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Programme

EXTERNAL BEAM AND INTERVENTIONAL RADIOTHERAPY TO REDUCE TOXICITY RISK AND INCREASE OUTCOME: WHAT'S NEW AND ON-GOING

A.R. Alitto[1], G. Mantini[2], V. Valentini[2]

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A significant evolution has been faced in cancer care that has allowed a decrease in mortality rate, even if the incidence is even higher.

As result of this evolution, an increasing number of people survive cancer but a significant proportion has side effects as a result of cancer care, which impairs their quality of life (QoL).

In this scenario, radiotherapy (RT) has became an important step in the management of cancer, and, over the past two decades, technologies and techniques has been developed, allowing for delivery of higher definitive radiation doses while limiting exposure of normal tissues.

Development of volumetric imaging techniques has allowed improving in QoL for patients undergoing definitive management of cancer. In particular, the next generation of 3DCRT, intensity-modulated radiation therapy and volumetric-modulated arc therapy (VMAT), have enabled even dose escalation to the target and sparing normal tissues. The possibility to use altered and unconventional fractionations and volumes has improved significantly outcomes, reducing toxicities.

Moreover, the recent development of proton therapy and also of brachytherapy treatment has opened new avenues for improving conformity and therapeutic ratio. The possibilities to implement also Image guided and MRI-guided treatment would open new frontiers in cancer treatment.

These new progresses, along with significant advances in systemic therapies, have improved survival in cancer care and decreased toxicities.

They have also brought to light new challenges and avenues, overall radiogenomics with the identification of genomic markers, predictive for the development of adverse effects resulting from cancer treatment with radiation. The integration of the "-omics" features in clinical practice, could lead to the development of clinical decision support systems based on prediction models of treatment outcome, enabling truly personalized and participative medicine.

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BLADDER CANCER AIRO-AIRB GUIDELINES PRESENTATION

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Bladder Cancer (BC) represents the second most frequent genito-urinary oncological disease, after prostate cancer, and the ninth most frequently diagnosed cancer worldwide.[1]

Radical cystectomy represented for many years the only therapeutic option for muscle -invasive BC. "bladder preservation" strategy, which consists of transurethral resection of bladder tumor (TURBT), followed by radio chemotherapy. This strategy is a valid option supported by several international guidelines.[2]

Neverthless, this conservative approach is still rarely used in Italian clinical scenario, whereas in some countries is routinely used.[3]

In consequence of that, the aim of these guidelines is to provide evidence-based recommendations, in order to support the radiation-oncologists in the management of BC in daily clinical practice.

The working group involved in the development of these guidelines was composed of radiation oncologists, medical oncologists, pathologist, radiologists, surgeons.

The level of evidence and the strength of the recommendation were weighed and graded according to Scots Network of intercollegiate guidelines (SIGN-www.sign.ac.uk). For these recommendations we took into consideration the NICE, NCCN, EAU and AUA/ASCO/ASTRO/SIU guidelines.[4-7]

Subsequently, guidelines has been analyzed and evaluated by two experts through the AGREE II system (Evaluation of the guidelines for research and evaluation).

In conclusion, this document is aimed to guide radiation oncologists, who are systematically involved in the treatment of BC, physicians interested in Uro-Oncology and all stakeholders.

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RADIOTHERAPY IN ORGAN PRESERVATION STRATEGIES FOR ANAL CARCINOMA. WHEN AND HOW TO ASSESS TREATMENT RESPONSE: WHAT THE RADIATION THERAPIST ASKS

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Standard treatment for squamous cell carcinoma of the anus is chemo-radiotherapy (CRT) with concurrent fluorouracil and mitomycin with curative intent. Salvage surgery is reserved to patients who have residual/recurrent disease.[1] A complete clinical response is defined as no evidence of residual tumor or nodal disease. Digital rectal examination and careful inspection of inguinal regions remain the main method for the response evaluation. Moreover, on the basis of several randomized trials, previous guidelines recommended the assessment of tumor response at 6–12 weeks after treatment, but discordance exists regarding early biopsy.[2] More recently, the post-hoc analysis of the randomized ACT II trial,[3-4] a UK phase 3 trial designed to investigate whether cisplatin in the CRT schedule improves the complete response rate, and whether maintenance chemotherapy (fluorouracil and cisplatin) after CRT increases progression-free survival, provided definitive evidence that anal tumor regression is a time-dependent event, that it can regress slowly and that it is acceptable to monitor partial responders carefully up to the 26° week from the start of CRT. In addition, the analysis underlined some critical aspects in the response evaluation. For example, the subjectivity of clinical response assessment and the variation in examiners and/or specific tools for response assessment could incorrectly label as incomplete clinical response in the early intervals. In fact, although an accurate identification of response is a crucial component to optimize patient management, the ideal method and timing of

response evaluation and when maximum response occurs after CRT remains unclear. Moreover, clinical examination had limitation to give response information for more deeply, non-palpable disease, as well as, problems in interpretation of response could be caused by radiotherapy-induced acute local effects. Finally, also the ability of endoanal ultrasound or MRI and the optimal time to assess response accurately is less well-defined 5. For these reasons, additionally, predictive imaging (i.e. early size-based MRI evaluation, 18F-FDG PET activity) and biological (i.e. circulating tumor DNA, HPV DNA sequences) markers able to allow real time analysis, that may be each other prospectively compared, could be of significant clinical benefit for those tumors with residual active disease where prompt surgical salvage is associated with improved outcomes 6.

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THE RADIOLOGIST'S POINT OF VIEW

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Anal cancer staging is essential for both prognostic information and correct therapeutic planning.

Accurate assessment of tumour size and depth of mural invasion is possible with endoanal ultrasound, due to excellent spatial detail but is best reserved for small T1 lesions as the small field-of-view limits assessment of regional lymph nodes and infiltration of structures beyond the anal canal.

MRI provides a detailed visualisation of the anal canal and nearby anatomical structures. Although the dentate line is not directly recognisable, its position can be inferred as it corresponds approximately to the upper portion of external sphincter muscles

In 2014 the European Societies, ESMO-ESSO-ESTRO, recommended MRI as the primary imaging modality to accurately stage anal cancer, taking into account the maximum tumour diameter, possible invasion of adjacent organs, and nodal involvement. Particular care should be applied to choosing the longest lesion diameter on T2-weighted images, since correct T parameter staging relies on this measure being below 2 cm, over 5 cm or intermediate.

Several different criteria exist to assist in identifying involved lymph nodes, including round shape, heterogeneity of appearance, irregular border, presence of mucin and/or calcifications, loss of the normal fatty hilum, and increased short-axis diameter. Although size was historically the most widely used criterion, results of studies suggests that additional criteria are crucial to accurate diagnosis of cancer of the lymph nodes on the basis of imaging.

The main impact of FDG PET/CT on therapy stems from its high sensitivity in identifying involved lymph nodes and influencing radiation therapy planning by defining sites of metabolically active tumour, which supports the use of PET/CT in radiation therapy planning.

Imaging also has a role in detecting residual or recurrent disease after therapy, with an emerging place for new molecular imaging techniques not only to detect early recurrence but also to predict response to further therapy and thereby guide escalation of treatment when appropriate.

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RADIOMICS PHENOTYPE

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Over the past decade a compelling body of literature has emerged suggesting a more pivotal role for imaging in the diagnosis, prognosis, and monitoring of diseases. These advances have facilitated the rise of an emerging practice known as Radiomics. It is an area of quantitative imaging research designed to maximize the extraction of mineable high-dimensional features from diagnostic imaging studies. The body of research advocating radiomics has a common promise: that the extracted information from images might prove to be complementary or interchangeable with other sources, i.e., demographics, pathology, blood biomarkers, and genomics.[1] Although medical images are commonly used by radiologists to describe a pathologic substrate, features extracted in the radiomic process are not part of radiologists' lexica since they are generally not visible to the naked eye. By analyzing the content of imaging data, we can potentially capture the underlying intratumoral and molecular structure of the lesions and their environment.[2] The final goal is to improve personalized medical decision-making: establishing reliable models that can stratify therapy outcomes and can be used for assessing patients' personal trade-off between the risks and benefits of different treatment options. Hence radiomics could potentially enhance the clinical decision making process of cancer care.[3] Our aim is to clarify the meaning of radiomics phenotype and the potential clinical utility of radiomics in solid tumor cancer care. First, we reviewed the literature in this field and underlined the potential contributions of radiomics to the improvement of cancer care at various stages of the decision-making process. Second, we discussed the limitations of the current process and explained the benefits of radiomics; third, we provided a description of the workflow of radiomics and explained how it relates to biomedical texture analysis.

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THE IMPACT OF SWOARS-SPARING IMRT AND EARLY SWALLOWING RE-HABILITATION ON THE QUALITY OF LIFE OF LONG-TERM SURVIVAL HEAD AND NECK CANCER PATIENTS

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Introduction: Radiation-induced dysphagia represents a real "Achille's heel" for patients affected by head and neck cancers (HNCs) often leading to a malnutritional status and risk of aspiration pneumonia. On the contrary, an organ preservation strategy should provide both the highest tumor control probability (TCP) and the minimum function impairment with the subsequent maximum therapeutic index gain.

Methods: Intensity Modulated RT (IMRT) might reduce the probability of post-radiation dysphagia by producing concave dose distributions with better avoidance of several critical structures such as swallowing organs at risk (SWOARs) which might result in better functional outcomes. Similarly, early and frequent involvement of Speech Language Pathologist (SLP) could be beneficial to evaluate swallowing function at baseline and prescribe rehabilitative interventions to prevent post-radiation swallowing impairment as well as to maximally restore these functions after treatment.

Results: Multiple studies have demonstrated that implementation of swallowing exercises during radiochemotherapy may help to preserve intra-treatment and post-treatment swallowing function.

Patients who either eat or exercise fare far better than those who do neither whereas those who both eat and exercise have the highest rate to return to a regular diet. The few available studies regarding SWOARS-sparing IMRT seem to show encouraging results on swallowing outcomes reporting an acceptable pattern of dysphagia compared with the historical data.

Conclusions: The maximum benefit of IMRT in swallowing function preservation has still to be thoroughly investigated, such that well-designed prospective trials specifically focused on this relevant endpoint are strongly encouraged by a panel of experts. In the meantime, we suggest taking the SWAORs into consideration in the plan optimization process, to maximally reduce irradiation without compromising target coverage, and to refer patients (mostly HPV-positive patients who are candidates for a radiochemotherapy curative treatment with a bilateral neck irradiation) to deglutologists for management and prevention of swallowing dysfunction, as recommended by current guidelines.

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TARGET THERAPY - IMMUNOTHERAPY: EMERGING OPPORTUNITIES IN COMBINATION WITH RADIOTHERAPY

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During the past decade, survival of patients with metastatic renal-cell carcinoma has dramatically improved since the advent of several targeted therapy and immunotherapy. Angiogenesis inhibitors (VEGF or mTOR inhibitors), tyrosinekinase inhibitors (TKIs) and immune checkpoints inhibitors (antiPD1; anti-CTLA-4) changed the therapeutic approach to this tumor.

This effort in developing systemic therapy has restricted the role of radiotherapy in non-metastatic management of renal-cell carcinoma, as evidenced by different guidelines, which focus mainly on radiotherapy with palliative intent. This preclusion is reasonable in the absence of level one clinical evidence and the poor results obtained with conventional radiotherapy (non-stereotactic, not image-guided, and conventionally fractionated). With the widespread availability of modern radiotherapy techniques such as stereotactic body radiotherapy, there are no longer technical barriers to adopt radiation in the treatment of renal-cell carcinoma, especially in combination with new drugs due to its biological mechanisms. Indeed, combinations of radiation with immune therapy may act synergistically in enhancing anti-tumour immune reactions, thus potentially increasing both tumor control and toxicity. Preclinical data, clinical experience, and challenges are herein reviewed and discussed.

COMBINING IMMUNOTHERAPY AND RADIOTHERAPY FOR CANCER TREATMENT: BIOLOGICAL BASES

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Several preclinical and few clinical studies have suggested that the combination of radiation therapy (RT) with immunotherapy (IT) may improve treatment outcomes by enhancing the immune system's ability to recognize and kill tumor cells both in localized and metastatic disease. In this presentation we summarize the underlying molecular mechanism of combination of RT and IT. Tumors have the ability to escape the immune system (IS) through a processes called 'immunoediting', which include impairment of the antigen presentation and processing apparatus, anergy of T cells, activation of negative costimulatory signals in microenvironment, elaboration of immunosuppressive factors and increased infiltration of immunosuppressive cells. The discovery of immune checkpoints modulating immune response has drastically chanced the landscape of cancer treatment. Immunotherapeutic agents act via mechanisms that depend on expression of immune checkpoints regulators (CTLA4, PD1 and its ligand PDL1). RT has both immunostimulatory and immunosuppressive roles, depending on the radiation dose, number of fractions, type of tumor and site of irradiation. RT acts as immunostimolatory by increasing antigen visibility through expression of major histocompatibility complex on tumor cells and release of tumor-associated antigens, leading to an in situ vaccine effect, and by enhanced expression of "danger signals" that trigger immune response, like calreticulin, ATP, HMBG-1, heat shock proteins and high mobility group box proteins. These proteins, also known as damage-associated molecular patterns (DAMPs), are responsible for the CD8+ T cell-mediated anticancer response. In addition to enhance antitumor activity, RT renders the tumor microenvironment conducive to effector T-cell recruitment and function, through vascular, endothelial and stromal inflammation. Radiation-induced modulation of the tumour microenvironment also may increasethe efficacy of co-administered immunotherapeutic agents. Figure 1 shows RT immunobio-

logy. Both RT and IT act synergistically, with complimentary mechanism. RT can modulate the expression of tumor antigens, immune checkpoints and influence cytokine expression promoting the action of immunotherapeutic agents. In turn, IT facilitates the action of RT by targeting and modulating various T-cell populations. However this synergistic relationship depends on the timing of RT and IT administration and on the presence of peculiar immunomodulatory agents in the tumor microenvironment. More translational studies are needed to evaluate whether RT can enhance the priming of tumor-reactive T cells and IT response.

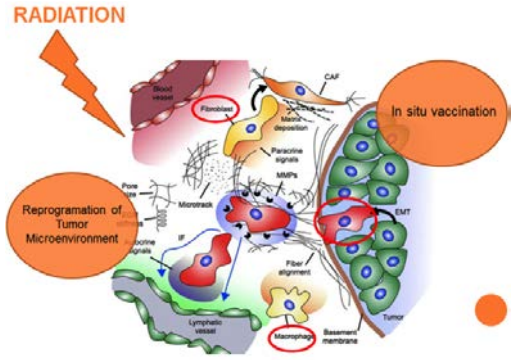

Figure 1. Immunobiology of RT.

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ROLE OF RADIOTHERAPY DURING IMMUNOTHERAPY: WHAT VOLUME?

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In 1953, was first introduced the term 'abscopal effects' (lat.: ab = away, scopus = target) to describe radiation effects 'at a distance from the irradiated volume but within the same organism'.[1]

Abscopal responses, were rarely reported in clinical practice in the past in multiple cancer type: many have considered these affect as anedoctal, because of the immunosuppressive role of radiotherapy.[2] From 2000's many studies were conducted on this theme and revealed that radiotherapy can generate an immune response more intensive and complex than before thought. First radiotherapy is not only able to induce anti-tumoral responses, but it can also induce immune suppression.

In the era of immunotherapy, a renewed interest arise on combination with radiotherapy, and data from pre-clinical and now also clinical, encourage us to consider the possibility that radiotherapy can enhance the efficacy of cytotoxic T lymphocyte antigen (CTLA)-4 and PD-1 blockade.[3]

Several questions must be tackled, detailing how we can take advantage of the abscopal effect and of the combination between radiotherapy and immunotherapy. Means to enhance fractionation schedules, the target volume determination, and the optimal doses represent crucial issues to maximize the benefit from this combination. Another unknown point is whether the location of the irradiated tumor field impacts the outcomes. So, when associating radiotherapy to immunotherapy, we have to consider that old conception of volume's radiotherapy, in particular treating the low and intermediate risk volume for some disease, probably is not the best choice. Similarly, large irradiated volumes that encompassing large volume of bone marrow contribute to immunosuppressive role of RT. In this sense is reported that the efficacy of agents targeting CTLA4 receptors overexpressed in draining lymphatic tissues could be hampered if large lymphatic tissues are concomitantly irradiated.[4] Moreover, some authors, have shown that RT induced cross-presentation of tumor-associated epitopes by DCs take place in the draining lymph nodes.[5]

Finally, recents study revelead that Tregs, a sub-set of CD4+ T-cells involved in the suppressive microenvironment, are more radioresistants to fractionated schedules than other T-cell subsets, potentially mitigating the immune response induced by RT when treating large volumes.[6] So some authors suggest to re-thinking completely volumes of RT both in radical treatment, really important for designing next sperimental trial and in palliative set.

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COMBINING RADIOTHERAPY AND CANCER IMMUNOTHERAPY: IT'S TIME FOR TIMING

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Aim: the use of immune checkpoint inhibitors for the treatment of advanced melanoma and other solid tumour entities is establishing immunotherapy as a pillar besides systemic surgery, radiotherapy, and anticancer treatments. The available data suggest great potential of the combination between immunotherapy and radiotherapy, however some concerns raise about dose, fractionation, and timing. We focuses on the immunological effects of irradiation with immunotherapy, looking at the most fruitful timing.

Methods: we review the evidence available on combination strategies.

Results: current clinical trials mostly start immunotherapy after curative radiation or they combine stereotactic body radiotherapy with immunotherapy regimens. However, the best fractionation and sequencing might differ depending on the applied immunotherapy, tumour type and patient inherent factors. Furthermore, radiotherapy might also be used when disease is refractory to immunotherapy in order to induce a secondary response with continuation of the treatment.

Conclusions: the combination of immunotherapy and radiotherapy might be a way to long-term cancer control and survival for a large number of cancer patients. Clinical trials may find an appropriate time window to combine these two treatments.

RADIOTHERAPY IN ELDERLY PATIENTS WITH BREAST CANCER: TO TREAT OR NOT TO TREAT?

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Breast conserving surgery (BCS) followed by radiotherapy (RT) is the standard treatment for patients with early stage breast cancer. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) analysis evaluated 17 randomised trials showing that RT after BCS reduced the 10-year risk of any first recurrence from 35.0% to 19.3% (absolute reduction 15.7%, 95% CI 13.7-17.7 $2p<0.00001$), but the benefit of RT varied when adjusted for age, estrogen receptor status and grade.[1] The management of elderly patients with breast cancer is at present a major issue of debate. Randomized trials showed that the omission of postoperative RT in elderly women with early stage breast cancer, treated with adjuvant hormonal therapy, is safe and associated with a low local recurrence rate without a detriment in overall survival.[2,3] Therefore, at present, the omission of postoperative RT in a selected group of elderly women is a challenge issue. Since in elderly patients with early stage breast cancer RT improves local control without a survival benefit, RT-related toxicity estimation is a pivotal issue, particularly in patients with comorbidities. Furthermore in elderly patients life expectancy estimation and a multidisciplinary approach, including a comprehensive geriatric assessment,[4] is crucial in order to define the optimal therapeutic strategy. Clinical trials including elderly patients and development of consensus guidelines for older adults cancer patients should be encouraged.

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MULTIDISCIPLINARY GERIATRIC EVALUATION IN THE PERSONALIZATION OF THERAPY

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Aims: To provide guidance regarding the multidisciplinary evaluation and management in older breast cancer patients.

Methods: A total of 55 studies were analyzed. Estimation of life expectancy and ability to undergo treatment might be improved by collaborative geriatric and oncology management, and a multidomain geriatric assessment.

Results: Many instruments are available for compliance assessment to therapy. Comprehensive geriatric assessment (CGA), that includes measures of function, comorbidity, nutrition, medication, socioeconomic issues and geriatric syndromes, should be used to identify vulnerabilities.[1-2] Preoperative assessment of cancer in the elderly (PACE), which includes CGA, has been used to assess suitability for surgery.[3] Chemotherapy is not feasible with attenuated autonomy so maintenance of functional autonomy must be assessed by Activities of Daily Living (ADLs) or Instrumental Activities of Daily Living (IADLs).[2] CGA can be time consuming, taking roughly 45 min to complete and usually implemented by a geriatrician. Therefore, the use of an abbreviated screening method is helpful to identify patients who would benefit from a full CGA.[2] Improvements in local recurrence rates are seen in elderly, with excellent breast cancer specific outcomes for older breast cancer patients with favorable tumor biology subtypes, even after de-intensified local-regional treatment. Thus, tumor biology, and not age, should be the driver in local therapy decision-making.[4-6]

Conclusions: Modified management strategies are often used for older individuals; however, the evidence for such approaches is poor. Age alone should not dictate any aspect of management for older individuals with breast cancer. All decisions should consider physiological age, estimated life expectancy, risks, benefits, treatment tolerance, patient preference, and potential treatment barriers. Our understanding of tumor biology continues to advance, treatment will increasingly be individualized based on the genetic composition of the tumor.

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ELDERLY PATIENTS AFFECTED BY HEAD AND NECK SQUAMOUS CARCINOMA: THERAPEUTICAL APPROACH WITH A FOCUS ON RADIATION VOLUMES AND CHEMOTHERAPY ASSOCIATION

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The demographics of squamous cell carcinoma of the head and neck (SCCHN) is marked by a growing number of patients aged 65 and over, which is in line with global projections for other cancer types. In developed countries, more than half of new SCCHN cases are diagnosed in older people, and in 15 years from now, the proportion is expected to rise by more than 10%. Still, a high-level evidence-based consensus to guide the clinical decision process is strikingly lacking. The available data from retrospective studies and subset analyses of prospective trials suffer from a considerable underrepresentation of senior participants. Nevertheless, it is becoming clear that, if treated irrespective of chronological age, fit elderly patients in a good general condition and with a low burden of comorbidities may derive a similar survival advantage as their younger counterparts. Despite that, undertreatment represents a widespread phenomenon and, together with competing non-cancer mortality, is suggested to be an important cause of the worse treatment outcomes observed in this population. Due to physiological changes in drug metabolism occurring with advancing age, the major concerns relate to chemotherapy administration. In locally advanced SCCHN, concurrent chemoradiotherapy in patients over 70 years remains a point of controversy owing to its possibly higher toxicity and questionable benefit. However, accumulating evidence suggests that it should, indeed, be considered in selected cases when biological age is taken into account. Results from a randomized trial conducted in lung cancer showed that treatment selection based on a comprehensive geriatric assessment (CGA) significantly reduced toxicity. However, a CGA is time-consuming and not necessary for all patients. To overcome this hurdle, geriatric screening tools have been introduced to decide who needs such a full evaluation. Among the various screening instruments, G8 and Flemish version of the Triage Risk Screening Tool were prospectively verified and found to have prognostic value. In light of these considerations, also in SCCHN, the application of elderly specific prospective trials and integration of clinical practice-oriented assessment tools and predictive models should be promoted. Finally, continuous efforts should be made toward sufficient implementation of supportive

care measures, not only in the palliative setting but throughout the whole treatment period. Oral mucositis, pain syndrome, and nutritional deficiency are among the most common problems to be timely addressed. In this respect, refinements in radiotherapy techniques, comprising, e.g., intensity-modulated radiation therapy (IMRT), offer an opportunity to reduce acute and late side effects and should be, therefore, promoted.

INTERVENTIONAL PARTIAL BREAST IRRADIATION

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Aims: Elderly breast cancer patients will become a critical health problem, because of the upcoming increasing life expectancy during the next decades. Some of them have geriatric frailty characterized by a limited life expectancy and comorbidities that increase with age in incidence and severity. On the other hand, there are elderly patients still working and socially committed, mainly the young elderly (up to 65 years). However, patients in both groups can have difficulties in receiving whole breast irradiation (WBI) after breast conserving surgery (BCS) because of uneasy transportation from home to radiation therapy centers or patients with homes in remote areas and jobs that do not permit time off for several weeks of daily treatment. Difficulty of compliance is also a point to consider in elderly breast cancer management. Taken all together these findings led the International Society of Geriatric Oncology to recommend the development of radiation therapy regimen specifically adapted to the elderly patients.

Accelerated partial breast irradiation (APBI) is a valuable compromise between WBI and endocrine sole therapy. It may improve the underutilisation of BCS by decreasing the treatment time, costs, side effects and fear of WBI, thus improving Quality of Life (QoL).

Methods: Interventional APBI can be delivered using:

- high dose rate (HDR) and pulsed dose rate (PDR) interstitial multi-catheter brachytherapy (IBRT) or balloon and hybrid applicators (intracavitary brachytherapy-INBRT) with ^{192}Ir;
- intraoperative radiotherapy (IORT) with electrons or low-energy photons at the time of surgery.

Results: APBI is well tolerated for elderly women with no detrimental impact on functional autonomy and QoL. APBI in well selected elderly patients allows to achieve a 5-year local control rate of around 98%.

IBRT emerged as the best for target coverage and versatility. Another advantage is that treatment is administered when the histological findings are available. It appeared non inferior to WBI in long-term phase II and phase III studies. Level of quality assurance and reproducibility, long-term experience, precision and independence on patients motions were almost the same for all techniques.

Conclusions: Interventional APBI may substitute WBI in well selected elderly patients. It is especially more convenient for high-volume radiation centers with long waiting lists, for patients who live far away from the radiotherapy centers. The departments have to be aware about this issue, to provide to elderly women with early breast cancer, the best therapeutic option combining optimal local control with good QoL in a cost-effective way. The choice of APBI techniques will be influenced by many factors whereby the strongest arguments are local experience and hospital budget size.

RADIOIMMUNOTHERAPY ASSOCIATION IN HEAD AND NECK CANCER

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Rationale of association: There is a strong rationale for combining radiotherapy (RT) with immune checkpoint inhibitors (ICIs): response to ICIs seems to correlate with neoantigen burden[1] and head and neck squamous cells carcinoma (HNSCC) express high levels of relevant neoantigens. RT can release neoantigens[2] thus activating T cell-priming, trafficking of T cells to tumors and eventually an antigen-specific anti-tumor response. However, RT also leads to the overexpression of PD-L1 in tumors and its microenvironment, which can be blocked by anti PD1/PD-L1 to enhance response to RT. There is also rationale for combining RT with cetuximab and anti-PD-1. Cetuximab adds may inhibit EGFR pathway but also induce antigen-dependent cell toxicity. Cytokines released by activated NK cells leads to increased expression of PD-L1 in the tumor, which can, again, be blocked by ICIs in enhanced response to cetuximab.[3]

Preliminary data on safety: In the phase II NCT02586207 trial in locally-advanced (LA) HNSCC, pembrolizumab in combination with weekly cisplatin-based CRT was safe and did not significantly impair RT or chemotherapy dosing.[4] In the phase 2 PembroRad trial comparing pembrolizumab versus cetuxmab plus RT, on 133 treated patients, cetuximab was found to be more toxic, mainly due to in-field toxicity.[5] In the Phase 3 REACH trial investigating avelumab, cetuximab, and RT versus a standard of care in LA-HNSCC, in 14 patients included in the experimental arm the safety stopping rule was not crossed.[6] Recently reported safety data for cohort 3 (cetuximab+ nivolumab + RT) of RTOG 3504 Trial showed that nivolumab is safe and feasible to administer concomitant with a cetuximab-RT regimen for patients with newly diagnosed intermediate/high risk HNSCC.[7] However, caution on safety should be taken: there does seem to be an increase in incidence of immune-related adverse events in RTOG 3504, as compared with single-agent nivolumab. For example, diarrhea was reported in 38% of patients in RTOG 3504 versus 7% in CheckMate 141. Also, preliminary data on safety of phase I PULA HNSCC trial combining anti-CTLA4, cetuximab and RT in LA

HNSCC showed that ipilimumab dose had to be de-escalated due to dose-limiting dermatologic toxicity in association with cetuximab.[8]

Results from ongoing trials will give better insight to which is the best sequencing and what is the best radiation dose and fractionation. Also, regarding single-agent or combination, the combination of anti-CTLA4 and anti-PD-1 has been approved for the treatment of metastatic melanoma, and this strategy's being studied in metastatic head and neck squamous cell carcinoma in first-line or second-line.

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OROPHARYNGEAL CARCINOMA HPV-POSITIVE: A SINGLE DISEASE OR MORE DIFFERENT ENTITIES?

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Head and neck squamous cell carcinoma (HNSCC) comprises a heterogeneous group of tumors that arise from the squamous epithelium of the oral cavity, oropharynx, larynx and hypopharynx. While many HNSCCs are related to classical etiologic factors of smoking and alcohol, a clinically, genomically, and immunologically distinct subgroup of tumors arise from the epithelium of the tonsil and the base of tongue as a result of infection with Human Papilloma Virus (HPV).[1] It is recognized that HPV-positive oropharyngeal squamous cell carcinoma (OPC) is associated with p16 overexpression and a better prognosis than HPV-negative OPC.[2] During the last years, several studies have hypothesized a de-escalation or de-intensification in HPV-OPC patients with the intent to improve the therapeutic ratio and treatment-related long-term complications.[3,4] However, to date, the interdisciplinary community recommend a larger consensus before changing the standard of care for patients with lower-risk HPV-associated OPC (*i.e.* patients with a minimal smoking history and a small tumor size). As a result, the dilemma that clinicians face is how to choose the appropriate treatment plan and when treatment deintensification is oncologically safe. Perhaps, the development of a tumor gene signature will allow for personalized medicine by providing information to individualize prognosis and treatment decisions. It could be intriguing to hypothesize that patients found to have a gene signature that predicts low risk of recurrence or mortality could be treated with a de-intensified schedules while those with a high-risk gene signature could be treated with a more intense regimen. In absence of evidences, future studies assessing clinical outcomes in OPC should consider advances in gene expression profiles to finalize the ongoing process of *Precision Medicine* in HPV-OPC.

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LECTURE SNR - NUOVO REGOLAMENTO UE: LA PROTEZIONE DEI DATI PERSONALI. SUGGERIMENTI DI BUONA CONDOTTA PER IL RADIOTERAPISTA ONCOLOGO

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Il nuovo regolamento della privacy andrà a sostituire in parte il Codice della Privacy, in vigore dal 2004. Introduce un nuovo modo di "pensare" il trattamento dei dati: l'obiettivo del GDPR è non solo quello di proteggere i nostri dati, e con essi i nostri diritti fondamentali di cittadini, ma anche quello di consentire, lecitamente, di fare circolare i dati. Promuove il principio dell'accountability o responsabilizzazione del Titolare, introducendo il ruolo del Responsabile della protezione dei dati personali (*Data Protection Officer*). Questa figura sarà obbligatoria per tutte le pubbliche amministrazioni e per le aziende. Il Regolamento rafforza la sicurezza dei dati personali e i diritti dell'interessato, adottando approcci e politiche che tengano conto costantemente del rischio che un determinato trattamento di dati personali possa influire sui diritti degli interessati. Il pieno rispetto dei principi di integrità, sicurezza e protezione dei dati personali rappresenta ormai una condizione indispensabile per il corretto svolgimento della professione medica. La nuova normativa dà grande rilievo all'informazione rispetto alla raccolta di atti formali di consenso. Il legislatore europeo ha precisato che per i trattamenti basati sul consenso dell'interessato, il titolare del trattamento dovrebbe essere in grado di dimostrare che l'interessato ha acconsentito al trattamento. E' opportuno prevedere una dichiarazione di consenso predisposta dal titolare del trattamento in una forma comprensibile e facilmente accessibile, che usi un linguaggio semplice e chiaro e non contenga clausole abusive. L'informazione diventa il punto centrale del processo e sarà il medico a dover dimostrare di avere assolto al proprio onere, molta attenzione va posta nell'indicare le interazioni tra professionisti e le condivisioni degli archivi. Lo schema di decreto attuativo del regolamento aggiunge che l'informativa va fornita preferibilmente per iscritto. Nell'informativa vanno dettagliati eventuali trattamenti particolari per scopi di ricerca, trial clinici, teleassistenza-telemedicina, per fornire altri beni o servizi all'interessato online, per l'implementazione del fascicolo sanitario elettronico e dei registri di patologia ed ogni altra attività che sui dati si intende fare oltre che il tempo massimo di conservazione. Il cittadino ha diritto di accesso ai suoi dati; il diritto di chiederne la rettifica o la cancellazione, o la limitazione del trattamento; diritto di opporsi al trattamento; diritto alla portabilità; diritto di revocare il consenso al trattamento in qualsiasi momento e di proporre reclamo all'autorità di controllo. Inoltre, occorre spiegare cosa succede se non si vuole comunicare i dati richiesti: in genere, non potrà essere offerto il servizio -certificazioni, rendicontazione delle prestazioni - ma va sempre assicurata la cura.

References

G.U.E. Atti Legislativi 8/4/2016 Regolamento del Parlamento Europeo e del Consiglio relativo alla protezione dei dati personali;

Camera dei Deputati Schema di decreto legislativo per l'adeguamento del Regolamento UE n. 679/2016;

L. Bolognini-E.Pelino-C.Bistolfi "il Regolamento Privacy europeo" Giuffrè Ed.

MOLECULAR CHARACTERIZATION OF SQUAMOUS CELL CARCINOMAS OF THE VULVA

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Aims: We wanted to investigate the presence of fusion gene in a series of squamous cell carcinomas (SCC) of the vulva as the detection and characterization of such tumorigenic transcript is of great importance both research-wise, diagnostically and may serve as therapeutic targets for antioncogenic drugs that interact directly with the molecular changes responsible for neoplastic transformation.

Methods: High-throughput paired-end RNA-sequencing was performed on 12 vulvar SCC.

Results: We found two recurrent fusions with the *STIP1-CREB3L1* and *ZDHHC5-GPR137* being present in two tumors each. The transcripts were detected only in the tumor samples, not in normal vulvar tissue from healthy donors used as control. The *CREB3L1* and *ZDHHC5* genes encode proteins involved in transcription suggesting that the chimeras may alter downstream events in their respective pathways. Expression analysis of the *CREB3L1* gene showed the presence of two distinct groups of tumors, one having fusion and downregulation of the gene and the other showing upregulation of C*REB3L1*.

ROLE OF INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY) IN VULVAR CANCER

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The purpose of this lecture is to discuss the current role of brachytherapy in vulvar cancer. The standard treatment for vulvar squamocellular carcinoma is surgery. External beam radiotherapy (EBRT), brachytherapy, and chemotherapy are either adjuvant or standalone treatment options.[1] Clinical data on the place of brachytherapy (BT) for treatment of vulvar carcinoma are poor. Brachytherapy is an optimal treatment option for primary and recurrent carcinomas of the vulva, especially in patients with serious comorbidities and contraindications for surgery.

Table 1. Literature review of interstitial salvage brachytherapy for vulvar cancer.

Study	Time period	Total pts	Salvage pts	Technique	Dose (Gy)	Outcome
Prempree and Amornmarn Florida (10)	1958-1977	21	21	LDR	55-85	5-year DFS 38%
Hoffman et al. Florida (10)	1985-1988	10	Unknown	LDR	70-90	3-year OS 80% all comers
Pohar et al. France (17)	1975-1993	34	15	LDR	60 (53-88)	5-year LC 19% for recurrence (vs. 80% for first presentation $p = 0.04$) 5-year OS 29% in all patients and 33% in salvage patients ($p = 0.64$)
Tewari et al. California (12)	1995-1992	11	5	LDR	28.66 (23.6–35)	MS 33 months all patients LC 2 years 82%
Dyk et al. Wash U (10)	2006-2012	50	Unknown*	HDR	51.3 (30–60)	1-year LC 72% all comers
Kellas-Sleczka et al. Poland (10)	2004-2014	14	8	HDR	15-43	1- and 3-year PFS for recurrent group 100 and 62.5% MS 28 months
Castelnau-Marchand et al. France (20)	2000-2015	26	3	LDR and PDR	60 (55-60)	3-year OS 81% and DFS 57% for all comers
Mahantshetty et al. India (11)	2001-2016	38	3	HDR	38.4 (35.5–46.7)	5-year OS 82% DFS 51% LC 77% for all comers

*16 salvage and total, 13 vulvar; unclear how many recurrent vulvar cancers.
DFS, disease-free survival; OS, overall survival; LC, local control; MS, median survival.

From Hughes KE et al (5)

This allows for the delivery of a very high radiation dose to the tumor while sparing organs at risk. The discussion will focus on clinical application of brachytherapy when used as a separate treatment or in combination with external beam radiotherapy (EBRT), in interstitial or in peri-operative modality. Finally, we will review the recent literature in disease management in terms of clinical outcome (Table 1). The results will be discussed when brachytherapy is used for the treatment of the primary locally advanced vulvar cancer and when BT is used in case of recurrent disease, where patients require extensive surgery or in cases where surgery is contraindicated or refused.[2-5]

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TOXICITY AND QUALITY OF LIFE AFTER TREATMENT. VULVAR CANCER

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Vulvar cancer is a relatively uncommon neoplasm responsible for 5% of gynecologic malignancies.[1] There has been an incremental rise over the last 2 decades, including in premenopausal women.[2] This could be related to changes in sexual behavior and to and increasing number of persistent human papillomavirus(HPV)infection. It common knowledge that 40% to 60% of vulvar cancer and up to 90% of intraepitheal neoplasia(VIN) are associated with HPV.[2,3] HPV-16 is the common serotype. Up to 95% of these cancers are squamous cell carcinoma (SCC) and occur on the labia majora and other primary sites such as labia minora, clitoris, and perineum. Over the years, surgical approach has become more conservative and radical vulvectomy plus en bloc inguinofemoral lymphadenectomy has been replaced by wide excision with macroscopic margins of at least 1 to 2 cm. The sentinel node biopsy has been introduced for a minimal invasive evaluation of the nodal status only early stage vulvar who are clinically node negative.[4] Radiation therapy (RT) has a major role in curative treatment of vulvar cancer patients RT can be used in various settings: 1)adjuvant RT with or without chemotherapy 2) Neoadjuvant and primary RT with or without chemotherapy. Intensity modulated RT (IMRT) improves the avoidance of critical structures, while maintaining adequate tumor volume coverage.[5] As in anal cancer, IMRT has rapidly become a standard option in vulvar cancer. Pelvic radiation therapy has several known acute and long term toxicities. Acute treatment-related toxicities include dermatitis, mucositis, diarrhea, and dysuria, among others . These side effects can generally be managed with skin creams, anti-diarrhea medications, and pain medications, and may resolve shortly after the completion of therapy. Long-term effects of pelvic radiation can include infertility, stenosis of the vaginal canal, loss of lubrication, premature menopause, late bladder/gastrointestinal problems such as chronic diarrhea or proctitis, lymphedema, pelvic insufficiency fractures and an increased risk of second malignancies.[6] The long-term effects of radiation may appear anywhere from months to years after exposure to radiation, and may be permanent for some patients. The most commonly reported instruments in the gynecologic literature related to radiation for general QOL are the European Organization for Research and Treatment of Cancer Quality of life Questionnaire Core 30 (EORTC QLQ C30),[7] and the Functional

Assessment of Cancer Therapy (FACT)[8] which similarly has disease-specific modules, though these are less commonly reported in the radiation literature. Toxicity in integrated treatments for neoplasms of the vulva can be particularly severe. Beware of comorbidity and predisposing factors. Preference to the choice of IMRT treatments where possible. The quality of life even after a long time is related to the treatment experience. Attention not only to critical organs but also to others "dimensions" of life of the patients on which we are affected.

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FUNCTIONAL IMAGING: HOW TO INCREASE THE SAFETY OF OUR TREATMENT

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In the last decades Radiotherapy (RT) underwent a number of technological innovations. Modern RT techniques, such as IMRT, VMAT, proton and heavy ion, mainly because of new accurate treatment planning systems, have improved the dose delivery. Functional and molecular imaging techniques have been developed and performed to quantitatively map the spatial distribution of parameters such as metabolism, proliferation, hypoxia, perfusion and ventilation of both organs at risk of tumor.

In radiotherapy optimization these imaging modalities allow the dose sparing to high functioning subregions of normal organs or dose escalation to selected subregions of tumor, as well as the potential to tailor radiotherapy to functional changes occurring during the course of treatment.

The mapping of the spatial variation of function, as identified by functional imaging, can be used to either spare high functioning normal tissue or escalate dose to hypoxic/hyperactive regions of the tumor, also using modern radiotherapy technologies that certainly contribute to this purpose.

Consequently, integration of functional imaging seems to be very promising for individualized RT treatment planning. The most common molecular images used for tumor volume delineation and assessment of tissue pathophysiological features are PET data.

The most popular tracer is fluorine-18 fludeoxyglucose (FDG) that provides metabolic and functional information useful during the radiotherapy process. In lung cancer PET/CT can direct the coverage of tumor volumes, dose escalation, and adaptive management.[2] Also for head&neck cancer PET/CT, as an adjunct to magnetic resonance imaging planning, is evaluated to dose escalation and delineation of avoidance organ at risk such as salivary glands or bone marrow.[3] Other PET tracers were used to visualize tumor hypoxia, a feature associated with treatment failure. Several studies tried to identify some surrogates for hypoxia, but most of them used different approach for thresholding – from visual, standardized uptake value (SUV) to kinetic analysis.[4] Only a few involved the dose painting based on Functional- Magnetic Resonance Imaging (fMRI). In some of them, dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) was employed. Diffusion-weighted MRI (DW-MRI) is another technique that may be applied in the personalized radiotherapy treatment planning.[5]

Modern radiotherapy planning is based on coregistration of a conventional MRI scan with a planning CT scan. In a feasibility study of four patients with low-grade glioma, Kovacs and colleagues[6] co-registered fMRI following acoustic, visual, somatosensory, and numeral stimuli to a planning CT scan. The study showed that with fMRI-based 3D conformal planning the radiotherapy dose to the superior and inferior temporal gyrus and the lingual gyrus could be reduced by about 50%. A subsequent study[7] of ten patients with brain tumours confirmed the role of fMRI in reducing the radiotherapy dose to vital organs without compromising the total target coverage of the tumour.

The introduction of three dimensional functional imaging with single photon emission computed tomography (SPECT) improved the assessment of pulmonary comorbidity and provided the localisation of healthy and defective tissue to enable lung dose optimisation by modifying beam orientations to avoid highly functioning lung. SPECT provides information about the distribution of blood flow, where the perfused areas can coincide with the functional sites.[8]

Lung function before RT is distributed unevenly. The tumour itself , by altering the function of different areas of the lung, and pre-existing lung comorbidity, such as chronic disease or smoking related alterations, may cause regional changes in perfusion. Furthermore, lung perfusion changes in a dose-dependent manner after RT. SPECT perfusion changes are correlate with the severity of radiation pneumonities and early reduction of lung perfusion after radiation therapy is associated with risk of late pulmonary toxicities.[9]

It is possible to coregister SPECT with CT simula-

tion images to consider these regional differences in treatment planning, in order to exclude the perfused and therefore functioning areas allowing to reduce the radio-induced damage or allow the dose escalation.[10]

Functional imaging in radiotherapy has great promise to guide radiation management target delineation as well as to monitor response to treatment and represents a large step forward in efforts to personalize radiotherapeutic care.

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CANCER CELL STEMNESS, PLASTICITY AND RADIORESISTANCE: PREDICTION OF RADIOTHERAPY OUTCOME AND SPECIFIC TARGETS FOR COMBINED TREATMENTS

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Aims: Tradional radiation biology, basing on the stocastic model, asserted that all cancer cells within the tumor are a clonal population of highly proliferating cells, with a high alpha/beta ratio and sensitivity to radiation1. The discovery that the hierarchical organization of tumors originates from a small population of cancerous stem cells (CSC) with a very low rate of proliferation, a higher radioresistance and that based on the intrinsic plasticity, non-CSCs can de-differentiate in CSC, have radically revolutionated radiation oncology2-3. Thus, understanding the molecular mechanisms regulating CSCs can be indispensable for the optimization of current treatment strategies.

Methods: Herein, we review the literature and present our preliminary in vitro- and in vivo data.

Results: DNA repair, ROS scavenging and anti-apoptotic pathways as well as the presence of hypoxic and acid microenvironmental nich partecipate in determing CSCs radioresistance. If high radiation doses appear to be more effective in killing CSCs, local recurrence suggests that this effect may result from a further slowing of the proliferation of CSCs. Radiation seem to sustain CSCs population by reprogramming non-CSCs into CSCs and inducing drastic pro-CSCs modifcations of the microenvironmental nich. Multicenter studies revealed a significant association of the expression of putative CSCs markers with locoregional tumor control after radiotherapy and the variability in biomarkers expression and a phenotypic switch during radiotherapy. Because of this complex scenario, strategies to enhance efficacy of radiotherapy by targeting cancer stem cells should target structures that are overexpressed in CSCs compared to non-CSCs or by inhibition of pathways that are of higher importance in CSCs compared to non-CSC. In this regard, HMG CoA reductase-, WNT-, HER2-, PI3K/AKT-, ATM/Chk2-, HDAC-inhibitor and immunotargeting drugs have been tested showing encouraging results4. Our data showed the role of Ephrin signaling in sustaining CSCs phenotype and the ability of a new pharmacological Ephrin targeting drug, named GLPG1790, to counteract radiation-induced CSCs enrichment, inducing a drastic radiosensitization of rhabdomyosarcoma CSC and non-CSC cells.[5]

Conclusions: Twenty years of research on radiobiology confirm that CSCs are a "mobile target" that could be difficult to trace and eradicate and that it is therefore necessary to identify new therapeutic strategies capable of radiosentizing CSCs and blocking CSCs repopulation from non-CSCs cells.

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ROLE OF SBRT IN THE OLIGOMETASTATIC PROSTATE CANCER PATIENT

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The oligometastic or recurrent cancer (cancer patients with 1–5 metastatic sites) could been considered as an intermediate state between localized lesions and those widely metastatic. In this state the disease is amenable to a curative therapeutic strategy and to a localized therapy.[1] Several authors reported the benefit of local therapy with favorable impact on both overall survival (OS) and time to progression (TTP) in this setting of patients.[2] Stereotactic radiotherapy delivered on the sites of metasasis and/or recurrence can be usefully employed both in case of metastatic hormone-sensitive prostate cancer (mHSPC) and in castrate resistant prostate cancer (mCRPC) patients.[3,4] Several dose' regimens were employed. In literature we are found studies showing that better results are obtained when biologically effective dose larger than 100 Gy (α/β=10 Gy) are delivered.[5] SBRT seems to be a safe approach to metastatic lesions that might provide disease control and defer androgen deprivation therapy (ADT) in mHSPC patients and sistemic therapy in mCRPC ones. Local control is better when higher radiation doses are employed.[6]

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THE ROLE OF SBRT IN OLIGOMETASTATIC BREAST CANCER

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Oligometastatic breast cancer represents a distinct subset of metastatic disease with a potentially more indolent biology, where metastases are limited in number and location.

The development of oligometastases in breast cancer patients is not a rare occurrence, as suggested from prospective trials performed for the first line treatment of metastatic breast cancer. In these series approximately half of patients recurred in a limited number of sites.[1]

Hellman and Weichselbaum first described the oligometastatic state in 1995.[2] Since then, many studies investigated the role of local therapies, such as surgery and radiotherapy, in the treatment of oligometastatic patients. Most of these studies are surgical series, but recent technological developments made stereotactic body radiotherapy (SBRT) an attractive option in this setting of patients.

In 2013, Tree and colleagues[3] reviewed the role of SBRT in the treatment of oligometastases and identified different factors affecting prognosis in oligometastatic patients (histology, size, location and number of metastases, disease-free interval and radiation dose delivered). Breast cancer histology resulted as favourable prognostic factor. Encouraging results derive from studies limiting the enrollment to breast cancer patients (4-6); in these series the reported two-year local control and overall survival rates ranged from 80% to 97% and from 66% to 95%, respectively. Moreover, radiation therapy was well tolerated, and no Grade ≥3 toxicity was documented.[5,6]

Unfortunately, given the lack of randomized prospective data, all our knowledge about the role of SBRT in oligometastatic breast cancer derives from retrospective case series or single arm dose escalation studies.

Multiple randomized trials (such as SABR-COMET and NRG BR002) are ongoing to determine if the SBRT in addition to standard of care systemic therapies improves clinical outcomes in selected patients with oligometastatic disease.

Waiting for these results, the selection of oligometastatic breast cancer patients who can benefit from SBRT remains a crucial aspect that should be discussed within a multidisciplinary team.

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BRAIN METASTASES IN HER2 POSITIVE BREAST CANCER: WBRT AND SRS IN THE AGE OF NEW SYSTEMIC THERAPIES

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The incidence of brain metastases (BMs) in breast cancer (BC) patients ranges between 10-30% and these rates are as high as 50% in patients with HER2-positive disease that is an important predictor factor for BMs development associated with young age. The success of the first-generation HER2-directed therapies (eg. Trastuzumab) has brought to improve overall survival and systemic disease control changing the natural history of this subtype BC. Nevertheless, approximately half of the patients with BMs die from intracranial disease progression at a median survival time after BMs diagnosis of 24 months.[1] Probably, the detectable BMs are the result of the aggressive biological behavior and the genetic heterogeneity and actionable mutations in HER2+ BC interposed between primary tumor and its BMs,[2] in a framework of selective resistance to the drug and/or the poor or non-penetration of the same, across the blood-brain barrier. New drug or old drug with new escape action mechanism would seem to achieve the control of brain micrometastatic or low-volume disease with a response rate of 65.9% and 1-year OS of 70%.[3,4] However, Aoyama *et al*.[5] showed that WBRT is able to prevent new BMs arising for a maximum of 6 months after treatment. Considering the longer than 1-year survival of these patients, outliving the benefits of WBRT and developing correlated negative effects,[6,7] could be a possible event. In the other hand, to improve intracranial disease control and to reduce neurological deaths, the rising evidences about radiosurgery (SRS/SFRT) use, also for multiple BMs,[8,9] may be the successful strategy avoiding WBRT that remains a valid support tool for patients with short life expectancy. This scenario opens a translational research field in which synergic multiple approaches lead improving OS in a disease subset that until a few years ago had a short prognosis.

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PREVENTION AND EARLY DETECTION OF RADIATION INDUCED HEART COMPLICATIONS: AN EMERGING NEED FOR MODERN RADIOTHERAPY

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The association between chest radiation therapy (RT) and cardiac complications is nowadays well known for patients cured from mediastinal lymphomas, breast cancer and lung cancers. Cardiac complications from thoracic irradiation were, anyway, considered rare and insignificant[1] for a long time, although the first report on the aftereffect of X-rays on the heart was described in 1897.[2] First detailed and reliable descriptions of radiation induced heart disease (RIHD) date back to occasional case reports published 40-50 years ago.[3-4] Hancock et al. from Stanford University subsequently established that the risk is related to doses to the mediastinum[5] in Hodgkin lymphoma (HL) patients. Since then, several studies have become available, focusing mostly on childhood, HL and breast cancer survivors, connecting cardiac RT dose with the risk of cardiac morbidity and mortality.[6-9] Acute complications (within 6 months by the end of the treatment) often manifest as pericarditis, which is usually transient and easily curable with anti-inflammatory therapy. Late deficits, conversely, are composed by miscellaneous events and, by affecting all the heart structures, manifest with chronic heart failure, unstable angina, myocardial infarction, valve impairment and arrhythmia. Late effects may rise up several years after the end of the treatment, usually appearing in the second to the third decade post-therapy.[10] Radiation induced heart disease has become an important argu-

ment of research nowadays, leading to intensive debate on the risk-benefit ratio of RT, particularly in lymphoma patients. However, the recent prominent improvement of RT techniques has significantly reduced the inadvertent irradiation of organs at risk, with a particular attention in the recent years for the heart. Techniques as intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT) and respiratory gating have the clear goal to decrease fields and doses of RT to all the organs at risk, including the heart, without compromising long-term disease related outcomes. For that reason, RIHD is expected to reduce dramatically in the future even though, given the long latency of these events, the magnitude of the residual risk is still uncertain. Purpose of this talk is to evaluate the potential contribution of modern RT techniques in reducing RIHD and to investigate the efficacy of new diagnostic tools in detecting radiation induced heart damage in the early preclinical phase.

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SAFE TRIAL: AN ONGOING RANDOMIZED CLINICAL STUDY TO ASSESS THE ROLE OF CARDIOTOXICITY PREVENTION IN BREAST CANCER PATIENTS TREATED WITH ANTHRACYCLINES WITH OR WITHOUT TRASTUZUMAB

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Anthracyclines and trastuzumab play a key role in preoperative and adjuvant BC treatment, and showed a significant survival benefit in several trials. Although acute cardiac toxicity is relatively infrequent and usually reversible in a dose-dependent manner, published data evidenced a clinically relevant early late cardiac toxicity, with a chronic progressive deterioration of LVEF, up to congestive heart failure. Late toxicity occurs in most cases within the first year following chemotherapy completion; therefore, an echocardiographic monitoring is strongly recommended for a longer time.The issue of a cardiotoxicity prevention strategy for these patients is strongly debated, but the Steering Committee of the SAFE trial does trust in multidisciplinary and accurate basal cardiological assessment.

The aim of our study is to find out the best approach to prevent cardiac toxicity in non-metastatic BC patients undergoing anthracycline-based chemotherapy, with or without subsequent anti-HER2 therapy with trastuzumab.

SAFE trial (CT registry ID: NCT2236806; EudraCT number: 2015-000914-23) is a multicentric randomized phase 3, four-arm, single-blind, placebo-controlled study that aims to evaluate the effect of bisoprolol, ramipril or both drugs, compared to placebo, on subclinical heart damage evaluated by speckle tracking cardiac ultrasound consequent to anthracycline-based therapy in non-metastatic BC patients. Cardioprotection is administered for 1 year, or until the end of trastuzumab therapy, when indicated. Dosages for all groups will be systematically up-titrated as tolerated at 1-week intervals, for a total of 3 weeks, up to the daily target dose of bisoprolol, ramipril and placebo. All patients undergo cardiac surveillance with echocardiogram and speckle tracking strain at baseline and every 3 months, until 2 years. Thereafter, patients will be followed up as per single center local policy and international guidelines recommendations. Patients will be allocated in a 2 × 2 factorial design to one of the four treatment arms (Table 1). Allocation of the participants in the trial arms will be conducted by a stratified randomization, using randomized permuted blocks within defined age and HER2 status strata, software-based. The analysis is based on intention to treat. Simple descriptive statistics will be used to compare the individual characteristics of patients allocated in the distinct groups at time 0 (baseline). The SAFE study is active and recruting, the results will be made available next year.

Table 1. Cardiac toxicity prevention in non-metastatic breast cancer patients treated with anthracycline-based chemotherapy: A randomized, placebo controlled, phase III trial – SAFE trial.

		INTERVENTION A (Bisoprolol)	
		YES	NO
INTERVENTION B (Ramipril)	YES	A+B	B
	NO	A	No intervention

DEEP INSPIRATION BREATH HOLD (DIBH) TECHNIQUES FOR ADJUVANT RADIOTHERAPY IN LEFT-SIDED BREAST CANCER

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Aims: To review the commonly used techniques and devices for Deep Inspiration Breath Hold (DIBH) for postoperative radiotherapy (RT) in left-sided breast cancer and to illustrate the experience with DIBH at the Radiotherapy Department - San Donato Hospital-Arezzo.

Methods: Modern breast cancer RT techniques, such as respiratory-gated RT in DIBH, have been shown to reduce the high dose exposure of the Organs at Risk (OARs) in RT for left-sided breast cancer, that might increase the relative and absolute risks of radiation-induced secondary lung cancer and ischemic heart disease. There are two very commonly used techniques for DIBH, voluntary DIBH (vDIBH), and moderate DIBH. With vDIBH respiratory motion is monitored through devices placed on the patient's chest, and the patient is instructed to hold her breath at certain points in the breathing cycle. The treatment beam can also be gated so that treatment is stopped when the breathing signal falls outside a preset threshold. Optical tracking systems can reconstruct the 3D surface of the patient, visualizing the alignment of the reference surface and the reconstructed surface at the region of interest to provide real-time position monitoring. Moderate DIBH is obtained for instance with devices typically utilizing a spirometer which allows for monitoring of air flow throughout the respiratory cycle and stopping air flow at a set threshold volume. In our Institution vDIBH is used. We retrospectively reviewed 90 left-sided breast cancer patients referred for adjuvant RT. Two treatment plans were generated for each patient: Free Breathing-3DCRT and DIBH-3D-CRT. Dosimetric parameters were obtained from Dose Volume Histograms. Results were compared using the T-Test. Results: for heart, Left Anterior Descending Coronary Artery (LADCA) and left lung, a significant dose reduction was found with DIBH. These results reported by several Authors are confirmed also by our study based on vDIBH technique.

Conclusions: all the analyzed techniques are very reproducible and enable a decrease of cardiac, LADCA and lung dose, thus potentially impacting on radiation-induced late sequelae.

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RADIOTHERAPY WITH DEEP INSPIRATION BREATH HOLD (DIBH) TECHNIQUE IN THE LOCO-REGIONAL TREATMENT OF LOCALLY ADVANCED LEFT BREAST CANCER

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Aims: The aim of the study was to compare the deep inspiration breath-hold (DIBH) 3D conformal irradiation technique with Free-breathing (FB) 3D conformal and volumetric modulated arc therapy (VMAT) for left sided whole breast and locoregional treatment to verify the robustness of DIBH delivery

Methods: An Elekta Synergy linac is used to simulate the treatment of ten patients. Three plans were generated in Monaco 5.0 for each patient with FB and DIBH 3D conformal and FB VMAT technique with a dose prescription of 50 Gy in 25 fractions. Plan quality was assessed considering target coverage, sparing of the contralateral breast, the lungs, the heart, LAD and the normal tissue. The Wilcoxon test was used for statistical analysis with a significance level of 0.05. Optical surface tracking technologies were used to support the DIBH gated treatments. The robustness of DIBH delivery was assessed by set-up verification with electronic portal images (EPID) and intra fraction monitoring via the optical system. EPID were acquired during the first three treatment fractions and one time week for and compared with the digitally reconstructed radiographs with a maximal acceptable tolerance of 5 mm. Intra-

fraction and intra-beam set-up variability were quantified over all the treatment fractions.

Results: DIBH 3D technique provided a significant dose reduction in Heart Mean Dose (0.9 Gy DIBH 3D, 1.8 Gy 3D FB vs 5.6 VMAT FB), and LAD V20 (1.7 Gy DIBH 3D, 17 Gy 3D FB vs 0.5 VMAT FB) . Better PTV coverage was found in DIBH 3D plans (PTV95%: 91.5% DIBH 3D, 85.2% Gy FB, 89.5% VMAT). No statistically significant difference was achieved for the ipsilateral lung parameters (V20 and Dmedia) although the expected damage is much lower in the DIBH technique since the lung parenchyma density (-562HU in DIBH vs -379,7HU in 3D o VMAT) decreases significantly (p<O.OS) . Contralateral breast and lung and the normal tissue were significantly spared in DIBH 3D irradiation. In particular, the low doses (the percentage of volume relative to the outer contour of the patient receiving SGy (VS), are considerably higher in the VMAT (VS 45Gy) treatments compared to the other 2 RT modalities (VS DIBH 19.6 and 3D 18). Set-up verification with EPID and intra-fraction monitoring via the optical system provided an Intrafraction variability <2.2 mm in translations and <1° in rotations.

Conclusions: Balancing target coverage and OAR sparing, DIBH 3D conformal can be considered the preferable of these investigated treatment options. With appropriate patient selection and adequate training, the DIBH technique for advanced left breast cancer is feasible and reproducibility. However, this technique is time-consuming, since the setup is complex, results in an increased time for treatment delivery, and needs patient cooperation and technical expertise.

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RE-IRRADIATION WITH CURATIVE INTENT IN PATIENTS WITH HEAD AND NECK CANCER: WHO, HOW AND HOW MUCH?

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The optimal treatment of locoregionally recurrent or second primary cancers of the head and neck remains to be defined. over the last 2-3 decades re-irradiation has been progressively recognized as a possible therapeutic approach in selected patients. This presentation attempts to review the more recent considerations in the application of re-irradiation in this population. The main focus will be on the identification of ideal candidates for re-irradiation, the timing between the two treatment courses, the modern radiotherapy techniques available to prevent excessive normal tissues damage, the treatment volumes and the optimal prescription doses.

LDR PROSTATE BRACHYTHERAPY

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Low dose rate brachytherapy (defined by the use of radiation source with a dose rate of less tha 2 Gy per hour) is one way to administer radiation therapy to treat low and intermediate-risk prostate cancer.

The term brachytherapy derived from Greek “brachus” or “brachy” and refers to a technique that used radiation sources into or very near target tissue. With this technique the volume of irradiated tissue is relative small compared with extermal beam radiotherapy and it makes dose escalation feasible.

Referred to prostate cancer, LDR brachytherapy is also named permanent prostate brachytherapy, given that the implanted radioactive sources are left within the prostate gland; it is different from the HDR technique, where w the source are temporarily placed and removed when the dose are delivered.

The rationale in using this technique is based on:

- The particular anatomical location of the prostate

- The degree of dose escalation (provided by LDR vs external beam radiotherapy-EBRT) may be more effective in tumor cells kill
- The possibility to give a focal "hot spots" to the peripheral zone (the critical zone for develop of cancer)
- The more favorable distribution of dose to the surrounding normal tissue

LDR brachytherapy requires a skilled working team (clinicians, physicists, dosimetrist, nurces) to perform a safe and reproducible technique. With the use of a real time TRUS images obtained immediately prior to the implant, a treatment plan is created: this intraoperative planning may prolong the time request in the operating room (vs a preplanned prostate brachytherapy technique) but in this way the need of a pre-procedural TRUS study is eliminated. During the procedure the TRUS guided the placement of a lot of hollow needles, preloaded with the sources. This sources are available in loose format or they can be linked together at regular interval: this format produce a better dose coverage because of the lower risk of migration outside the periprostatic tissue. The sorces commercially avalaible are 125I, 103Pd and 131Cs: they differ for the physical characteristics (half life and average energy) and for prescription dose utilized in clinical trial. Despite the radiobiological consideration of the prostate cancer (the longer half life of 103Pd and 131Cs may confer a possible advantage with a more rapid delivery of radiation dose) large retrospective study have confirmed the equivalence in oncologic outcomes of the different radionuclides.

LDR brachytherapy is an estabilished treatment for localized prostate cancer, but an appropriate patient selection is mandatory: this selection is based on oncological stratification and patient's characteristics.

The data about the oncological statification regard the risk (and than the need of additional EBRT) of tumor extension beyond the prostate. This considerations remain uncertain so there is no level I evidence investigating appropriate patient selection (in particular about intermediate risk and LDR brachyrìtherapy manotherapy). Clinical patient selection is very important to minimize the risk of treatment related toxicity: volume and morphology of the gland, urinary function, prior TURP, are factors that should be considered in the shared decision process between physician and patient.

Although randomized studies comparing brachytherapy, EBRT and radical prostatectomy (RP) are lacking, several large series reported excellent results for patients treated with LDR technique. The BFS for low risk patients is greater than 90% and in intermediate risk desease is between 75 and 90%. Furthermore in this series the cause-specific survival is over 95%. Under evaluation is, in particular, the subgroup of intermediated risk, in which the distinction between favorable and unfavorable group is too much important. In this cases the factor driving concerns about the choise of LDR brachytherapy monotherapy or in addition to EBRT is the risk of tumor extension beyond the prostate.

Another question about the efficacy of LDR brachytherapy is the role of androgen deprivation therapy (ADT) in improving cancer control rates: there is a little evidence to demonstrate a benefit of adding ADT to brachytherapy in low and favorable intermediate risk.

Acute and late genitourinary (GU) adverse effects are the most reported data of toxicities in these patients: acute effects peak between 1-3 month (irritative and obstructive symptoms) and ranges (G3 symptoms) between 5-10% in retrospective large series. The early side-effects for prostate brachytherapy have been well characterized: in particular, urinary symptom scores return to baseline within 6 and 12 month after the treatment. Late GU effects are less than 3% for Grade 3-4.

G3 gastrointestinal (GI) toxicity rates are reported between 1-3%: rectal ulceration is uncommon and occours in less than 1% of patients. Although there are only retrospective study, the data about QOL show similar findings among the modality of treatment (LDR brachytherapy vs EBRT vs RP). However each modality impact specific symptoms: urinary and sexual functions QOL are better in patient undergoing brachytherapy than those undergoing RP. Urinary bother and bowel function are worse in patients undergoing brachytherapy. There is a little difference between EBRT and brachytherapy in favour of interstitial treatment, about sexual function and bowel symtoms.

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Selected Oral Communications

COS001

CURATIVE RADIOTHERAPY IN MUSCLE-INVASIVE BLADDER CANCER PATIENTS, OUR EXPERIENCE

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Aims: To evaluate clinical results in selected bladder cancer patients treated with curative radiation therapy.

Materials and Methods: We reviewed clinical records of bladder cancer patients treated in two Radiotherapy Centres of Sicily (Papardo Hospital and Policlinico G. Martino in Messina) from March 2013 to February 2018. The toxicity was evaluated with RTOG acute and late morbidity scoring.

Results: Twenty five patients (3 female and 22 male) were evaluable. The median age was 86 years (range 77-92). All patients were submitted to TURB (transurethral bladder resection) both to define the istotype and to debulk. 1/25 patients had cT1G3; 19/25, cT2G2-G3; for 5 patients disease stage was unknown. Systemic chemotherapy was administered in 2/25patients; 2/25 had local chemotherapy instillation; 1/25 had concomitant radiochemotherapy. The radiotherapy techniques used were: IMRT in 4/25 patients, IMRT-IGRT in 7/25 patients, VMAT in 1/25, 3DCRT in 3/25 patients and 3DCRT-IGRT 10/25 patients. The median delivered dose was 60Gy (range 36-66 Gy), with a fraction dose of 200 cGy in 19/25 patients, 210 cGy in 6/25 patients.The median follow-up, included who died, was 23 months (range 6- 62 months). 23/25 patients completed planned treatment; In 1/25 patients treatment has been interrupted at 36 Gy,1/25 at 54 Gy for G3 toxicities. Genitourinary acute toxicities were: G0 in 4/25 patients, G1 in 5/25 patients, G2 in 12/25 patients, G3 in 4/25 patients. Gastrointestinal G1 toxicity was observed in 4/25 patients. A complete response was observed in 12/25 (48%) cases; a partial response in 1/25 (4.6%) was recorded. Two patients were submitted to radical cystectomy for locally recurrent disease,6 and 18 months after treatment respectively. No significant late toxicities was observed. At the last follow-up both median TTP and OS have not been reached.

Conclusions: Also in elderly bladder cancer patients suitable to radical cystectomy, radiotherapy treatment is an excellent therapeutic option, which should be considered at the time of therapeutic choice.

COS002

A NATIONWIDE SURVEY TO IMPROVE CLINICAL RESEARCH ON BREAST CANCER RADIOTHERAPY BY THE ITALIAN SOCIETY OF RADIATION AND CLINICAL ONCOLOGY (AIRO) BREAST GROUP

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Aims: In clinical research, surveys get a "snapshot" of the current medical practice about gray issues and stimulate a discussion leading to the development of tailored trials. This study reports Italian radiotherapy practice in the management of breast cancer (BC) on 3 topics of common interest: post-mastectomy or regional nodal hypofractionated radiotherapy (hRT), re-irradiation (rRT) for BC recurrence and radiotherapy (RT) after neoadjuvant chemotherapy (NAC).

Methods: A nationwide, 21-points questionnaire was distributed online via Survey Monkey to the Italian radiation oncologists. Items referred to general topics (country, center, experience in BC) and for each issue to: clinical decision making; treatment volumes; RT techniques; dose prescription.

Results: 78 Centers answered the Survey for 34164 patients (pts) affected by BC. In most centers, the pts number treated was superior to 200/year and in almost all cases an experts multidisciplinary discussion was performed to choose the best treatment for each patient. 16734 (49%) pts were treated with hRT. The 95% of centers used this treatment approach as clinical practice after breast-conserving surgery (BCs) for early stage BC, mostly in women older than 50 years (45%) affected by invasive ductal carcinoma (89%). Dose prescription ranged between 34-45Gy with high use of moderate hRT (40Gy/15fr and 42.5Gy/16fr in 62% of cases). In early stage BC, the 60% of centers used partial breast RT with different techniques. In locally advanced BC, the post-mastectomy or regional nodal hRT was still rarely applied, 13% and 15% respectively. 216 (0.6%) pts received rRT after BC recurrence. In 80% of cases, the rRT was given more than 5 years after primary RT. 3879 (11%) pts received RT after NAC. In the 55% of cases a clinical disease evaluation was performed at the end of systemic therapy and in 40% before the start of NAC. Disease staging included sentinel node biopsy before and after NAC in 40% and 60% respectively. In this setting, breast RT was administrated in 97% of pts after BCs, with hRT in 49% of cases.

Conclusions: This survey demonstrated the high interest for breast RT in the majority of Italian Centers. Some practices as rRT and RT omission in particular clinical settings need further verification before entering in current clinical practice. Future national clinical collaborative studies are advocated in order to investigate these controversial topics about BC RT.

COS003

HYPOFRACTIONATED WHOLE-BREAST IRRADIATION WITH OR WITHOUT BOOST IN ELDERLY PATIENTS: CLINICAL EVALUATION OF AN ITALIAN EXPERIENCE

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Aims: To examine local control, disease-free survival and toxicity in elderly (≥65 years) breast cancer patients treated with hypofractionated radiotherapy (hypo-RT) with or without a boost to the tumor bed.

Methods: The study was conducted on 752 patients treated from April 2009 to February 2017. Patients received 42.4 Gy in 16 daily fractions (2.65 Gy per fraction). A boost was only administered in cases of grade 3 primary tumor and close or positive margins. Acute and late toxicity was prospectively assessed during and after hypo-RT, based on the RTOG scale. Disease-free survival (DFS) and local recurrence-free survival (LRFS) were estimated using the Kaplan-Meier method for cumulative probability. Log-rank tests were used to identify differences by subtype. Cox's proportional hazard models were used to investigate the impact of various factors on the risk of disease progression.

Results: Among the 752 patients treated, 41 (5.5%) experienced disease progression including: 7 (17.1%) exclusively local recurrences; 1 (2.4%) local and nodal recurrence; 1 (2.4%) local and nodal recurrence plus metastasis; 7 (17.1%) nodal recurrences plus metastases; and 25 (61%) exclusively distant metastases. The 5-year DFS, LRFS, breast-cancer-specific survival and overall survival rates were 91.8% (95% CI 88.6-94.2), 98.0% (95% CI 96.1-99.1), 98.2% (95 CI 96.5-99.1) and 87.5% (95% CI 83.8-90.5), respectively. On univariate analysis, the administration of a boost, grading (G1-G2 vs G3), and molecular subtype (triple-negative or Her2-positive, or luminal B vs luminal A) significantly affected disease progression ($p<0.01$), and these findings were also confirmed by multivariate analysis.

Conclusions: Our study showed that hypo-RT is effective and well tolerated in the elderly population, and that routine use of a boost for patients over 65 years could be no justified. Further studies on the boost issue are strongly advocated.

COS004

CIRCULATING TUMOR CELLS (CTCS) IN PATIENTS WITH LOCALLY ADVANCED HEAD AND NECK CARCINOMA: RESULTS OF LONG-TERM FOLLOW-UP

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Aims: CTCs have been described as prognostic and predictive factors in a variety of solid neoplasms. In 2012 we anticipated that CTCs could have a role in predicting prognosis and response to combined radical treatment in patients (pts) with locally advanced head and neck carcinoma (LA-HNC). We here present updated results after a longer follow-up.

Methods: Pts were prospectively enrolled, treated and followed-up at 4 oncologic Institutions in Italy as per initial protocol. CTCs analysis was performed with the CellSearch System (Menarini-Silicon Biosystems, Bologna, Italy). Pts for whom no clinical information was available at the date of December 2016 were considered lost to follow-up and not eligible for analysis.

Results: Sixty-five out of 73 pts were eligible for response and survival analysis. After a median follow-up of 64 months, 24 (37%) and 30 (46%) pts were relapsed and dead, respectively. Median relapse-free survival (RFS) and overall survival (OS) for the whole cohort were 56 and 64 months, respectively. Eleven (17%) pts had a median of 2 CTCs/7.5 mL blood (range 1-43) at baseline before any treatment. CTCs resulted prognostic of shorter median RFS (21 vs not reached months, p 0.05) and OS (33 vs not reached months, p 0.163). The presence of baseline CTCs correlated with a poorer overall responce after radical CRT.

Conclusions: The results of this study extend our previous observations and confirm the data subsequently published in the literature. The presence of CTCs in LA-HNC pts and the absence of their clearance during treatment identify a subpopulation of pts with a more aggressive disease regardless of known prognostic categories. Further studies are warranted.

COS005

SAFETY AND FEASIBILITY OF CONCURRENT GAMMAKNIFE RADIOSURGERY AND IMMUNE CHECKPOINT INHIBITORS. A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Aims: Radiosurgery (RS) is the standard treatment for patients with limited number of brain metastases (BMs) and controlled extracranial disease. Recently, growing interest is addressed to immune checkpoint inhibitors (ICIs) in the treatment of melanoma, lung and kidney cancer with evidence of clinical benefit in terms of disease control and integrated clinical management. Lack of dataare available about safety of concurrent RS and systemic therapy with ICIs.

Aim of this study is to evaluate safety and synergistic activity of concurrent GammaKnife Radiosurgery (GKRS) and ICIs treatment.

Material and Methods: We retrospectively analyzed data from patients treated with GKRS for BMsand anti-CTLA4 (Ipilimumab) or anti-PD1(Nivolumab) agents from January 2014 to March 2016. Time interval between last ICIs administration and GKRS was no more than 6 weeks. We evaluated response to treatment using magnetic resonance imaging acquired at 45 days, 3 and 6 months after treatment, according to iRANO (Immunotherapy Response Assessment in Neuro-Oncology) criteria and neurotoxicity.

Results: Twelve patients were treated for a total number of 61 BM from melanoma (n=5), lung (n=6) and kidney (n=1). Median number of treated lesions was 3 per patient (1-16). Median age was 55 years (32-77); median DS-GPA was 2 (1-4). GKRS was delivered in a single fraction for a median dose of 21 Gy (15-24). Median treatment volume was 9.45 cm3 (1.75-220.35). Systemic treatment was anti-CTLA4 in 3 patients (13,1% of lesions) or anti-PD1 in 8 patients (60,7% of lesions). 1 patient was treated with both anti-CTLA4 and anti-PD1 agents (26,2% of lesions). Complete response, partial response and stable disease were achieved in 7 (11,5%), 22 (36,1%) and 32 (52,4%) lesions at the 45 days MRI. At 6 months in 4 cases (6,6%) MRI showed progression of treated lesions and in 5 patients (41,7%) appeared new cerebral localizations. At a median follow up of 9,6 months (6,3-30,6) one death was due to brain progression; 5 patients died for systemic progression. Acute neurotoxicity after GKRS didn't verify, while radionecrosis occurred in 1 patient. Only BRAF mutation was significantly related to local control (p=0,029).

Conclusions: Combination of ICI and GKRS is feasible and safe. In BRAF mutated melanoma brain metastases, defective mechanisms of DNA repair could be

the basis of better local control. Further studies are needed with more patients and translational research, to investigate this finding.

COS006

LOCALLY ADVANCED NSCLC (LA-NSCLC): RESULTS FROM A NATIONAL SURVEY ON TREATMENT PRACTICE FROM ITALIAN THORACIC ONCOLOGIST COMMUNITY

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Aims: Concomitant Radio-Chemotherapy (cRT-CHT) is the standard of care for locally advanced NSCLC (LA-NSCLC), but treatment is variously managed in reason of manifold presentation at diagnosis. The aim of the Survey is the evaluation of pattern of care for LA-NSCLC among national specialists involved in thoracic oncology. It seems necessary for subsequent possible strategies of implementation of multidisciplinary approaches.

Methods: A 15 multiple choice web-questions on diagnostic-therapeutic course of LA-NSCLC were submitted between February and April 2018 to Italian Pneumologists (PN), Thoracic Surgeons (TS), Radiation (RO) and Medical Oncologists (MO). Questions regarded: demography, diagnostic and therapeutic approaches, choices in different clinical scenarios.

Results: Most of responders were RO (42%), followed by PN (22%), MO (20%) and TS (15%) with 69% of participants with more than 5 years experience in lung cancer treatment, and 59% of specialists devoting more than 70% of their clinical practice to lung oncology. Multidisciplinary fortnightly discussions guided therapeutic integrate treatment in 80% of cases, in 72% are performed even weekly. Less multidisciplinar facilities emerged in responders from southern regions of Italy. Histological or cytological proof of lung cancer was considered adequate to define treatment by 63% of specialists, while 37% reputed necessary addictive molecular data. In 51% of cases, the definition of diagnostico-stadiative process is made by PN. In case of cN2 single nodal involvement, 48% of specialists address patients to RT-CHT, 52% to surgery upfront. Inoperable patients, with stable disease or partial response after neoadjuvant treatment would be addressed to RT in most of cases (68%): to RT-CHT in 49% and to RT alone in 19%. When RT-CHT was elective treatment, 54% of thoracic oncologists preferred concomitant approach while 46% have rather decided for sequential therapy due to logistical and expected toxicities.

Conclusions: The critical point of interest emerging from our survey is the need for adequate patient selection for cRT-CHT. Furthermore, a real multidisciplinary approach through regular meeting needs to be increased and widely spread in all Italian Centers particularly in the era in which very promising results were obtained by the associations with immunotherapy.

COS007

CHEMORADIATION IN ELDERLY PATIENTS WITH HEAD AND NECK CANCER: IS CONCOMITANT CHEMOTHERAPY SAFE AND USEFUL? A SINGLE INSTITUTION EXPERIENCE

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Aims: Concomitant chemotherapy (CC) in elderly patients (age > 70 years) treated with radiotherapy for head and neck cancer has shown no survival benefit with higher toxicity rates in several series. Despite that, in clinical routine CC is still often used also in elderly patients with good performance status (KPS). The aim of this study is to investigate possible factors related to toxicity incidence and survival outcomes in this specific population.

Materials and Methods: From January 2013 to March 2018, 197 patients consequently treated at a single Institution were retrospectively identified. Most of them were male, smoker and drinker, with good KPS. Median age was 77 years (range 70-92). Patients usually presented with locally advanced disease (stage IV 65%). Curative and post-operative setting were almost equally distributed. Of all patients 30% received CC (basically weekly cisplatin).

Results: CC was administered more often in patients with good KPS (KPS > 80, p .001) and with a higher stage of disease (stage > III, p .002). Patients treated with CC were also significantly younger than patients treated with only radiotherapy (median age 73 vs 78 years, p .000). CC was associated with higher hematological toxicities: anemia > G2 (p .000), leukopenia > G2 (p .000) and thrombocytopenia > G2 (p .000). Weight loss was also more severe (p .025), with a higher need of nutritional support (p .050) in patient treated with CC. Otherwise we didn't see any significant increase of local toxicities except the slight worsening of acute skin reactions > G2 (p .034) and acute and late dysgeusia (p .050 and p .021, respectively). No significant correlations were found between concomitant chemotherapy and survival: at 12 months local control (LC) was 81% and 85% (p ns), cancer specific survival (CSS) was 91% and 90% (p ns) and overall survival (OS) was 84% and 87% (p ns) in patients treated with or without CC, respectively. At multivariate analysis the only variables that impacted on LC, CSS and OS were the stage of disease and the KPS (Table 1).

Conclusions: our results confirm that CC in elderly is more toxic and it does not offer a survival advantage. Its administration in this specific population should therefore be given cautiously.

Table 1. Multivariate analysis

Endpoint	Variable	Relative Risk [Confidence Interval]	p value
Local Control	Stage (III-IV vs I-II)	3.0 [0.8-13.4]	.063
	KPS (≥ 80 vs < 80)	3.2 [1.4-7.4]	.003
Overall Survival	Stage (III-IV vs I-II)	5.7 [1.4-23.7]	.001
	KPS (≥ 80 vs < 80)	2.1 [1.1-3.7]	.016
Cancer Specific Survival	Stage (III-IV vs I-II)	8.3 [2.0-34.1]	.000
	KPS (≥ 80 vs < 80)	2.5 [1.5-4.4]	.001

COS008

RADIOTHERAPY AND ACUTE TOXICITY IN ELDERLY CANCER PATIENTS: IS VULNERABLE ELDERS SURVEY-13 A SCREENING METHOD FOR FRAILTY?

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Aims: Vulnerable Elders Survey-13 (VES-13) is an instrument used to identify vulnerable patients. The aim of this study was to describe the VES scores in a cohort of older cancer patients, to evaluate its accuracy in predicting risk of radiotherapy acute toxicity and its association with completion of treatment. Vulnerability assessment of geriatric patients with cancer may contribute to improve anti-cancer treatment with maximal results and minimal side effects.

Methods: From October 2016 to February 2018, 75 patients aged > 70 years with diagnosis of solid cancer, treated with radiotherapy, were enrolled in this prospective study. 54,6% of patients were > 75 years. Palliative treatment was performed in 23 patients. Neaodjuvant, radical and adjuvant treatments was performed in 52 patients, with or without sistemic therapy. Most frequently primary cancer site in radical radiotherapy treatments were breast, prostate and head and neck cancer. VES-13 was give at the beginning, at the end of radiotherapy and 3, 6 and 9 months later. Score ≥3 identified high risk of frailty. We evaluated whether baseline VES-13 score was associated with acute toxicity according to CTCAE v.4.0 scale, completation of radiotherapy and clinical outcomes.

Results: VES-13 identified 41 patients (53,3%) as vulnerable with a baseline score>3. 7 patients (9%) did not complete radiotherapy. These patients had higher VES-13 score compared to those who completed treatment. Head and neck and brain cancer showed a worsening of VES-13 score at the end of radiotherapy. At 3, 6 and 9 months there is no significant improvement in VES-13 score. Acute toxicity was associated with higher VES-13 score in palliative treatment. About 10 head and neck radiotherapy treatment, 3 patients (with VES-13 >3) interrupted or stopped radiotherapy, 2 patients of them reported G4 acute toxicity. Five of six patients treated for brain metastasis with palliative radiotherapy had VES-13 score>3 and die 2 months later end radiotherapy. At 12,2 months follow-up , 18 patients died,16 of whom had high VES score

Conclusion: VES-13 is usefull predictor for survival and toxicity. It has been used as a simple tool for assessing the vulnerability of elderly in various clinical settings, with higher scores reflecting greater risk of health deterioration. These vulnerable older adults would definitely benefit from a more carefully planned treatment strategy and/or multidisciplinary supportive care.

COS009

INDUCTION CHEMOTHERAPY FOLLOWED BY CHEMORADIOTHERAPY IN LOCALLY ADVANCED ANAL CANAL CARCINOMA

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Aims: Several studies identified clinical features as large primary tumors and extensive regional nodal involvement associated with poor prognosis and treatment failure in locally advanced anal canal carcinoma (LAACC). The aim of this study is to evaluate the impact of induction chemotherapy (ICT) in LAACC patients with large primary tumors, involvement of perianal skin and adjacent organs and extensive regional nodal disease.

Methods: Patients with histologically proven squamous carcinoma of the anal canal staged clinically T4N3M0 were eligible. All patients underwent temporary colostomy. ICT consisted of 3 cycles of Cisplatin (75 mg/m^2 q28) plus 5-fluorouracil (5-FU, 750 mg/m^2/d ci). CRT was standard “Nigro regimen”. RT was delivered using IMRT at 45 Gy in 25 fractions to pelvic and inguinal nodes; an additional 14 to 23.4 Gy (1.8 Gy/die 5/w) were delivered to primary tumour and involved nodes. Clinical response was assessed with CT and MRI after each treatment. Primary endpoints were local control (LC), symptomatic improvement and treatment feasibility.

Results: Between January 2007 and December 2016, 84 patients with anal canal cancer were treated. Four of them presented with a T4N3M0 clinical stage, a 10 cm median tumor longitudinal extension (range 7-12) and involved perianal skin. All were female (median age 62 years) and presented pelvic pain and infected perianal wounds. All patients completed ICT achieving complete pain resolution. Only toxicity recorded was anemia (G1) in 1 patient. Restaging MRI showed partial response (PR) in all patients. CRT was completed without interruptions nor severe toxicities: dysuria, radiodermatitis and diarrhoea G1 were recorded. At 3 months from CRT, there were 1 complete response (CR) and 3 PR. Of those 3 patients, 1 gained CR, 1 showed local disease progression and underwent Miles’ resection and 1 presented lung metastases at 6 months follow-up. After a median follow-up of 16

months (range 13-46), all patients were alive with LC, although 2 had distant metastases.

Conclusions: In some patients with LAACC even a Miles' resection cannot be performed. Thus, ICT may be proposed in these selected cases. The ICT in our study achieved a stable LC, rapid symptoms improvement and a significative disease volume reduction that made the RT feasible, both technically and clinically.

COS010

NOVEL SBRT FOR BULKY TUMORS EXPLOITING RADIATION-HYPOXIA-INDUCED BYSTANDER AND ABSCOPAL EFFECTS WITH PARTIAL HIGH-DOSE IRRADIATION OF THE HYPOXIC TUMOR SEGMENT

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Aims: New SBRT technique, exploiting bystander and abscopal effects has been developed at our institute for treatment of unresectable bulky disease. Behind our approach were pre-clinical studies which showed for the first time that high-dose partial tumor irradiation of hypoxic segment resulted in significant radiation-hypoxia-induced bystander (R-H-IBE) and abscopal effects (R-H-IAE). Hypothesis of presented study is that high-dose irradiation of exclusively hypoxic tumor segment will generate regression of whole partially-irradiated bulky (due to R-H-IBE) but also of unirradiated metastatic lesions (due to R-H-IAE). Primary endpoint was time to tumor progression. Secondary endpoints included local and distant response rates.

Methods: This prospective study involved 30 metastatic patients whose only bulky tumors of lung, head and neck, kidney, skin, adrenal glands and lymph nodes were partially irradiated. We defined "Bystander Tumor Volume (BTV)" (hypoxic segment) based on morphologic and functional tumor proprieties in PET and contrast-enhanced CT, as a hypovascularized-hypometabolic (SUV cut-off 3) junctional zone between the central necrotic and peripheral hypervascularized-hypermetabolic tumor segment. Based on tumor site and volume, BTV (without additional margins: CTV nor PTV) was irradiated with 1-3 fractions of 10 or 12 Gy to 70% isodose-line. SBRT plan was calculated on Monaco-TPS and delivered by 6MV FFF photons. Before each treatment, a cone-beam CT was performed. No patient received chemotherapy or immunotherapy.

Results: Targeted BTV corresponded to 30% bulky. With median follow-up of 10 months (range: 2-22) local response rate was 97%. Average bulky shrinkage was 60% (range: 40-100%) with 4 complete responses. 87% of patients remained free of progression. Distant response rate was 50% with mean reduction of untreated metastases of 50% (range: 50-100%). No patient experienced acute or late toxicity of any grade.

Conclusions: SBRT-PTI for bulky tumors was effective and safe. The results confirmed our hypothesis showing high potential for induction of R-H-IBE/R-H-IAE resulting in improved local control and prolonged time to tumor progression. Relevance: conversion of unresectable lesions into resectable as a neoadjuvant option (palliative into curative treatment), more suitable (1-3 days) treatment schedule for patients in poor general condition, better cost/effectiveness-profile, very safe re-irradiation by relapse.

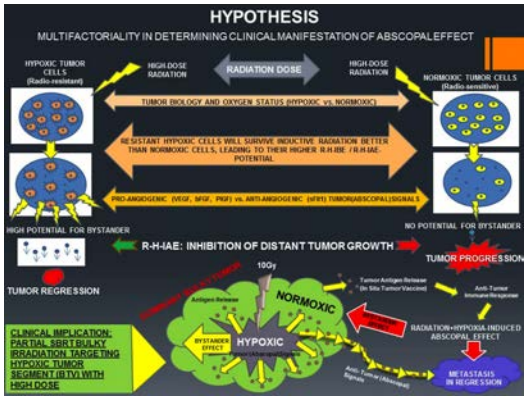

Figure 1.

AIRO GIOVANI
Oral Communications

CG001

MIDDLE HALF BODY RADIOTHERAPY IN BONE METASTASES FROM PROSTATE CANCER: A PHASE I STUDY

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Aims: In 2001 a clinical randomized trial from IAEA tested 2D Half Body Irradiation (HBI) for palliative treatment of multiple bone metastases demonstrating that a dose of 12 Gy in 4 fractions, twice a day, had the same effectiveness and tolerability of a total dose of 15 Gy in 5 daily fractions. However, the 2-days treatment was more comfortable and time-saving for patients (pts), in a variety of metastatic malignancies, with the exception of prostate cancer. In fact, in metastatic prostate disease, better outcome and lower toxicity were observed with a longer therapeutic schedule. Aim of our study was to evaluate the possibility to deliver the higher dose (15 Gy) in 4 fractions twice a day, in the specific setting of HBI defined as middle half body (MHB: pelvis, femurs and lumbar spine) by using a multiple field 3D-conformal technique to reduce toxicity.

Methods: A phase I trial in 3-dose escalation steps was designed: 13 Gy (3.25 Gy-fractions), 14 Gy (3.5 Gy-fractions), and 15 Gy (3.75 Gy-fractions). The eligibility criteria included prostate cancer with painful bone metastatic disease in MHB fields, ECOG performance status ≤3, life expectancy > 3 months, no severe bone marrow dysfunction. Treatment was delivered in 2 days with twice-daily fractionation and at least 6 hours interval. Pts were treated in cohorts of 6-12 to define the maximum tolerated dose (MTD). The dose-limiting toxicity (DLT) was defined as any acute toxicity of grade 3 or greater, using the RTOG scale. Pain was recorded using a visual analogue scale. IAEA pain and drug score were also registered.

Results: 25 patients were enrolled. Only grade 1-2 acute toxicity was recorded. No pts experienced DLT. With a median follow-up of 7.4 months, only two case of G1 skin late toxicity were observed. The overall (complete plus partial) response rate for pain was 84% (21/25 pts): 9 pts had complete pain relief (VAS=0), 10 pts showed at least 30% VAS reduction, 2 pts showed an improvement in pain score and drug score with 20 and 25% VAS reduction respectively.

Conclusions: The MTD of short course MHB radiotherapy in patients with bone metastases is 15 Gy. Preliminary data on palliative efficacy are promising.

CG002

DOSIMETRIC EVALUATION IN A LARGE SERIES OF BREAST CANCER PATIENTS (BCP) TREATED WITH POST OPERATIVE RADIOTHERAPY WITH DEEP INSPIRATION BREATH HOLD (DIBH)

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Aims: To analyze dose to organs at risk (OAR) and target coverage in BCP treated with DIBH and Intensity Modulated Radiotherapy (IMRT) technique in our department.

Methods: From January 2016 to December 2017 we evaluated clinical dose plans of 218 left sided BCP consecutively treated at our department. We performed DIBH treatment procedure for breast or chest wall irradiation (with or without nodal fields) using an optical gating method, Varian Real Time Position Management (RPM) System, and two tangential inverse planned intensity modulated beams with dynamic dose delivery. In our series, 189 patients (pts) (87%) received whole breast hypofractionated treatment (42.4 Gy/16 fractions/2.65 Gy) and 29 pts (13%) received local and nodal treatment with conventional fractionation (50 Gy/25 fractions/2 Gy). We analyzed the following OAR doses: heart (mean heart dose (MHD), maximum dose, 1 cc maximum dose, V5 Gy, V10 Gy, V20 Gy), left anterior descending coronary artery (LADCA) (mean and maximum doses), ipsilateral lung (mean dose and V20 Gy). The target coverage (PTV) was evaluated by studying the coverage of 95% and 93% of the prescribed dose as well as 1 cc maximum and minimum doses.

Results: The MHD for all patients was 0.81 Gy (0.03-2.6). The mean values of maximum dose, 1cc maximum dose, V5 Gy, V10 Gy, V20 Gy of the heart for all pts were 16.9 Gy (3.0-46.9), 7.6 Gy (0.9-41.7), 0.59% (0-10.3), 0.04% (0-7.9), 0% (0-1.9), respectively. Mean and maximum LADCA doses were 2.9 Gy (0.7-31.4) and 10.2 Gy (2.1-42.5), respectively. MHD and LAD maximum dose were significantly higher in pts receiving both local and nodal treatment: 1.4 Gy (0.7-1.4) vs 0.8 Gy (0.4-2.6) ($p<0.001$) and 20.8 Gy (6.1-42.5) vs 12.4 Gy (2.01-39.1) ($p< 0.001$), respectively. Mean and V20 ipsilateral lung doses were 4.6 Gy (2.5-12.1) and 8.4% (1.1-23.3), respectively. Mean PTV V95% and V93% coverage were 96.7% (78.7-99.6) and 98.5% (84.6-99.9), respectively; the mean value of 1 cc maximum was 106% and the minimum dose was 85.6%.

Conclusions: Althought a longer follow up is needed to evaluate clinical benefits and toxicity, we found, in our large series of pts, that DIBH and IMRT significantly reduce the dose to the heart and LADCA without compromising target coverage, in according to literature data.

CG003

PRODIGE 1.0: A BLADDER TOXICITY PREDICITIVE MODEL IN PROSTATE CANCER

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Purpose: Future challenges in oncology include development of predictive models able to support decision making. The aim of our study was to analyze some dosimetric parameters to predict late bladder toxicity and elaborate a model in prostate cancer patients.

Materials and methods: A prospective study was performed on prostate cancer patients treated with radiotherapy by volumetric technique, via Simultaneous Integrated Boost, and Image Guided Radiotherapy methods. Clinical Target Volumes (CTV) included: prostate gland (CTV1, 80 Gy) and seminal vesicles (CTV2, 72 Gy) in most of the sample. Late bladder toxicity data were collected via RTOG and CTCAE 4.03 scales, and cumulative Dose Volumes Histograms (DVH) were exported for each patient. Data were analyzed by using RStudio Software version 3.3.1 and by an in house developed software package "Moddicom". A p value < 0.05 was used as level of significance. Vdose (a value of dose to a specific volume of OAR) and Dvolume (a value of Volume where is distributed a specific value of dose) impact were analysed through Mann-Whitney rank sum test. A logistic regression was used as final model. The model was validated internally, by using a bootstrap analysis, and externally, by using a dataset from different centre. The area under the ROC curve and the calibration plot (Hosmer-Lemeshow GOF test) were used to evaluate the performance of internal and external validation.

Results: Data from a total of 175 patients were collected for internal dataset. Median follow-up was 39,09 months (C.I. 6.34-113.18). We performed Mann-Whitney rank sum test with continuity correction, in the subset of patients with late bladder toxicity grade ≥ 2 (in terms of haematuria, cysititis and dysuria), we observed a statistical significant correlation with a Vdose equal to 51.43 Gy (p.value 0.025) (Figure 1) Regarding V51, by a boostrap method of 2000 patients, the AUC of the ROC curve was respectively 0.63 for the internal validation and 0.62 for the external validation. No significant deviation of the Hosmer-Lemeshow GOF test was found in the calibrations plot of internal and external validation ($p>0.05$).

Conclusions: The development of prediction models, toxicity and more personalized treatments is a desirable and persuasive goal. Our results could help to optimize treatment planning procedures and seems defi-

nitely encouraging thus allowing to personalize treatments and reduce late toxicity.

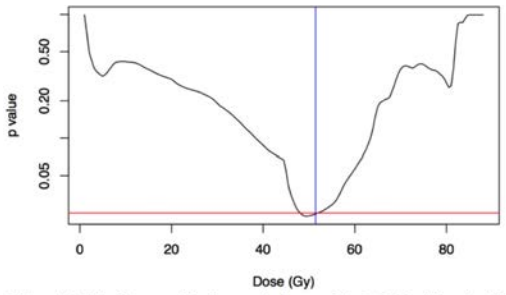

Fig.1: statistical significant correlation between development of late G≥2 GU toxicity and a Vdose

CG004

PRELIMINARY RESULTS OF AN AIRO PALLIATIVE STUDY GROUP INVESTIGATION ON ROLE OF PROGNOSTIC SCORE IN CLINICAL PRACTICE AND RESEARCH: PROPHET TRIAL

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Aims: Palliative Radiotherapy (PR) for bone metastases is a possible treatment for metastatic patients but often clinical practice and absence of shared guidelines can limit choice of correct regimen. Prognostic scores can help clinician to tailor time, dose and volume in PR. In this study we investigate about decision variance after application of Mizumoto Prognostic Score (MPS) to 5 clinical cases.

Methods: Five clinical cases were selected with a complete indication of MPS parameters. Two cases were of A class (prognosis > 6 months), 1 case of B class (prognosis between 6 and 12 months) and 2 cases were of C class (prognosis between 12 and 24 months). Six Radiotherapy Oncologists (ROs) with different grade of experience (in training RO, Junior RO, Expert RO, Junior RO Team Palliative member, Expert RO Team Palliative member) underwent a questionnaire to explore what RT regimen would chose before and after MPS application. Descriptive statistical analysis and concordance Fleiss' kappa test were used to discriminate variance of answers between groups.

Results: A questionnaire with 5 clinical cases was administered to 6 ROs. All participants complete the questionnaire. Median conversion rate of RT dose prescription after MPS application was 26.8% (0-50%). According to Fleiss' kappa parameters, evaluation of agreement in dose prescription showed an improving in 13.44% (from 37.33% [poor level] to 50.67% [Intermediate/Good level]) at the overall analysis after MPS application. Analytical case evaluation of agreement showed a basal good level of concordance between ROs in C class cases (40-66.7%), with an implement of agreement between 0 and 26.7%. A and B class cases showed a poor level of basal agreement (6.67-26-67%), that after MPS rise since to 46.67%. Analytic analysis of agreement of ROs showed a mean global implement of 18.75% (0-33.4%) after MPS application.

Conclusions: This preliminary investigation about prognostic score use in palliative radiotherapy has showed that MPS application can change RT prescription in 26.8% of participant, globally increasing also agreement in final dose prescription. A further analysis with 9 clinical cases to be administered to 25 ROs is scheduled, in order to confirm results and define how much experience and prognostic class can influence agreement.

CG005

PREOPERATIVE HYPOFRACTIONATED IMRT-SIB VERSUS CONCOMITANT BOOST RADIOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER PATIENTS: OUTCOME AND TOXICITY

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Aims: To compare treatment outcome and toxicity between a hypofractionated neoadjuvant radiochemotherapy (hN-RCT) with IMRT-SIB and conventionally fractionated neoadjuvant radiochemotherapy (cN-RCT) with concomitant boost, through a retrospective comparison with historical series from our Department.

Methods: Between April 2014 and February 2017,

37 patients with locally advanced rectal cancer were treated with a hN-RCT regimen (55 Gy in 2.2 Gy/fr); this series was compared with our historical series of 138 patients affected by locally advanced rectal cancer treated with cN-RCT with concomitant boost (45 Gy in 1.8 Gy/fr plus 1 Gy biweekly boost up to 10 Gy). Concomitant fluoropyrimidine was administered in both regimens. Surgery was performed after median 9 weeks (range 5-18) from the completion of neoadjuvant regimen. Pathological complete response, downstaging, treatment and surgery-related toxicity, local control and survival were evaluated.

Results: Pathologic complete response and T-downstaging rates were 22.2% versus 19,1% (P=0.5) and 64.8% versus 51.4% (P=0,05) in the hN-RCT and cN-RCT cohorts, respectively. hN-RCT was associated with a lower incidence of local relapse than cN-RCT (0% versus 13.2%; p 0.015) and the actuarial 2 years local control is 97.1% and 90.1 (P=0,25) for hN-RCT and cN-RCT, respectively. At the uni- and multivariate analysis patients who achieved a major or complete pathological response reported a better survival and a lower incidence of local relapse, regardless of treatment schedule. No differences in acute and late G3-4 toxicity were observed (10.81% and 10.89% for hN-RCT and cN-RCT, respectively). No differences in surgical morbidity and time to the recanalization were observed.

Conclusions: IMRT-SIB with total dose of 55 Gy (2,2 Gy/fr) is feasible, with tolerable acute and late toxicity and no increase in surgical morbidity. Early results showed good outcome in terms of pathological complete response and T-downstaging. A longer follow-up and a larger series are necessary to better assess the effectiveness of the hypofractionated schedule.

CG006

SAFETY AND EFFICACY OF HYPOFRACTIONATION FOR YOUNG BREAST CANCER PATIENTS TREATED WITH CONSERVATIVE SURGERY: A MONO-INSTITUTIONAL LARGE SERIES

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Aims: Adjuvant whole breast radiotherapy, with or without boost on tumor bed, represents the standard of care after breast conserving surgery. For decades, conventional fractionation has been widely used; however, many important experiences have showed comparable outcomes in terms of local control and toxicity using hypofractionated schedules. Nevertheless, there is currently no uniform consensus among Countries regarding the use of hypofractionation in younger breast cancer patients. The aim of our experience is to assess safety and efficacy of this approach.

Methods. We retrospectively analyzed data from 343 patients aged less than 60 treated from January 2013 to December 2016 at our institution with hypofractionated radiotherapy after breast conserving surgery. We evaluated local control, acute and late treatment-related toxicity, fibrosis and cosmesis at 6 months and 12 months.

Results: Mean patients age was 49.5 years (range 29-60). Eighty-two had undergone previous adjuvant chemotherapy, with or without anthracyclines, while 16 patients received primary systemic therapy. Two hundred-sixteen patients received adjuvant endocrine therapy. Schedule of 44 Gy in 16 fractions with or without boost in conventional fractionation was used. We experienced 0.9% rate of G2-G3 edema at the end of treatment. Fifty-nine patients (17%) had G2 erythema and only one patient presented G3 erythema at the end of radiotherapy, while wet desquamation (5 grade I, and 2 grade II) was observed in 7 patients (2%). Late G1 fibrosis was documented in 20 patients (6%) and G2 in 3 patients at 1-year evaluation (0.9%). Breast cosmesis resulted worsened after treatment in 49 patients (14.3%). Sixteen patients experienced mild breast pain at 6 months, 8 at 12 months evaluation. At a median follow up of 3 years, 99.7% of patients were alive. We registered 3 cases of loco-regional recurrence (0.9%). Two patients (0.6%) developed distant metastasis.

Conclusions. Our large experience demonstrated that hypofractionated whole breast radiotherapy for young patients is feasible, safe, and effective, showing an acceptable rate of acute and long term toxicities and a very low rate of disease failure.

CG007

USE OF A PDRN-BASED CREAM FORMULATION IN THE PREVENTION AND TREATMENT OF RADIODERMATITIS: A MONO INSTITUTIONAL EXPERIENCE

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Aims: This study was designed to assess the efficacy and tolerability of a PDRN (Polideoxyribonucleotides)-based cream formulation in the prevention and treatment of radiodermatitis in patient with breast cancer treated with hypofractionated radiotherapy. PDRN is a well-known registered drug with tissue repairing, anti-ischemic and anti-inflammatory properties.

Methods: Patients with breast cancer has been randomized to use a cream, standard of care in our institution or a PDRN-based cream, throughout the duration of radiotherapy and for two weeks afterwards. Patients were monitored before therapy, weekly during therapy, and for 2 weeks after radiotherapy was completed, using RTOG skin toxicity grading scale. Patients received a 3D conformal hypofractionated radiotherapy schedule (50-57.5 Gy with SIB technique on breast and tumor bed) in daily fractions of 2-2.3 Gy with 6-15 MV photons). Several clinical variables has been assessed on these patients as tumor histology, skin phototype,

use of chemo or hormone therapy, concomitant medical conditions and CTV breast-volume.

Results: Between december 2016 and march 2017, 120 consecutive patients, were enrolled in this study. Median age of the patients was 52.5 (range 36-81). At 4th week, 28/60 patients in the PDRN group vs. 42/60 patients in the control group had G2 grade of skin toxicity (p=0.0095). Moreover, between phototype 3 patients, 20/36 (55%) patients in the PDRN group vs. 21/26 (81%) patients in the control group had G2 grade of skin toxicity (p=0.038). At the end of the treatment (5 weeks), 40/60 patients in the PDRN group vs. 50/60 patients in the control group had G2 grade of skin toxicity (p=0.035). After 10 days from the end of the treatment, 9/60 patients in the PDRN group vs. 18/60 patients in the control group had G2 grade of skin toxicity (p=0.049). Moreover, between phototype 3 patients, 8/36 (22%) patients in the PDRN group vs. 13/26 (50%) patients in the control group had G2 grade of skin toxicity (p=0.022). After 40 days from the end of the treatment, 2/60 patients in the PDRN group vs. 8/60 patients in the control group had G1 grade of skin toxicity (p=0.047).

Discussion: PDRN based cream improves the acute skin toxicity profile of patients undergoing radiation therapy after conservative surgery for breast cancer. In these patients, the maximum skin toxicity grade is lower and the complete skin healing is faster. We need more patients and a longer follow up to assess late toxicity.

CG008

SWALLOWING ORGANS LATE COMPLICATION PROBABILITIES AND DOSIMETRIC CORRELATIONS IN HNCS: RESULTS OF A MONO-INSTITUTIONAL PROSPECTIVE STUDY

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Aims: To investigate late radiation-related dysphagia in HNCs candidates for a non-surgical curative treatment using a SWOARs-sparing IMRT. We report the correlations between doses received by the SWOARs and FEES dysphagia scores.

Methods: Eligibility criteria: nasopharynx and oropharynx cancers requiring bilateral neck irradiation. Objective instrumental assessment was made by FEES at baseline, at 6 and 12 months post-therapy to assess the severity of pharyngeal residue according to Farneti pooling score (P-score) for 3 different consistencies: water (L=liquid), marmalade (SS=semisolid) and cracker (S=solid). For the intent of the analysis, P-score was dichotomized as follows: 4-5 (no dysphagia) and 6-7 (mild dysphagia) vs 8-9 (moderate dysphagia) and 10-11 (severe dysphagia). SWOARs were assembled, based on the physiology-and-anatomy concept, into 5 Functioning Swallowing Units (FSUs): superior, middle and inferior constrictor muscles (Pharyngeal constrictors), supraglottic and glottic (Whole larynx), cricopharynx and cervical esophagus (Cricoesophageal muscolature), the two parotid glands (Parotids) and base of tongue (BOT). The differential and cumulative DVHs of the FSUs were computed and the following features were extracted: V30, V35, V40, V45, V50, V55,V60, V65, Dmean, Dstd, Dmin/Dmax and the dose received by the maximum number of cc (Dpeak). Each DVH feature was compared between patients with low/mild dysphagia and moderate/severe dysphagia (4-7 vs 8-11 P-scores) both for SS and S, using two-sample t-test with significance level $p<0.05$.

Results: A total of 38 patients were enrolled. Results are reported in the Table 1. P-score for S at 6 months resulted significantly correlated to V60 and V65 to the BOT. P-score for S at 12 months resulted significantly correlated to V50 and V55 to the BOT, to Dpeak, Dmin and Dmean to the Parotids and to V40, V55, V60, V65 and Dmean (p=0,03) to the Pharyngeal constrictors. P-score for SS at 6 months resulted significantly correlated to V55, V60, V65 and Dmean to the BOT and to V60, V65 and Dpeak to the Parotid glands.

Conclusions: Doses to BOT and Parotids significantly correlated to swallowing impairment both for SS and S whereas doses to constrictor muscles correlated to swallowing impairment for S.

Table 1. Dosimetric correlation between FEES scores and dose to SWOARs.

FEES/S t-6m						
FSUs	Features	Group A		Group B		p-value
		Mean	SD	Mean	SD	
BOT	V60 (%)	32.05	27.19	52.56	30.47	0.0438
	V65 (%)	17.03	18.74	34.18	25.27	0.0299
FEES/S t-1a						
FSUs	Features	Group A		Group B		p-value
		Mean	SD	Mean	SD	
BOT	V50 (%)	60.11	35.26	85.18	27.97	0.0425
	V55 (%)	46.68	36.23	72.96	32.08	0.0456
PAROTIDS	Dpeak (Gy)	12.29	7.05	21.08	12.19	0.0168
	D99 (Gy)	6.89	5.05	11.17	6.13	0.0418
	Dmean (Gy)	23.07	6.19	28.59	8.60	0.0463
PHARYNGEAL CONSTRICTORS	V40 (%)	74.70	25.03	90.30	10.15	0.0430
	V55 (%)	46.16	25.93	63.53	18.62	0.0487
	V60 (%)	28.71	20.23	46.12	22.80	0.0327
	V65 (%)	16.84	13.21	28.96	13.98	0.0200
	Dmean (Gy)	48.34	11.00	55.72	5.06	0.0326
FEES/SS t-6m						
FSUs	Feature	Group A		Group B		p-value
		Mean	SD	Mean	SD	
BOT	V55 (%)	55.95	36.30	87.87	10.84	0.0423
	V60 (%)	36.15	28.73	73.77	15.14	0.0040
	V65 (%)	19.83	20.36	54.93	16.23	0.0004
	Dmean (Gy)	53.32	9.78	63.28	2.33	0.0196
PAROTIDS	V60 (%)	2.04	3.23	5.72	6.34	0.0408
	V65 (%)	0.51	1.23	1.91	2.53	0.0453
	Dpeak (Gy)	16.07	10.84	27.83	19.07	0.0427
FEES/SS t-1a						
No Significative Results						

FEES- Fiber optic Endoscopic Evaluation of Swallowing S-Solid SS-Semisolid BOT- Base Of Tongue FSUs- Functioning Swallowing Units

CG009

SIB-IMRT IN THE TREATMENT OF ANAL CANCER PATIENTS, BY TOMOTHERAPY: SAFETY AND EFFICACY IN A SINGLE-CENTER EXPERIENCE

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Aims: To evaluate safety, clinical response (CR) and survival in Anal Cancer (AC) patients treated by chemoradiotherapy (CRT), with a simultaneous integrated boost (SIB)-IMRT with TomoTherapy (TT).

Methods: A cohort of 38 patients affected by AC, treated with TT between September 2014 and April 2018, was retrospectively analyzed. Concurrent chemotherapy (cCT) was always administered, except in unfit patients. The preferred CT regimen was 5-fluorouracil (5FU)-Mitomycin C (mitC). A SIB-IMRT approach was used, with total doses prescribed to PTV1, PTV2 and PTV3 ranged between 61.6–50 Gy, 50.4–45 Gy, 45–37.5 Gy, respectively, at corresponding dose/fraction ranges of 2.2–1.8 Gy for PTV1, 2–1.68 Gy for PTV2 and 1.8–1.5 for PTV3, delivered in 25–30 fractions. Acute gastrointestinal (GI), genitourinary (GU), dermatologic, and hematologic toxicities were scored, according to CTCAE scale, v. 4.02. CR was assessed at 12 weeks after the end of treatment via digital rectal exam or anoscope. Survival analysis were calculated from the end of treatment to the date of first local or distant recurrence for the disease-free survival (DFS) and to the date of death from any cause for the overall survival (OS).

Results: CR has been analyzed in 36/38 patients (95%), median follow-up (FUP) was of 9.5 months (range 2-43). Baseline clinical features of patients are summarized in Table 1. Twenty patients (53%) had nodal positive disease (stage IIIA/B) and 16 cases (42%) had a stage IIIB disease (stage IIIB). cCT was given to 30 patients (81.1%), 23 of them (76.6%) having been treated with 5FU–MitC. In 30 (79%) patients, RT schedule was 55 Gy to PTV1 and 45 Gy to PTV2, in 25 fractions, without any PTV3. In 17 patients (45%) treatment was completed without any interruptions, while the median duration of treatment breaks was 7 days (range 1-16) in the remaining group. The rate of G3 diarrhea and dermatitis was 8.1% and 13.5%, respectively. No G3 GU and hematological toxicities were reported. About CR, 29/36 patients (80.6%) achieved a complete response, while 6 (16.7%) showed a partial response; none had a stable disease and 1 patient (2.8%) had local progression. At last FUP, only 1 patient died. The 2-year OS and DFS were 96.2% and 74%, respectively.

Conclusions: CRT with TT for AC showed a good acute toxicity profile and excellent efficacy results, in terms of both clinical response and survival. A longer FUP is needed to confirm the long-term benefit and to evaluate any late toxicity.

Table 1.

Patients features	n	%
N. of patients	38	
Male	11	29
Female	27	71
Median age, y	66	
range	39-84	
Diagnosis Performance Status		
0	30	79
1	8	21
Tobacco smoke		
<10 packs/year	31	82
10-20 packs/year	3	8
>20 packs/year	4	10
Status HIV		
Positive	3	8
Negative	35	92
Stage of disease		
I	1	3
II	17	44
IIIA	4	11
IIIB	16	42
Status p16/HPV		
Not evaluated	32	84
Positive	5	13
Negative	1	3
Simulation PET/CT		
yes	28	74
no	10	26
Caratteristiche	n	%
Numero di pazienti	38	
Maschi	11	29
Femmine	27	71
Età mediana	66	
range	39-84	
PS alla diagnosi		
0	30	79
1	8	21
Fumo		
<10 pacchi/anno	31	82
10-20 pacchi/anno	3	8
>20 pacchi/anno	4	10
Status HIV		
positivo	3	8
negativo	35	92
Stadio di malattia		
I	1	3
II	17	44
IIIA	4	11
IIIB	16	42
Status p16/HPV		
Non valutato	32	84
positivo	5	13
negativo	1	3
PET/TC di centraggio		
si	28	74
no	10	26

CG0010

VMAT FOR THE TREATMENT OF LOCALLY ADVANCED OESOPHAGEAL AND JUNCTIONAL CANCER

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Aims: To report, dosimetric results, safety, toxicity profile and clinical outcomes of a consecutive series of patients affected with oesophageal cancer (both squamous cell - SCC and adenocarcinoma – ADK histology) treated with volumetric-modulated arc therapy (VMAT), having either a definitive (DE) or pre-operative (PO) intent.

Methods: We retrospectively analysed 66 patients who received VMAT at our Institution between 2013 and 2017 (PO:35; DE:31) with curative intent. In the PO cohort, the more common schedules used were 41.4 Gy/23 fractions (fr) and 45 Gy/25 fr. In the DE cohort, the most commonly used regimens were 54 Gy/27 fr

and 60 Gy/30 fr. All patients in the PO group and 23 in DE group received concurrent chemotherapy. The more common regimes used were Cisplatin/5-fluorouracil and Carboplatin/Paclitaxel.

Results: Median follow-up was 11 months (range:4-40 months) in PO and 14 months in DE (range:2-43 months) groups, respectively. In the PO cohort, ADK were 34.3% and SCC 65.7%. In the DE group ADK were 12.9% and SCC 87.1%. In the PO cohort the disease was localized in the cervical and upper thoracic oesophagus (CUT) in 14.3% of patients, in 28.5% in the middle thoracic (MT) and in 57.2% in the lower thoracic (LT) and gastro-oesophageal junction (GEJ). In the DE cohort the disease was localized in 38.7 % in the CUT, in 38.7% in MT and in 22.6% in LT and GEJ. Dosimetric parameters regarding both treatment volumes and organs at risk are presented in Table 1. Maximum acute toxicities were: anorexia-G3 (PO:22.9%; DE:29%); esophagitis-G3 in 14.3% of patients in PO group and -G4 in 3.2% in DE cohort; asthenia-G3 (PO:14.3%; DE:32.3%); nausea-G3 (PO:8.6%; DE:3.2%); diarrhea-G2 in 2.9% of patients in PO group and -G1 in 16.1% in DE cohort. One-year overall survival was 59.9% [95% confidence interval (CI):39.9%–75.2%] in PO cohort and 42.1% (95% CI:24.24%-58.97%) in DE group, while cancer-specific survival was 72.6% (95% CI:50.3%-86.1%) in PO and 46.9% in DE cohort (95% CI:27.3%–64.3%). One-year local-regional control rate was 75.3% (95% CI:50.9 - 88.7%) in PO and 47.2% (95% CI:27.3%-64.7%) in DE group.

Conclusions: Our clinical results support the use of VMAT as a safe and effective radiotherapy option in the combined modality treatment of oesophageal cancer with consistent dosimetric results in terms of both target coverage and normal tissue sparing and a mild toxicity profile. Short-term oncological outcomes are in line with those reported in the literature.

Table 1. Dosimetric results.

Volumes	Parameters	Neoadjuvant RT			Definitive RT		
		Cervical/Upper	Middle	Lower/GEJ	Cervical/Upper	Middle	Lower/GEJ
Intestine	Mean dose (Gy)	0.15 (0.02)	2.15 (3.77)	7.17 (3.89)	0.23 (0.18)	0.42 (0.47)	3.64 (6.25)
	D_1 cc (Gy)	0.31 (0.08)	13.57 (16.53)	37.56 (11.19)	0.71 (0.88)	4.94 (7.77)	17.72 (18.75)
	V_{30} (%)	0.00 (0.00)	0.72 (1.62)	4.58 (4.21)	0.00 (0.00)	0.00 (0.00)	0.82 (1.62)
	V_{40} (%)	0.00 (0.00)	0.05 (0.15)	0.92 (1.14)	0.00 (0.00)	0.00 (0.00)	0.02 (0.03)
Heart	Mean dose (Gy)	1.45 (0.89)	19.43 (7.88)	20.88 (5.93)	8.14 (7.67)	18.94 (10.20)	26.93 (7.24)
	D_1 cc (Gy)	12.1 (16.29)	44.77 (8.13)	41.95 (12.03)	35.21 (18.93)	52.88 (5.49)	53.50 (1.68)
	V_{30} (%)	0.10 (0.21)	20.45 (15.92)	21.66 (13.74)	8.33 (13.25)	27.26 (19.85)	33.57 (18.00)
	V_{40} (%)	0.00 (0.00)	6.15 (7.72)	5.13 (5.21)	3.22 (6.02)	12.06 (10.56)	15.72 (7.76)
	V_{45} (%)	0.00 (0.00)	1.94 (5.43)	1.48 (4.03)	1.43 (3.10)	6.44 (6.84)	8.57 (5.30)
Left kidney	Mean dose (Gy)	0.09 (0.04)	2.03 (2.20)	5.85 (4.47)	0.18 (0.15)	1.13 (3.03)	2.32 (3.56)
	D_1 cc (Gy)	0.14 (0.05)	13.58 (15.72)	26.97 (13.20)	0.27 (0.19)	4.18 (11.77)	11.72 (18.85)
	V_{15} (%)	0.00 (0.00)	5.89 (8.96)	19.40 (19.29	0.00 (0.00)	3.49 (11.05)	6.48 (12.96)
	V_{20} (%)	0.00 (0.00)	1.71 (2.85)	9.92 (11.97	0.00 (0.00)	1.81 (5.71)	4.00 (7.99)
	V_{30} (%)	0.00 (0.00)	0.49 (0.96)	2.78 (4.49	0.00 (0.00)	0.55 (1.75)	0.96 (1.92)
Right kidney	Mean dose (Gy)	0.10 (0.02)	0.57 (0.61)	3.84 (3.28	0.21 (0.25)	1.00 (2.57)	1.23 (1.88)
	D_1 cc (Gy)	0.19 (0.08)	3.73 (5.46)	17.67 (12.37	0.39 (0.52)	3.97 (10.97)	8.25 (14.85)
	V_{15} (%)	0.00 (0.00)	0.33 (0.94)	11.65 (17.75	0.00 (0.00)	2.94 (9.31)	2.99 (5.99)
	V_{20} (%)	0.00 (0.00)	0.03 (0.10)	4.47 (6.33)	0.00 (0.00)	1.45 (4.59)	1.39 (2.78)
	V_{30} (%)	0.00 (0.00)	0.00 (0.00)	0.51 (1.15)	0.00 (0.00)	0.39 (1.24)	0.12 (0.25)
Liver	Mean dose (Gy)	0.20 (0.03)	4.49 (4.34)	12.92 (3.91)	0.50 (0.35)	2.14 (3.52)	6.59 (6.74)
	D_1 cc (Gy)	0.5 (0.06)	30.59 (19.07)	43.88 (3.24)	4.02 (6.62)	14.92 (15.69)	27.49 (24.98)
	V_{20} (%)	0.00 (0.00)	7.45 (8.17)	20.12 (11.33)	0.01 (0.02)	3.06 (8.70)	7.47 (10.84)
	V_{30} (%)	0.00 (0.00)	3.42 (3.61)	9.68 (6.86)	0.00 (0.00)	1.91 (6.03)	3.37 (4.61)
Lung	V_{20} (%)	15.20 (3.90)	16.74 (3.99)	12.31 (7.93)	19.78 (4.48)	21.56 (5.63)	17.78 (11.13)
	V_{10} (%)	27.34 (3.10)	33.37 (5.62)	28.67 (12.43)	31.82 (6.06)	35.51 (8.32)	35.46 (7.93)
	V_5 (%)	36.46 (4.92)	48.65 (6.72)	46.32 (13.77)	43.22 (12.10)	48.31 (9.49)	55.31 (9.68)
	MLD	8.07 (0.98)	9.56 (1.03)	8.25 (2.86)	10.36 (2.12)	10.89 (2.37)	10.73 (3.25)
Stomach	Mean dose (Gy)	0.22 (0.08)	9.36 (10.15)	29.99 (6.69)	0.66 (0.67)	3.02 (4.96)	20.15 (22.62)
	D_1 cc (Gy)	0.28 (0.20)	24.90 (21.95)	45.13 (1.50)	2.40 (3.87)	12.88 (20.01)	23.18 (24.87)
	V_{30} (%)	0.00 (0.00)	10.69 (13.87)	60.68 (20.77)	0.00 (0.00)	1.66 (4.25)	22.60 (41.16)
	V_{45} (%)	0.00 (0.00)	0.76 (1.10)	3.10 (5.51)	0.00 (0.00)	0.53 (1.60)	12.02 (24.04)

		Dose	Tumor Location	D_2 (Gy)	D_{98} (Gy)	V_{95} (Gy)	V_{105} (%)
PTV - tumor	Neoadjuvant RT	41.4 (Gy)	Middle	44.71	38.7	94.26	10.2
			Lower/GEJ	44.49 (0.70)	38.46 (0.68)	93.83 (3.76)	10.59 (6.52)
		45 (Gy)	Cervical/Upper	47.97 (0.45)	41.71 (0.62)	94.16 (1.97)	7.25 (4.44)
			Middle	47.85 (0.63)	49.99 (21.27)	94.46 (0.62)	6.22 (3.72)
			Lower/GEJ	47.16 (0.93)	42.33 (0.31)	96.09 (1.52)	2.71 (3.33)
	Definitive RT	54 (Gy)	Cervical/Upper	55.84 (4.25)	48.80 (3.78)	95.15 (0.87)	9.52 (3.57)
			Middle	57.57 (1.20)	50.53 (0.20)	94.96 (0.98)	7.95 (7.63)
			Lower/GEJ	56.60 (0.80)	50.02 (0.70)	88.86 (9.29)	2.53 (2.21)
		60 (Gy)	Cervical/Upper	64.12 (1.87)	56.06 (0.71)	95.58 (1.43)	14.16 (17.17)
			Middle	64.42	56.09	95.19	11.48
			Lower/GEJ	-	-	-	10.2
PTV – elective volumes	Neoadjuvant RT	45 (Gy)	Middle	47.88	39.01	97.96	65.56
	Definitive RT	54 (Gy)	Cervical/Upper	56.93 (1.12)	44.05 (2.19)	96.49 (3.13)	55.27 (29.40)
			Middle	57.06 (1.02)	42.87 (1.34)	98.1 (1.45)	74.27 (17.61)
			Lower/GEJ	55.19 (2.14)	43.66 (2.16)	96.73 (0.66)	50.86 (12.54)
		60 (Gy)	Cervical/Upper	63.57 (1.76)	49.58 (2.38)	98.07 (0.84)	77.19 (7.55)
			Middle	60.45	49.21	99.03	48.16

CG0011

DEEP INSPIRATION BREATH-HOLD RADIOTHERAPY VERSUS FREE-BREATHING INTENSITY MODULATED RADIOTHERAPY FOR LEFT-SIDED BREAST CANCER

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Aims: During radiotherapy (RT) of left-sided breast cancer, parts of the heart are irradiated, which may lead to late toxicity. We report on the experience of single institution with cardiac-sparing RT using deep inspiration breath hold (DIBH-RT) and compare with free breathing intensity modulated RT (FB-IMRT) technique.

Methods: Left-sided breast cancer patients, treated at our department with postoperative whole breast DIBH –RT, were considered for inclusion. All patients were immobilized in a supine position (Posiboard frame, Civco Inc.®, Orange City, IA, USA) and underwent to a FB and DIBH planning computed tomography (3 mm slide thickness) without intravenous contrast media. A clinical target volume (CTVbreast) was obtained encompassing breast glandular, while the whole breast planning target volume (PTVbreast) was defined adding a 5 mm expansion in the transverse plane and 8 mm in cranial–caudal direction to the CTVbreast. PTVboost was generated using a 5 mm isotropic expansion on CTVboost (tumor bed). A total dose of 50 Gy and 60Gy (25 fractions) were prescribed to PTVbreast and PTVboost. FB and DIBH treatment plans were obtained with 2-4 tangential fields, with IMRT. Dose volume histogram parameters for heart was compared between FB and BH.

Results: Between March 2017 and March 2018, 38 patients were analyzed. Compliance to treatment was 100%, all patients completed the planned RT without interruption. All patients suffered from early breast cancer (T1-2 N0 M0) and have a median age of 49 years (range 39-58). The average of PTV breast was 550 cc (range 200-1240). When compared with FB, DIBH resulted in a significant reduction of average median cardiac dose from 1.1 +/- 0.5 to 0.8 +/- 0.2 Gy ($p<0.0001$), the average of D2% cardiac dose from 5.3+/- 5.1 to 2.4 +/- 0.9 Gy ($p<0.0001$) and average cardiac V5Gy from 2.4 +/- 2.6 to 0.0 +/- 0.6% ($p<0.0001$). The session time was 7 min/fraction for DIBH and 4min/fraction for FB.

Conclusions: When compared with FB, DIBH-RT showed a significant reduction of cardiac doses without an excessive increasing of session time. The relative low dose of cardiac exposure due to FB or DIBH –RT should be investigated to evaluate the real clinical impact.

CG0012

LONG-TERM OUTCOME OF DUCTAL CARCINOMA IN SITU OF THE BREAST TREATED WITH INTRAOPERATIVE RADIOTHERAPY WITH ELECTRONS AS ADJUVANT RADIATION TREATMENT AFTER BREAST-CONSERVING SURGERY: THE EXPERIENCE OF THE EUROPEAN INSTITUTE OF ONCOLOGY

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Aims: According to American Society for Therapeutic Oncology and Radiology (ASTRO) guidelines on partial breast irradiation (PBI), based mainly on reports using MammoSite, ductal carcinoma in situ (DCIS) has recently been included in the suitable category. As of now, no data have been published regarding the use of intraoperative electrons (IOERT) in DCIS. This study aims at investigating the local control rate and disease-free survival in patients (pts) affected by DCIS and treated with breast conservative surgery (BCS) and PBI with IOERT.

Methods: From 1998 to 2010, more than 1450 pts with DCIS underwent BCS at the European Institute of Oncology in Milan. Out of them, 216 (15%) were treated with IOERT as the sole adjuvant radiotherapy. Intermediate/high-grade tumors based on vacuum-assisted core biopsy and/or radiological extent of microcalcifications ≤2 cm represented the main eligibility criteria for IOERT. Immediately after removing the lesion with BCS, pts received 21 Gy at 100% isodose of prescription. Adjuvant hormonal therapy (HT) was offered at clinicians' discretion, according to pts' preference.

Results: Clinical and pathological data were collected for 180 (83%) pts, with a median age of 57 (range 29-75) years. DCIS median pathological size was 1.3 (range 0.2-5.0) cm. Necrosis was present in 62.2% of the cases, microcalcifications were found in 75.6% of pts and multifocality was detected in 16.7% of specimens. Among them, 31.7% of DCIS were grade 3. Adjuvant HT has been administered to 43.3% of pts. Over 10-year follow-up, 60 oncologic events were recorded: 52 occurred within the IOERT-treated breast,

leading to a cumulative incidence of in-breast tumor reappearance (IBR) of 28.9%. In details, 53.8% were invasive recurrences and 42.3% were in situ. Second IBRs occurred in 5 pts after salvage therapy (surgery, radiotherapy, HT, chemotherapy). Ten-year overall survival rate was 95.9%. Analyses of clinical, pathologic, and treatment-related variables (such as tumor grade, necrosis, receptor status, KI-67, cerbB2 status, margins of excision and the use of adjuvant hormonal therapy, size of IOERT collimator, histological subtypes) related with the development of local recurrences are currently being performed.

Conclusions: IOERT-based PBI should be evaluated with caution in DCIS. Ongoing subset analyses will help selecting pts for whom IOERT may confer an acceptable risk of IBR and represent a valid alternative to whole breast irradiation.

CG0013

PARTIAL BREAST RE-IRRADIATION USING EXTERNAL BEAM RADIOTHERAPY FOR LOCAL RECURRENCE AFTER PREVIOUS WHOLE BREAST RADIOTHERAPY: EXPERIENCE OF EUROPEAN INSTITUTE OF ONCOLOGY

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Aims: Although the standard treatment of in-breast recurrence (IBR) after breast conservative surgery (BCS) and whole breast radiotherapy (WBRT) is still represented by mastectomy, over the last decade there has been an increasing attitude towards performing a second BCS followed by further radiotherapy (RT) with different techniques (intraoperative RT, brachytherapy, external beam RT). The aim of the study is to evaluate acute toxicity and local control of partial breast re-irradiation (re-PBI) with intensity modulated RT (IMRT), using a hypofractionated scheme.

Methods: Eligibility criteria included patients previously treated with WBRT who experienced IBR and were operated on with second BCS. Re-irradiation was limited to the tumor bed and was performed using either TomoTherapy® IMRT with helical modality or BrainLab-VERO® IMRT step-and-shoot. Planning target volume (PTV) was generated by clinical target volume (CTV) with a margin of 5 mm. Daily image-guided RT was applied by megavoltage fan beam computerized tomography (CT) for TomoTherapy® and kilovoltage cone beam CT for VERO®. For target volume, the PTV planning objectives were V100%≥95%, V95%≥98%, V90%≥100%, Dmax≤110%. Toxicity was evaluated using RTOG/EORTC criteria.

Results: Between 6/2012 and 3/2016, 61 patients were treated with re-PBI (Table 1). Prescription dose was 37.05 Gy in 13 fractions. Fifteen (25%) patients were treated with TomoTherapy® and 46 (75%) with VERO®. Overall, median follow-up was 21 (7-41) months. Data of acute toxicity within 6 months are available for 31 (51%) patients: no acute toxicity >G2 has been observed, while 5%, 8% and 5% of patients report desquamation G1, erythema G1 and edema G2, respectively. Twelve (20%) patients showed a subsequent oncologic event 24±12 months after the retreatment: 1 patient had a second IBR distant from the re-PBI field (1.6% cumulative incidence of IBR), 7 patients developed distant metastasis (lymph nodes, lung, bones and brain) and 4 had other primitive tumors (including 1 contralateral breast).

Conclusions: Re-PBI after second BCS represents a feasible alternative to mastectomy with regard to local control, showing good toxicity profile. Longer follow-up is needed to evaluate late toxicity and to establish the role of this treatment modality in local control. This abstract is the basis for a future article.

Table 1. Patients' characteristics.

Characteristics	Tot = 61
Mean age ± standard deviation (years)	61 ± 11
Tumour side	
Right, n (%)	29 (47.5)
Left, n (%)	32 (52.5)
CTV, median (range) [cm^3]	39.8 (31.6-73.6)
Adjuvant therapy	
Chemotherapy (alone or with hormonotherapy), n (%)	20 (32.8)
Hormonotherapy alone, n (%)	36 (59.0)

CG0014

PRELIMINARY RESULTS OF ACUTE TOXICITY IN PATIENTS UNDERGOING VMAT PARTIAL BREAST IRRADIATION: A PHASE II PROSPECTIVE STUDY

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Aims: To report preliminary results of partial breast

irradiation (PBI) using Volumetric Arc therapy (VMAT) in patients (pts) with early stage breast cancer.

Methods: A prospective phase II study started at National Cancer Institute in June 2015. Pts with early stage breast cancer (Stage I), who underwent breast conservative surgery (BCS), were recruited. Pts received a PBI with a hypofractionated schedule of 30 Gy in 5 fractions delivered on consecutive days. The radiotherapy treatment (RT) was delivered using Volumetric Arc Therapy (VMAT) with a TrueBeam® (Varian Medical Systems, Inc.,CA). Toxicity was assessed according to RTOG/EORTC criteria.

Results: At the time of this analysis, 66 pts were enrolled in this study. Thirty-six women had right and 30 had left-side breast cancer. Median age was 70 (range 46-92). Pathological stage was IA, IB and IC in 14, 29 and 23 pts, respectively. Fifty-seven women had Luminal A and 9 had Luminal B breast cancer. Pts were treated from March 2014 to November 2017. Acute toxicity, assessed at the end of RT, consisted of G1 erythema in 14/66 (21.2%) pts. No > G1 skin toxicities occurred. Fibrosis G1 was reported in 6/66 (9%) pts and G2 in only one patient (1,5%). No episodes of pneumonitis or pericarditis were registered at the RT end or later. Edema G1 occurred in 4/66 (6%) pts and asthenia G1 in only one (1,5%). With a median clinical follow-up of 11 months (range 6-35), no Grade 2 or more of any toxicity was reported.

Conclusions: Our preliminary data about early toxicity of PBI with hypofractionated schedule of 30 Gy in 5 fractions delivered on consecutive days are promising. PBI with VMAT is feasible and is a valid alternative treatment option after BCS in selected early breast cancer pts according to ASTRO guidelines. A longer follow-up is needed to assess late toxicity.

CG0015

DOSE INTENSIFICATION IN LOCALLY ADVANCED RECTAL CANCER PATIENTS, USING RECTAL MRI FOR BOOST VOLUME DELINEATION: MONO-INSTITUTIONAL EXPERIENCE

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Aims: Thanks to the dose-response in rectal cancer patients, a boost intensification to the tumor could represent a potential strategy to improve oncological outcomes. T2 weighted Magnetic Resonance Imaging (MRI) is considered the gold standard for local staging of rectal tumor. It represents a valid tool for target volume delineation in order to perform a dose intensification. The aim of our retrospective analyses is to evaluate the impact of GTV delineated with MRI regards to treatment tolerability and toxicities, and treatment response and outcomes, in patients treated with neoadjuvant chemoradiotherapy (CRT).

Methods: Between 2012 and 2018, 81 (M:58;W:23) locally advanced rectal cancer patients were treated in our Radiotherapy Department. A diagnostic rectal MRI was performed and co-registrated with CT scan simulation. Boost volume was defined as GTV plus correspondent mesorectum, plus 1 cm in cranio-caudal direction. RT was performed by 3D RT, with a total dose of 4500 cGy, 180 cGy/die, on the pelvic nodes, with a concomitant boost of 1000 cGy (100 cGy/die, 2 times/week; total dose 5500 cGy), or with SIB/IMRT technique with a total dose of 5500 cGy (220 cGy/die). All patients received concurrent capecitabine. The pathologic response was evaluated according to Mandard tumor regression grade (TRG) score. The Memorial Sloan–Kettering Cancer Center score was used for the evaluation of anal sphincter function.

Results: Median follow-up was 29 months (range: 1-71 months). The median age was 68 (range: 39-87) years. A pathological complete response (pCR) was obtained in 23 (28.4%) patients (TRG 1). Nine (11.3%) patients showed local recurrence. The 5-year disease-free-survival (DFS) and overall survival (OS) rates were 42.3%±14.4% and 77.8%±9.4%, respectively. Acute toxicities were reported in Table 1. One patient presented late skin toxicity ≥G3, one late GI and one late GU toxicity ≥G3. Overall sphincter function resulted excellent in 22 (27.2%) patients, good in 8 (9.9%), fair in 6 (7.4%) and poor (incontinence) in 11 (13.6%) patients. Twenty-two patients presented stoma.

Conclusions: MRI resulted as a good tool for boost volume delineation. Our results showed a benefit of dose intensification in terms of pCR (28.4%), with acceptable acute and late toxicities, and good results in terms of clinical outcomes. These results need to be confirmed in a larger population study.

Table 1. Acute Toxicities using the Radiation Therapy Oncology Group (RTOG) scale

Acute Toxicities	G0	G1	G2	G3
Skin Toxicity	54 (66.7%)	18 (22.2%)	8 (9.9%)	1 (1.2%)
GI Toxicity	26 (32.1%)	39 (48.2%)	15 (18.5%)	1 (1.2%)
GU Toxicity	58 (71.6%)	21 (26.0%)	2 (2.4%)	0 (0%)
Hematologic Toxicity	67 (82.7%)	8 (9.9%)	6 (7.4%)	0 (0%)

CG0016

NEOADJUVANT RADIO-CHEMOTHERAPY IN RECTAL CANCER: NEW STRATEGY USING SIB TECNIQUE FOR INCREASING RADIATION DOSE AND IMPROVING LOCAL CONTROL

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Purpose/Objective(s): Our goal was to evaluate the efficacy and tolerance increasing the single fraction (fr) and total dose of radiotherapy with SIB tecnique given

concurrently with chemotherapy in locally advanced rectal tumors as neoadjuvant treatment.

Materials/Methods: 43 patients (pts),median age 64 (33-80), mean P.S. 1(0-2), with stage II 25%, III 72%, IV 3%, 51% located inferiorly (26% middle and 23% superiorly) were treated with capecitabine (750 mg/m^2, twice daily for 5 days/week) and concomitant RT. After PET/CT simulation 3 volume were identified: BTV was treated by 55 Gy (2.2 gy/fr) while CTV1 and CTV2 received 50 Gy (2.0 Gy/fr.) and 45 Gy (1.8 Gy/fr.) by VIMAT tecnique, in 5 weeks. After 8-12 weeks pts were restaged and went to surgery.

Results: 44% of TRG4/3, 46% of TRG2 and 12% of TRG 1 were obtained. 77% of pts avoided abdomino-perineal resection. Local control was 98% (mean 22 months of follow-up). G.I. acute grade 3 toxicity was 3%, anastomotic leakage was 2.5% and overall survival at 4 years was 96%.

Conclusions: Preoperative chemotherapy concurrently with intensified radiotherapy appears efficacy with 44% of clinical complete remissions. The low acute and late toxicity allows to apply this schedule safetly and offers the possibility to investigate new dose regimens with selected volumes.

CG0017

MRI FOR GROSS TUMOR VOLUME DELINEATION IN PANCREATIC CANCER: A MULTI-INSTITUTIONAL CONTOURING STUDY BY THE AIRO STUDY GROUP FOR GASTROINTESTINAL CANCERS

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Aims: Currently, Computed Tomography (CT) is the standard imaging modality for pancreatic tumor delineation in radiation treatment planning. Due to the high soft tissue resolution, Magnetic Resonance Imaging (MRI) could improve the accuracy of tumor delineation compared to CT scan. A multi-institutional contouring dummy-run study was proposed to evaluate the impact of Magnetic Resonance Imaging on inter-observer agreement in Gross Tumor Volume (GTV) and duodenum delineation in radiation therapy planning for pancreatic cancer compared with CT.

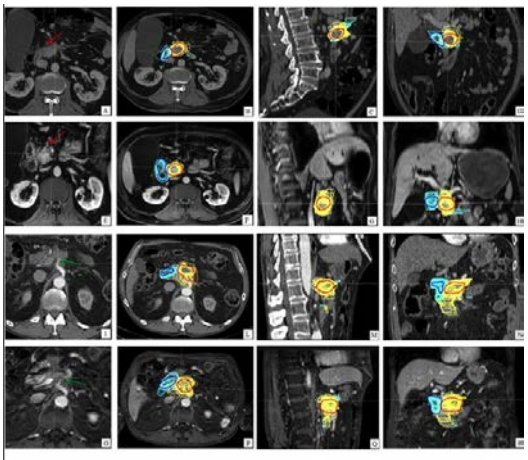

Figure 1. Graphic representation on axial (Panels A, B, E, F, I, L, O and P), sagittal (Panels C, G, M and Q) and coronal (Panels D, H, N and R) planes of inter-observer variation between 31 Centers for CT (Panels A, B, C and D) and MRI (Panels E, F, G and H) GTV and duodenum of Case 1 (borderline resectable) and for CT (Panels I, L, M and N) and MRI (Panels O, P, Q and R) GTV and duodenum of Case 2 (unresectable). GTV and duodenum benchmark delineations are represented in red and blue solid outline, respectively. Yellow and light blue solid outlines represent GTVs and duodenum contours of the remaining 30 participating Centers. Panels A, E, I and O represent axial CR and MRI images of Case 1 (borderline resectable) and Case 2 (unresectable) without contours. Panels A and E: borderline resectable case for the encasement of the superior mesenteric vein (red arrow); Panels I and O: unresectable case for the tumor infiltration of the celiac trunk (green arrow).

Methods: Two clinical cases of borderline resectable (Case1) and locally advanced unresectable (Case 2) pancreatic cancer were selected by two radiologists and two radiation oncologists expert in pancreatic cancer. In two sequential steps, diagnostic contrast-enhanced CT scan and MRI sequences were sent to the participating centers. CT-GTVs were contoured while blinded to MRI data sets. Dice Similarity Index was used to evaluate the spatial overlap accuracy of both GTV and duodenum of all centers with respect to the benchmark.

Results: Thirty-one radiation oncologists from different Institutes joined the study and submitted the delineated volumes for both cases on CT scans and MRI images, respectively (Figure 1). CT- and MRI-GTV volumes were 21.6±9.0 cm^3 and 17.2±6.0 cm^3, respec-

tively for Case1, and 31.3±15.6 cm^3 and 33.2±20.2 cm^3, respectively for Case 2. MRI-GTV mean volume resulted significantly smaller than CT-GTV in the borderline resectable case ($p<0.05$), whereas no significant GTV differences between the two different imaging modalities were reported in Case 2. A substantial agreement was shown by the median DICE index for CT- and MRI-GTV resulting as 0.74 (IQR: 0.67-0.75) and 0.61 (IQR: 0.57-0.67) for Case1; a moderate agreement was instead reported for Case 2: 0.59 (IQR:0.52-0.66) and 0.53 (IQR:0.42-0.62) for CT- and MRI-GTV, respectively.

Conclusions: An acceptable agreement for GTV delineation was reported in the borderline resectable case. Intravenous contrast-enhanced diagnostic CT scan resulted comparable to MRI in inter-observer variability of GTV and duodenum delineation. Based on these results, CT scan can still be considered as the gold standard for volume delineation in pancreatic cancer, even when more conformed techniques such as IMRT, VMAT and/or SBRT, are used.

CG0018

SPATIAL PATTERN OF RECURRENCE AS A BASIS FOR TARGET VOLUME DEFINITION IN PRIMARY AND RECURRENT GLIOBLASTOMA

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Aims: To compare the patterns of recurrence in patients with irradiated and re-irradiated Glioblastoma (GBL) in order to evaluate re-irradiation volumes and confirm our target volume definition protocols.

Methods: Imaging and clinical data from 28 consecutive patients with recurrent GBL were analyzed. The spatial pattern of recurrences, both after Stupp protocol and re-irradiation, was analyzed according to the RANO-HGG criteria. In re-irradiation protocols we proposed a target volume containing the T1 weighted contrast enhancing lesion as the gross tumor volume (GTV) and a margin of 3 mm to generate the planning target volume (PTV), without clinical target volume (CTV). For analysis, all pre- and post- radiation as well as all follow- up images were analyzed and then we defined three categories of recurrent tumors: in field, marginal and distant recurrence. In field recurrence was defined if > 80% of the tumor recurrence resided within the prescription 95% isodose surface; marginal if 20% to 80% of the lesion was inside the 95% isodose surface. Distant recurrence was defined if the occurrence of contrast-enhancing lesions not received radiation dose. Furthermore, progression-free (PFS) and overall survival (OS) from primary diagnosis and from recurrence were analyzed by the Kaplan–Meier method.

Results: Median age of analyzed patients was 49 years and mean Karnofsky Performance Status was ≥ 80. More patients had undergone surgical resection followed by Stupp protocol at primary diagnosis of GBL. All of these patients, at recurrent disease, were treated with hypofractionated stereotactic radiotherapy. Fourteen patients received 30 Gy in 5 fractions, 11 received 25 Gy in 5 fractions, 2 received 20 Gy in 4 fractions while only one 48 Gy in 6 fractions. Most of patients (81%) showed in field relapses, both after Stupp and after re-irradiation; only few patients in both groups had a marginal relapsed (19%). No statistical significant difference in terms of pattern of recurrence was showed between primary and salvage radiotherapy. Median OS from primary diagnosis was 713 days and median OS from re-irradiation was 244 days. PFS from primary diagnosis to re-irradiation was 582 days.

Conclusions: Our data demonstrated that the target volume definition based on T1 contrast-enhancement of recurrent GBL without further margins is safe and adequate to avoid marginal relapse.

CG0019

PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: WHOLE BRAIN OR WHOLE BRAIN WITH HIPPOCAMPAL SPARING?

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Aims: One of the main limiting factor of a whole brain radiation therapy (WBRT) is the neurocognitive functions (NCFs) decline. Significant preclinical and clinical evidence shows that it is mainly caused by the radiation-induced injury to the hippocampus. It is hypothesized that conformal hippocampal avoidance during the course of WBRT might provide meaningful NCFs preservation. This study evaluates the correlation between the site of (Primary Central Nervous System Lymphoma) PCNSL lesions and the hippocampal region in order to explore the feasibility of routinely sparing of the hippocampus during a WBRT to prevent neurocognitive decline.

Methods: Patients (>18 years, ECOG <4) with pathologically proven PCNSL and MRI image pre-

treatment were retrospectively reviewed. All patients had received high-dose of methotrexate (HD-MTX) before WBRT. T1-weighted, post-contrast axial MR image sets obtained prior to cranial irradiation were imported on Varian Eclipse treatment planning system, version 11 (Varian Medical Systems) and registered with the simulation CT. The hippocampus as well as each PCNSL lesions were contoured. Three dimensional envelopes surrounding the hippocampus were generated adding 5, 10, and 15 mm and the distance of brain lesions were recorded as <5 mm, 5 to <10 mm, 10 to <15 mm, and >15 mm from the hippocampus. The minimum margin of 5 mm was taken into account for systematic setup error and dose fall-off between whole brain clinical target volume and the hippocampus.

Results: Between 2005 and 2018, 38 patients were treated and 36 pts with 57 lesions were eligible for this study. PCNSL lesions' locations were: deep brain structures (26%), parietal lobe (23%), frontal lobe (19%), temporal lobe (14%), occipital lobe (7%), brainstem (5%), other sites (6%). Nine patients were affected by multiple lesions. In 18/57 lesions (31.6%) the distance from the hippocampus region was less than 5 mm and seven of them (12.3%) involved the hippocampus. Lesions over 15 mm from the hippocampus were observed in 30 cases (52.6%), while only the 15,8% was between 5 and 15 mm.

Conclusions: These data show that routinely sparing of the hippocampus region is not recommended. Anyway, it should be considered in selected patients, when the spatial distribution of PCNSL is far more than 5 mm from the lesion.

CG0020

"RESIDUAL SITE" RADIOTHERAPY (RSRT) AND IMMUNOCHEMOTHERAPY IN PRIMARY MEDIASTINAL B CELL LYMPHOMA: PRELIMINARY RESULTS

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Aims: To evaluate, in patients with primary mediastinal lymphoma (PMBCL), the efficacy of RSRT after immunochemotherapy (ICHT) on local control, PFS (progression free survival) and OS (overall survival).

Methods: This study includes 34 patients (range 19-67 years at diagnosis), with PMBCL, treated between 2006 and 2014 with immunochemotherapy and radiotherapy. STAGE: 8/34 was I, 12/34 was II, 4/34 was III, 10/34 was IV. All patients were treated with ICHT (R-MACOP-B: 23 patients; R-CHOP: 11 patients). Nine patients performed early intensification with high-dose chemotherapy and stem cell transplantation. The gross tumor volume (GTV) included the morphological mediastinal residual disease after ICHT and the PTV was defined by expanding the corresponding GTV of a 5-mm margin, in the three dimensions, according to the surrounding healthy structures. The percentage of local control, the PFS and OS were assessed.

Results: At the end of immunochemotherapy and before radiotherapy all patients were evaluated with CT with mdc and CT PET. According to the PET, we recorded 16/34 Complete metabolic response and 18/34 partial metabolic response. All patients received consolidation radiotherapy with dose of 30-40 Gy. The median follow-up was 72 months (range 43-145 months). Only one recurrence was observed (1/34; 3 %) after a median follow-up of 9 months. The 5-yrs PFS and 5-yrs OS were 97.1% and 97% months (range 37-136 months).

Conclusions: Although preliminary, our experience showed that the "Residual Site" volume of radiotherapy treatment does not seem to result in a decrease in local control and survival in PMBCL patients treated with immunochemotherapy protocols.

CG0021

DIFFERENCES IN INTERNAL MOVEMENT EVALUATION OF GROSS TUMOR VOLUME (GTV) AND MESORECTUM IN PATIENTS IN PRONE AND SUPINE POSITION, BASED ON CONE BEAM COMPUTED TOMOGRAPHY FOR RECTAL CANCER TREATMENT

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Aims: Due to a reported dose-response relationship in rectal cancer radiotherapy, a greater interest in dose intensification on small boost volume arises. In this scenario, organ motion evaluation could be mandatory. This study aimed to use CBCT for the evaluation of internal movement (IM) of GTV and mesorectum, in rectal cancer patient treated with neoadjuvant radiochemotherapy, underlying the differences in prone and supine position.

Methods: Twenty-four patients, (M:16, W:8), with II-III stage rectal cancer, underwent CT scan simulation, 12 in prone and 12 in supine position, with controlled bladder filling. GTV (tumor site and corresponded rectum) and mesorectum (from the sacral promontory to the level where the levator ani muscle inserts into the rectal wall) were delineated on MRI imaging co-registrated with CT scan simulation. CBCTs were performed once a day during the first 5 fractions, then once or twice a week during all treatment, by Elekta X-Ray volume imaging system (XVI). The IM was estimated for GTV on all CBCTs co-registrated with CT scan simulation. Bladder was also delineated. Co-registrations were performed on RayStation platform

(RaySearch Laboratories, Stockolm, Sweden) by bone landmarks and corrected for set-up errors. IM evaluation was obtained for both prone and supine position, as mean shift in left and right (L-R), postero-anterior (P-A) and cranio-caudal (C-C) directions and volumes variability were calculated by DICE index, as well as precision, sensitivity and specificity.

Results: A total of 222 CBCTs were performed and retrospectively analysed: 110 in prone and 112 in supine position. Detailed values are reported in Table 1. Mean DICE index for GTV, mesorectum and bladder was 0.74, 0.86, 0.68, respectively in prone position, and 0.77, 0.89, 0.71 respectively in supine position.

Conclusions: In our study, GTV and mesorectum IM, evaluated in patients in prone and in supine position, were less than 4mm in all directions. Despite the small number of patients evaluated, supine position resulted in 1 mm less deviation compared to prone position. Anyway, in both set-up, CBCT resulted effective for IM assessment and could represent a valid method for appropriate treatment intensification.

Table 1. Mean shift in left-right (L-R), postero-anterior (P-A) and cranio-caudal (C-C) directions, mean volumes and DICE index, precision, sensitivity and specificity for GTV, mesorectum and bladder in prone and supine position.

110 CBCT (prone pts)	L-R (cm)		P-A (cm)		C-C (cm)		Volume (cm^3)	DICE index	Precision	Sensitivity	Specificity
GTV	-0.16	0.15	0.29	-0.38	0.14	-0.22	55.00	0.74	0.59	0.72	0.79
Mesorectum	-0.13	0.13	0.21	-0.25	0.15	-0.23	337.11	0.86	0.76	0.86	0.87
Bladder	-0.29	0.24	0.37	-0.40	0.52	-0.82	206.79	0.68	0.53	0.63	0.81
112 CBCT (supine pts)	**R-L (cm)**		**A-P (cm)**		**C-C (cm)**		**Volume (cm^3)**	**DICE index**	**Precision**	**Sensitivity**	**Specificity**
GTV	-0.09	0.18	0.25	-0.25	0.10	-0.11	44	0.77	0.64	0.75	0.80
Mesorectum	-0.10	0.09	0.16	-0.13	0.12	-0.15	279	0.89	0.80	0.87	0.91
Bladder	-0.19	0.19	0.49	-0.39	0.72	-0.38	259.95	0.71	0.56	0.82	0.48

CG0022

OPTIMIZATION IN ADJUVANT RADIOTHERAPY FOR BREAST CANCER: EARLY TOXICITY RESULTS OF A CONCOMITANT PHOTON BOOST DELIVERY (CO.M.BO STUDY)

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Purpose: Adjuvant radiotherapy (RT) for breast cancer (BC) is mandatory after conserving surgery. A sequential boost to tumour bed is often recommended to reduce local relapse rate. The possibility of reducing treatment time can be useful in terms of cost/effectiveness and quality of life of the patient. This study investigates the preliminary results in terms of efficacy and local recurrence of a concomitant boost in photons regimen.

Material and Methods: From January 2017 all the patients (pts) who underwent lumpectomy for BC and adjuvant RT with boost were enrolled. We excluded pts with less than 12 months of follow up. Tumor bed (CTV1) was contoured using pre-operative exams, surgery description and when possible also clips in site. A margin of 0.8 mm was given in all directions for PTV1, not exceeding breast (PTV2). In this way, a daily boost dose to tumour bed was given using two isocentric tangential treatment plans with 3D-conformal RT technique. According to risk class, patient received an EQD2tumor (α/β 4) between 60.4 and 67.7 Gy on tumor bed, an EQD2acute_effects (α/β 10) between 58.9 and 65.1 Gy and an EQD2late_effects (α/β 3) between 61 and 68.8 Gy. Acute and late toxicity were reported according to CTCAEv4.03.

Results: 49 pts were prospectively monitored during RT and follow up. Mean age was 54 years (36-76). Thirty pts (61%) with negative margins, 14 pts (28.5%) with close margins and 5 pts (10.5%) with focal invasive positive margin underwent respectively a daily dose to tumor bed of 2.3, 2.4 and 2.5 Gy in 25 fr, concomitant to whole breast irradiation +/- nodal irradiation 50/2 Gy. Acute toxicities were: 14 pts (28.5%) G1 skin, 10 pts with G2 skin (10.4%), 1 pt (2%) with G3 skin and 2 pts (4%) with chest pain G2. Late toxicities recorded during follow up were: 20 pts (40%) with subcutaneous G1 and 7 pts (14.2%) with subcutaneous G2. At 12 months of follow up no pts presented local relapse, only 2 pts had distant metastases.

Conclusion: A concomitant photon boost added to adjuvant RT for BC seems to be a feasible and safe option to reduce overall treatment time with good local control. Further studies and larger series are needed for results confirmation.

Oral Communications

CO001

PREDICTIVE FACTORS FOR SURVIVAL IN OLIGOMETASTATIC PATIENTS FROM COLORECTAL CANCER TREATED WITH STEREOTACTIC BODY RADIATION THERAPY

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Aims: Colorectal cancer (CRC) represents one of the major leading causes of death from cancer worldwide. The prolongation of survival of metastatic CRC patients with the introduction of new systemic treatments increased the relevance of local approaches in the oligometastatic setting. Aim of the present study was to analyze pattern of care and recurrence of oligometastatic CRC patients, and to evaluate predictive factors of survival.

Methods: We included patients with histologically confirmed colorectal adenocarcinoma and maximum of 5 metastases. Previous or concomitant systemic treatments were allowed. Tumour response was classified according to EORTC-RECIST criteria version 1.16. End points of the present study were the outcome in terms of Local control of treated metastases (LC), progression free survival (PFS), and overall survival (OS). Univariate analysis was performed with the log-rank test, and Cox proportional hazards regression was used to estimate hazard ratios (HR). Stepwise Cox regression was performed for multivariable analysis to evaluate the association between predictive factors and survival.

Results: 270 patients were treated with SBRT on 437 metastases. Lung was site of metastases in 48.5% of cases, followed by liver (36.4%) and lymph nodes (12.4%). Systemic treatment was administered before SBRT in 199 patients (73.7%). Median follow-up time was 22.6 months (3- 98.7). Rates of LC at 1, 3 and 5 years were 95%, 73% and 73%, respectively. Time from diagnosis of metastases to SBRT was the only factor predictive of LC (HR 1.62, p=0.023). Median PFS was 8.6 months and both control of treated metastases (HR 1.86, p=0.000) and single line of systemic treatment before SBRT (HR 1.86, p=0.000) were positively correlated to PFS. Rates of OS at 1, 3 and 5 years were 88.5%, 56.6%, and 37.2%, respectively. Lesion greater than 30 mm (HR 1.82, p=0.030), presence of metastases in organ different from lung ((HR 1.67, p=0.020), the use of systemic treatment before SBRT (HR 1.82, p=0.023), and progression of treated metastases (HR 1.80, p=0.007), were all predictive of worse OS (Figure 1).

Conclusions: Stereotactic body radiation therapy represents an effective approach in the management of oligometastatic CRC. Control of treated metastases was a strong positive predictive factor for both PFS and OS.

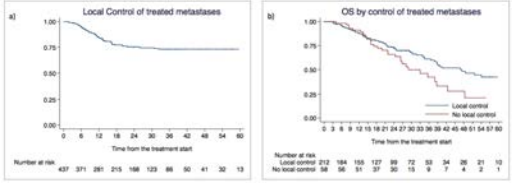

Figure 1. Kaplan-Meier curves of local control for treated metastases (a) and overall survival according to local control of treated metastases (b).

CO002

PREDICTIVE FACTORS FOR RESPONSE AND SURVIVAL IN OLIGOMETASTATIC PATIENTS TREATED WITH STEREOTACTIC BODY RADIATION THERAPY

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Aims: To evaluate patients, treatment or disease characteristics that could predict response to SBRT and survival in a database of oligometastatic patients from different solid tumors.

Methods: Patients treated with SBRT for oligometastatic disease between January 2014 and December 2015 were included in this analysis. Patients were defined as oligometastatic if they were affected by maximum 5 active lesions in 3 different sites. They had to be treated with SBRT with radical intent. Primary endpoint of the study was overall survival; secondary end points were local control, disease free survival and progression free survival. Local control and survival times were calculated from the day of SBRT.

Results: 358 patients were included in the study. Main patients and treatment characteristics are listed in Table 1. Patients received different RT schedules according to number, site and size of the metastases. Treatment was generally well tolerated, no acute or late G3-4 toxicity was recorded. Complete response, partial response or stable disease were recorded in 152 (42.5%),160 (44.7%) and 40 (11.1%) patients respectively. Six patients (1.7%) experienced local progression at first evaluation, while other 69 (19.6%) patients experienced local relapse during follow up. With a median follow up time of 22.2 months (range 2-49.9 months) actuarial local control time at 6, 12 and 24 months was 94.6%, 84.3% and 78.9% respectively. Distant progression was recorded in 279 patients (77.9%). Actuarial DMFS at 6, 12 and 24 months was 67.1%, 38.3% and 20.9% respectively. Actuarial PFS at 6, 12 and 24 months was 66.1%, 36.3% and 18.4% respectively. At last follow up, 195 patients (54.5%) were still alive, in 59 cases with no evidence of disease. Actuarial median overall survival (OS) was 26.4 months, OS at 6, 12 and 24 months was 96%, 85.2% and 63.6%. At univariable analysis sex and number of treated lesions were found to be correlated with LC. Previous medical therapies, number of treated lesions, number of involved organs ,presence of inactive extra-target disease, "adjuvant" medical therapies and local response correlated with DMFS and PFS. Age at stage IV diagnosis, presence of inactive extratarget disease and local response were statistically correlated with OS.

Conclusions: SBRT for oligometastatic patients is safe and effective. Local response is strongly correlated with patients' prognosis, underlying the relevance of local control also in a metastatic setting.

Table 1.

Variable	Median (Interquartile range)/Patients (%)
Age at diagnosis of primary tumour	63.60 (55.5 – 72.7)
Sex	
Male	207 (57.82%)
Female	151 (42.18%)
Primary tumour site	
Colon-Rectum	108 (31.17%)
Lung	85 (23.74%)
Upper GI	47 (13.13%)
Breast	26 (7.26%)
Gynaecological	22 (6.15%)
Prostate	12 (3.35%)
Kidney	11 (3.07%)
Other*	47 (13.13%)
Histology of the primary tumour	
Adenocarcinoma	224 (65.57%)
Other**	134 (37.43%)
Treatment of the primary tumour	
Exclusive surgery	119 (33.24%)
Exclusive medical therapy	16 (4.47%)
Exclusive radiotherapy	8 (2.23%)
Surgery + Medical therapy	128 (35.75%)
Surgery + Radiotherapy	15 (4.19%)
Radiotherapy + Medical therapy	15 (4.19%)
Surgery + Radiotehrapy + Medical therapy	57 (15.92%)
Age at diagnosis of Stage IV disease	65.7 (57.6 – 73.9)
Disease free interval	13.6 (4.5 – 30.7)
Comorbidities	
Absent	85 (23.74%)
Present	273 (76.26%)
ECOG Performance status	
0	185 (51.68%)
1	134 (37.43%)
2	37 (10.34%)
3	2 (0.56%)
Type of metastases	
Synchronous	76 (21.23%)
Type of oligometastatic state	
De novo	142 (39.66%)
Induced	157 (43.85%)
Oligoprogression	59 (16.48%)
Previous local ablative therapies	
No	217 (60.61%)
Yes	141 (39.39%)
Previous medical therapies	
No	121 (33.80%)
1 line	133 (37.15%)
2 lines	64 (17.88%)
3 lines or more	40 (11.17%)
Number of treated metastases	
1	199 (55.59%)
2	94 (26.26%)
3	47 (13.13%)
4	15 (4.19%)
5	3 (0.84%)
Metastatic sites	
Lung	138
Brain	61
Liver	95
Adrenal gland	19
Lymph nodes	91
Number of treated organs	
1	314 (87.71%)
2 or more	44 (12.29%)
Presence of extra-target disease	
No	316 (88.27%)
Yes	42 (11.73%)
BED	105 Gy (78.7-105.6)
Concomitant medical therapies	
No	345 (96.37%)
Yes	13 (3.63%)

*Other primary tumour sites: soft tissues, thymus and pleura, urinary bladder; **Other primary tumour histologies: squamous cell carcinoma, infiltrating ductal carcinoma, clear cell carcinoma, neuroendocrine tumour, sarcoma, papillary carcinoma, melanoma, cholangiocarcinoma, hepatocellular carcinoma, adenoid cystic carcinoma, urothelial carcinoma

CO003

REIRRADIATION OF BRAIN METASTASES (BM) WITH RADIOSURGERY (SRS): COMPARISON BETWEEN OUR PREVIOUS AND MORE RECENT RESULTS

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Aims: In our previous published trial on SRS of recurrent BM after whole brain radiotherapy (WBRT), Karnofsky performance status (KPS) and administered dose conditioned outcome and late toxicity. A suboptimal result of this trial was the appearance of brain radionecrosis in 6% of patients (pts) (Maranzano E et al. Reirradiation of brain metastases with radiosurgery. Radiother Oncol 2012; 102: 192-7). Starting from this experience, BM pts were recruited for reirradiation with SRS using a tighter selection with the aim to obtain similar satisfactory outcomes and limit radionecrosis.

Methods: Between November 2008 and December 2016, 60 patients recurring after WBRT were recruited for reirradiation with SRS. Only patients with good KPS (> 70), good neurologic functional score (NFS 0-1) and lesions with a diameter ≤ 20 mm were considered eligible for retreatment. Dose exceeding 20 Gy was never administered. A comparison between our previous and more recent results are reported.

Table 1. Comparison of patient outcome between previous trial and current trial.

Trials	N. of patients /lesions	Patients with KPS >70	Patients with controlled extracranial disease	Median interval between WBRT and SRS	Median lesion diameter (volume)	Median administered SRS dose (range)	Complete plus partial response	Duration of response at 1 and 2 years	N. of patients with brain radionecrosis
Previous	69/137	75%	72%	11 months	12 mm (1 cc)	20 Gy (12-25 Gy)	28%	74% and 69%	4 (6%)
Current	60/130	100%	77%	15 months	9 mm (0.5 cc)	18 Gy (14-20 Gy)	44%	85% and 83%	0

Legenda: KPS, Karnofsky performance status; WBRT, whole brain radiotherapy; SRS, stereotactic radiosurgery.

Results: The 60 patients reirradiated had 130 BM with a diameter range of 6-20 mm. At time of analysis, all but 3 patients had died. Median interval between prior WBRT and SRS was 15 months and median SRS administered dose was 18 Gy (range 14-20 Gy). Complete and partial response (CR, PR) was obtained in 44% of patients with 1 and 2 years of control rate of 85% and 83%, respectively. Median overall survival (OS) after reirradiation was 15 months. No radionecrosis was detected. Characteristics and outcomes of patients recruited in the current trial are summarized and compared with results of our previous trial in Table 1.

Conclusions: Analysis of our current data suggests that a tighter selection of pts (KPS > 70; NFS 0-1, BM with ≤ 20 mm of diameter and SRS dose ≤ 20 Gy) allows a high OS rate, a good percentage of CR and PR which last for > 2 years, and no brain radionecrosis. Considering that on this topic there are neither phase III randomized trials nor prospective ones, our current experience can be of interest in patient selection and dose prescription for the reirradiation of brain metastases with SRS after WBRT.

CO004

STEREOTACTIC RADIOTHERAPY IN OVARIAN CANCER: MULTICENTRIC RETROSPECTIVE POOLED ANALYSIS (MITO-RT PROJECT)

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Aims: Stereotactic body radiotherapy (SBRT) represents an interesting opportunity in the treatment of ovarian cancer (OC) isolated recurrences or residual lesions after systemic treatment, and a valid tool to lengthen the free time of re-challenge with platinum. Studies on this topic are sporadic and with few cases. Aim of this multicentric retrospective pooled analysis was to collect the largest unselected real-life dataset of OC patients treated with SBRT in the attempt to define the safety and efficacy. Secondary objectives were to identify the best dose/fractionation regimen in terms of local control as well as to describe acute and late toxicities.

Methods: Eight Italian cancer Centers were firstly started the project giving their adhesion to this retrospective pooled analysis. A specific data-set for standardized data collection for ovarian cancer SBRT treatment was developed. Participants were required to fill a data sets including: age, histotype, site of irradiation, previous treatments, best response, toxicity as well as technical/dosimetric data about SBRT treatment. Results: Data on 73 OC patients (median age: 63.5, range 40-83) carrying a total of 120 lesions were considered suitable for analysis. Between 2005 and 2018 all patients underwent SBRT in single or multiple fractions with a median biological equivalent dose (BEDα/β 10) of 76.8 Gy (range 7.5-262.5). Patient and treatment characteristics as well as acute toxicity are detailed in Table 1. Safety. 52 patients (71.3%) did not experience acute toxicity, the others 21 (28.7%) experienced low grade

acute toxicity with no patient showing > grade 2 toxicity. With a median follow-up of 18 months (range: 1 - 120), 68 patients (93.1%) did not experienced late toxicity, the others 5 (6.9%) experienced low grade late toxicity with no patient showing > grade 2 toxicity. Efficacy. On a per-lesion basis, the 12-and 24-months actuarial local control inside SBRT field were 88.3% and 86.2%, respectively. BED10 > 50Gy was correlated with a better 12-months local control (91.7% versus 72.9%, p=0.034).

Conclusions: Preliminary results on a population-level confirm that SBRT delivered in 1-10 consecutive fractions is safe and well tolerated notwithstanding several previous surgical and systemic treatments. Therefore, this treatment can be considered as a further resource in order to lengthen the free time of re-challenge with platinum.

Table 1. Patients' characteristics, treatment details and acute toxicity.

		No. patients (%)	No. lesions (%)
		73	120
Age, years, median (range)		63.5 (40-83)	
Histotype			
	Serous		85 (71.0)
	Endometrioid		21 (17.5)
	Clear cell		5 (4.1)
	Mixed epithelial		2 (1.7)
	Indifferentiated		5 (4.1)
	Mixed malignant Mullerian tumor		1 (0.8)
	Other		1 (0.8)
Type of lesion (%)			
	Lymph Node metastases		62 (51.7)
	Parenchymal lesions		56 (46.6)
	Bone metastases		2 (1.7)
Patients treated by previous chemotherapy cycles		68 (93)	
N° of chemotherapy schedules, median (range)			3 (1-7)
Patients treated by previous surgery		73 (100)	
Gross tumor volume (cc), median (range)			3.9 (0.04-88.4)
Planning target volume (cc), median (range)			16.16 (0.04-118)
Median SBRT dose (Gy), range			36 (5-75)
Median SBRT dose BED 10 (Gy), range			76.8 (7.5-262.5)
Median SBRT dose per fraction (Gy), range			7.5 (5-30)
SBRT N° fractions			1-10
Reference dose			
	ICRU 62/Isocenter		54 (45.0%)
	Target mean		51 (42.5%)
	Specific isodose		15 (12.5%)
Acute toxicity			
	Grade 0	52 (71.3)	
	Grade 1: Gastrointestinal (11), pain (2), other (2)	15 (20.5)	
	Grade 2: Gastrointestinal (2), pain (2), other (2)	6 (8.2)	

CO005

30 GY SINGLE DOSE STEREOTACTIC BODY RADIATION THERAPY (SBRT): REPORT ON OUTCOME IN A LARGE SERIES OF PATIENTS WITH LUNG OLIGOMETASTATIC DISEASE

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Aims: to evaluate local control (LC), long term adverse effects and survival in a series of patients with oligometastatic to the lung disease who received 30Gy in single dose with stereotactic technique.

Methods: Between December 2008 and April 2016, a total of 160 lung metastases in 123 patients affected by oligometastatic disease were treated, at our Institution, with stereotactic body radiotherapy (SBRT) delivered in a single dose of 30 Gy. The primary tumors in most cases were non small-cell lung cancer and colon-rectum cancer (46.3% and 29.2%, respectively). Prognostic factors were also assessed.

Results: The median follow-up was 38 months. Twenthy-three (14.3%) lesions in 20 patients progressed locally. Intra-thoracic progression (new lung lesions or thoracic lymph node metastases) occurred in 58 (47.1%) patients. Distant progression occurred in 43 (34.9%) patients after a median time of 14 months. The 3- and 5-year local relapse-free survival (LPFS) were 80.3% and 79.5% (median not reached), respectively. Late toxicity was evaluated in 148 patients (follow-up >6 months): 50 (33.7%) had grade ≤2 fibrosis, 10 (6.7%) experienced grade 3 fibrosis. Two (1.3%) cases of rib fracture occurred. One case of toxic death (grade 5) has been reported. Median OS was 39 months. Prognostic factor at the univariate analysis was: lesion diameter ≤18 mm correlated significantly with a longer LPFS (p=0.001). Prognostic factors at the multivariate analysis were: lesion diameter <18 mm was predictive for longer LPFS (p=0.006); oligometastases from primary colon cancer predicted significantly for worse LPFS (p=0.041) and progression-free survival (p=0.04).

Conclusions: To our knowledge, the current study represents the largest series on the use of SBRT 30 Gy single dose for lung metastases. The proposed schedule showed to be effective and safe, when administered in selected oligometastatic patients. These results could be evaluated in further prospective series with the aim of investigating the safety of this schedule in selected candidates.

CO006

TEN-YEARS STEREOTACTIC RADIOSURGERY ACTIVITY USING A LINEAR ACCELERATOR WITH ROBOTIC ARM IN THE TREATMENT OF BRAIN METASTASES AND PRIMARY AND METASTATIC EXTRACRANIAL TUMORS AT THE UNIVERSITY HOSPITAL OF MESSINA

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Aims: To report the crude number of stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) for brain metastases and extracranial tumors using a CyberKnife system.

Methods: we retrospectively analyzed the crude number of SRS for brain metastases and SBRT for primary and metastatic extracranial lesions in our Centre from January 2008 to December 2017. From this analysis have been excluded primary benign brain tumors (i.e. meningiomas, neurinomas, pituitary adenomas) and non-tumors treatments (i.e. arterovenous malformations, trigeminal neuralgia).

Results: A total of 908 brain metastases have been irradiated. Period 2008-2009, 73 treatments have been delivered; period 2010-2011, 143 SRS; period 2012-2013, 271 SRS; period 2014-2015 248; period 2016-2017, 174 SRS. As regard the SBRT, a total of 418 primary and metastatic lesions have been treated. Period 2008-2009, 28 treatments have been delivered; period 2010-2011, 38 SBRT; period 2012-2013, 88 SBRT; period 2014-2015 122; period 2016-2017, 142 SBRT. Regression analysis showed no statistically significant results.

Conclusions: We observed a growing trend from 2008-2013 with a crude number decrease in the last four-years period for SRS, conversely SBRT had an opposite behavior showing a progressive increase from 2008 to 2017. It is noteworthy to underline that, in 2009, LinAc had 20 days stop and in 2016 2 months stop both for LinAc upgrade. Notably, the reduction of the overall crude number of treatments could be associated with the activation of a new LinAc performing Volumetric Arc Therapy and IMRT. This observation confirms the necessity for a single Center which has high technology (i.e. CyberKnife)to have all the possible facilities to offer the best therapeutic choice for single patient.

CO007

SBRT FOR LUNG OLIGOMETASTASES IMPACTS ON SYSTEMIC TREATMENTS FREE SURVIVAL: A COHORT STUDY

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Aims. To analyze the impact of SBRT on systemic treatment free survival in a cohort of patients affected by different clinical presentations of lung oligometastases.

Materials and Methods. Inclusion criteria of this study were: 1-5 lung oligometastases; absence of extrathoracic disease; Karnofsky performance status (KPS) > 70; a biologically equivalent dose (BED) ≥100 Gy; and at least 6 months of follow up after SBRT. Three groups of patients were identified: 1) those with oligometastases as first clinical presentation for whom SBRT was adopted as primary treatment option ('oligometastases group'), 2) those oligoprogressive after systemic therapy ('oligoprogressive group'), and 3) those with oligopersistent disease after systemic therapy ('oligopersistent group'). The primary study end-point was the systemic treatment free-survival for each group of patients, whereas distant progression free survival (DPFS), local control (LC), and overall survival (OS) were the secondary end-points.

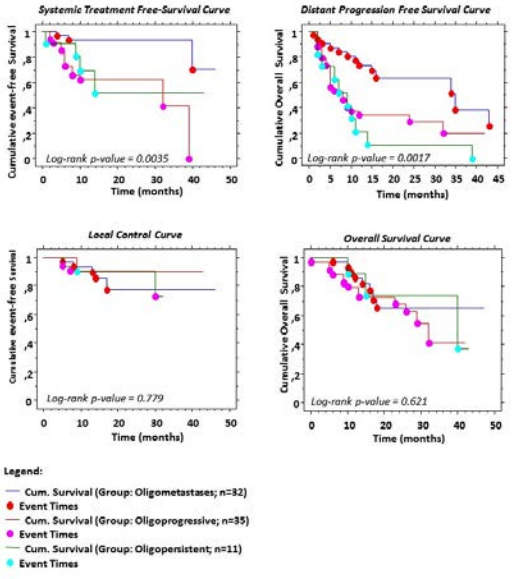

Figure 1.

Results. Seventy-eight patients and 114 lung metastases were analyzed. Of these, 32 patients were treated with SBRT for lung oligometastases, whereas the remaining patients underwent SBRT for oligoprogressive disease (n=35) or oligopersistent disease (n=11) after systemic therapy. In the whole cohort, the systemic treatment free-survival was 16±11 months (mean ± SD), LC was 18±11 months, DPFS was 14±11 months and OS was 19.6±11 months. The Kaplan-Meir survival analysis showed that the 'oligometastases group' had better clinical outcomes in terms of systemic treatment free-survival (log-rank test p=0.0035) and DPFS (log-rank test p=0.0017) compared to the two other groups of patients. Conversely, LC and OS did not significantly differ among the three groups.

Conclusions. In the present experience, SBRT has shown to be an important curative therapeutic option in patients with lung oligometastases, especially in those affected by metachronous lesions in which SBRT is offered as first treatment therapy. In this last clinical scenario, SBRT has shown a significant beneficial effect on systemic treatments free survival. It is currently hard to demonstrate if delaying systemic therapies means also longer survival for these patients. Undoubtedly, in several cases, delaying systemic treat-

ments could delay or avoid the most relevant adverse events related to the use of antiblastic drugs.

CO008

CAN STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASIS BE SAFELY COMBINED WITH SYSTEMIC THERAPIES?

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Aims: Stereotactic Radiotherapy (SRT) is an effective treatment for brain metastases (BM) and is generally safe. Aim of this retrospective study was to compare toxicities and efficacy of SRT alone and in combination with systemic therapies in patients with BM.

Methods: We analyzed all patients treated between 2010 and 2017 at our institution with SRT for BM, with or without concurrent systemic therapy (defined as administered within four weeks of SRT).We evaluated in this cohort of patients the haematological and neurological toxicities, brain progression free survival (bPFS) and overall survival, stratifiyng patients for yes/no systemic therapy.

Results: Data on 45 patients were obtained. Median age at diagnosis of BM was 66 years (range 37-90 yrs). At the time of initial presentation of BM, the majority of patients had ECOG perfomance status of 0-2. The most common primary tumors were lung, breast, melanoma and kidney. Sixty percent of SRT treatments were delivered concurrently with systemic therapy, of which 56% were with conventional chemotherapy and 44% with targeted and immunotherapy agents. Patients were divided in two groups: SRT alone and SRT/systemic therapy. No differences between the two groups of patients in terms of clinical and treatments characteristics were found. Median follow up was 10 months (range 1-65 months). In all patients myelosuppression was minimal after treatment, with 9% grade 2-4 toxicity; grade >=2 neurological symptoms were reported in 11% of patients, with one grade 5 neurological toxicity. There was no difference in haematological (p=0.79) and neurological (p=0.96) toxicities between the two groups. Histologically confirmed radionecrosis was reported in 2 patients (one in SRT alone and one in SRT-systemic therapy group) and radiologically suspected radionecrosis in 2 patients both in the group of concurrent therapy (one with chemotherapy and one with target therapy). Median bPFS was 12.1 months, without any significant difference between the two groups (p=0.49). To date 29 patients have died, of which 3 for brain progression, 13 for systemic progression and two for both systemic and brain progression. Nine patients were died for no tumor related causes and 2 patients for unknown causes. Median OS for entire group was 8.13 months without any difference between the two groups of patients. (p=0.37).

Conclusions: Systemic therapy can be safely given concurrently with SRT for BM without increase of toxicity.

CO009

LONG-TERM OUTCOME OF PATIENTS WITH VESTIBULAR SCHWANNOMAS (VS) AFTER LINAC STEREOTACTIC RADIOSURGERY

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Aims: Vestibular Schwannomas are benign tumors arising mostly from vestibular component of the vestibulocochlear nerve. Hearing loss is the most common initial presenting symptom. This report regards patients with sporadic VS undergone SRS with a follow-up period of >10 years.

Methods: Between August 2002 and January 2008, 53 patients with 53 sporadic VS were treated with SRS. Twenty-six (49%) patients were female. The median age was 59 years (range, 23-83). The median tumor volume was 1,7 cc (range, 0.09-7.4). Before SRS, in 9 (17%) patients a subtotal and in 5 (9%) patients a total resection had been performed. In these cases SRS was performed as salvage therapy for recurrent or progressive tumors. Patients not able to discriminate words or could not hear at all, were scored as 'non-serviceable hearing'. Trigeminal and facial nerve function was assessed asking the patient about facial pain/paraesthesia. The majority of patients (94%) had hearing loss as an initial symptom and forty-five (85%) patients a "non-serviceable" hearing function. Ataxia/disequilibrium, tinnitus, trigeminal and facial pain/paraesthesia were presenting symptoms in 19, 15, 7,5 and 19% of the patients, respectively. Median dose of SRS was 16Gy (range, 11-20 Gy).

Results: Considering that 5 patients were lost to follow up, 48 (92%) patients with 48 VS were evaluable for analysis of treatment response and toxicity. At a median follow-up of 11 years (range, 10-16), 12 patients (25%) had an objective improvement of pain/paraesthesia their initial symptoms with a MRI response classifiable in stable, partial or complete remission in 8,3,1 patients, respectively. 27 (56%) patients had a stationary of symptoms, with a MRI findings of stable disease, central tumor necrosis with temporary increase in tumor size, or partial remission in 17,5,1 patients, respectively. 9 (19%) patients worsened trigeminal or facial neuropathy in 4 and 5 cases, respectively. This deterioration was transient in 5 patients and persistent in 4. Patients who developed transient toxicity had received a median dose of 16 Gy, the others 20 Gy. The crude tumor control rate at 5 and 10 years was

94% and 94% (45/48), 3 (6%) patients developed a radiographic progression at a median time of 20 months, 1 of these required surgery for hydrocephalous.

Conclusions: Long-term follow-up confirmed the excellent tumor control associated to LINAC SRS of VS. Iatrogenic toxicity was rather low and similar to that reported in literature.

CO010

CLINICAL OUTCOMES OF RECTAL SQUAMOUS CELL CARCINOMAS TREATED WITH CHEMORADIOTHERAPY WITH OR WITHOUT SURGERY: A RARE CANCER NETWORK STUDY

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Aims: To report the results of a Rare Cancer Network study on Rectal Squamous Cell Carcinomas (R-SCC).

Methods: This study included 77 adult non-metastatic R-SCC patients (pts) treated in 13 American and European Institutions (M/F=54/23). Median age was 59 years (range: 25-87). Radiotherapy (RT) was delivered to 72 pts, usually with concomitant CT (CRT, n=62) as radical (n=47), neoadjuvant (n=17) or postoperative treatment (n=8). All patients received RT on internal iliac and presacral nodes, + external nodes (n=17) or external and inguinal nodes (n=39), up to a median total dose of 45Gy (range:30–65Gy, 1.8–3Gy/fraction). A boost was delivered in 40 pts, with external beam RT (n=36), up to a median total dose of 18Gy (range:5.4–30.6Gy), or with brachytherapy (n=4) up to a total dose of 25-33.4Gy. Surgery was delivered in 30pts, as LAR (n=9), APR(n=14), or Trans-Anal Resection (n=5).

Results: Median follow-up was 59.6 months (Range, 3.1–268). 5-year OS, cancer specific survival, local control (LC, at the anal level), loco-regional control (LRC, at the anal and/or the pelvic nodes level), metastases-free survival and disease-free survival were 83%+7% (95% CI), 85%+7%, 85%+7%, 83%+7%, 82%+7% and 76%+10%, respectively. Better 5-year LRR rates were reported in patients receiving exclusive chemoradiotherapy (CTRT) compared to those who received combined surgery and CTRT (88% vs 71%, Log-rank p-value 0.03). Noteworthy, no differences were seen in terms of distribution of stages amongst these 2 therapeutic approaches. At univariate analysis, T stage (T1-2 vs T3-4), N status (N0 vs N+), and Stage (I-II vs IIIA-B) did not statistically influence the 5-year LRC rate. Patients with a IIIB stage presented a statistically lower 5-year LRC rate (66% vs 85%, p-value=0.003). Salvage APR was realized in only 2/47 pts who received exclusive CRT. Toxicity data were available for all the pts: 51/77 pts presented a G1-4 acute toxicity (66%), while late G1-4 toxicity was reported in 32/77 pts (41%).Acute and late toxicity scores were available for 57 (74%) and 64 (83%) pts, respectively. The rates of grade >3 acute and late toxicity were 14% and 12%, respectively.

Conclusions: CRT seems to be the treatment of choice for R-SCC, as it allows good clinical outcomes and sphincter saving procedures, with acceptable severe toxicity rates. Stage IIIB patients present lower LRC rates and are probably the best candidates to multidisciplinary approaches

CO011

RE-IRRADIATION WITH INTRAOPERATIVE RADIATION THERAPY (IORT) COMBINED WITH SURGICAL SALVAGE FOR RECURRENT SOFT TISSUE SARCOMA AFTER MULTIMODALITY TREATMENT

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Background: The management of local recurrence of soft tissue sarcomas (STS), previously treated with multimodality approach including external beam radiotherapy (EBRT), is challenging. Aim of this study is to evaluate safety, feasibility and efficacy of re-irradiation with IORT alone and salvage surgery in patients (pts) affected by local recurrence of extremity and retroperitoneal STS.

Materials and Methods: We retrospectively analyzed data of pts with local recurrences of STS, after previous preoperative EBRT (40.5-50Gy) +/- Chemotherapy and Surgery +/- IORT, treated at our Institute.

Results: Data of 43 pts, 19 (44%) female and 24

(56%) male, treated between March 2001 and March 2018, were available. Median ECOG PS was 0 (range 0-1). The most common histologies were Liposa 20pts (46.5%) and Leiomyosa 6pts (13%); 20 (46%) pts had high grade disease and all by one M0. Median size of disease was 7cm (range 3-10). Site of primary tumor was limb in 13 (30%), trunk in 10 (23%) and retroperitoneum (RPS) in 20 (47%) pts respectively. All pts had received previous EBRT and 22 pts (51%) of them had also IORT. Curative treatment intent was considered in 34pts (79%). R0 resection was achieved in 20 (46%) pts (9 limb, 5 trunk and 6 RPS), 21 (49%) had R1 resection (4 limb, 5 trunk and 12 RPS) and 2 (5%) pts with RPS had R2 resection. All pts with extremity STS underwent to limb sparing surgery. IORT was given after tumor removal, using electrons of 6-16Mev energy, with a median dose of 15Gy (range 12.5-18Gy). Median PTV was 7 cm in size (range 3-12) shaped with applicators of respectively diameter. Partial IORT PTV overlapping was necessary in (36%) of 22 IORT pretreated pts. Major Grade III postoperative complications were reported in 3 (7%) pts: bleeding in 2 of them and bowel occlusion in1, all required surgical treatment. Grade II complications were reported in 9 (21%) pts, consisting of late neuropathy; only 3 (33%) of these pts received Re-IORT. At a median follow up of 36 months (range 6-162), 17 (40%) pts are alive without disease.

Conclusions: Re-irradiation with full dose of 15Gy IORT, combined with surgical salvage in recurrent STS pts, appears safe with acceptable morbidity. Re-IORT in selected cases may be considered. This combined approach could represent a feasible option for conservative surgical salvage for recurrent extremity STS. The data of desease control is encouraging.

CO012

WHOLE LUNG IRRADIATION FOLLOWING HIGH DOSE CHEMOTHERAPY WITH BUSULFAN AND MELPHALAN IN PATIENTS WITH EWING SARCOMA: TOXICITY AND OUTCOMES ANALYSIS IN A MULTICENTRIC ITALIAN STUDY

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Aims: To evaluate toxicity, Overall Survival (OS), Event-Free Survival (EFS) e Pulmonary Relapse Free Survival (PRFS) after High Dose Chemotherapy (HDCT) with Busulfan and Melphalan, Ematopoietic Stem Cells Transplantation (TCSE) and Whole Lung Irradiation (WLI) in patients (pts) with Ewing Sarcoma localized or metastatic at time of diagnosis.

Methods: Pts were enrolled in 10 Italian Centres between 1st november 1999 and 31st January 2017 with localized or metastatic Ewing Sarcoma at time of diagnosis. Clinical (particularly lung toxicity) and radiological data were collected. OS, EFS, and PRFS were calculated based on Kaplan Meier method.

Results: 68 pts (36 male, 32 female) were collected from 10 Italian Centres, with median age of 14 years (range: 8 months-35 years), and median follow-up of 34 months; 48.5% of pts had Ewing Sarcoma of limbs; 82.3% pts had pulmonary metastases at time of diagnosis. Spirometries were collected at each step of treatment: before and after HDCT, after WLI, and during follow-up, showing pulmonary function changes in 6.4%, 25.0%, 38.4%, and 35.9%, respectively. Low-intermediate and severe toxicity were recorded in 22.6% and 2.9% of pts, respectively. Three-year EFS, OS, and PRFS were 60.4% 72.5%, and 65%, respectively.

Conclusions: Our study showed the feasibility of combined treatment with HDCT based on Busulfan and Melphalan followed by WLI. We recommend to perform spirometry at each step of treatment. Further studies are needed to evaluate the efficacy of the described treatment.

CO013

RADIOTHERAPY TREATMENT FOR MERKEL CELLS CARCINOMA (MCC): THE EUROPEAN INSTITUTE OF ONCOLOGY (EIO) EXPERIENCE BASED ON MULTIDISCIPLINARY TEAM APPROACH

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Aims: To review the treatment of Merkel Cells

Carcinoma (MCC) patients (pts), based on a multidisciplinary team discussions.

Methods: In the period 2003 – 2016 we review the radiotherapy treatment of 21 pts affected by the uncommon and aggressive skin Merkel Cells Carcinoma (MCC) at European Institute of Oncology (EIO) in the contex of a multisciplinary tumor board (MTB) discussions, with the presence of surgery, oncology, nuclear medicine and imaging specialists. If the pts have MCC diagnosed in other hospitals, in most of the cases an EIO pathology specimens review was performed.

Table 1.

N. of patients	21
Average age (years)	66,4
Primary tumor localization	Limbs (19,04 %), Buttocks Region (19,04 %), Head&Neck (23,81 %), Unknown (38,09 %)
Stage	III (61,9%), I (14,9%), II (4,5%), IV (4,5%), N.D. (14,2%)
Ki-67	> 20% (available in 6 out 21 pts)
Polyoma virus detection.	38% positive, 14,3% negative , 47,6% not rated

Results: Table 1 shows the characteristics of the pts. Radical surgery with wide negative margins and postoperative radiotherapy were the cornerstone in the pts management: 85% of our patients underwent an adjuvant radiant treatment, compared with a remaining 15% for which the treatment was palliative, because these pts were found metastatic before the RT start or not candidate for radical surgery. Two pts underwent neoadjuvant chemotherapy before surgery. In 47.6% was adopted a modulated intensity RT technique (IMRT), in 33.3% a 3D conformational technique, in 9.5% the stereotactic RT (SBRT), in 4.7% (one patient) was performed high dose rate (HDR) brachytherapy and for one patient (4.7%) were used electrons. As part of the adjuvant treatment, the average dose delivered was 53 Gy with 2.1 Gy a fraction. Still in the context of patients who underwent adjuvant treatment, the average progression-free survival (PFS) was 40.6 months. At present 9 pts are alive with no evidence of disease, while 9 pts died for the progression of the disease and 3 pts have been lost at follow-up. The principal sites of progression were lymph nodes (28,57%), Bones (4,76%), and Peritoneal nodes (4,76%). At progression the most of the pts had 1st line chemotherapy (CHT) mainly with Carboplatin and Etoposide; some pts for several disease progressions had 2nd and 3rd line CHT Carboplatin and Etoposide re-challenge and with temozolomide or FOLFIRI regimen.

Conclusions: MCC is characterized by a high incidence of early locoregional relapse and distant metastases. Because of its rarity and the resulting lack of prospective randomized trials, data regarding the optimal treatment of MCC are limited. Multidisciplinary management in this setting appear to be the best way to optimize the chance of cure.

CO014

RADIOSURGERY FOR HAEMANGIOBLASTOMAS: MONOINSTITUTIONAL ANALYSIS

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Aims: Hemangioblastomas (HB) of the central nervous system are rare indolent WHO grade I vascular tumors of controversial origin that may occur sporadically or in association with von Hippel–Lindau (VHL) disease. Though primary therapy for HB is surgical resection, for patients with subtotally excised or unresectable lesions and for patients with poor clinical status who are not good candidates for surgery, as well as those wishing a minimally invasive approach, radiotherapy (RT) or radiosurgery (SRS) can be an effective alternative. RT and SRS have been associated with good rates of local control in a 60–90% range, especially in patients with VHL. The aim of this study is to evaluate the efficacy and safety of SRS for patients with diagnosis of intracranial and spinal HB in terms of local control and toxicity.

Methods: We conducted a retrospective analysis of 22 patients with a total of 37 HB: 23 intracranial HB and 14 spinal HB treated at our Institute from January 2012 until February 2017. A regular radiological follow-up with MR imaging was scheduled at 4–6 month intervals after SRS procedure. The radiosurgical procedures were performed using a CyberKnife® system, characterized by a 6MV linac mounted on a robotic arm for multiple, non-isocentic, non-coplanar beams sets delivery. Statistical analysis was carried out using SPSS 21.

Results: Twenty-two patients were followed for a median of 42 months (range 3–72 months). Median age at the time of SRS was 44 years (range 19-79), 8 patients were female and 14 male. The diagnosis of HB was based on the histological findings, except in 7 patients without surgical removal. Seven patients had multiple lesions and 30 patients had a single lesion. The median tumour volume pre-SRS was 417 mm3 (range, 40-15779 mm3). The mean prescription dose was 18 Gy (range, 10-25 Gy) in 1-5 fractions with median isodose line of 81% (range, 73-88%). Two patients (9%) developed a recurrence, 12 (55%) showed stable disease and 8 (36%) partial response. There was no significant toxicity after treatments.

Conclusions: SRS, both in single and multi-fractions settings, is potentially attractive for patients with VHL disease where multiple HBs may develop either concurrently or sequentially and may be difficult to

treat or retreat with repeated surgery and/or conventional radiation techniques without the risk of toxicity. Our results show that SRS can be considered a safe and effective treatment for intracranial and spinal HB.

CO015

THE ROLE OF PRIMARY SURGERY AND EXTERNAL BEAM RADIATION THERAPY IN THE MANAGEMENT OF NON-METASTATIC DUCTAL PROSTATE CANCER: 20-YEAR OUTCOMES FROM A SINGLE INSTITUTION EXPERIENCE

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Aims and Introduction: Ductal prostatic carcinoma (DAC) is a rare histological subtype of prostate cancer (PC). Although it is reported to be an aggressive tumor, often with locally advanced and/or metastatic disease at presentation, the optimal therapeutic approach is still controversial as a consequence of the lack of current literature regarding treatment recommendations. The outcomes of our 20-year experience of multidisciplinary management of non-metastatic DAC (nmDAC) are presented in this paper.

Materials and Methods: A retrospective analysis of our Urology and Radiation Oncology Institutional database was performed. Patients affected by DAC undergoing radical treatment were included. All the cases were discussed during a multidisciplinary tumor board in order to plan a highly personalized treatment. The cohort was divided into three groups according to treatment: Group A underwent surgery alone (either radical prostatectomy or cystectomy), Group B surgery and post-operative radiation therapy (RT, either adjuvant or salvage) and Group C RT alone. Statistical analysis was performed using SPSS statistical software v20 (SPSS Inc, Chicago, IL, USA). Survival outcomes were estimated using Kaplan-Meier method, after adjustment for predictive variables (age, comorbidities, pathological stage, histology).

Results: From 1997 to 2016, about 8470 PC patients underwent radical treatment at our Institution, of which 71 were diagnosed with nmDAC (0.84%): Group A was composed by 21 patients (29.6%), Group B by 27 patients (38%) and Group C by 23 patients (32.4%). Characteristics of the population in study are summarized in Table 1. Histological examination showed 17 pure DAC (23.9%) and 56 mixed DAC and acinar adenocarcinoma (78.9%). At a median follow-up time of 60 and 120 months, overall survival (OS) was respectively 86% and 70% for Group A, 100% and 92% for Group B, 65% and 49% for Group C (p=0.054). Pure DAC undergoing surgery showed an OS of 34% at a median follow up of 60 months, while the addiction of post-operative RT led to an OS of 100% (p=0.029).

Conclusions: DAC is a rare, often aggressive subtype of PC, especially when presenting with pure histological form. Our relatively large series of patients seems to support the role of an aggressive combined therapeutic approach, when feasible, in order to improve local disease control and long-term survival outcomes.

Table 1. Population features (Tot. 71 patients).

	Group A (21 patients)	Group B (27patients)	Group C (23 patients)
Age at diagnosis, median (range)	66 (49-75)	65 (46-72)	71 (46-81)
PSA, median (range)	8.8 (2.1-64)	10 (1.3-53.9)	10 (2.2-232)
Karnofsky Performance Status, mean	86.7	89.6	87.4
cT4	2 (10%)	2 (7%)	5 (22%)
cT3	8 (38%)	22 (82%)	6 (26%)
cT2	11 (52%)	3 (11%)	9 (39%)
cT1	0	0	3 (13%)
cN+	4 (19%)	4 (15%)	2 (9%)
Pure ductal histology	4 (19%)	4 (15%)	9 (39%)
Mixed acinar histology	17 (81%)	23 (85%)	14 (61%)

CO016

TEMOZOLOMIDE PLUS 3D-CRT AFTER HIGH DOSE METHOTREXATE IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: A PROSPECTIVE PHASE II STUDY

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Aims: Aim of this study is to evaluate the addition of temozolomide (TMZ) to radiotherapy in patients with primary cerebral lymphoma (PCNSL) previously treated with high dose Methotrexate (MTX-HD) in terms of overall survival (OS).

Materials and Methods: Patients with histologically proven diagnosis of PCNSL treated with high doses MTX and subsequently subjected to radiation therapy plus Temozolomide were considered for this analysis. Two clinical Target Volum (CTV) were defined: CTV2 was represented by Whole Brain plus leptomeninges until C2, reaching a dosage of 30 Gy in 15 daily fractions, while CTV1 comprising the initial disease location and residue if present. The total dose delivered on CTV1 was related to the type of response had to treatment with MTX-HD (complete response = 6 Gy, partial response = 10 Gy, progression disease = 16 Gy). Temozolomide was administered concomitantly at the dose of 75 mg/mq/die according to our previous escalation study.

Results: Thirty-three patients were enrolled from March 2004 to December 2017: 18 male and 15 female. Median age was 64,5 yrs (range 50-76). Twenty-two out of 33 patients received two cycle of MTX-HD, 9 patients received only one cycle of HD-MTX because of hematological toxicity and 2 patients did not received any cycle due to poor performance status. Nine patients underwent macroscopic surgical excision, while 24 patients received biopsy. Twenty five patients received radiotherapy in association with TMZ. At a median follow up of 80 months (range 3-169), 9 of 33 patients (27%) are alive (7 without disease and 2 with stable disease), 22 patients died because of disease and two patients died because of other causes. Median OS for all patients was 23.1 months with at 1 yrs OS of 64% and at 3 yrs OS of 43% of patients (Figure 1). The use of concomitant TMZ significantly impact the OS (p=0.004).

Conclusions: This prospective analysis shows that, despite the limit of possible patient selection, the addition of TMZ at the dose of 75 mg/mq seems to have a better outcome compared to RT alone.

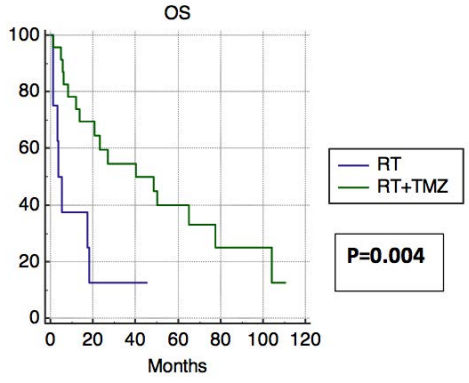

Figure 1.

CO017

WHICH TREATMENT APPROACH FOR ELDERLY PEOPLE WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK? A NATIONAL SURVEY ON BEHALF OF THE ITALIAN ASSOCIATION OF RADIATION ONCOLOGY(AIRO) HEAD AND NECK STUDY GROUP

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Aims: Although the majority of cases with head and neck cancer (HNC) occur between the fifth and sixth decade of life, the onset of the disease in patients older than 60 years is common with up to 24% of HNC cases diagnosed in patients older than 70 years. Moreover, compared with younger subjects, HN elderly patients are more frequently burdened with treatment-induced severe acute toxicity, multiple comorbidities and non-cancer related death although age is not an independent negative prognostic factor in head and neck cancer treatment. Nevertheless, the treatment of HNC elderly patients remains controversial. Here we report the results of a national survey investigating radiation oncologists' behavior in regard to treatment of HNC elderly patients.

Methods: In February 2018 a 41-item questionnaire, concerned locally advanced HN patients with age >-70 years, was sent to all Italian radiotherapy centers by a national electronic survey and it was completed by Italian physicians that are familiar with Head and Neck Cancer. Three –section have been identified: 1) general information, 2) treatment in curative setting and 3) treatment in palliative setting. Data referred to patients treated in 2017 were required.

Results: Overall 69 responders completed the survey. During 2017 a median of 25 pts (range 2-100) age >70 y were treated in 69 Radiotherapy Departments. In the interdisciplinary team, nurse practitioner in 55.8%, speech language pathologist in 27.9%, pain therapist in 46.5%, nutrition specialist in 65.3%, but only in 9.3% geriatric oncologist as supportive care were represented. In pretreatment evaluation none comorbidity score is adopted by 55% of the physicians. In the radical setting the majority of pts received radiotherapy (RT) alone (27,5%), surgery followed by adjuvant RT (23.2%), concomitant CTRT (19.5%). When chemotherapy is employed, CDDP 40 mg/m^2 by 57%, CETX by 18% and CDDP 100 mg/m^2 by 17% of responders was used. IMRT is adopted in 84.5% of the patients. Only 41% of physicians think that elderly pt need hospitalization a little more compared with younger pts. In palliative setting 30 Gy in 10 fraction is the most used scheme and RT was delivered only to GTV by 68% of responders.

Conclusions: In absence of evidence-based recommendations there is an urgent need for clinical trials aimed at assessing a greater uniformity and the best choice of treatment in elderly population.

CO018

ROLE OF HYPOFRACTIONATED ELECTRON BEAM RADIOTHERAPY IN NON-MELANOMA-SKIN-CANCER IN ELDERLY PATIENTS

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Aims: Non-melanoma skin cancer (NMSC) represents the most common type of malignancy in white population. The 99% of the NMSC is represented by keratinocyte carcinomas (BCC) and squamous cell carcinomas (SCC). Usually lesions appears in elderly patients and the age limits therapeutics options. Aim of this study is to evaluate the effectiveness and the safety of hypofractionated electron beam RT in terms of local control (LC), toxicity and cosmetic outcome.

Methods: Between January 2011 and December 2016, 229 pts (77% men and 33% women) were treated in our center with electron beam RT for NMSC. Median age was 83 yrs. Lesions were localized in most cases on the scalp, front, ear, eyelid or nose. In 112 pts RT was the unique treatment, instead in 117 pts RT was delivered after surgical excision with or without persistence of local disease. The treated lesions were BCC in 71 cases, SCC in 148, untyped in 10 cases. In the 82% of cases the tumor dimensions were between 2 and 5 cm. The lesion treatment to a depth of 3-5 mm with a 4 or 6 MeV electron beam was produced by Linac. The delivered dose was 60 Gy/10fx in definitive treatments and 30, 48 or 60 (6Gy/fx) in post-operative cases. Toxicities were assessed by CTCAE 4.0 criteria and results were evaluated every 2 months for the first 6 months after the end of RT and then every 6 mth.

Results: Median follow-up was 9,8 mth. LC ratio was 93% (144 pts with complete response at the first control and 47 complete response achieved at the second/third control). 12 pts presented local progression with a mean time to progression of 16 months. 2 pts developed lymph nodal metastases (SCC with local complete response on primary cancer). Grade 2 acute toxicity was observed in 12 pts and grade 3 just in 1 case. No case of chondronecrosis was detected. In 180 pts cosmetic outcome was excellent with normotrophic skin in the site of treatment.

Conclusions: In our experience hypofractionated electron beam radiotherapy for NMSC is safe and a high rate of LC can be achieved with low toxicity and good to excellent functional and cosmetic results. Furthermore, the comparison in terms of LC between pts who received definitive RT and those who received RT as a post-operative treatment, demonstrates that definitive RT is a valid alternative to surgery with the advantage to be a less invasive technique while having the same high rate of LC. These results of our study are particularly relevant in the treatment of elderly pts.

CO019

INDIVIDUALIZED TREATMENT OF HEAD NECK SQUAMOUS CELL CARCINOMA PATIENTS AGED 70 OR OLDER WITH RADIOTHERAPY ALONE OR ASSOCIATED TO CISPLATIN OR CETUXIMAB: IMPACT OF WEEKLY RADIATION DOSE ON LOCO-REGIONAL CONTROL

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Aims: To evaluate if, in elderly HNC patients, loco-regional control (LRC) is influenced by average weekly radiation dose (AWD).

Materials and Methods: From 2009 to 2017 the medical records of 150 consecutive HNC elderly patients were reviewed. AWD was calculated by dividing the total dose in Gray by overall treatment time in weeks. Patients were divided in 2 groups according to age: Group 1 (70-75years) and Group 2 (>75 years). Primary endpoint was LRC; secondary endpoints were overall survival (OS) and compliance to planned treatment.

Table 1. Patient characteristics

Patient charateristics		All patients	%	Group 1	Group 2	p
Number of patients				N (%)	N (%)	
Gender						0,3454
	Male	113	75	57 (79)	56 (72)	
	Female	37	25	15 (21)	22 (28)	
Primary site						0,0029
	Oral cavity	23	17	5 (7)	18 (23)	
	Oropharynx	47	36	28 (39)	19 (24)	
	Larynx	62	47	26 (36)	36 (46)	
	Hypopharynx	0	0	13 (18)	5 (6)	
cT stage						0,0192
	Tis-T2	58	39	35 (49)	23 (29)	
	T3-T4	92	61	37 (51)	55 (71)	
cN stage						0,0684
	N0	62	41	24 (33)	38 (49)	
	N+	88	59	48 (67)	40 (51)	
Stage						0,8368
	0-II	28	19	14 (19)	14 (18)	
	III-IV	122	81	58 (81)	64 (82)	
RT						1
	Adjuvant	37	25	18 (25)	19 (24)	
	Radical	113	75	54 (75)	59 (76)	
Treatment completed						0,7474
	Yes	140	93	68 (94)	72 (92)	
	No	10	7	4 (6)	6 (8)	
RT tecnique						0.000
	3DCRT	75	50	27 (37)	48 (62)	
	IMRT/VMAT	75	50	45 (63)	30 (38)	
RT schedule						0.928
	Standard	103	69	49 (68)	54 (69)	
	Slight accelerated	47	31	23 (32)	24 (31)	
Systemic therapy						0.002
	Chemotherapy	34	23	26 (36)	8 (10)	
	Cetuximab	26	17	17 (23)	9 (11)	
	No	92	60	30 (41)	62 (79)	
PS						0,0374
	0	84	56	49 (68)	35 (45)	
	1	49	33	18 (25)	31 (40)	
	2	14	9	4 (6)	10 (13)	
	3	3	2	1 (1)	2 (3)	

Results: The median age was 76 years (range: 70-92), the distribution of patients by age was 72 and 78 patients in Group 1 and in Group 2, respectively; overall median follow up was 23 months (range 0-99). Table 1 shows patients characteristics. Patients in group 1 (70-75 years) underwent to RT concomitant to systemic therapy and were treated with a IMRT technique more frequently than those in group 2 (p= 0.000 and 0.002, respectively). Group 1 was associated to lower T stage (p=0.0192) and high PS (p=0.037). The AWD was assessed for all but 10 patients (excluded because they did not completed RT: 1 died after 21.2 Gy and the others presented important cognitive impairment). The mean AWD was 9.28±0.92. Optimal cut-off of AWD for LRC was 9.236 (p=0.018). Median OS was 73 months. In univariate survival analysis low PS (p=0.005), T3-T4 (p=0.021), Stage III-IV (p=0.046) and AWDLow (p=0.018) were significantly associated with lower LRC; low PS (p<0.001) and Group 2 (p=0.006) were also associated with lower OS. Considering patients treated with radiotherapy alone AWDLow was significantly associated with lower LRC (p=0.04) whereas among patient treated with concomitant chemoradiotherapy AWD did not affected LRC (p=0.18). The multivariate analysis confirmed the independent significant value of PS for the prediction of both LRC and OS (p=0.035 and p<0.001, respectively). As regards compliance evaluation, 38 (25.3%) patients interrupted RT treatment due to toxicity for a median time of 1 day (range: 1-9), 20 and 18 patients were in group 1 and group 2, respectively (p= 0.508).

Conclusions: In elderly patients an AWD of >9.236 Gy was found to be beneficial for RT alone regimen but not chemoradiotherapy regimen.

CO020

RADIOSURGERY OR FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES IN ELDERLY PATIENTS

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Aims: For selected patients with brain metastases (BMs), the role of stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (SFRT) is well recognized. Nevertheless, limited experiences have been conducted in elderly patients affected by BMs. Aim of the current analysis was to analyze SRS/SFRT linac-based for elderly people with BMs in terms of feasibility and clinical results.

Materials and Methods: Patients with life expectancy > 3 months, number of BMs < 10, diameter < 3cm and controlled or synchronous primary tumor, were recruited to receive SRS/SFRT. From this population data-set, patients over 65 years old were selected for the present analysis. The prescribed total dose and fractionations were performed based on BMs size and proximity to organs at risk (total dose 15–30 Gy, 1–5 fractions). A Volumetric Modulated Arc Therapy (VMAT) plan was generated with one or two coplanar partial arcs or 5 no-coplanar arcs by HyperArc. Toxicity was assessed according to CTCAE v4.0. MedCalc v18.2 was utilized for statistical analysis.

Results: From April 2014 to December 2017, 200 patients with more than 450 BMs were treated with linac-based SRS/SFRT. Forty patients were elderly (median age 70, range 65-83) with 110 brain lesions. With a median follow-up time of 28 months (range 4-43 months), median overall survival and 1-year overall survival were 9 months and 39%, respectively; median intracranial progression free survival was 6 months. No difference in terms of outcomes were observed between patients under or over 70 years (p=0.2 and p=0.18). At the time of the analysis, local control was reported in 109/110 BMs (99.1%): 12 BMs had a complete response (10.9%); 51 BMs (46.4%) a partial response; 46 BMs (41.8%) a stable disease. One BM (0.9%) progressed after 2 months from SRS, probably due to the prescription dose (18Gy in 1 fraction). Eighteen out forty patients (45%) experienced an intracranial progression in terms of appearance of new BMs: 16 out 18 elderly patients underwent re-irradiation (11 patients received SRS; 5 patients received whole brain RT). Acute and late toxicities were mild: no adverse events more than grade 2 were recorded. Forty-five percent of patients are still alive, no patient died for brain disease.

Conclusions: These preliminary findings highlighted the feasibility and safety of Linac-based SRS/SFRT in elderly patients affect by oligo or multiple BMs. Prospective studies with a longer follow-up are advocated to define the correct treatment approach in this setting.

CO021

ADVANCED HEAD AND NECK (H&N) CANCER IN ELDERLY PATIENTS: RESULTS OF A SHORT-COURSE ACCELERATED PALLIATIVE RADIOTHERAPY

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Aims: To assess the safety and efficacy of a SHort-course Accelerated RadiatiON therapy (SHARON) regimen in the palliative treatment of H&N locally advanced or metastatic cancer in elderly patients.

Methods: Eligibility criteria for the analysis were: 1) histological confirmed H&N cancers, 2) age ≥ 80 years, 3) expected survival > 3 months and 4) Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 3. A total dose of 20 Gy was delivered in 2 consecutive days with a twice daily fractionation (5 Gy per fraction) and at least 6-8 hour interval. Primary endpoint was the symptoms response rate.

Results: Twenty-four patients (male/female: 12/12; median age: 85.0 years; range: 80-98) were included in the analysis. ECOG performance status was < 3 in 13 patients (54%). Patients with different cancer types were included in the analysis, in particular the primary were: oral cavity (N°=8; 33.3%), larynx (N°=4; 16.6%), oropharynx (N°=3; 12.5%), salivary gland (N°=3; 12.5%), lip (N°=2; 8.3%), nasal cavity (N°=2; 8.3%), maxillary sinus (N°=1; 4.1%) and ethmoid sinus cancer (N°=1; 4.1%). With a median follow-up time of 2.0 months (range, 1 to 16 months), one (3.2%) G3 acute skin toxicity, 2 (6.4%) G2 acute pharyngeal toxicity, 4 (12.9%) G1-G2 acute skin toxicities and 3 (9,6%) G1-2 mucositis were recorded. Among overall 24 symptomatic patients, 19 showed an improvement or resolution of baseline symptoms (overall palliative response rate: 79%). No detrimental effects in terms of quality of life were observed after the treatment. With a median survival time of 12.6 months, the median symptoms free survival was 11.3 months. Five of 24 (20,8%) patients required a retreatment that was performed in median after 6 months (range: 2,9 - 8,6 months) from the previous one.

Conclusions: Short-course accelerated radiotherapy in palliative setting of Head & Neck cancers is effective in terms of symptom relief and well tolerated even in elderly patients.

CO022

RADIOTHERAPY FOR RADICAL TREATMENT OF HEAD AND NECK CANCER IN ELDERLY PATIENTS: A MONO-INSTITUTIONAL RETROSPECTIVE ANALYSIS

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Aims: To evaluate results of radiotherapy (RT) in a cohort of 74 elderly-patients (≥70 year) affected by head and neck carcinoma (HNSCC), treated with radical intent.

Methods: From January 2009 to February 2018, 74 patients (pts) older than ≥70 years, affected by HNSCC, underwent RT with Tomotherapy (IG-IMRT). 77% of cases were stage IVA-B. Histological type was squamous in 87%. Most frequent subsite was Oropharynx (42 pts). HPV-status (DNA) was evaluated in 25 pts and it resulted positive in 23. Patients received (89%) a total dose of 66 Gy in 30 fractions to CTV at high risk of local recurrence and 60 Gy and 54 Gy to CTV at intermediate and low risk, respectively, using Simultaneous Integrated Boost (SIB); 11% of pts received standard fractionation with sequential plans to 50/60/70Gy. 47% of pts received concurrent systemic therapy (once/three-weekly Cisplatin (CDDP: 17%) or Cetuximab (CTX: 30%)).

Table 1.

	Median	Percentage (of 74 pts)		RT alone (39 pts)		RT + CDDP (13 pts)		RT + CTX (22 pts)		p
		%	N°	%	N°	%	N°	%	N°	
Age	74 years (70-89)									
Age<75		54,1%	40	35,9%	14	84,6%	11	68,2%	15	
75-79		32,4%	24	38,5%	15	15,4%	2	31,8%	7	**0,001**
Age≥80		13,5%	10	25,6%	10	0,0%	0	0,0%	0	
Performance Status (PS)	0 (0-2)									
PS 0		75,7%	56	69,2%	27	84,6%	11	81,8%	18	
PS 1		23,0%	17	28,2%	11	15,4%	2	18,2%	4	0,161
PS 2		1,0%	1	2,6%	1	0,0%	0	0,0%	0	
Charlson Comorbidity Index (CCI)	1 (0-5)									
CCI 0-1		63,5%	47	51,3%	20	76,9%	10	77,3%	17	
CCI 2-3		31,1%	23	38,5%	15	23,1%	3	22,7%	5	**0,023**
CCI 3-4		5,0%	4	10,2%	4	0,0%	0	0,0%	0	
SUBSITES OF DISEASE										
Others		9,6%	7	10,2%	4	7,7%	1	9,1%	2	
Oral Cavity		6,8%	5	2,6%	1	15,4%	2	9,1%	2	
Nasopharynx		8,1%	6	12,8%	5	7,7%	1	0,0%	0	
Glottic Larynx		8,1%	6	15,4%	6	0,0%	0	0,0%	0	0,289
Hypopharynx		10,6%	8	12,8%	5	7,7%	1	9,1%	2	
Oropharynx		56,8%	42	46,2%	18	61,5%	8	72,7%	16	
STAGE										
I-II		9,5%	7	18,0%	7	0,0%	0	0,0%	0	
III		13,5%	10	20,5%	8	0,0%	0	9,1%	2	**0,002**
IVA-B		77,0%	57	61,5%	24	100,0%	13	90,9%	20	
TUMOR STADIATION										
cT1x-cT1a-b		10,8%	8	18,0%	7	7,7%	1	0,0%	0	
cT2-cT3		32,4%	24	41,0%	16	7,7%	1	31,8%	7	**0,005**
cT4a-cT4b		56,8%	42	41,0%	16	84,6%	11	68,2%	15	
NODAL STADIATION										
cN0		18,9%	14	33,3%	13	0,0%	0	4,5%	1	
cN1		18,9%	14	20,5%	8	7,7%	1	22,7%	5	
cN2a-cN2b		33,8%	25	28,2%	11	46,2%	6	36,4%	8	**0,001**
cN2c-cN3		28,4%	21	18,0%	7	46,2%	6	36,4%	8	
Acute Toxicities CTCAE (Grade 3)		**47,3%**	35	**23,1%**	9	**69,2%**	9	**77,3%**	17	
Erythema (Grade 3)		20,3%	15	10,3%	4	30,8%	4	31,8%	7	**0,001**
Mucositis (Grade 3)		28,4%	21	10,3%	4	38,5%	5	54,5%	12	
Dysphagia (Grade 3)		24,3%	18	7,7%	3	38,5%	5	45,5%	10	
Interruption		20,3%	15	**15,4%**	6	**23,1%**	3	**27,3%**	6	0,394
Premature Discontinuation		6,8%	5	**2,6%**	1	**15,4%**	2	**9,1%**	2	0,963
Complete Response		78,4%	58	**87,2%**	34	**76,9%**	10	**63,9%**	14	0,189
Locoregional Recurrence		27,0%	20	**17,9%**	7	**15,4%**	2	**50,0%**	11	0,489
Metastases		13,5%	10	**10,3%**	4	**7,7%**	1	**22,7%**	5	0,821
Median PFS (months)				**48 m**		**62 m**		**19 m**		0,523
Median OS (months)				**50 m**		**62 m**		**36 m**		0,421

Results: Median age was 74 years (70-89), 76% of pts presented with a PS 0 and 45% with a Charlson Comorbidity Index (CCI) 1. Of all pts, 6 interrupted treatment definitively; 15 pts suspended RT temporarily (median time of interruption was 4 days). 23% of pts showed G3 acute toxicity (CTCAE) in the RT only group and 77% in the RT-CTX group and 69% in the RT-CDDP group. No G4-5 toxicity was observed. A complete response (CR) was obtained in 67%, 87% and 91% in RT-CTX, RT alone and RT-CDDP groups, respectively. The median progression-free survival (PFS) was 62 months (RT-CDDP), 48 months (RT alone) and 19 months (RT-CTX). Overall survival (OS) was 62 months (RT-CDDP), 50 months (RT alone) and 36 months (RT-CTX) (see Table 1). Multivariate analysis showed that stage, age and CCI were correlated with the choice of treatment (RT alone vs RT/CT or RT/CTX). Age, PS and CCI were not correlated with acute toxicities, local recur-

rence and complete response.

Conclusions: Within an elderly population, age, PS, CCI were not statistically correlated to treatment interruption, nor affected the response or acute toxicity. In selected elderly patients, radical radiotherapy even associated with systemic treatment seems to be safe and feasible. The relative merits of the different approaches have to be analyzed prospectively.

CO023

MANAGEMENT OF ELDERLY PATIENTS WITH LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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Aims: In patients with locally advanced squamous cell carcinoma of the head and neck, and in order to obtain the best organs preservation, concurrent chemotherapy with 3 weekly cisplatin and radiotherapy offers the best benefits in terms of overall survival (OS) and disease free survival (DFS); however these clinical outcomes appear to depend to the age of the population analyzed. In fact, this benefit seems to reduce in elderly patients. The aim of this study is to evaluate the impact of adding chemotherapy to the radiotherapy in terms of OS e DFS in elderly patients treated in our deprtment.

Methods: Five hundred pts with head and neck cancer were treated in our department with Volumetric Arc Therapy/RapidArc®. Retrospectively, we considerered only pts with an age of 65 or more, with squamocellular, locally advanced carcinoma of the oropharynx, hypopharynx, oral cavity and larynx. The pts were treated either with only radiotherapy (RT) or with concurrent chemo-radiotherapy (cCT-RT), scheduled 100 mg/m^2. Only 33% of pts treated with chemotherapy received the three cycles prescribed.

Results: One hundread and seven pts (75 male and 32 female) were evalueted; median follow up was 26 months. 67 pts were treated with RT, and the median age at diagnosis was 72 (65-90) years; 40 pts were treated with cCT-RT and median age was 68 (65-70) years. OS at 2 years is 63% in RT group and 81% in second cCT-RT group (p:0.297). DFS was calculated in 81 pts beacuse 26 pts presented residual disease al the post tretment restaging; DFS at 2 years in the group treated with RT was 70% while in cCT-RT group was 84% (p:0.203). The percentage of recurrence/residual locoregional disease was 46% and 28% respectively in RT and cCT-RT groups.

Conclusions: The results obteined from our study confirm that cCT-RT doesn't improve OS and DFS in elderly patients, with head and neck cancer in locally advanced stage, as shows in the literature. Further analysis of compliance and comorbidity, limiting the administration of chemotherapy prescribed, may allow identificaion of subgroups where the cCT-RT proves a significant effectiveness.

CO024

CLINICAL OUTCOMES AND CLINICAL/BIOLOGICAL PROGNOSTIC FACTORS IN ELDERLY PATIENTS WITH GLIOBLASTOMA

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Aims: To investigate the impact of co-morbidities and other clinical and biological factors on overall survival (OS) of elderly patients with newly diagnosis of glioblastoma (GBL) treated with chemo-radiation in order to identify the prognostic parameters that can guide the therapeutic choice.

Methods: From January 2013 to December 2017, 34 patients, with newly diagnosis of GBM were treated with postoperative radiotherapy, with concomitant and adjuvant chemotherapy with Temozolomide (TMZ). Twenty one patients received 60 Gy in 30 fractions (but one did not finish the treatment), 9 received 45 or 40,05 Gy in 15 fractions and 4 patients with 25 or 30 Gy in 5 fractions. Charlson Index Co-morbidity (CCI) was used to assess the co-morbidities and Prognostic Nutritional Index (PNI) score was calculated to evaluate the nutritional and immune status of these patients. Both parameters were linked to the clinical outcomes. Survival analyses were performed by the Kaplan-Maier and influence of CCI and PNI by log-rank test.

Results: In our study the median age was 70 years (range 65-79) and mean Karnofsky performance status was ≥ 70. The median OS was 12.1 months (range 8.0-22.5) and median progression free survival (PFS) was 12.1 (range 10.3 +∞). At univariate analysis, KPS and type of surgery were associated with OS (p=0.0339 and p=0.00782) and only the type of surgery with PFS (p=0.0182). Using log rank test we identified as the optimal PNI cut-off level the value of 42; the best cut-off value of CCI was 2 for OS and 3 for PFS. Univariate analysis showed that 14 patients with a PNI< 42 had a median survival of 13.10 months versus 8.38 months for those patients with a PNI ≥ 42 (p=0.63). The 1 year OS rate for patients with a PNI < 42 was 25% while the corresponding value for patients with PNI > 42 was 54%. Univariate analysis showed that 9 patients with a CCI > 2 had a median survival of 8 months versus 14.2 months for those patients with CCI<2 (p= 0.0766). Patients with CCI≥ 3 showed a median PFS of 5.9 months versus 12.3 months for those patients with CCI<3 (p=0.0113).

Conclusions: Our analysis showed that CCI and PNI are strong predictive parameters of OS in elderly patients with GBL treated with standard therapy. Use of these parameters can be useful to select elderly patients can be treated with standard therapy or those patients that can beneficed of palliative approach alone.

CO025

ASSESSMENT OF SEXUAL FUNCTION AND QUALITY OF LIFE IN ENDOMETRIAL CANCER PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY

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Aims: Endometrial cancer (EC) is the most common genealogic malignancies in developed countries. Treatment choice for EC is stage dependent and includes surgery, with or without chemotherapy followed by pelvic radiotherapy (RT) and/or vaginal brachytherapy. The objective of this study was to evaluate the quality of life (QoL) and sexual function of women ≤ 65 years affected by EC and undergone to adjuvant EBRT +/- vaginal brachytherapy using EORTC QLQ-EN24 questionnaire.

Methods: We selected from our records 29 women ≤ 65 years with EC undergone to surgery and adjuvant radiotherapy from December 2010 to December 2017. We administered an Italian version of the EORTC QLQ-EN24 questionnaire. The questionnaire contains 24 items divided into two sections. In the first section, questions are aimed at evaluating genitourinary symptoms, fecal incontinence and body image; the second section is focused on sexual and vaginal functioning. For each item, patients could assign a score from 1 (not at all) to 4 (very much). Patients could compile independently the questionnaire or, if necessary, with the physician help. In addition two more questions were submitted to patients to evaluate feasibility and utility of the assessment. The questionnaire was administered during follow up visit after 3 months to the end of radiotherapy after acute toxicity resolution.

Results: Based on selection criteria, we enrolled 29 patients, in regular follow up. Twenty-three of 29 selected patients answered the questionnaire with a compliance of 79%. The median age was 60 years. Fifty-seven percent of our sample (13/23) was sexually active after treatments. Answers were reported in Table 1. We highlight that the majority of the first section answers (92%) were 1 (not at all) or 2 (a little). Considering the second section of questionnaire, the 76% of sexual active patients reported vaginal dryness and the 77% judged sexual activity little or not at all enjoyable. The totality of patients expressed a favorable opinion about the feasibility and utility of the questionnaire.

Conclusion: The EORTC QLQ-EN24 questionnaire is a useful and simply method to assess QoL in endometrial cancer patients. Sexual dysfunctions after adjuvant RT resulted to be an issue of some concern for our selected patients.

Table 1. Patients answers.

	NO	POCO	MOLTO	MOLTISSIMO
1 Ha avuto crampi addominali?	15	6	2	0
2 Ha avuto problemi intestinali (diarrea, stipsi)?	12	7	3	1
3 Ha presentato sangue nelle feci?	22	1	0	0
4 Ha urinato con maggiore frequenza?	10	8	4	1
5 Ha avuto bruciore o dolore al passaggio delle urine?	15	6	2	0
6 Ha avuto perdite di urine?	15	7	1	0
7 Ha avuto difficoltà a svuotare la vescica?	17	4	1	1
8 Ha avuto gonfiore di una o entrambe le gambe?	19	4	0	0
9 Ha avuto dolore alla schiena?	15	7	0	1
10 Ha avuto formicolio o intorpidimento alle mani o ai piedi?	16	4	3	0
11 Ha avuto irritazione o indolenzimento vaginale o vulvare?	12	9	0	2
12 Ha avuto perdite vaginali?	17	6	0	0
13 Ha avuto sanguinamento vaginale?	23	0	0	0
14 Ha avuto vampate o sudorazione intensa?	12	10	0	1
15 Si è sentita meno attraente fisicamente a causa della malattia o del trattamento?	16	4	3	0
16 Si è sentita meno femminile a causa della malattia o del trattamento?	16	6	1	0
17 Si è sentita insoddisfatta del suo fisico?	15	5	2	1
18 Si è preoccupata che i rapporti sessuali potessero essere dolorosi?	16	5	1	1
19 E' stata sessualmente attiva?	9	12	1	0
	NO	POCO	MOLTO	MOLTISSIMO
20 Ha avvertito secchezza vaginale durante il rapporto sessuale?	3	4	4	2
21 Ha avuto l'impressione che la Sua vagina fosse meno profonda?	6	4	2	1
22 Ha avuto l'impressione che la Sua vagina fosse più stretta?	4	6	2	1
23 Ha avuto dolore durante i rapporti sessuali o altre attività sessuali?	5	5	2	1
24 Ha trovato piacevole l'attività sessuale?	2	8	3	0

CO026

SHOULDER GIRDLE IMPAIRMENT AFTER ADJUVANT RADIOTHERAPY FOR BREAST CANCER: AN ALGORITHM PROPOSAL FOR A PRESERVATION STRATEGY

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Aims: Pain and functional impairment of the ipsilateral shoulder girdle in patients who underwent surgery and radiotherapy (RT) for breast cancer (BC) is a reported late toxicity. Herein, we describe a correlation with dosimetric parameters and propose an algorithm for sparing strategies.

Methods: 111 patients (pts) treated for BC underwent complete physical and multidimensional evaluation by physiatrist and radiotherapist during follow up. Pts with severe arthrosis and/or rheumatologic diseases were excluded. A scapula-humeral articulation (SHA) standardized contouring was performed retrospectively on Eclipse®. A possible correlation between functional impairment at Disability of the Arm, Shoulder and Hand (DASH) Score, Range of Motion

(ROM) and dosimetric parameters (MeanDose and Dmax) was investigated on both treated (TA) and healthy arms (HA). Statistical analysis results were summarized into a proposal of algorithm for sparing SHA.

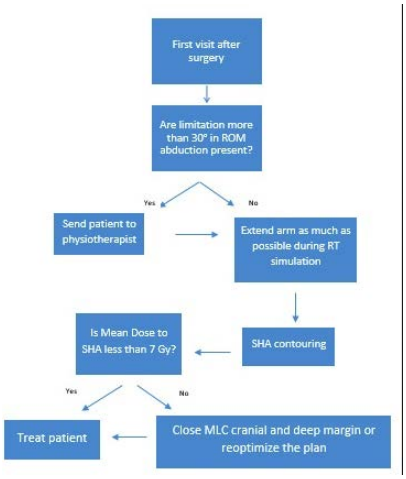

Figure 1.

Results: 111 patients were evaluated. Mean age was 60 years (41-85). 110 pts (99%) underwent axillary surgery with breast surgery. Fifty-two pts (46.8%) presented a reduction of ROM abduction on the TA at the observational analysis. Mean ROM abduction reduction was 13°06' (0-100°). DASH score results were: excellent in 79 pts (71.2%); discrete in 15 pts (13.5%); good in 15 pts (13.5%); sufficient in 2 pts (1.8%). Median Dmax at SHA was 18 Gy (0.22-51.9) and median MeanDose at SHA was 2 Gy (R 0.04-24.32 Gy). Univariate analysis showed a linear correlation between DASH Score and ROM of Abduction of TA (△=-0,7), ROM of Abduction and ROM of Flexion in TA (△=0.8), ROM of Abduction and ROM of Flexion in HA (△=0.8). A difference in ROM abduction between the two arms was found at Chi-square test ($p<0.05$ at $\chi 2$ CI = 95%). Cox's Linear Regression confirmed the correlation between DASH score and ROM abduction on TA ($p<0.0001$). Multivariate analysis confirmed a correlation between MeanDose and Age ($p<0.05$), DASH score ($p=0.006$) and ROM abduction on TA ($p=0.005$). The MeanDose > 7Gy and ROM abduction >30° were found related with DASH score reduction of level in our series.

Conclusions: This generating hypothesis study introduces an algorithm using for sparing SHA toxicities and improve quality of survivorship. ROM evaluation at first contact after surgery, early physiotherapy, standard contouring and planning adaptation represent possible indications to preserve SHA. Further prospective studies are needed to confirm results.

CO027

QUALITY OF LIFE IN THE FIRST FIVE YEARS AFTER RADICAL RT FOR PROSTATE CANCER: RESULTS FROM A PROSPECTIVE OBSERVATIONAL TRIAL

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Aims: To analyze the evolution of Quality of Life (QoL) in the first 5 years after RT for prostate cancer (PCa) as determined by EORTC QLQ-C30 vers. 3.0 (ERTC-QLQ).

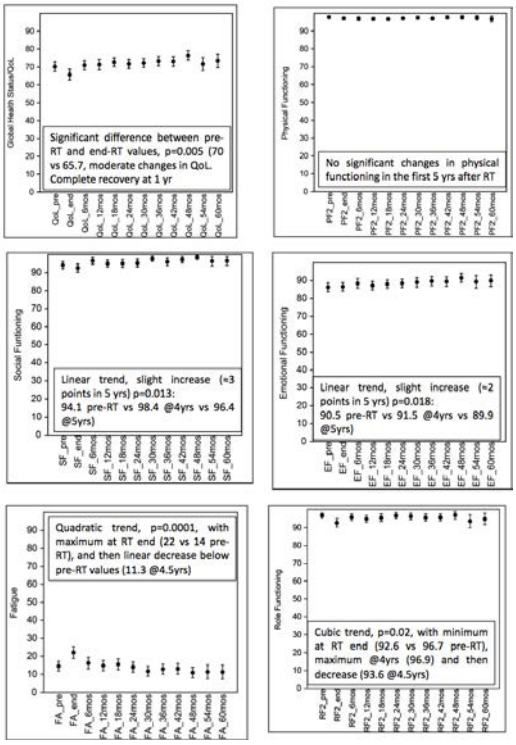

Figure 1.

Patients and Methods: Patients (pts) enrolled in an observational trial aimed at evaluating toxicity and QoL after radical radiotherapy (RT) for PCa were included RT-induced changes in QoL were assessed by means of EORTC-QLQ, which includes QoL scales evaluating Global health status (QL2), functional scales and Symptom scales. For the purpose of this analysis, variations of QL2, Physical functioning (PF2) , Social functioning (SF), Emotional functioning (EF) and Role functioning (RF2) were evaluated. Among symptoms, only Fatigue (FA) was selected. Questionnaires were filled in before RT, at RT end and then every 6 months

till 5 years. Longitudinal evaluation of QoL in the first 5 yr after RT was analyzed by means of ANOVA for multiple measures.

Results: A total of 170 pts had data at baseline, 96 pts had at least 9/12 questionnaires and were considered for ANOVA. Mean age was 68 years (range: 46 to 83 yrs). 147/170 pts (86.5%) underwent conventionally fractionated RT at 78Gy, while 23 pts (13.5%) had hypofractionated RT (65 Gy, 2.6Gr/fr). 55.2% of pts received pelvic lymph node irradiation and 72.1% underwent neadjuvant/adjuvant hormone therapy. QoL was high before RT: median values were above 90 for all functional subscales and median global QL2 was >70. A moderate deterioration of QL2 and an increase in FA emerged between pre-RT and end of RT (p=0.005 and p=0.0001, respectively), but with complete recovery at 1 yr. No significant modification in PF2 was reported in the first 5 yrs; evolution of SF and EF over time was characterized by a linear trend with slight increase of 3 and 2 points in 5 yrs, respectively. RF presented a cubic trend with a minimum at RT end, a maximum at 4 yrs and then a decrease. Detailed description of evolution of QoL scales is presented in the Figure 1.

Conclusions: PCa pts receiving radical RT show high QoL levels before RT and no significant variations with respect to baseline QoL in the long term period (5 years). Some items (QL2, FA, RF2) exhibit, as predictable, a slightly worsening at the end of RT, but there is a complete recovery within the first year, with some aspects (SF and EF) steadily improving.

These data endorse one more time that RT for PCa is safe for this class of long surviving patients.

CO028

IATROGENIC SEXUAL DYSFUNCTION, FOLLOWING EXCLUSIVE ENDOVAGINAL BRACHYTHERAPY (BRT). A COMPARATIVE RETROSPECTIVE STUDY REGARDING THE INTRODUCTION OF A SUPPORTIVE THERAPY: THE OUTCOME OF A BETTER PERCEPTION OF QUALITY OF LIFE

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Aims: BRT treatments can cause permanent sexual dysfunction due to shortening and vaginal shrinkage induced by fibrosis and post-treatment stenosis as a permanent toxic effect. We evaluated the introduction of supportive therapy (SuBRT) vs control group (CBRT).

Methods: From January 2010 to September 2017, 207 patients histologically proven endometrial carcinoma treated with BRT exclusively, with or without supportive therapy during treatment. BRT treatment involved a total dose of 30 Gy with a daily fraction of 6 Gy. Supportive therapy: daily endovaginal lavender with clorexidina and 12 hours after endovaginal ovules of hyaluronic acid low weight. We have formulated a psychological check-list for short interview to assess quality of life and impact on sexual activity after BRT, respecting privacy. We defined following areas: 1) social relationships and personal emotions, 2) intimacy of couples and sexuality, 3) impact of treatment on sexuality, 4) relationship doctor-patient before BRT.

Results: Evaluable 199 pts.; median follow up 44 months (range 8-93); median age 62 years (40-88). Histological examination resulted 5 squamous and 194 adenocarcinoma; grading G1 for 15%, G2 for 65% and G3 for 20% of cases; all stage pT1B; lymph node status Negative in 149 (75%) and NX in other 50 (25%). Diameter of the cylinder used in 168 (84%) pts. it was 3-4 cm the remaining 31 (26%) diameter 1-2. Only 3 (1.5%) pts. disease progression. Psychological evaluation performed on 142 pts. (median age 61, range 44-71) the rest 57 not interested because not sexual active. Two groups: 69 CBRT vs 73 pts. SuBRT. First area the change of social activity recorded as “very, very much” was 33 of CBRT vs 22% of SuBRT, in the emotional state we found 42 of CBRT vs 29% SuBRT. Second area: intimacy of couple; 71 vs 49% said they had undergone change; with repercussions on her relationship 49 vs 32% and 81 vs 48% of women reported decreased sexual desire. Third area impact on sexuality: BRT changed your sex life? 46 vs 21% of SuBRT “very, very much”. With sexual intercourse painful for 73 vs 48% of the interviewees and to the question “Are sexual relations satisfactory?” 91 vs 60% of respondents answered “NO”. Fourth area when we asked “Have you been informed that BRT could have an impact on sexuality?” 58 vs 80% of the patients answered “YES” while at the question “Did they advise you to have sex with your partner?” 71% vs 81 of the women received these indications. Unexpectedly, 13 vs 1% SuBRTof patients explicitly requested psychological support.

Conclusions: Regardless of grading and lymph node depletion, BRT is effective in preventing disease recurrence. Although cylinders with larger diameter are used, the problem of post BRT toxicity management remains. Introduction of supportive therapy during treatment and best patient doctor relationship reduced the impact on quality of life of these patients.

CO029

LONG-TERM CLINICAL AND VOICE OUTCOME IN PATIENTS WITH EARLY STAGE GLOTTIC CANCER TREATED WITH EXCLUSIVE RADIOTHERAPY VERSUS LASER MICROSURGERY

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Aims: Oncological outcome of patients affected by early glottic cancer (EGC) treated with radiotherapy (RT) either Laser microsurgery (LM) is similar, but

voice quality (VQ) outcome and voice quality handicap following these treatment modalities are not clear. The aim of our study is to report clinical outcomes focalizing on voice quality of patients who received either RT or LM.

Methods: We evaluated 45 EGC patients (Tis, T1 and T2 stages) submitted to primary RT or LM between 2008-2017. Overall survival (OS), progression free survival (PFS) and radiation induced toxicities according to CTCAE v4.0 scale were evaluated. For a subsample of this ECG population a prospective VQ evaluation is ongoing. Enrollment of patient for VQ evaluation will include at least 20 patients, performing multi-modality voice analyses. Voice evaluation includes: Voice Handicap Index (VHI-30), objective analysis using PRAAT software and perceptual rating performed by speech therapist (GRBAS scale). A clinical examination is performed jointly with radiation oncologist, otolaryngologist and speech pathologist, involving laryngeal evaluation with videostroboscope (VS) and laryngoscope. Statistical analysis will be performed to compare voice outcome and clinical evaluation of larynx in two treatment modalities (RT and LM).

Table 1, 2, 3, 4.

Table 1. Summary of averages obtained from VHI-30 questionnaire in RT and LM groups

Variable	RT group	LM group	For each scale	Global
Functional	7,75 (3-13)	25,5 (22-29)	Normal (≤10)	Normal (<30)
Physical	11,25 (4-26)	26,5 (18-35)	Mild (11-20)	Mild (31-60)
Emotional	13 (2-24)	31 (22-40)	Moderate (21-30)	Moderate (61-90)
Global	**32 (10-63)**	**83 (62-104)**	Severe (31-40)	Severe (91-120)

Table 2. Summary of GRBAS in RT and LM groups

Variable	RT group (%)	LM group (%)
Overall grade		
Normal	0	0
Mild	50	0
Moderate	33,3	50
Severe	16,7	50
Roughness		
Normal	16,7	0
Mild	33,3	50
Moderate	16,7	50
Severe	33,3	0
Breathiness		
Normal	50	0
Mild	33,3	0
Moderate	16,7	50
Severe	0	50
Asthenia		
Normal	50	0
Mild	33,3	0
Moderate	16,7	50
Severe	0	50
Strain		
Normal	83,3	50
Mild	16,7	50
Moderate	0	0
Severe	0	0

Results: A total of 30 patients, average age of 73 years (range 52-86), received RT with a total dose of 66-70 Gy, 2Gy/day, using 3-dimensional conformal technique. 15 patients received LM. Overall tumor stage distribution was: Tis (13.3%), T1 (83.3%), and T2 (3.34%). All patients except one achieved a complete response after definitive RT. The median follow-up was 53 months (range 5-115 months), but LM patient had a shorter follow-up (range 6-24 months). In RT group mean OS and PFS were 52 and 50 months, 18 months both OS and PFS for LM group; 1 patient experienced disease failure 24 months after radical RT. No long-term RT toxicities greater than G2 occurred. From the original sample of 45 patients, in the context of ongoing VQ analyses 8 patients were evaluated to date. In tables we reported the summary of average VHI-30 and GRBAS scores, vocal acoustic analysis and VS evaluation in both groups.

Conclusions: The preliminary results from the limited recorded data seem to show a more favorable voice outcome in RT patients. We attempt to complete this study and to perform a comparative statistical evaluation RT vs LM group, in order to confirm this result.

Table 3. MPT and vocal acoustic analysis of LM and RT groups

Variable	RT group (mean ± SD)	LM group (mean ± SD)
Fo (Hz)	140,5 ± 24,19	185,1 ± 40,60
MPT (sec)	10,16 ± 3,06	10,51 ± 6,34
Jitter (%)	1,85 ± 0,51	0,78 ± 0,17
Shimmer (%)	10,43 ± 8,03	10,52 ± 5,69
HNR(dB)	13,44 ± 8,55	14,55 ± 2,51

Fo (Hz): Fondamental frequency; MPT: Maximum fonation time, Jitter (%): Frequency variation; Shimmer (%): amplitude variation; HNR (dB): Harmonics -to-Noice ratio.
Treshold for pathologic voice: Jitter ≥ 1.04 %, Shimmer ≥ 3.81 %

Table 4. Laryngeal videostroboscopy evalution in RT and LM groups

Variable	RT group (%)	LM group (%)
Vocal cord motion (Normal vs reduced)	66,7 vs 33,3	50 vs 50
Vocal cord vibration (Normal vs increased)	66,7 vs 33.3	50 vs 50
Edema/erythema (normal vs edema)	66,7 vs 33,3	0 vs 100
Glottic closure (complete vs incomplete)	66,7 vs 33,3	0 vs 100

CO030

QUALITY OF LIFE IN SURVIVORS HEAD AND NECK CANCER USING UW-QOL AFTER INTENSITY MODULATED RADIATION THERAPY WITH TOMOTHERAPY

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Aims: Radiotherapy in head and neck is associated with side effects that impact on the quality of life of patients. In this abstract we have analyzed patients who had a squamous carcinoma in oropharynx nasopharynx, mouth, tongue and larynx treated with IMRT Tomotherapy simultaneous integrated boost to primary tumor and cervical lymph nodes.

Methods: We have analyzed 76 patients, aged 31-89, with 23 months follow-up who have received simultaneous integrated boost to primary tumor and cervical

lymph nodes. We used University of Washington quality of life scale with a direct interview of all partecipants. The UW-QOL questionnaire consists of 12 domains that pertain to the degree of quality of life in the categories of pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder function, taste, saliva, mood, and anxiety.

Results: 23 months after completed radiotherapy 24% of patients rated their overall quality of life as "good" and 7,8% "very good". 32% consider their quality of life "fair" and 16% "poor". Most frequent discomforts are related to changes in saliva production which prevent normal swallowing and to difficult chewing due to loss of dental elements. Also in 55% we observed a relevant impairment in daily life and recreational activities. Two important items of the UW-QOL concern mood and anxiety: 34% of patients has reported to be neither in a good mood nor depressed about cancer and 41% is anxious about it.

Conclusions: IMRT with Tomotherapy is well tolerated in head and neck cancer patients, but their quality of life remain still unsatisfactory at long term follow-up because of mood and anxiety related to cancer independently from the type of therapy administred (Radiotherapy, Surgery and/or Chemiotherapy). Further studies are needed to intensify psychological and social support.

CO031

RADIOTHERAPY-RELATED ALOPECIA IN PATIENTS TREATED FOR BRAIN TUMORS MAY BECOME TRANSIENT: RESULTS OF A SCALP-SPARING VMAT TECHNIQUE

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Aims: Radiotherapy (RT) may induce permanent hair loss with a huge psychological impact. Sparing the scalp during focal cranial RT for brain tumors is a challenging issue because the scalp is often strictly adjacent to the target. Moreover, clear constraints for this structure are not available in the literature. The aim of this study is evaluating dosimetry of areas of transient and permanent alopecia for patients with brain tumors treated with a scalp-sparing approach in conventionally fractionated VMAT.

Methods: The scalp was defined as a region of interest (ROI) including the tissue between the skin and the skull and avoiding the hairless skin of the face and the neck. At the moment of the end of RT and during the follow-up, the patient was asked to wear the thermoplastic mask so that the areas of alopecia were defined with a wire. Then, a CT scan was performed to the mask and these images were coregistered to the simulation CT to obtain a dosimetric evaluation in areas of alopecia. Grade of alopecia was assessed according to CTCAE version 4.0. For all the patients clinical data (age, gender, smoking, histotype of tumor, chemotherapy, antiepileptic therapy, RT prescribed dose) were collected.

Figure 1.

Results: A total of 101 patients were included in the study. All the patients received a limited-volume RT with conventionally fractionated VMAT technique. In the inverse planning process constraints for the scalp were set. 5 patients who were treated for deep tumors did not develop any area of alopecia. Their scalp received very low doses (16 Gy <10cc; 20 Gy <5cc; 30 Gy <1cc). At the end of RT, 96 patients out of 101 developed acute alopecia (G1 n=11; G2 n=52; G1+G2=33). Mean Dscalp without alopecia was 7.7 Gy (range 0.9-25 Gy), whereas Dscalp in areas of alopecia G1 was 16.6 Gy (range 1.6-36.1 Gy) and Dscalp in areas of alopecia G2 was 20.2 Gy(range 1.9-41 Gy). Unexpectedly, alopecia at the end of RT developed also in areas that received low doses. Trichological follow-up was available for 64/101 patients. 60 patients (93.8%) completely recovered from alopecia. Median time to recover was 5,6 months (range 59-447). Only 4 patients (6.2%) had permanent alopecia in areas that received very high doses (mean D max to the scalp was 57,7 Gy).

Conclusions: Treating patients with this Scalp sparing approach alopecia at the end of radiotherapy may develop also in areas that receive low doses, but in the majority of patients complete recovery will be obtained within some months.

CO032

EVALUATION OF QUALITY OF LIFE IN MEN WITH PROSTATE CANCER AFTER RADIATION THERAPY

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Aims: To evaluate health-related quality-of-life (QOL) outcomes in patients with prostate carcinoma after radiotherapy (RT) at a time-point during follow-up.

Methods: QOL outcomes were assessed using the FACT-P QOL questionnaire administred during a whole month at a time-point during follow up. Mean scores of individual domains/scales were compared between different categories of patients (men in hormonal therapy or not, men who had undergone to radical prostatectomy and adjuvant RT or RT alone, men who had undergone to RT to pelvic nodes and men after RT to prostate or prostatic bed alone) using 't' test.

Results: 60 patients (mean age 65.2 years) were included in the analysis. The median follow up was 46 months (range 3-134). 16 patients (25.8%) were taking hormonal therapy at the time of the examination, 26 patients (42.6%) underwent surgery before RT and 35 patients (57.4%) RT alone, and in 22 patients (36.1%) RT was delivered also to the pelvic lymph nodes. Several general (emotional functioning, role functioning, social contact) as well as prostate cancer-specific (sexuality, bowel and bladder function) QOL domains were analysed. Importantly, all the QOL domains were worse in patients in hormonal therapy, but only the functioning QOL domains in a significant way ($p<0.05$). Prostatectomy patients reported worse outcomes in bladder function and emotional well-being, but the difference wasn't statistically significant. There were no differences in the level of sexual activity between patients undergoing surgery and not, even if 16 pateints (26.6%) didn't answer the question. Moreover, we didn't find QOL discrepancies between patients who had undergone to RT to pelvic nodes and men after RT to prostate or prostatic bed alone. There were no differences in all QOL domains in patients with > 75 years, even if emotional weel being is worse in the younger group with a trend towards statistically significant. Patients with a follow up longer than 6 years didn't report worse QOL scores than those with a follow up of 6 years or less.

Conclusions: At a time point during follow up we didn't find significant discrepancies for all the QOL domains in the different categories of patients except for patients in hormonal therapy, who reported worse score in the functioning QOL domains. An analysis on a larger sample of patients is needed to confirm these preliminary data.

CO033

11C- METHIONINE PET/CT IN PATIENTS WITH ADENOID CYSTIC CARCINOMA TREATED WITH CARBON IONS RADIOTHERAPY

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Background: MRI is the mainstay for staging and for treatment response evaluation in adenoid cystic carcinoma (ACC), whereas the role of molecular imaging is controversial. Methionine (MET) is a neutral essential amino acid for protein and polyamine synthesis and its altered metabolism plays a central role in tumor growth, resulting in an over uptake of MET in the cancer cells. It is possible to note this metabolic net¬work by PET using radiolabeled MET.

Aims: To evaluate the usefulness of MET PET in assessing treatment response, patients' outcome and survival rate in adenoid cystic carcinoma (ACC) treated with carbon ion radiotherapy (CIRT).

Methods: This is a retrospective cohort study involving 85 patients with pathologically confirmed ACC treated with carbon ions radiotherapy (CIRT) between May 2013 and May 2017 at CNAO. All patients underwent MET-PET and MRI examination before and after CIRT. MET uptake in the tumor was evaluated using SUV (max and mean), TBR, metabolic tumor volume, delta volume and delta SUV. Metabolic findings were compared with the morphological characteristics in the best response MRI (best-MRI) and in the latest MRI. Thus, we classified each MET-PET as complete metabolic response (CMR), partial metabolic response (PMR), stable metabolic disease (SMD) and progression metabolic disease (PMD) and we compared these findings to best and latest MRI classified as complete response (CR), partial response (PR), stable disease (SD) and progression disease (PD). Metabolic results were correlated with clinical outcome and patient characteristics.

Results: Considering best-MRI, SUVmax and SUVmean of primary tumor in planning MET PET were significantly higher in SD-patients vs CR patients ($p<0.01$) and in MET-PET after CIRT, SUV (max and mean) of primary tumor and TBR (max and mean) were effective in distinguishing CR from PR, SD and PD ($p<0.01$). As regards last-MRI, CR patients had lower tumor SUV (max and mean) values compared to PR, SD and PD ($p< 0.01$). Patients with metabolic response (CMR and PMR) after CIRT, had a trend to a better survival (p: 0.052) and in our analysis CMR patients survived longer (p: 0.042). There were no correlation

between MET PET findings and patients' characteristics.

Conclusions: In our study MET-PET is useful for predicting the outcomes of patients with ACC treated with CIRT.

CO034

PREDICTING GRADE 2+ ACUTE SKIN ERYTHEMA AFTER ADJUVANT BREAST CANCER RT: IDENTIFICATION OF GENE PROFILES ASSOCIATED TO INCREASED RISK OF TOXICITY

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Aims: To identify gene expression profiles (GEP) associated to increased risk of grade 2+ acute skin erythema after adjuvant breast cancer (BCa) radiotherapy (RT).

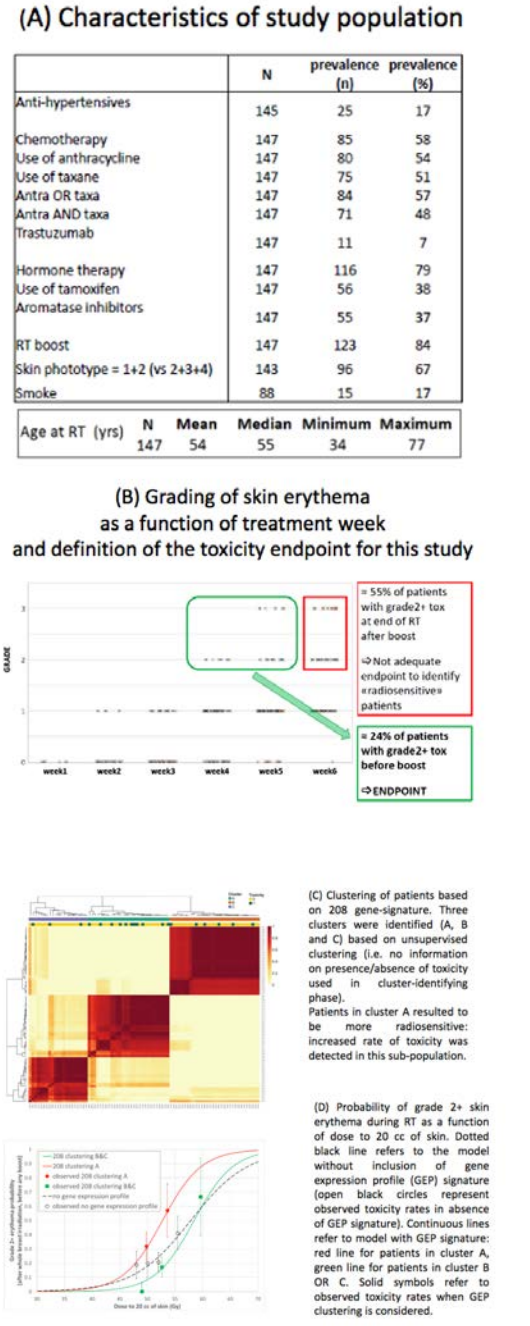
Materials and Methods: BCa pts treated with 3DCRT after breast conserving surgery were considered: 50Gy (2Gy/fr) whole breast photon RT followed in some cases by 10 or 16Gy photon or electron boost to the tumour bed. Acute skin erythema (AE) was assessed using RTOG scoring system before RT and every 5 fractions. Grade 2+ AE before boost was considered as the primary endpoint. Relevant clinical risk factors were prospectively recorded, dosimetric features were extracted from skin dose-volume histogram, with skin defined as the difference between the body contour and a 5mm inner isotropic contour from the body. Peripheral blood was obtained, RNA extracted from mononuclear lymphocytes (after in vitro expansion) and GEP determined using Illumina HumanHT-12 v4 Expression BeadChip (≈47000 probes, ≈37000 genes). Unsupervised clustering was used to reduce the dimensionality of data (partition around medoids). Dosimetric, clinical and genetic variables were included into logistic regression.

Results: 147 pts were available, 35/147 (24%) pts with grade2+ AE before boost, 82/147 pts had GEP information. Unsupervised clustering selected 208 genes identifying 3 clusters of pts: 38% toxicity in cluster A, 19% and 14% in clusters B and C, respectively (OR=5 for A vs "B OR C", p=0.01). Cluster A was mainly characterized by underexpression of genes involved in immunoregulation, inflammatory processes, antioxidant activity, cell cycle progression and differentiation.

p=0.01). The Figure 1 shows details on study population, GEP clustering and predictive model curves.

Conclusions: Gene expression profiling resulted in the identification of a signature of enhanced radiosensitivity for acute toxicity after BCa RT. This signature was included in a predictive model leading to significant improvement in calibration, likelihood and discrimination.

This study was funded by a grant of Mrs M. Bonatti and Mr G. Mameli and by the LILT Lega Italiana per la lotta contro i tumori



	N	prevalence (n)	prevalence (%)
Anti-hypertensives	145	25	17
Chemotherapy	147	85	58
Use of anthracycline	147	80	54
Use of taxane	147	75	51
Antra OR taxa	147	84	57
Antra AND taxa	147	71	48
Trastuzumab	147	11	7
Hormone therapy	147	116	79
Use of tamoxifen	147	56	38
Aromatase inhibitors	147	55	37
RT boost	147	123	84
Skin phototype = 1+2 (vs 2+3+4)	143	96	67
Smoke	88	15	17

Age at RT (yrs)	N	Mean	Median	Minimum	Maximum
	147	54	55	34	77

Figure 1.

Multivariable regression resulted in a 3 variable clinical/dosimetric/genetic model including dose to 20cc of skin (p=0.02, OR=1.4 for 1Gy increase), skin phototype (p=0.05, OR=1.9 1+2 vs >2), GEP cluster (p=0.01, OR=5 A vs B+C). Inclusion of GEP clustering improved likelihood (-86.6 vs -78.9, p=0.05), calibration slope (0.86 and R2=0.01 vs 0.93 and AUC (0.62 vs 0.83,

CO035

RADIOMIC: PREDICTION OF ACOUSTIC NEUROMA RESPONSE TO THE CYBERKNIFE TREATMENT

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Aims: The objective of this study is to analyse MR images acquired before Cyberknife treatment, to predict the response and avoid unnecessary radiosurgery for patient.

Materials: T1 weighted MR images of 38 patients presenting an acoustic neuroma treated with Cyberknife® at our institute (52.6% responders with Volume Reduction) were selected and analysed. Analysed images were acquired on 1.5T machines with contrast enhanced T1-weighted sequences in the axial plane. Semi-automatic tumour segmentation was carried out on MR images using the 3DSlicer image analysis software. Shape-based, intensity-based and texture-based features were extracted. An evolutionary algorithm (a TWIST system based on KNN algorithm) was used to subdivide the dataset into training and test set and select features yielding the maximal amount of information. After this pre-processing, a predictive model based on a training-testing crossover procedure was developed. The best neural network obtained was a 2-layers feed forward back propagation algorithm with 8 input variables containing the maximal amount of information.

Results: The neural network was used twice inverting the training/testing set. In the first analysis the sensitivity was 100%, while the specificity, was 77.78%. These two results gave a global accuracy of 88.89%. In the second analysis the sensitivity was 61.54% and the specificity 100%, with a global accuracy of 80.77%. The mean value of the global accuracy was 84.83%.

Conclusions: The obtained results show that Machine Learning coupled with radiomics has a great potential in distinguishing responders with volume reduction from responders without volume reduction to radiosurgery, before the treatment.

CO036

CREO PROJECT (COLLABORATIVE MULTI-SOURCES RADIOGENOMICS APPROACH FOR PERSONALIZED ONCOLOGY IN NON-SMALL CELL LUNG CANCER): EXPLORATORY RADIOMICS FOR PREDICTING ADAPTIVE RADIOTHERAPY

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Aims: The primary goal of precision medicine is to minimize side effects and optimize efficacy of treatments. Recent advances in medical imaging technology allow the use of more advanced image analysis methods beyond simple measurements of tumor size or radiotracer uptake metrics. The extraction of quantitative features from medical images to characterize tumor pathology or heterogeneity is an interesting process to investigate, in order to provide information that may be useful to guide the therapies and predict survival. The aim of this study was to investigate whether the radiomic features of initial imaging were able to predict tumor reduction during radio- chemotherapy (RCT) in patients with stage III non-small cell lung cancer (NSCLC).

Methods: We studied 91 patients with stage III NSCLC treated with concurrent RCT: 50 patients were treated at radical dose with adaptive approach (adaptive group), 41 patients underwent radical concurrent RCT in the same period, but who did not achieve target reduction (non-adaptive group). Clinical characteristics of these patients are listed in Table 1. The characteristics investigated were extracted from the initial simulation CT on which the Clinical Target Volume was manually delineated by expert radiation oncologists, providing a 3D ROI. Given each 3D ROI in the images, we computed the radiomic features using our in-house software tool coded in MATLAB (Mathworks Inc, MA, U.S.A.), taking into consideration 12 statistics features and 230 textural features extracted from the CT images. In our study, we used an ensemble learning method to classify patients' data into either the adaptive or non-adaptive group during RCT on the basis of the starting CT simulation. All the experiments were conducted according to a 10-fold cross validation, i.e., a model validation technique which provides a nearly unbiased estimate using only the original data.

Results: Figure 1 shows the final performance, the area under the receiver operating characteristic curve (AUC). To the best of our knowledge, this is the first trial investigating radiomic strategy to predict tumor shrinkage during RCT and our data suggests that a specific signature can be identified (AUC 0.82).

Conclusions: The initial results of CREO Project obtained are an original and innovative topic that opens up new research in the field of personalized medicine in radiation therapy. The identification of the external validation dataset is actually ongoing.

Table 1. Patients' characteristics.

	Adaptive group (%) (n=50)	Non-Adaptive group (%) (n=41)	Total (n=91)
Age:			
< 70 years	19 (38%)	18 (44%)	37 (41%)
≥ 70 years	31 (62%)	23 (56%)	54 (59%)
Sex:			
Male	39 (78%)	30 (73%)	69 (76%)
Female	11 (22%)	11 (27%)	22 (24%)
Histology:			
Adenocarcinoma	16 (32%)	23 (56%)	39 (43%)
Squamous	28 (56%)	15 (37%)	43 (47%)
NOS	3 (6%)	3 (7%)	6 (7%)
No histologic subtype available	3 (6%)	0 (0%)	3 (3%)
Stage:			
IIIA	29 (58%)	26 (63%)	55 (60%)
IIIB	21 (42%)	15 (37%)	36 (40%)
Chemo before RCT:			
Yes	23 (46%)	28 (68%)	51 (56%)
No	27 (54%)	13 (32%)	40 (44%)
Concurrent chemo:			
Duplets	19 (38%)	20 (49%)	39 (43%)
Mono	31 (62%)	21 (51%)	52 (57%)

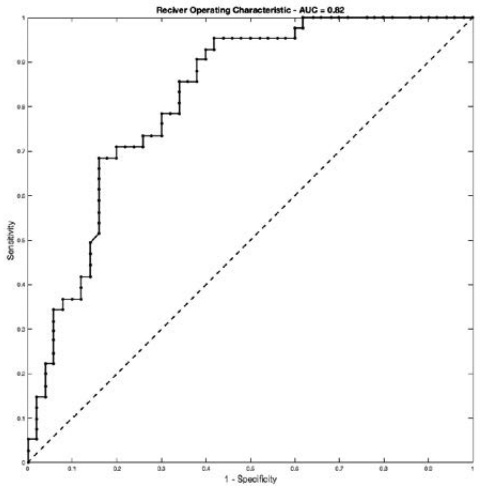

Figure 1. ROC curve of the proposed system.

CO037

RADIOMICS BY NEURAL NETWORKS FOR HISTOLOGICAL CHARACTERIZATION OF MENINGIOMAS: POSSIBLE IMPLICATION FOR SURGICAL PROCEDURE AND ADJUVANT RADIOTHERAPY

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Aims: Most meningiomas are classified as benign lesions (WHO grade I) while the other 20% are reputed high-grade tumors (WHO grade II-III). A preoperative MRI assessment is crucial because it might aid important prognostic informations for the morbidity, mortality, recurrence rates, surgical planning and following adjuvant radiotherapy planning. We propose a MRI based Convolutional Neural Network (CCN) model to detect meningioma WHO grade.

Methods: 80 meningiomas cases were reviewed for preoperative Magnetic Resonance Imaging (median age: 61 years, WHO grade I:55 patients , WHO grade II-III: 25 patients) on a 1.5 Tesla Signa unit (General Electric and Philips Healthcare). Axial T2-weighted images, ADC and T1 weighted images with contrast enhancement, previously imported into treatment planning console, were manually contoured by a fully trained neuroradiologist and the gross tumor volume (GTV) was obtained. The vitreal body of the eye was also contoured to obtain a signal intensity normalization. A Convolutional Neural Network (CNN) with 3 convolution layers was then trained on normalized as well as raw MRI slices to classify the hystological grade. The dataset was split in train (65%), validation (15%), testing set (20%). The testing set never entered the training process. Accuracy and performance parameters by slice and by patient were obtained from 100 testing iterations. A patient was considered well classified if at least 50% of its slices were correctly classified.

Results: The CNN trained on T2-WI showed the best accuracy values on testing set. -Accuracy values on normalized images: mean by-slice accuracy on testing set: 0.852 (0.782-0.905); mean accuracy per-patient classification on testing set: 0.894 (0.872-0.915). - Accuracy values on not normalized images: Mean by-slice accuracy on testing set: 0.813 (0.737-0.874); Mean accuracy per-patient classification on testing set: 0.874 (0.853-0.895)

Conclusions: Convolutional Neural Network is a rather accurate and reliable tool able to make predictions on meningiomas WHO grade histology based on presurgical MRI assessment without the need for explicit feature extraction. The per-patient accuracy is higher after normalization procedure but not significantly different from un-normalized images. The possibility to detect histology only using MRI could have important implications for operated, multifocal, not operable or recurrent lesions before radiotherapy planning, above all in doubtful cases.

CO038

INCLUSION OF GENETIC FEATURE IN NORMAL TISSUE COMPLICATION PROBABILITY MODELS AFTER RADIOTHERAPY FOR PROSTATE CANCER

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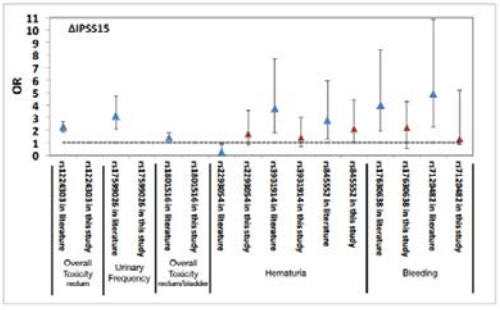
Aims: Inclusion of molecular markers into validated models for prediction of toxicity (tox) after prostate cancer (Pca) radiotherapy (RT) could improve the probability to identify radiosensitive patients (pts) and provide intervention to reduce side effects. We evaluated the effect of Single Nucleotide Polimorfisms (SNPs) inclusion in a previously published predictive models for acute urinary tox (Palorini 2016)

Methods: 8 A cohort of pts treated with radical RT for PCa was considered. A multivariable model predicting severe worsening of acute urinary symptoms of at least 15 points (ΔIPSS≥15) as assessed by the International Prostate Symptom Scores (IPSS) was applied to this population. For each pt, we calculated the predicted tox risk using their clinical-dosimetric features. The distribution of residuals (observed tox – predicted tox probabilities) was used to select pts whose tox were not correctly predicted by the model. That is, pts who showed tox but had very low predicted probabilities (radiosensitive pts) or, vice versa. 108 pts were identified for genetic investigations. A panel of selected published SNPs (rs17599026, rs1801516, rs12243039, rs3931914, rs2293054, rs845552, rs7120482 and rs17630638) associated to increased risk of tox after RT of PCa was considered. Between October 2016 and May 2017, a peripheral whole blood EDTA sample was collected from each pt for DNA extraction.

Results: Severe acute urinary tox (ΔIPSS≥15) was reported in 8/108 pts (7.5%). Rounding this value, we chose 10% model predicted probability as discriminative cutoff to "label" a patient as "at high risk" of tox: so pts with predicted tox probability ≤10% were classified as "at high risk" of tox while pts with predicted probability >10% were classified as "at low risk" of tox. The 8 pts with severe acute urinary tox had predicted probability ≤10%, when using the clinical-dosimetric model (without genetic information). When introducing the genetic information 3/8 (37.5%) are re-classified as "at high risk" of tox, thus highlighting the enhanced ability of the genetic-extended model of classifying pts as "at high risk" of tox

Conclusions: SNPs already identified as associated with increased risk of tox were confirmed in this validation study. They could improve clinical utility of previously developed clinical-dosimetric NTCP models. Development of such biologically-extended predictive models could prompt personalization of RT, with impact on the patients' Quality of Life

Odds Ratios for acute severe urinary toxicity for the SNPs analysed in this study: values reported by the literature vs values in this trial.



Normal Tissue Complication Probability (NTCP) model for prediction of acute severe urinary toxicity as a function of the dosimetric parameter (DSHwa8.5=absolute bladder surface receiving more than 8.5 Gy/week, Palorini RO 2016) and of presence of 0, 1 or 2 risk SNPs (rs3931914, rs845552)

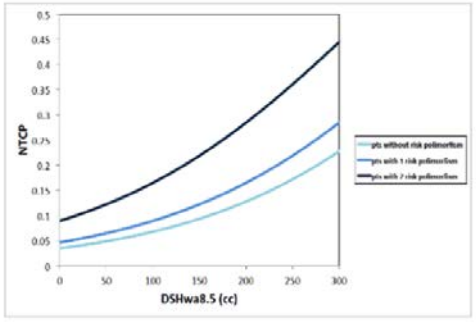


Figure 1.

CO039

DELTA RADIOMICS FEATURES ANALYSIS FOR THE PREDICTION OF PATIENTS OUTCOMES IN GLIOBLASTOMA MULTIFOME (GLI.F.A. PROJECT): AN OBSERVATIONAL PROSPECTIVE MULTI-INSTITUTIONAL STUDY

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Aims: Glioblastoma multiforme (GBM) is the most frequent and most lethal primary brain tumors in adults. The correlation between tumor images features and clinical outcomes has already been the subject of different studies conducted in order to create predictive models. A multi-centric study, the GLI.F.A. (Glioblastoma: advanced Imaging Features Analysis) Project, was performed for a comprehensive analysis of GBM heterogeneity to increase the power of decision support models.

Methods: In this first phase of the study, the imaging features of preoperative MRI in adult patients affected by GBM, that undergo to surgery and standard chemo-radiotherapy according to EORTC 26981-22981-NCIC trial, were analyzed. Gross Tumor Volume (GTV) was contoured in the T1 post contrast and T2-FLAIR weighted images. In order to standardize data collection we created a brain cancer ontology and developed the platform for sharing and combining multiple datasets (SPIDER BOA System for Patient Individual Data Entry and Recording Beyond Ontology Awareness). Therefore, we have used the MODDICOM software for the extraction of preoperative MRI features. The significance of the radiomic features was evaluated on the T2-Flair and T1mdc images through the Wilcoxon Mann Whitney test, Log-rank test for Kaplan-Meier curves, considering Overall Survival, Progression Free Survival and Response to radio-chemotherapy (RTCT) as main outcomes.

Table 1.

MRI sequence	Outcome	Feature	Feature order	p-value
contrast-enhanced T1 weighted	OS	Grey level non-uniformity normalised	II	0.02
		Run entropy	II	0.03
	PFS	Inverse difference normalised	II	0.007
		Inverse difference moment normalised	II	0.0025
		First measure of information correlation	II	0.014
	Response to RTCT	Uniformity	I	0.022
T2-FLAIR weighted	OS	Kurtosis	I	0.06

Results: We collected data of 27 patients with a median age of 61 years (range: 45-75). At the time of the analysis 20 patients were still alive. Using the implemented software 94 features were analyzed. Significant features divided by MRI sequence and outcome are reported in Table 1. The second order textural features showed the most significant result for OS and PFS on contrast-enhanced T1, while the first order statistical features resulted significant for response to RTCT on T1 and for OS on T2-FLAIR weighted MRI.

Conclusions: Preliminary univariate analysis of radiomics features related to survival and clinical outcomes suggest that there is a valuable possibility to stratify patients according MR based quantitative imaging. A higher number of patients, multivariate analysis and external validation are next steps for getting reliable predictive models.

CO040

TUMOR SHRINKING DURING ADAPTIVE CHEMO-RADIATION IS A BIOMARKER FOR OUTCOME IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (LA-NSCLC)

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Aims: To investigate the relationship between the shrinkage of tumor volume during treatment and long-term results, and the rate of tumor shrinking as predictor of outcome and survival.

Materials and Methods: A matched analysis between two groups of patients who underwent concurrent chemoradiation for locally advanced NSCLC between 2012 and 2014 was performed. Patients were divided in two groups according to the occurrence of tumor shrinkage or not during treatment. Two groups of patients were identified, named Adaptive Group (AG) and Non-Adaptive Group (NAG), in case of occurrence or absence of tumor shrinkage. Then the rate of tumor shrinking as predictor of outcome was analyzed. Receiver operating characteristics (ROC) analysis was performed to analyze the predictive value of the tumor volume reduction in determining changes in survival. Patients were grouped according to the cut-off values obtained (0-29%, 30-49%, >50%). Toxicity was evaluated according to RTOG/EORTC scale. The differences between the two groups were compared by Fisher's exact test (two tail) or χ^2 when appropriate. The Progression Free Survival (PFS) and Overall Survival (OS) curves were calculated with the Kaplan-Meier method, and a log-rank test was used to carry out between-group comparisons. This study was reviewed and approved by the Institutional Review Board.

Results: Out of 91 patients, 88 could be evaluated for long term results. No differences in term of survival outcome have been reported, while a benefit in lung toxicity was recorded for AG patients. Regarding the tumor shrinkage, advantage was reported for patients with a reduction from 30 to 49% of the basal clinical target volume. The subgroup of patients with a tumor reduction between 0 and 29% and with a reducing volume > 50% obtained the worst survival (25.1 and 23,1 months, respectively). The median value of PFS was 16.5 months for patient reducing 30-49% and 7.6 and 7.4 months for patients shrinking 0-29 and >50%, respectively.

Conclusions: The present report can be considered a hypothesis generating study. Further molecular investigations are ongoing to find out correlations between molecular prognostic factors and biological aggressive-

ness of the disease. Future studies on larger populations will shed light on the existence or not of a group of NSCLC with different clinical behaviors, mirroring an unknown biological aggressiveness.

CO041

INFLUENCE OF TUMOUR MICROENVIRONMENT SIGNALS ON MIGRATION AND INVASION FEATURES OF PANCREATIC CANCER CELLS EXPOSED TO LOW AND HIGH LET RADIATION

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Aims: Several reports described that photon radiation may increase the migration and invasiveness of cancer cells surviving after radiotherapy whereas the fewer studies with carbon ions performed so far showed a different modulation. We evaluated the influence of the microenvironment released factors on cancer cell invasion analysing the effects of microenvironment released factors on irradiated pancreatic cancer cells using different radiation qualities and doses. Since significant attention has been given in the last years to the ability of individual cell to switch between mesenchymal and amoeboid mobility, we also evaluated the amoeboid-mesenchymal transition plasticity of migrating and invading Aspc-1 cells with regard to radiation dose and type.

Methods: Boyden chamber assays were used to test the migration and invasive behaviour of irradiated Aspc-1 with different cells/chemoattractants placed in the lower. Migrated cell morphology was scored as amoeboid type or mesenchymal type, and the percentage of cells of each morphological type was determined.

Results: Conditioned medium collected from irradiated tumour cells as attractant highly increased the migration ability of photons and carbon ion irradiated Aspc-1 cells suggesting a positive interaction in tumour progression induced by cell-released factors following radiation. Irradiated-Aspc-1 cells migration was then investigated seeding irradiated fibroblasts in the lower compartment: even if low doses seemed to not greatly influence cell mobility, 4Gy dose decreased of 37% and 56% when photons and carbon ions respectively were employed. The presence of unirradiated fibroblasts differently affects the invasiveness capability of irradiated Aspc-1 cells: while photons seemed to slightly increase the invasiveness of pancreatic cancer cells when co-cultured with fibroblasts, factors released from pancreatic cancer cell following carbon ions radiation appeared to induce a stronger response in fibroblasts promoting inhibition of cancer cells invasion.

Conclusions: The changes in migratory behaviour, migration and invasiveness of Aspc-1 cells that we observed, are likely due to the reciprocal release of soluble factors by cancer cells and normal fibroblasts whose production is differently modulated after high or low LET radiation. These results point out how important it is to consider the role played by tumour microenvironment when effects of radiation are evaluated.

CO042

IN VITRO EVALUATION OF THE EFFECTS OF L-DOPA PRETREATMENT ON T98G GLIOBLASTOMA CELLS KINETIC, MIGRATION AND HIGH-LET RADIATION RESPONSE

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Aims: A role of L-DOPA for the diagnosis and treatment of glioblastoma has been hypothesized. In the diagnostic field, L-DOPA can be used labelled by F-18 and visualized with Positron Emission Tomography (PET) in order to obtain more radiodiagnostic information of the disease. In the experimental therapeutic field, to improve the efficacy of Boron Neutron Capture Therapy (BNCT), L-DOPA pretreatment has recently been proposed with the aim of increasing the efficiency of Boronophenylalanine (BPA) incorporation by tumour cells. The aim of this study was to assess the effects of pretreatment with L-DOPA on the biological behaviour of human T98G cells in vitro.

Methods: We investigated how the 4-hour pretreatment with 50 μg/mL or 100 μg/mL of L-DOPA can influence the growth rate, the ability to form colonies, and the migratory capacity of these cells, in basal conditions and after carbon ion irradiation. Migration of T98G cells was assessed through transwell chambers containing a membrane with a pore size of 8μm. To monitor the collective motion of the cells in two dimensions the wound healing assay was also performed. Carbon ion irradiations were performed with the clinical beam at the CNAO Foundation in Pavia.

Results: Our results pointed out that L-DOPA pretreatment, at the concentrations suggested in literature, determines significant changes in T98G cells behaviour. An important decrease in cell proliferation with a minor tendency to aggregate is associated to a more efficacy in migration, both as collective motion of the cells in two dimensions (wound healing assay) and as single cell migration (transwell assay). More evident effects by T98G L-DOPA pretreated cells were observed on the response to carbon ion irradiation. Pretreated cells showed significant increase in migration capabi-

lity and a dramatic enhance in clonogenic survival after both 2 Gy and 4 Gy Carbon ion irradiation compared to unpretreated cells.

Conclusions: These aspects have never been previously evaluated and open further questions about the utility of L-DOPA preload in BNCT and need to be investigated deeper for a possible application in PET with 18F-DOPA.

CO043

TESTOSTERONE-MEDIATED ACTIVATION OF ANDROGENIC SIGNALLING SUSTAINS IN VITRO THE TRANSFORMED AND RADIORESISTANT PHENOTYPE OF RHABDOMYOSARCOMA CELL LINES

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Aims: Rhabdomyosarcoma (RMS), the most common soft-tissue sarcoma in childhood, rarely affects adults, preferring male. RMS expresses the receptor for androgen (AR) and responds to androgen; however, the molecular action of androgens on RMS is unknown.

Methods: Herein, testosterone (T) effects were tested in embryonal (ERMS) and alveolar (ARMS) RMS cell lines, by performing luciferase reporter assay, RT-PCR, and western blotting experiments. RNA interference experiments or bicalutamide treatment was performed to assess the specific role of AR. Radiation treatment was delivered to characterise the effects of T treatment on RMS intrinsic radioresistance.

Results: Our study showed that RMS cells respond to sub-physiological levels of T stimulation, finally promoting ARdependent genomic and non-genomic effects, such as the transcriptional regulation of several oncogenes, the phosphorylation-mediated post-transductional modifications of AR and the activation of ERK, p38 and AKT signal transduction pathway mediators that, by physically complexing or not with AR, participate in regulating its transcriptional activity and the expression of T-targeted genes. T chronic daily treatment, performed as for the hormone circadian rhythm, did not significantly affect RMS cell growth, but improved RMS clonogenic and radioresistant potential and increased AR mRNA both in ERMS and ARMS. AR protein accumulation was evident in ERMS, this further developing an intrinsic T-independent AR activity.

Conclusions: Our results suggest that androgens sustain and improve RMS transformed and radioresistant phenotype, and therefore, their therapeutic application should be avoided in RMS post puberal patients.

CO044

ENHANCEMENT OF SOFT TISSUE SARCOMA CELL RADIOSENSITIVITY BY POLY (ADP-RIBOSE) POLYMERASE-1 INHIBITORS

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[1]Department of Experimental and Clinical Biomedical Sciences, Section of Radiation Oncology, University of Florence; [2]Department of Orthopaedic Oncology, Azienda Ospedaliera Universitaria Careggi, Florence, Italy

Introduction: Soft-tissue sarcomas (STS) are aggressive tumors with a poor prognosis and there is a major clinical need for new strategies. Poly-ADP ribose polymerase (PARP)-1 promotes base excision repair and DNA strand break repair. PARP inhibitors (PARPi) have shown to enhance the cytotoxic effect of irradiation. We evaluated the effect of PARPi on STS cell lines survival and DNA damage after irradiation.

Materials and Methods: For clonogenic assays, STS cell lines were irradiated at 2, 4 or 6 Gy, with or without olaparib (1 μM), iniparib (10 μM) or veliparib (5μM) pretreatment. The impact of PARPi on γ-H2AX and Rad51 foci formation was evaluated by immunofluorescence in rhabdomyosarcoma cells treated with olaparib and irradiated at 4 Gy. Phospho-ERK, cleaved caspases 3 and PARP1 protein expression was evaluated by western blot in rhabdomyosarcoma cells treated with olaparib and irradiated at 4 Gy.

Results and discussion: PARPi induced significant radiosensitization in STS cells. Rhabdomyosarcoma showed the greatest increase in radiosensitivity, with a radiosensitization enhancement ratio at 50% survival (ER50) of 3.41 with veliparib. Fibrosarcoma showed an ER50 of 2.29 with olaparib. Leiomyosarcoma and liposarcoma showed the higher radiosensitization with veliparib (ER50 of 1.71 and 1.84, respectively). The combination of olaparib and radiation in rhabdomyosarcoma cells caused an increased number of γH2AX and Rad51 foci compared to olaparib or irradiation alone. Rhabdomyosarcoma cells treated with the association of olaparib and irradiation showed a slightly increased cleaved caspases 3 protein expression compared to olaparib or irradiation alone. Moreover, olaparib enhanced

PARP-1 cleavage, and decreased radiation-induced phospho-ERK protein expression. We showed that PARPi are potent radiosensitizers on human STS in vitro models: they reduced cell survival, inhibited DNA damage repair and pro-survival ERK signaling in STS cells when used in combination with irradiation.

Conclusions: These data warrant further investigations that evaluate irradiation plus PARPi in STS.

CO045

RADIOTHERAPY RESPONSE IS LINKED TO MICRORNA-146A AND MICRORNA-34A EXPRESSION THROUGH OXIDATIVE STRESS IN RHABDOMYOSARCOMA CELL CULTURES?

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Aims: Many studies have indicated that cellular exposure to radiation therapy induces various responses including DNA damage processing, cell cycle arrest, differentiation and altered gene expression. Oxidative stress and the overproduction of reactive oxygen species (ROS) represent the main causes of the radiation-induced cytotoxicity and the metabolic and morphologic cellular changes during radiotherapy response. MicroRNAs (miRNAs) are small non-protein coding RNA that play an important role in gene regulation. These RNA molecules function as post-transcriptional regulators, usually resulting in translational repression or target mRNA degradation and gene silencing. Accumulating evidence has demonstrated the involvement of microRNAs dysregulation in radiotherapy response. In this study, we evaluated the effect of oxidative stress induced by radiotherapy on the regulation of miR-146a and miR-34a expression levels in human rhabdomyosarcoma cell lines cultures.

Materials and Methods: Embryonal and alveolar rhabdomyosarcoma cell lines (RD and RH30) were stimulated with different doses (0.5-1-2-3-5 Gy) of radiation. After treatment the cells were collected and processed for the subsequent analyses. The percentage of survival cells after radiotherapy was analyzed by clonogenic assay; mitochondrial ROS production was detected by flow cytometry and the antioxidant enzymes superoxide dismutase (SOD)-2, catalase (CAT), glutathione peroxidase (GPx), the transcriptional factor nuclear factor erythroid 2 like 2 (NRF2), as well as the selected miRNAs were analyzed by qRT-PCR.

Results: The percentage of survival cells was significantly reduced by radiation, in a dose dependent manner, in comparison to basal condition. Oxidative stress induced by radiotherapy was confirmed by a significant increase in superoxide anion production and a significant modification of SOD-2, CAT, GPx and NRF2 gene expression. Furthermore, irradiation significantly modulated the expression levels of miR-146a and miR-34a, and level of miR146a and mir-34a are strictly linked to radiotherapy response.

Conclusions: Our preliminary results demonstrated for the first time the modification of miR-146a and miR-34a in rhabdomyosarcoma cell lines; these miRNAs seem to be involved in the sensitivity to radiotherapy response through oxidative stress.

CO046

TOLERANCE OF BRAIN TO STEREOTACTIC RE-IRRADIATION OF GLIOMA: A SYSTEMATIC REVIEW

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Aims: Radiation necrosis (RN) and other major neurological complications remain primary concerns in re-irradiation of high grade glioma (HGG). Following conventional re-irradiation, radiation-induced normal brain tissue necrosis occurs beyond an EQD2 cumulative around 100 Gy. With increasing conformality of radiotherapy, a higher radiation dose might be tolerated. Studies on stereotactic re-irradiation of glioma were examined to obtain information on the tolerance dose and treatment volume of normal human brain tissue.

Material and methods: Literature search was performed on May 1, 2018, via PubMed for publications from 2000 to 2018. Only human studies and English-language publications reporting toxicity about the use of stereotactic radiotherapy for recurrent glioma were included. Meta-analyses of published rates of radiation necrosis and other major neurological complications were performed. The studies were analysed by using the linear quadratic model to derive information on the cumulative equivalent doses in 2-Gy fractions (normalized total doses, NTDcumulative) for the healthy human brain.

Results: Sixty-six papers totaling 3441 patients were included. Worsening of pre-existing neurologic symptoms, increase in seizure activities, dizziness, headache, fatigue, brain edema, intratumoral bleeding, and radio-necrosis were described as side effects of re-irra-

diation. Fifty-five papers reported the incidence of severe toxicity of stereotactic radiotherapy (pooled rate 6.2%, range 0-86.7%), with 52.7%) studies reporting no cases of severe toxicity. Sixty-four papers reported the incidence of RN (pooled rate 9.9%, range 0-64%) and the number of patients who required salvage craniotomy due to RN (pooled rate 2.0%, range 0-28%). Mean cumulative NTD was 118.8 Gy (range 84-210 Gy). The pooled rate of RN was 2.9 and 10.8% (p=0.02) in studies with mean cumulative NTD lower and higher than 100 Gy, respectively. The pooled estimates of median progression free survival and median overall survival did not significantly differ in studies with mean cumulative NTD lower and higher than 100 Gy (7.0 and 8.7 months for PFS, and 11.0 and 11.9 for OS, respectively).

Conclusions: Even when using very conformal techniques such as stereotactic radiotherapy, limiting the cumulative NTD to 100 Gy might be a safer option as compared to higher cumulative doses. On the other hand, there seems to be no evidence of improved survival outcomes with cumulative NTD higher than 100 Gy.

CO047

TOLERANCE OF HEAD AND NECK ORGANS AT RISK TO REIRRADIATION: A SYSTEMATIC REVIEW ON BEHALF OF THE AIRO REIRRADIATION STUDY GROUP

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Aims: Reirradiation is becoming an established treatment option for recurrent-new primary cancer disease. The AIRO reirradiation study group aimed to analyze the impact of reirradiation in terms of toxicity for specific sites. Here, we present the preliminary results of the AIRO Head and neck (H&N) reirradiation working group.

Methods: A systematic review of published Pubmed and Embase' reports regarding reirradiation for the period 2000-2018 was perfomed between march and May, 2018 according to the PRISMA guidelines with the following inclusion criteria: at least 10 patients included, English language, full papers. Abstracts, commentaries and reviews were excluded.

Results: Inclusion criteria were met by 45 studies (7 prospective, 38 retrospective) from the initial 1295 citations retrieved. Publication period ranged from 2003 to 2017. A total of 3144 patients were included. Median follow up was 24,9 months. IMRT-only technique was used for 12 studies (26,6%). Stereotactic radiotherapy (sbrt) was used in eight studies (17.8%), hadron therapy (proton-carbon ions) were reported in three studies as well as 3D conformal radiotherapy. Brachitherapy was used in two studies. Other studies (37,8%) used mixed techniques. Median Reirradiation doses ranged from 50,4 to 70 Gy with conventional fractionation and from 30 to 44 Gy for sbrt cases. Elective nodal irradiation was omitted by most studies. Severe (≥G3) toxicities were reported by most studies. The most common grade 3-4 toxic effects were radionecrosis, dysphagia requiring feeding tube replacement, trismus. Fatal events occurred mostly due to mucosal bleeding and carotid blowout syndrome. The preliminary data analysis indicated Clinical target volumes > 50cc, planning target volumes > 100 cc, reirradiation interval < 20 months, single fraction SBRT (vs fractionated SBRT) as possible independent predictors of long-term toxicities.

Conclusions: H&N Reirradiation at curative doses is feasible; however, an experienced and multidisciplinary management of the common severe toxicities occurring due to reirradiation is required. The risk of fatal complications is low but not negligible. A further analysis of the systematic review raw data, looking for potential correlation between carotid and mucosal dose, radionecrosis and the risk of G5 toxicity is ongoing.

CO048

IL-1 BETA AND ACTIVATION OF NLRP3 INFLAMMASOME AFTER RADIOTHERAPY

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Introduction and objecties: Exposure to radiation can result in the activation and damage of peripheral immune cells, particularly macrophages, and proinflammatory cytokine release, which in turn may limit the therapeutic benefit. Immunostimulatory activity can occur through release from RT-damaged cells of DNA (which enhances the activity of antigen-presenting cells) and ATP, which activates the inflammasome with release of IL-1ß. Our goal is to demonstrate that RT induces NLRP3 inflammasome through IL-1 ß release in the microenvironment.

Materials and Methods: *In vitro* experiments: Peritoneal macrophages were isolated as described (Zhang X, *et al.* 2008). At first, mice were killed by excess anesthesia, and 5 mL sterile PBS was injected

into the peritoneal cavity. The peritoneum was gently massaged, and fluid recovered. Peritoneal macrophages were collected by centrifugation at 200 x g for 5 minutes at 4°C then a total of $3x10^5$ cells/well are added to 24-well tissue culture plates. Then, peritoneal macrophages were exposed to 60Co radiation source to attain the desired doses. PBMCs (peripheal blood mononuclear cells) were isolated from human blood by Ficool-Paque density gradient centrifugation. Blood was diluted with an equal volume of phosphate-buffered saline, pH 7.4 (PBS). Diluted blood was layered over 25 ml of the Ficoll-Paque PLUS (GE Healthcare). Gradients were centrifuged at 400×g for 30 min at room temperature in a swinging-bucket rotor without the brake applied. The PBMC interface was carefully removed by pipetting and washed with PBS by centrifugation at 250×g for 10 min then a total of 5x105 cells/well are added to 24-well tissue culture plates. Then, PBMCs were exposed to 60Co radiation source to attain the desired doses. *In vivo* experiments: Mice were exposed to whole-body radiation by timed exposure to 60Co radiation source. After 4h blood samples were collected from the submandibular vein of mice. Then, supernatants from peritoneal cavity were isolated. Blood samples were processed for obtain plasma (centrifugation 1,000 x g, 10 minutes at 4°C). IL-1ß measurement: Mouse plasma and cell-free culture supernatants were tested using ELISA kit following the manufacturer's instructions. Statistical analysis: The data are expressed as the mean ± S.E.M and analyzed for statistical significance using Microsoft Excel (Microsoft Co.). Student's t-tests was used to detected statistical significance. $p < 0.005$ (***), $p < 0.01$ (**) and $p < 0.05$ (*) were considered significant.

Results: Our preliminary results showed that RT at different doses induces pro-inflammatory cytokine release, such as IL-1ß. in supernatant of peritoneal macrophages and in peritoneal washes and blood of irradiated mice we found high levels of IL-1ß (detected by ELISA assay) compared to untreated control. Finally, we evaluated NLRP3 inflammasome activation in PBMCs (peripheal blood mononuclear cells) obtained from human blood and we found that RT induces IL-1ß release as well.

Discussion: RT is able to activate the NLRP3 inflammasome inducing release of IL- 1ß. We detected the IL-1ß either *in vitro* from cultured peritoneal macrophages after irradiation or *in vivo* in peritoneal washes and blood of mice irradiated. We demonstrated NLRP3 activation also in PBMCs obtained from human patients.

CO049

68GA-PSMA-11 PET/CT IN PROSTATE CANCER PATIENTS WITH BIOCHEMICAL RECURRENCE AFTER RADICAL PROSTATECTOMY AND PSA <0.5 NG/ML: EFFICACY AND IMPACT ON TREATMENT STRATEGY

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Aims: Primary aim of this retrospective, single-center analysis was to assess the performance of 68Ga-PSMA-11 PET/CT in prostate cancer (PCa) patients in early PSA failure after radical prostatectomy (RP). Secondary aim was to assess potential impact of 68Ga-PSMA-11 PET/CT on treatment strategy

Methods: A retrospective analysis about patients enrolled between March 2016 and July 2017 has been performed according to these inclusion criteria: a) RP as primary therapy; b) proven BCR c) PSA values between 0.2 - 0.5 ng/mL at the time of 68Ga-PSMA-11 PET/CT investigation; d) no Salvage Radiation Therapy (S-RT). The performance of 68Ga-PSMA-11 PET/CT was evaluated as detection rate on a per-patient and a per region basis (local vs. distant lesions). We further performed an intention-to-treat (ITT) analysis. Patient cohort was grouped into three different sub-population, blinded to 68Ga-PSMA-11PET/CT results, according to different pattern of treatments: a) S-RT (±systemic treatment), b)stereotactic body radiotherapy (SBRT) (± systemic treatment) c)systemic treatment. Treatment strategy was re-evaluated taking into consideration 68Ga-PSMA-11 PET/CT images.

Results: One hundred-nineteen (119) PCa patients were enrolled (mean age 66 years old; range 44-78), mean PSA value at the time of 68Ga-PSMA-11 PET/CT was 0.34 ng/mL (median 0.32;SD ±0.09 range 0.20-0.50 ng/ml). 68Ga-PSMA-11 PET/CT was positive in 41/119, resulting in an overall detection rate of 34.4%. 68Ga-PSMA-11 uptake was observed in prostate bed (3/119; 2.5%),in pelvic lymph nodes (21/119; 17.6%), in retroperitoneal lymph nodes (4/119; 3.4%) and in the skeleton (21/119; 17.6%). Regarding ITT, 81/119 patients (68.1%) were considered as possible candidates for S-RT in prostate bed and 0/111 (0%) for SBRT. According to 68Ga-PSMA-11 PET/CT results, the intended treatment was changed in 30.2% of cases (36/119). According to PET/CT, S-RT was recommen-

ded in 70/119 (58.8%) of which 58/119 (48.7%) in prostate bed and SBRT in 29/119 (24.4%) patients. When 68Ga-PSMA-11 PET/CT resulted positive, the intended RT planning was modified in 87.8% of cases (36/41)

Conclusions: In our series we observed a detection rate of 34.4% for 68Ga-PSMA-11 PET/CT. In the ITT analysis 30.2% of patients had a change in the intended treatment. These data support the hypothesis that 68Ga-PSMA-11 PET/CT is a useful procedure in the management of PCa patients showing early recurrence after RP and should be implemented in clinical practice.

CO050

68GA-PSMA PET/CT IN PATIENTS WITH BIOCHEMICAL RECURRENCE OF PROSTATE CANCER AFTER RADICAL SURGERY

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Aims: The aim of the study is to evaluate the impact of 68Ga-PSMA PET/CT in patients with persistent or recurrent prostate cancer after radical prostatectomy (RP), who are elegible to salvage radiotherapy (SRT).

Methods: We have prospectively included patients from November 2016 to April 2018. All patients performed 68Ga-PSMA PET/CT before SRT. In case of PSA>1 ng/ml, patients underwent first 18F-choline PET/CT and if negative 68Ga-PSMA PET/CT. All focal uptakes higher than background were considered as positive findings. Dubious findings were explored by other imaging techniques and defined as true positive or negative by a multidisciplinary team. In case of negative 68Ga-PSMA PET/CT or local relapse, patients were sent to SRT. In case of lymph nodes relapse or distant metastases the management was modified on the basis of 68Ga-PSMA PET/CT. Association between PET positivity and clinical patterns was evaluated by Fisher's test.

Results: A total of 74 patients (median age 70y, range 52-82) were enrolled. Patological T stage was T1c-T2b-c in 46 patients (62%), T3a-b in 26 patients (36%) and not reported for 2 patients. Gleason Score (GS) was ≤7 in 56 (75%) and ≥8 in 18 (25%) patients, respectively. Persistence or biochemical recurrence (BCR) were found in 13 (18%) and 61 (82%) patients, respectively. Median time of BCR was 25 months (range 1-148). Median PSA value at the moment of 68Ga-PSMA PET/CT was 0,54 ng/ml (range 0,23-8,9) with a median PSA doubling time (DT) and PSA velocity of 7,6 months (range 0,6-264,8) and 0,4 ng/ml/y (range 0-30,2), respectively. 68Ga-PSMA PET/CT was positive in 22/74 patients (31%). According to PSA level 68Ga-PSMA PET/CT was positive in 8/38 patients with PSA >0,2 and ≤0,5 ng/ml, in 6/22 patients with PSA >O,5 e ≤1, in 4/7 patients with PSA >1 e <1,5 ng/ml and in 4/7 with PSA ≥1,5 ng/ml. Recurrence was on prostate bed in 5 patients, in lymph nodes in 13 patients and as single bone lesion in 4 patients. PET positivity was significantly correlated with T ≥3 stage (p=0,029), low PSA DT (p=0,015; 3.1 in PET+ vs 8,7 months in PET-) and high PSA velocity (p=0,020; 0,8 in PET+ vs 0,4 ng/ml/yr in PET-). Patient management was modified in 25 cases (34%) on the basis of 68Ga-PSMA PET/CT findings.

Conclusions: Preliminary data suggest that 68Ga-PSMA PET/CT can be clinically useful to guide treatment strategy in these patients. In this setting a good selection of patients that could benefit of 68Ga-PSMA PET/CT before SRT is mandatory.

CO051

INTENSITY MODULATED RADIATION THERAPY BOOST IN LOCALLY ADVANCED CERVICAL CANCER: IS IT A SAFE AND FEASIBLE ALTERNATIVE WHEN BRACHYTHERAPY IS NOT PRACTICABLE? AN UPDATE

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Aims: Standard treatment in locally advanced cervical cancer is External Beam Radiotherapy (EBRT) concomitant to platinum based chemotherapy, followed by intracavitary/interstitial brachytherapy (BRT). We questioned if an Intensity Modulated Radiation Therapy (IMRT) boost is safe and feasible in patients (pts) unfit for a BRT boost.

Methods: We retrospectively analyzed data of 25 women (median age 54.9 years, range 29.3–81.6) with cervical cancer who underwent EBRT to pelvis ± lombo-aortic lymph nodes and sequential IMRT boost with BrainLab VERO® between July 2014 and December 2017. Pts were considered unfit for BRT because of technical limitations, comorbidity or poor compliance. Clinical International Federation of Gynecology and Obstetrics (FIGO) Stages I, II, III, and IV was present in 1 (4%), 9 (36%), 4 (16%), and 11 (44%) pts, respectively. All but two pts underwent a Pre-boost MRI. Clinical Target Volume (CTV) was contoured considering the initial extent of disease and Planning Target Volume (PTV) achieved adding 3-5 mm to CTV. Constraints to organs at risk were borrowed from the BRT ones. Image Guided Radiotherapy (IGRT) was performed at every fraction in all pts. Toxicity, Local Recurrence (LR), Progression Free Survival (PFS) and Overall Survival (OS) were asses-

sed. Acute and late toxicity were evaluated by CTCAE Version 4.

Results: Median follow-up was 21.1 months (4 – 65.1). Median radiation dose to pelvis ± lombo-aortic lymph nodes was 50.4 Gy (45-50.4), boost treatment was homogeneously performed to a total dose of 25 Gy in 5 fractions (alternating days). Median overall treatment time was 73 days (61-101). According to CTCAE scoring criteria 9 pts experienced gastrointestinal (GI) and genitourinary (GU) grade G1-2 acute toxicity. G2 rectal late toxicity requiring laser-coagulation was registered in 2 pts, there were no GI or GU acute or late toxicities ≥ G3. LR occurred in 4 pts (16%), 6 (24%) experienced distant progression (1 pt had both). 2-yrs PFS and OS rates for all stages were 69% and 69%, respectively. At the time of assessment, 17 pts are alive with no evidence of disease (2 underwent subsequently pelvic evisceration for LR), 7 died for cervical cancer, 1 is alive with stable disease from the end of IMRT boost.

Conclusions: Our preliminary data show the feasibility of IMRT boost in terms of toxicity. Local control after IMRT boost was satisfactory. This approach seems to be reasonable alternative when BRT is not practicable.

CO052

ACUTE AND INTERMEDIATE TOXICITY OF A 3-WEEK SCHEDULE HYPOFRACTIONATED RADIOTHERAPY WITH A SIMULTANEOUS INTEGRATED BOOST IN 287 EARLY BREAST CANCER, USING TOMODIRECT: MONO-INSTITUTIONAL PROSPECTIVE STUDY

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Aims: To report toxicity of a mono-institutional prospective study on hypofractionated whole-breast (WB) intensity-modulated radiotherapy (RT) with a simultaneous integrated boost (SIB) to the tumor bed (TB) using Tomotherapy® (Accuray Inc, Sunnyvale, CA) in Direct modality.

Methods: A prospective cohort of patients (pts) with early breast cancer undergoing breast-conserving surgery followed by RT in 15 daily fractions (fr) to WB (prescription dose 40.05 Gy, 2.67 Gy/fr) and to the TB with SIB (prescription dose 48 Gy in 15 fractions, 3.2 Gy/fr), was enrolled between 2013 and 2017. Primary endpoint was acute and intermediate toxicity assessed at the end of RT and within 6 months since RT, according to RTOG scale. Mc Nemar's test was used to compare any grade of toxicity, while univariate and multivariate analysis were used to examine predictive factors for severe toxicity at any time. Secondary endpoints included early chronic toxicity for pts with a follow up >6 months using the LENT-SOMA scale and cosmesis using Harvard criteria.

Results: Pts enrolled for the primary endpoint were 287. Overall, 127 (44%) pts experienced a Grade 2 toxicity and 84 (29%) a Grade 1 toxicity, while for 14 (5%) pts we did not observe any toxicity nor at the end of RT or within 6 months since the end of RT. A statistically significant difference was noted between the two time points, with a large part of pts reporting no severe toxicity at 6 months (Table 1). At univariate analysis, age <40 years, breast volume >1000 cm^3 and Dmax≤115% of prescription dose were predictive factors of severe toxicity (Grade≥2) at any time with a significant relative risk of 2.02, 1.8 and 3.2 respectively. At multivariate analysis, only age and breast volume were confirmed as predictive factors with a significant relative risk of 2.02 and 1.84, respectively. One-hundred-twelve pts had a follow up >12 months (median=12.3 months) with 57/112 (51%) reporting toxicity Grade<2, while cosmetic evaluation was available for 102 pts with a good-excellent opinion for 88/102 (86%) pts.

Conclusions: Hypofractionated whole-breast intensity-modulated RT with a SIB to the TB delivered with TomoDirect is a safe and well-tolerated treatment with a large part of pts reporting no toxicity after the end of RT and a good-excellent cosmesis. Predictive factors of severe toxicity might be considered during the treatment planning in order to further reduce side effects. This abstract is the basis for a future article.

Table 1. Frequency of acute skin toxicity according to the RTOG scale at two time points.

Toxicity/Grade	At the end of RT N = 287 (%)	Within 6 months since the end of RT N = 183 (%)	*p*-value*
Erythema			**<0.0001**
0	33 (11)	153 (84)	
1	203 (71)	27 (15)	
2	51 (18)	3 (2)	
G2	51 (18; 95%CI: 14-23%)	3 (2; 95%CI: 0-5%)	
Desquamation			**0.005**
0	265 (93)	178 (97)	
1	17 (6)	4 (2)	
2	4 (1)	1 (1)	
G2	4 (1; 95%CI: 0-4%)	1 (1; 95%CI: 0-3%)	
Edema			0.22
0	224 (78)	139 (76)	
2	63 (22)	44 (24)	
G2	63 (22; 95%CI: 17-27%)	44 (24; 95%CI: 18-31%)	
Any toxicity			**<0.0001**
0	24 (8)	118 (64)	
1	164(57)	19 (10)	
2	98 (34)	46 (25)	
G2	98 (34; 95%CI: 29-40%)	46 (25; 95%CI: 19-32%)	

Note: significant *p*-values are in bold.
*Mc Nemar's test for any grade of toxicity (N=183 patients with data on both time points)

CO053

THE FAST APPROACH AS ADJUVANT WHOLE BREAST IRRADIATION IN EARLY STAGE OF BREAST CANCER: A SAFE ALTERNATIVE FOR FRAIL PATIENTS

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Aims: To evaluate early and late reactions, local control and survival of elderly breast cancer (BC) patients (pts) treated with adjuvant once-weekly hypofractionated radiotherapy (RT).

Methods and Materials: From 7/2011 to 4/2018, 271 BC pts treated with breast-conserving surgery received 5.7 Gy once a week for 5 weeks to the whole breast. No boost was applied. Pts entered a dedicated databank in the context of a research project called "Adjuvant radiation treatments with intensity-modulated radiotherapy and/or hypofractionated schedules for breast cancer" which was notified to the IEO Ethical Committee. Pts were considered as candidates for receiving such a scheme if affected by T1-T3 invasive BC, with no or limited axillary invasion. The age threshold was 65 years, but also younger women were offered the once-weekly scheme if affected by disabling disease.

Results: Median age was 76 (45.5-86.4) years. Pts were followed for a median of 23 (6-71) months. Most of BC were T1 (76.8%), while the remaining were T2 (21.8%), T3 (0.4%) and Tx (1%). Axillary status was negative in 68.6%, minimally involved in 14.8% (pN1) and not assessed in 16.6% of the cases (Nx). Most of the women received hormonal therapy (86%), while 10% received chemotherapy. Maximum acute toxicity at the end of RT was as follows: grade (G) 1, 2 and 3 erythema in 63%, 7% and 0.4% of pts, respectively. G2 edema was detected in 10% of pts. Desquamation occurred in 4% as G1 and 1.5% as G2 of cases. At median 2-year follow up, LENT-SOMA assessment was available for 112 (41%) pts. Various grade of fibrosis (G1 and G2 in 44% and 10%, respectively) and skin changes (G1 and G2 hyper- or hypo-pigmentation in 14% and 3% respectively, G1 and G2 telangiectasia in 2 pts) were observed. A minority complained pain of G1 (18 pts) and G2 (1 pt) intensity. Patient- and treatment-related factors as predictor for toxicity and local failure are being evaluated. At the time of writing, there were neither local recurrences nor breast cancer-related deaths. At the last follow-up visit, of 177 (65%) pts analyzed, 175 pts were alive without disease and 2 were alive with disease.

Conclusions: Mild early and long-term toxicities were observed with such a hypofractionated RT scheme. Although with a short follow-up, local control was excellent. Such a scheme was well accepted by pts, in particular by those with difficulties in commuting and with disabling associated disease. This abstract is the basis for a future article.

CO054

STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR UNRESECTABLE LOCALLY ADVANCED PANCREATIC CANCER: CLINICAL OUTCOMES ON 106 PATIENTS

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Aims: Pancreatic adenocarcinoma is characterized by a poor prognosis. Surgery is the gold standard of care, however more than 50% of patients are unresectable at the time of diagnosis. In patients with locally advanced pancreatic cancer (LAPC), the integration of chemotherapy (CT) and chemo-radiation treatment (CRT) is the current therapeutic option, associated with a significant toxicity rate and with a disappointing overall survival (OS). In the last years, the role of stereotactic body radiotherapy (SBRT) in the treatment of LAPC was investigated. Higher local control related to the high doses employed, short overall treatment time and sequential integration with systemic therapy, represent the crucial advantages of SBRT over conventional CRT. Scope of this study is to assess the efficacy of SBRT in patients with inoperable LAPC.

Methods: Patients with unresectable LAPC with maximum tumor diameter ≤5cm, without limph node disease and without distant metastasis were treated with SBRT, after multidisciplinary board evaluation. Prescription dose was 45Gy in 6 fractions. Primary end-point was freedom from local progression (FFLP). Secondary end-points were overall survival (OS), progression-free survival (PFS), and toxicity. Local control (LC) was defined according to RECIST v1.1 criteria. Acute and late toxicity was scored according to the NCI Common Terminology Criteria for Adverse Events (CTCAE) v3.0.

Results: Between January 2011 and September 2017, 106 patients (48 male-58 female) with LAPC were treated with SBRT at Humanitas cancer Center. Median age was 71 years (range 41-88 years). 60 patients (57%) received CT before SBRT, for a median time of 5 months (range 3 - 11 months). In 46 patients (77%) gemcitabine-based CT was administered, whe-

reas 20 patients (33%) received FOLFIRINOX. Median follow-up was 86 months (range 2-88 months). FFLP was 82% and 76% at 1 and 2 years, respectively. At univariate ($p<0.03$) and multivariate analysis ($p<0.001$), lesion size was significant for LC. Median PFS was 7 months (95% CI 4.76-8.23). Median OS was 12 months (95% CI 8.76-13.21). CT administered before SBRT ($p<0.005$) and FFLP ($p<0.002$) were significantly correlated with OS. Grade 3 gastrointestinal toxicity was detected in 2% of patients.

Conclusions: SBRT is an effective and safe local therapy for selected patients with LAPC. Our results suggest that the stereotactic treatment may be a promising therapeutic option in the multi-modality treatment of these patients.

CO055

HIGH-PRECISION SALVAGE RE-IRRADIATION FOR ISOLATED LOCAL RECURRENCE OF PROSTATE CANCER: MONO-INSTITUTIONAL SERIES OF 64 PATIENTS

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Aims: To evaluate high-precision external beam re-irradiation (re-EBRT) for local relapse of prostate cancer (PCa) after radiotherapy.

Methods: This retrospective study included patients with biochemical failure and evidence of isolated local recurrence of PCa after radical/salvage EBRT or brachytherapy that received image-guided re-EBRT. Biopsy was not mandatory if all diagnostic elements were univocal (Prostate Specific Antigen evolution, choline-positron emission tomography or magnetic resonance imaging). Re-EBRT was delivered with intensity modulated RT and/or stereotactic technology (RapidArc®, VERO® and CyberKnife®). Biochemical failure after the primary therapy was defined as two consecutive risings in PSA level >0.2 ng/ml post radical prostatectomy and PSA nadir +2 ng/ml above the nadir after primary RT. Updated data of some pts published by Zerini et al (2015) were included.

Results: Data of 64 patients were included, median age at re-EBRT was 73.2 years, median pre-re-EBRT PSA was 3.89 ng/ml. Median total dose was 30Gy in 5 fractions, biologically effective dose (BED) of 150Gy. One acute G3 genitourinary (GU) event and 1 late G3 GU event were observed. No G≥3 bowel toxicity was registered. At the median follow-up of 26.1 months, tumor progression was observed in 41 patients (64%). Eighteen patients (28%) experienced local relapse. Median time-to-progression was 14 months. Two-year local control, biochemical and clinical relapse free survival rates were 75%, 40% and 53%, respectively. Considering re-EBRT BED (≥130Gy vs. <130Gy), statistically significant differences were found for the one-year biochemical progression free survival rate (85% vs. 60%, p-value=0.0006) and one-year clinical progression free survival rate (90% vs. 73%, p-value=0.0026), as shown in the Kaplan–Meier curves(Fig. 1). No statistically significant differences between patients treated with a total BED<130 Gy or ≥130 Gy were found for local control at 2 years (85% vs. 65%, p-value=0.09) and overall survival at 2 years (95% vs. 90%, p-value= 0.38). At the last follow-up, 23 patients (36%) showed no evidence of disease.

Conclusions: High-precision salvage re-EBRT for isolated local PCa recurrence is a feasible and noninvasive treatment, offering satisfactory tumor control without significant complications if BED superior to 130Gy is administered. Further prospective studies are warranted to define the optimal patient selection and establish the optimal dose and volume parameters.

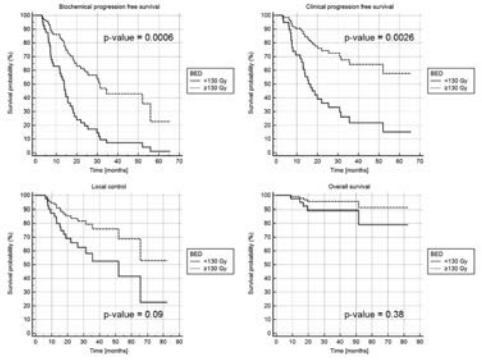

Fig. 1. a) Biochemical progression free survival rate (b-PFS), b) Clinical progression free survival rate (c-PFS), c) Local control (LC), d) Overall survival (OS) by BED <130 Gy (solid line) and BED ≥130Gy (dashed line).

CO056

STEREOTACTIC INTRACRANIAL ABLATIVE RADIATION THERAPY FOR MULTIPLE BRAIN METASTASES WITH HYPERARC: PRELIMINARY CLINICAL DATA

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Introduction: Brain metastases (BMs), the most common intracranial tumors in adults, affected about 20–

40% of cancer patients. Considering the absence of increasing overall survival when the irradiation of the entire brain is proposed, the ablative RT for BMs, including Stereotactic Radiotherapy (SFRT) or Radiosurgery (SRS) is increasing, also for multiple BMs. Aim of the present study is to evaluate safety and efficacy of SRS/SFRT for multiple BMs, using a new mono-isocenter technique with multiple non-coplanar arcs (HyperArcTM Varian Medical System).

Materials and Methods: Patients aged >18 years with a diagnosis of multiple BMs with a diameter inferior to 3 cm, a life expectancy more than 3 months, and Karnosky Performance Status (KPS) ≥70 were eligible for SFRT/SRS with HyperArcTM. Gross Tumour Volume (GTV) was delineated by the fusion between Magnetic Resonance Imaging and Computed Tomography. A Planning Target Volume (PTV) was obtained from GTV by adding a 2-mm isotropic margin. The prescribed dose (Dp) ranged between 15-27 Gy in 1-3 fractions. For each patient, a mono-isocenter volumetric modulated arc therapy plan was generated with 5 non-coplanar 180°-arcs (couch at 0°, ±45°, ±90°). A dose normalization of 100%Dp at 98%PTV was adopted, while D2%(PTV) <150% Dp was accepted. Corticosteroids were administered for all patients during SFRT/SRS.

Results: From August 2017 to May 2018, 382 BMs in 64 patients were treated with HyperArc SRS/SRT. The median number of BMs for each patients as 7 (range 1-21). From a clinical point of view, with a median follow-up time of 6 months (range 2-9 months), 209 out 229 evaluated lesions were controlled (40 BMs, 19%, had a Complete response; 97 BMs, 46%, a partial response, 72 BMs, 35% a stable disease), while 20 BMs out 229 (8%) showed a progression disease. No acute toxicity, in terms of nausea or vomiting o cefalea, were registered during treatment. In terms of dosimetrical data, the mean average value of BMs PTV was 8.6 cc (range 0.5-27.9 cc); the mean dose to the brain-minus-PTV was 2.78 Gy and the V12 (volume of brain that received 12Gy) was 19.9 cc. The total treatment time for each session was 13 minutes.

Conclusions: The present data showed that a mono-isocenter technique with multiple non-coplanar arcs (HyperArcTM Varian Medical System) is safe for BMs patients. The utilization of SFRT/SRS for multiple BM is controversial and should be explored in randomized trial.

CO057

EVALUATION OF ITALIAN RADIOTHERAPY RESEARCH FROM 1985 TO 2015: PRELIMINARY ANALYSIS. AN AIROGIOVANI ITALIAN ASSOCIATION OF RADIATION ONCOLOGY-YOUNG MEMBERS WORKING GROUP EVALUATION

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Aims: Radiotherapy (RT) provides significant benefits to cancer population in terms of overall survival. In the last decades, the indication to use RT in all stage of cancer disease is increased based on data deriving from clinical trials. Aim of the present review is to evaluate the Italian RT research production during a 30 years period (1985-2015). Second endpoint was to analyze how many young (under 40) Radiation oncology (RO) are devoted to research, analyzing the age of first author.

Methods: PubMed database was searched for English literature published from 1985 to December 2015 using keywords “radiotherapy” or “radiation” combined with “Italy”. Studies eligible for inclusion in this analysis were as follow: case reports, clinical and dosimetric retrospective or prospective studies (Phase I-II-III) in which RT was used, metanalysis, reviews, radiobiological studies. Exclusion criteria were: study do not conducted in Italy, study in which RT was not used or it was not investigated, study in which no Italian RO were in the author list, study without abstract.

Results: The systematic search identified 8823 records from PubMed and for the present preliminary analysis of a 20 years period (1985-2005) 4750 papers were evaluated. After the exclusion of duplicates, abstract review, cross-referencing and paper that do not respect the inclusion criteria, 1207 papers were included in the analysis. Based on the type of study, retrospective analysis, prospective Phase I-II trial and literature review were 44%, 20% and 14.5% of all published data, respectively. The number of published papers increased during a 20 years period (R2: 0,8) with a linear increase of retrospective studies, reviews and prospective phase I-II studies over all the period. Randomized trials increased in numbers from 2000, however their absolute value remains low comparing to others type of trials (4%). The Northen Italy produced the majority part of the Italian research (58.7%), while the Southern Italy published only 7.2% of all the studies analyzed. For 716 papers out 1207, the contribution of

young RO was evaluated: in 382 papers, the first author was a young RO.

Conclusions: The Italian radiotherapy research increased during the last decades. The present analysis reveals that retrospective studies were the most represented even if a linear increase of prospective studies was shown. Unfortunately, Phase III trials were underrepresented. The update of the present analysis to 2015 is ongoing.

CO058

A PROSPECTIVE REAL LIFE STUDY EVALUATING ABIRATERONE ACETATE PLUS PREDNISONE (AAP) FOR METASTATIC CASTRATION RESISTANT PROSTATE CANCER (MCRPC) (ABITUDE STUDY)

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Aims: According to an emerging need to investigate effectiveness in routine clinical practice, the ABITUDE study was designed to evaluate abiraterone acetate plus prednisone (AAP) in a real-world setting on chemotherapy-naïve patients with metastatic Castration-Resistant Prostate Cancer (mCRPC). Here we present the main results of the first interim analysis.

Methods: ABITUDE is a prospective, observational cohort study. Patients were consecutively enrolled in 49 Italian centers at the beginning of AAP and will be followed for 3 years. The primary objective is to evaluate PSA decline rate, radiographic progression-free survival (rPFS) and clinical benefit maintenance according to PCWG3 during AAP. Patient's quality of life and pain were measured every 6 months with the Functional Assessment of Cancer Therapy–Prostate (FACT-P; score range: 0-156) and the Brief Pain Inventory (BPI; score range: 0-10).

Results: Among 481 enrolled patients, 453 (94.2%) were evaluable for analyses: 330 (68.6%) were managed in oncology centers, while 65 (13.5%) and 58 (12.1%) in urology and radiotherapy centers, respectively. The median observation duration per patient was 8.8 months. Main baseline characteristics are shown in Table 1. Patients with oligometastatic disease, defined as patients with < 3 metastases, were 35.6% of the total sample, more frequent in radiotherapy and urology centers. During the treatment with AAP, 242 patients (60.3%) had a ≥50% PSA decline (N=401). The 1-year probabilities for radiographic progression-free survival and for clinical benefit maintenance were 73.9% (standard error: 2.9%) and 76.0% (standard error: 2.9%), respectively (N=439). At enrollment, median (25th-75th percentile) FACT-P total score was 110 (95; 120) points (N=421); during observation period, 218 patients (71.9%) did not show any functional decline (N=303). Median (25th-75th percentile) baseline BPI worst pain score was 2 (0;4) points (N=388); After 1 year, 70.9% if patients did not report any worsening in pain(N=439). Serious adverse events were 16.8% but only 0.6% were possibly, probably or certainly correlated to study drug. Of note, 21.5%, 37.9% and 38.2% of patients treated in urology, radiotherapy and oncology centers had at least 2 baseline comorbidities.

Conclusions: These data suggest that AAP was active and safe in a real world study population. Further analyses with a longer follow up are awaited.

Funding: The study was sponsored by Janssen-Cilag.

Table 1. Baseline characteristics.

	Urology	Radiotherapy	Oncology
Age (mean)	75.1	75.6	76.2
≥75 years	50.8%	58.6%	60.6%
PSA (ng/mL)	8.1	10.5	16.5
Extent of desease			
Bones	66.2%	60.3%	72.7%
Lymphnodes	44.6%	60.3%	50.3%
Visceral	6.2%	0	10,3%
Prostatic bed	16.9%	5.2%	0,6%
Bone mets			
≤3	23 (53.5%)	15 (42.9%)	75 (31.4%)
≥10	6 (14.0%)	7 (20.0%)	49 (20.5%)
Time from castration to AAP (median)	51 m	41.1 m	31.1 m
ECOG PS,			
0	30.6%	48.2%	62.8%
1	51.6%	44.6%	34.8%
≥2	17.7%	7.1%	2.5%
Comorbidities			
0	35.4%	20.7%	33.6%
1	43.1%	41.4%	28.2%
≥2	21.5%	37.9%	38.2%

CO059

ONTOLOGY OF HEAD AND NECK CANCER RE-IRRADIATION: FUNDAMENTALS FOR A SHARED MULTIDIMENSIONAL NETWORK DATABASE WITHIN THE RE.VOL.V.E.R. (RE-TREATMENT VOLUMES VALUE FOR PREDICTION OF EFFECTS OF RE-IRRADIATION) PROJECT FRAMEWORK

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Background: The aim of the RE.VOL.V.E.R. (RE-treatment VOLumes Value for prediction of Effects of Re-Irradiation) Project is to develop Decision Support Systems (REVOLVER.DSS) based on ad-hoc data mining processes from a multicenter Standardized Data Base (REVOLVER.SDB) including DICOM and DICOM-RT objects to guide treatment personalization in oncological patients treated with Re-irradiation. The REVOLVER.SDB will be the result of this multi-institutional data collection and implies a stand¬ardization of any considered variable. Herein the consensus among the participating centers upon the ontology in Head and Neck (H&N) Cancer re-irradiation is reported.

Materials and Methods: The RE.VOL.V.E.R. project was started in December 2017 with the establishment of a Consortium of 26 Radiotherapy Units. Each Center indicated who has the responsibility of the project for the local unit. A task group of Radiation Oncologists (ROs) elaborated a preliminary proposal of the ontology for H&N cancers re-irradiation. Each variable was fully and unambiguously described by a name, a definition, and a measurement. To reach a consensus on the ontology, every representative of the Centers participating to the REVOLVER project was invited to answer a web-based survey. They were invited to rate the value of each variables on a 4 points scale (1:irrelevant; 2:optional, 3:recommended; 4: mandatory) Thereafter the mean score of each variable was computed and weighted based on the experience and the H-Index of each participant . To cross validate the ontology and define the most relevant variables, twenty recently published papers on the same topic have been reviewed.

Results: The preliminary proposal of the ontology included 600 variables. The survey was on-line from January to February 2018. Seventeen /26 (65.3%) ROs within the Consortium participated to the survey. Three hundred and forty eight variables gained a weighted mean score of at least 3 points and were considered as recommended. One hundred and nine variables have been reported in the M&M or in the result section of the papers that have been reviewed. All these variables were among those defined as "recommended" by the R0s who participated to the survey.

Conclusions: A consensus about the ontology of H&N cancers re-irradiation was reached. Relevant variables that have to been included in the shared multicenter Standardized Data Base (REVOLVER.SDB) have been defined and prioritized.

CO060

IMPLEMENTING IN CLINICAL PRACTICE A MODERATELY HYPOFRACTIONATED RADIOTHERAPY REGIMEN FOR PROSTATE CANCER: DELINEATION PECULIARITY AND ORGAN AT RISK CONSTRAINTS COMPARISON BASED ON PHASE III TRIALS EVIDENCE

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Aims: To implement in clinical practice a moderately hypofractionated radiotherapy (MHR) scheme in men with low, intermediate and high-risk localized prostate cancer (PCa), according to evidence from phase III trials based on radiobiologic rationale that the alpha-beta ratio of PCa is considered low compared to most other neoplasms (ranging from 1 to 2 Gy).

Materials: Literature was reviewed focusing not only on outcomes, but also on delineation and constraints to organs at risks used.

Results: Four superiority trials, and three noninferiority trials were analyzed (CHHiP, RTOG 0415 and PROFIT). Collectively, the superiority trials failed to demonstrate differences in efficacy after 5 years, in terms of metastasis-free, cancer-specific survival or overall survival. On the other hand, the noninferiority trials, CHHiP, RTOG 0415 and PROFIT, overall demonstrated that the safety and efficacy of MHR is similar to that of conventional fractionated radiotherapy (CFR). The strongest evidence supported 60 Gy in 20 fractions of 3 Gy. In the PROFIT trial, dose-volume criteria were based on rectal and bladder wall contours. In all remaining trials, dose-volume criteria were based on solid organ contours. Constraints to organs at risks used were compared in Tables 1 and 2. Because International Commission on Radiation Units & Measurements (ICRU) 83 report recommended delineation of the wall for hollow organs, we adopted the dose-volume constraints based on rectal and bladder wall contours as suggested in PROFIT trial.

Conclusions: MHR for localized PCa is safe and effective. Based on several large randomized studies, MHR with 60 Gy in 20 fractions of 3 Gy over 4 weeks can be considered a standard of care for localized PCa.

This MHR regimen was chosen in our Institution for a widespread use because was used in two different randomized trials, was tested in all risk groups, and was evaluated both in the presence and absence of androgen deprivation therapy.

Table 1.

Dose (Gy)	Dose [%]	Max Vol [%]
RECTUM		
24,6	41	(80)
32,4	54	(70)
40,8	68	60
48,6	81	50
52,3	88	30
56,7	95	15
60	100	3
	Dose [%]	Max Vol [%]
BLADDER		
40,8	68	50
48,6	81	25
60	100	5
	Dose [%]	Max Vol [%]
FEMORAL HEADS		
40,8	68	50
40,8	68	50
	Dose [%]	Max Vol [cc]
BOWEL		
40,8	68	17
	Dose [%]	Max Vol [%]
PENILE BULB		
40,8	68	(50)
48,6	81	(10)

Table 2. Constraints from PROFIT trial.

ORGAN AT RISK	VOLUME (%)	MAX DOSE (Gy)
RECTAL WALL	50	<37
	70	<46
BLADDER WALL	50	<37
	70	<46
FEMORAL HEADS	5	<43

CO061

A MULTICENTER RANDOMIZED, PHASE II/III STUDY, TO COMPARE THE EFFICACY OF NBTXR3, IMPLANTED AS INTRATUMOR INJECTION AND ACTIVATED BY RADIOTHERAPY, WITH RADIOTHERAPY ALONE IN PATIENTS WITH LOCALLY ADVANCED SOFT TISSUE SARCOMA OF THE EXTREMITY AND TRUNK WALL

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Aims: Comparison between the antitumor activity in terms of Pathological complete response rate of intratumor injection of NBTXR3 activated by EBRT and EBRT alone, in patients with locally advanced soft tissue sarcoma of the extremity and trunk wall.

Methods: This Phase II/III has been a prospective randomized, multi-center, open-label and active controlled 2 arms study. Patients, stratified by histologic subtype, have been randomized in a 1:1 ratio, to receive either NBTXR3 as intratumor injection, activated by EBRT or EBRT alone, as preoperative treatment. NBTXR3 is a suspension of inert, crystalline nanoparticles (Hafnium oxide), with hydrodynamic diameter of 50 nm; functionalized by phosphate groups, which determine a negative surface charge. They have no specific target or interaction within the tumor cell. They are designed to generate oxygen free radicals to selectively destroy cancer cells, after activation by EBRT. After completing the treatment, surgery was performed in all patients. A biased coin dynamic method is used to avoid extreme imbalance of treatment assignment within histologic stratum. All patients received EBRT according to the current medical practice, 25 fractions, 2 Gy/fraction up to a total dose of 50 Gy, given as 5 fractions/week. 3D-RT and IMRT were both allowed.

Results: Seven patients were enrolled in the protocol at IOV-IRCCS of Padua, 4 were randomized to the experimental arm and completed NBTXR3 injection, EBRT, and surgery; 3 were assigned to the control one and completed EBRT as well. In the experimental group, after corticosteroid administration, according to the size, shape and topography of the tumor, echo or CT-guided 4 or more punctures were performed, with a suspension volume equivalent to 10% of baseline theoretical tumor volume calculated as the product of the 3 longest dimensions assessed by diagnosis MRI. No leakage of NBTXR3 into surrounding tissues occurred and intratumor NBTXR3 levels were maintained during EBRT. No NBTXR3 related adverse events occurred.

Conclusions: A single injection of NBTXR3 at 10% of TV with preoperative EBRT is technically feasible with manageable toxicity. Clinical activity was observed because all the patients enrolled in the experimental arm showed a superior response to treatment: at the pathological assessment they got a better EORTC-STBSG response score: A, B, B, B vs. D, D, E and a superior volumetric reduction according to the RECIST criteria: 89, 74, 50 and 25% vs. 47, 13 and 0%.

CO062

INDUCTION CHEMOTHERAPY REGIMEN WITH GEM-OX AND STEREOTACTIC BODY RADIOTHERAPY FOR LOCALLY ADVANCED PANCREATIC CANCER: PRELIMINARY RESULTS OF A PROSPECTIVE MONOCENTRIC STUDY

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Aims: Evaluating preliminary safety and effectiveness results of an induction chemotherapy (CHT) regimen followed by SBRT in locally advanced pancreatic cancer (LAPC).

Methods: Patients (pts) with non-metastatic inoperable LAPC were enrolled on a prospective single-institution study. Four CHT cycles with Gemcitabine and Oxaliplatin (GEMOX) (day 1-8 of a 21-day cycle) were administered. If no progression was observed after induction CHT, pts received 3 fractions of 8, 10 or 12 Gy (total dose 24-36 Gy) of SBRT based on tumor location in relation to stomach and duodenum. 4D-CT with oral and i.v. contrast was used for treatment planning and IGRT-IMRT for delivery. Seven weeks after SBRT tumour re-staging and evaluation for surgery was performed. Toxicity was scored according to CTCAE v4. Progression free survival (PFS), freedom from locoregional progression (FFLRP), freedom from distant metastasis (FFDM) and overall survival (OS) were calculated using the Kaplan-Meier method.

Results: Between February 2014 and December 2017 we enrolled 14 pts. All pts received four CHT cycles, except one because of an intercurrent myocardial infarction. Two pts developed distant metastases after induction CHT, 12 received SBRT. Total SBRT dose was: 36 Gy (2 pts), 30 Gy (3 pts) and 24 Gy (7 pts). At present 3/12 pts underwent resection without complications. With an overall median follow-up of 17.6 months (range, 3–40), for all patients the locoregional control rate was 57.1% (8/14). Median PFS, FFLRP, FFDM and OS were 12.2, 19, 14, 18.3 months respectively; estimated 1-year PFS, FFLRP, FFDM and OS rate were 64.3%, 92.9%, 64.3% and 78% respectively. Three pts developed acute G3 or greater hematologic toxicity (1 anemia and 2 neutropenia), 1 pt developed acute G3 gastrointestinal pain, no further G3 or greater acute nonhematologic toxicity was observed. One patient developed G2 gastric ulcer and G2 gastric haemorrhage that were medically managed. Late G3 or greater toxicities were not observed.

Conclusions: Induction CHT and SBRT in three fractions resulted in excellent local control and seems to improve survival outcomes, with a low rate of side effects. Evaluation upon enrolment conclusion is awaited to provide final results that may provide the rationale to further intensify research into modification/modulation of locoregional treatment strategies for LAPC.

CO063

STEREOTACTIC RADIATION THERAPY IN TREATMENT OF RESIDUAL DISEASE AFTER 3D CONFORMAL RADIATION THERAPY IN PATIENTS WITH NSCLC

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Aims: to evaluate local control of disease and toxicity of stereotactic body radiation therapy (SBRT) after 3D conformal RT (3D-CRT) in patients affected by residual disease from pulmonary carcinoma (PC).

Methods: We reviewed patients treated for non small cell and small cell lung cancer in our Department. We evaluated acute and late toxicities (primary endpoint) and local control disease (secondary end –point). This study has been approved by Ethical Committee (Prot. Numb. 0003722- 28/2/18).

Results: Twelve consecutive patients (11 M and 1 F, mean age 63,2 years, range 43 - 87) with PCs [12 non-small cell lung carcinomas (NSCLCs)] involving right lung (7 pts) and left lung (5 pts), underwent SBRT for remnant disease after 3D-CRT due to PCs from 2012 to 2018 at our University Hospital with a median dose of 19,5 Gy in 3 fractions delivered with linear accelerator equipped with robotic arm. Previous treatment consisted in 3D-CRT at the therapeutic dose of 60-66 Gy in 30-33 fractions. Seven patients underwent CHT in association with RT, 1 of them discontinued CHT because of haematological toxicity and the remaining 5 received only RT (1/5 because of impaired renal function). Patients were followed-up with Computed Tomography (CT) examinations every three months after SBRT. RECIST criteria 1.1 were used to assess response. In cases of equivocal findings, response was evaluated with 18F-fluorodeoxyglucose (18F-FDG) Positron Emission Tomography/Computed Tomography (PET/CT) was used to evaluate response. Patients were followed-up for a median of 36 months: 2/12 patients lost follow-up controls; 7 patients died, with a median 18 months OS, two of them died for brain metastases and one for lung metastases. 3/12 patients are still alive, two of them had a complete response and one had disease progression for bone metastases. No other additional toxicities were found in our patients.

Conclusions: Our study has proved that, in patients undergoing SBRT for residual disease after 3DCRT, SBRT is well tolerated with a significant local control of disease. SBRT should be considered in this set of patients but further studies are required.

CO064

GUROPA SURVEY: GENITO-URINARY RADIATION ONCOLOGY PRESCRIPTION ATTITUDES

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Aims: to investigate the role of Radiation Oncology in the management of genito-urinary (GU) cancer excluding prostate and penile cancer.

Methods: The questionnaire was focused on the evaluation of the degree of involvement of radiation oncologists in the work-up of bladder, renal cell carcinoma and testicular cancer.

Results: 88 radiation oncologists completed the survey. The majority (85.4%) of participating radiation oncologists were senior consultants (> 5 years of experience). Sixty-four (73.6%) carried out a multidisciplinary tumor board discussion of GU cases, while 23 (26.4%) did not. Seventy-five percent of responders reported that, every year, visited < 50 GU patients (pts), 18.1% visited 50-100 pts and 6.9% visited >100 pts. Bladder cancer (BC), curative radiotherapy (RT) as part of trimodality approach was claimed to be adopted in less than 10 cases per year. Regarding renal cell carcinoma (RCC) patients, primary tumor directed RT was adopted only in 8 cases (9.4%) in at least 10 pts per year. Palliative RT was more frequent in RCC (48.2%) in over than 10 pts per year. In case of testicular cancer (TC) the prescription of RT was limited (< 10 patients per year) due to the low incidence of disease and recent shift to surveillance as a first option in stage I seminoma.

Conclusions: our survey showed that radiation oncologists are rarely involved in the decision making strategy of GU cancer, despite many clinical trials support RT use. These patients probably deserve a more uniform approach based on updated, detailed and evidence based recommendations.

CO065

DIFFERENT CAROTID ARTERY CONTOURING APPROACHES RESULT IN RELEVANT DOSIMETRIC VARIABILITY AND SIGNIFICANT ANATOMICAL MISSING: DO WE NEED TO MOVE TOWARD A STANDARDIZED CONTOURING STRATEGY?

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Aims: A Carotid artery (CA) sparing approach is a field of increasing interest owing to long life expectancy of patients with early glottic cancer (EGC). A CA delineation consensus lacks with no internationally recognized dose constraints for this structure. Here we compare, in terms of anatomical and dosimetric variability, three of the most common CA delineations found in literature.

Methods: CA of 10 cT1a N0 EGC patients were outlined using 3 different approaches: 1) the whole CA from its origin up to the internal carotid entry into skull base (Contour 1); 2) the tract of CA from its origin up to at least 2.5 cm above the hyoid bone (Contour 2); 3) the tract of CA 1 cm superior and inferior to PTV (Contour 3). The carotid bulb was contoured 2 cm inferiorly and superiorly to carotid bifurcation according to the Framingham Heart definition due to its role in the radio-induced atherosclerosis. A 1 mm isotropic carotid and bulb margin was added to compensate the changes during cardiac cycle. Thirty VMAT CA sparing plans were generated and CA Dmax, Dmean, V35% and V50% were compared across the different contouring approaches. T-test for paired data with logarithmic transformation was used to compare dosimetric parameters. A two-sided p-value < 0.05 was the significance threshold.

Results: In terms of carotid structures missing, Contour 3 did not include the entire bulb in 100% of contoured carotids while Contour 1 and 2 always included it entirely. A significant variability in ipsilateral and contralateral CA Dmean and ipsilateral CA V35% were found among the three contouring approaches with the lowest, intermediate and highest mean values found for Contour 1, Contour 2 and Contour 3, respectively (Table 1). No consistent variability was found for bilateral CA Dmax and V50% and for contralateral CA V35% across the three contouring approaches (Table 1).

Conclusion: Here we document the need for a stan-

dardized CA delineation since a relevant dosimetric variability and a significant missing of important structures have been documented among the three most frequent used contouring approaches. Based on our data, we suggest to delineate the whole bulb and whole CA from its origin up to the skull base entry to decrease interobserver variability among clinicians.

Table 1. Dosimetric comparison of three different carotid artery delineation approachesin VMAT planning.

Dosimetric parameter	Contour 1	Contour 2	Contour 3	P value Contour 1 vs 2	Contour 1 vs 3	Contour 2 vs 3
Ipsilateral carotid						
Dmax (Gy)	45,2 (40,9-49,5)	44,7 (39,5-49,9)	44,4 (39,6-49,2)	0,47	0,31	0,33
Dmean (Gy)	10,1 (8,4-11,9)	12,6 (10,3-14,9)	27,7 (20,6-26,8)	<0,0001	<0,0001	<0,0001
V35%	4,6 (1,5-7,7)	5,7 (1,9-9,5)	10,9 (3,4-18,3)	0,001	0,01	0,01
V50%	0,1 (0-0,32)	0,12 (0-0,4)	0,23 (0-0,8)	0,40	0,35	0,34
Contralateral carotid						
Dmax (Gy)	19,1 (15,6-22,7)	19,1 (15,6-22,7)	17,3 (11,9-22,7)	0,6	0,34	0,34
Dmean (Gy)	4,8 (4,1-5,5)	5,8 (4,8-6,7)	10,8 (8,8-12,8)	<0,0001	<0,0001	<0,0001
V35%	0	0	0	NA	NA	NA
V50%	0	0	0	NA	NA	NA

Values are presented as Mean (confidence interval 95%). Contour 1: whole carotid from its origin to skull base entry; Contour 2: from carotid origin to at least 2,5 cm above hyoid bone; Contour 3: 1 cm superiorly and inferiorly to PTV; V35: volume percentage receiving ≥ 35 Gy; V50: volume percentage receiving ≥ 50 Gy; NA: not assessable.

CO066

THE USE OF PERFUSION SPECT TO PRESERVE FUNCTIONAL LUNG IN RADIOTHERAPY FOR NON-SMALL-CELL LUNG CANCER (NSCLC) PATIENTS

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Aims: Single Photon Emission Computed Tomography (SPECT) can be used to avoid, the High perfusion AREA in non-small-cell lung cancer (NSCLC) patients, to potentially reduce lung toxicity. The aim of this study is compare two different 3D-conformal treatment plans, with and without CT/SPECT informations.

Methods: Radiotherapy planning computed tomography (CT) scans was accurately co-registered with SPECT scans and three different perfusion areas, based on SPECT intensity, were segmented: Low Perfusion (LP), Medium Perfusion (MP) and High Perfusion (HP). Two different 3D-conformal plan, with co-planar e non co-planar fields, were generated, one according to nonfunctional Lung information (Anatomic Plan, A) the other one using the perfusion area geometries (Functional Plan, F). Each plan was performed with Varian Eclipse treatment plan System and calculated with Anisotropic Analytical Algorithm (version 10.0.28).

Results: Nine patients, affected by stage III NSCLC, underwent Radiotherapy with 50,4Gy in 28 fractions. A Dose-Volume Histogram (DVH) is used to evaluate the dose to the Target and to the Organs at Risk. F plans produce a significant reduction of dose in HP areas, in particular a reduction V20 HP (p=0,046), of homo-lateral V20Gy HP (p=0,028) and homo-lateral Dmean HP (p=0,039). The V20Gy HP values were reduced by an average of 15Gy to 8Gy, the V20 omo-HP from 38Gy to 22Gy and Dmean omo-HP from 16Gy to 12Gy. There are no significant differences for Dmean, V38Gy and V42Gy of Heart and Dmean, V35Gy and V50Gy of Esophagus and Dmax of Spinal Canal PTV's Homogeneity and Conformity Index.

Conclusions: With Functional Plans, it is possible to avoid HP areas and reduce dose in the HP regions of healthy Lung, especially in homo-lateral lung. This goal is achieved without worsening DVH's constrains in Spinal Canal, Esophagus and Heart, and with comparable PTV's Homogeneity and Conformity Index. The use of perfusion SPECT would allow potentially benefits as prevent lung toxicity and permit a dose escalation.

CO067

INTENSITY MODULATED RADIOTHERAPY – SIMULTANEOUS BOOST IN COMBINATION TO SYSTEMIC THERAPY FOR LOCALLY ADVANCED OROPHARYNGEAL CANCER: LOW RATE OF SALVAGE PHARYNGOLARYNGEAL SURGERY

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Aims: To evaluate the oncologic outcome in term of survival and organ function preservation in patients (pts) with locally advanced oropharyngeal cancer (LAOPC) treated with Intensity Modulated Radiotherapy-Simultaneous Boost (IMRT-SIB) in combination to systemic therapy (ST).

Methods: We conducted a retrospective analysis of 101 consecutive pts treated at Centro di Riferimento Oncologico in Aviano between January 2010 and June 2017. Pts were included if met the following inclusion criteria: age > 18years, clinical and histological proof of LAOPC, no evidence of distant metastases, treatment delivered with IMRT-SIB, concomitant or sequential ST. Salvage Surgery Free Survival (SS-FS) was calculated between the end of radiotherapy and the salvage pharyngolaringectomy for local relapse. SS-FS, relapse-FS (RFS) and Overall Survival (OS) curves were elaborated with Kaplan-Meier methods. A subgroup analysis in relation to TNM stage, ST and Human Papilloma Virus (HPV) status was performed.

Results: Median age was 65 years and 77 (76%) pts were male. Initial TNM stage was III, IVA and IVB in 17 (17%), 66 (65%) and 18 (19%) pts, respectively. HPV status was available in 84 pts and in 47 (47%) pts

was positive. Median dose was 70.95 Gy and delivered in 33 fractions. ST included induction chemotherapy (IC), concomitant cisplatin or cetuximab in 74 (73%) and 27 (27%) pts, respectively. Median follow up was 26.2 months. Six pts (6%) underwent SS for local relapse and all these events were recorded in the first 3 years. Three years SS-FS, RFS and OS rates were 93%, 66% and 75%, respectively (Figure 1). TNM stage was significantly associated with RFS (p=0.01) as well as IC with OS (p=0.002) (Figure 2). HPV related LAOPC showed better RFS and OS (p=0.0009 and p=0.005). None of the analyzed factors was related to higher rate of SS. Late toxicity (LT) was recorded in 36 (36%) pts: grade 1-2 and grade 3-4 LT was found in 35 and 1 pts, respectively.

Conclusions: In our cohort IMRT-SIB with sequential or concurrent ST was well tolerated and showed low rate of salvage surgery for local recurrences. RFS and OS were considerable and influenced by stage, ST and HPV status. None of the factors in analysis was associated with augmented percentage of SS. Further prospective analysis and randomized controlled trials are needed to confirm our findings in particular regard to the optimal combination with systemic chemotherapy.

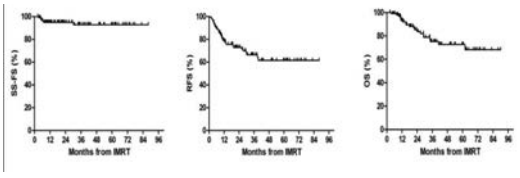

Figure.

CO068

RETREATMENT OF UVEAL MELANOMA LOCAL RECURRENCES AFTER INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY): SINGLE INSTITUTION EXPERIENCE AND SYSTEMATIC REVIEW OF LITERATURE

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Purpose: To report the results of a second course of brachytherapy in a group of patients with locally recurrent uveal melanoma.

Methods: A total of 414 patients underwent brachytherapy treatment in our center between December 2006 and December 2016 were identified. In this group of patients, five that received a second course of treatment with a plaque after local recurrences were included in the study. The reirradiation was performed with Ruthenium 106 plaque (prescribed dose to the apex 100 Gy) or with Iodine 125 (prescribed dose to the apex 85Gy). The dose limiting to the sclera was < 1000 Gy (including first plus second treatment) in order to prevent scleral necrosis. The principal parameters taken into account were local control, metastasis and toxicity profile with particular attention to visus. Furthermore a systematic literature search was conducted through three electronic databases from their inception until February 2018 including Medline/PubMed, Scopus and Embase.

Results: All patients were initially treated with Ruthenium 106 plaque; the reirradiation was performed with Ruthenium 106 plaque in three cases and with Iodine in two cases. The mean time between the first and the second plaque was 56.8 months (range 25-93 months). After a median follow-up of 44.2 months (range 26-65 months) from retreatment all patients evolved with worsening of the visual acuity (median visual acuity was 0.42 at time of recurrence and decline to 0.24 at the most recent follow-up); cataract occurred in two cases, no patient developed scleral necrosis. The local tumor control rate was 100%, no patient underwent secondary enucleation owing to retreatment failure. Distant metastasis occurred in 1 patient after a time of 6 months from retreatment. We identified 103 papers but only 2 met our inclusion criteria and were included in our review.

Conclusions: In selected cases, especially in presence of marginal local recurrence, retreatment with plaque can offer a high probability of tumor control and eye preservation but a worsening in the visus.

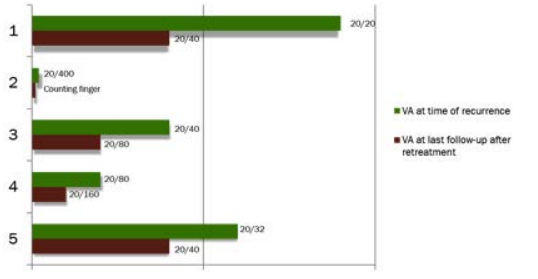

Figure 1.

CO069

T3 LARYNGEAL SCC: A RETROSPECTIVE ANALYSIS OF DIFFERENT THERAPEUTIC APPROACHES IN POLICLINICO SAN MARTINO, GENOVA

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Aims: Optimal treatment for pts with T3 laryngeal cancer is still considered a "grey zone". Different surgery approaches and organ preservation (OP) strategy such as RT or CTRT are available. Our aim was to evaluate the appropriateness of a multidisciplinary team's (DMT) choices retrospectively.

Methods: 144 consecutive pts with T3 laryngeal carcinoma from 2005 to 2016 were evaluated. Each clinical case was discussed by a tumour board. The decisions of the DMT about the best treatment modality for each pt are based on guidelines concerning T3 laryngeal cancer, tumor features, pt factors and pt choice. We considered 2 groups of pts: group A for the surgical treatment and group B for the non surgical modality. For pts in group A transoral re-excision was performed in case of deep or more than one superficial positive margins. Those with persistent tumor after reexcision, perineural invasion, angioembolization, multiple positive nodes or ECE were submitted to adj treatment. For group B the choice to do CTRT was mostly for those pts who were candidates to TL. RT dose ranged from 69.9 to 70Gy in 33-35 fr. Different regimen CT were used.

Results: 106pts were in group A and38 in group B. In groupA 40/106pts received neck dissection and 37/106 (35%) pts underwent adj treatment (RT alone 29pts, CTRT 8 pts). In groupB 15/38pts received RT alone and 23/38pts combined CTRT. Median FU was 35 months, overall 31 pts died, 11 for PD and 20 for other causes. 4pts are alive with disease, 83 are alive and free from disease. 30/144pts had a recurrence:19(18%) in groupA and 11(29%) groupB. 12pts received TL due to recurrence: 8belonged to groupA and 4 to groupB. Consequently concerning the OP rate, an open surgical approach and the presence of recurrence decrease the probability to spear the larynx(OR 6. 05 and OR 7.40 respectively). On the other hand, belonging to group B increase the OP rate (OR 0. 61). OS rates were 89%,80%and64%and DFS rates were 88%, 77%and 77% respectively at 1-3-5 years. For groupA 1-3-5 years DFS rate was 89%,83%and 83% and for group B 82,6%,62% and 62% respectively.

Conclusions: We registered a better but no statistically difference in OS, DFS in group A than in group B. Primary endpoint in OP is survival but also laryngoesophageal function so unimodality treatment is auspicable. To choose the best treatment modality for the single pt a DMT must consider different factors often not clear measurable with high interobserver variability such as pt fitness and motivation or tumor resectability.

CO070

TOWARDS ORGAN PRESERVATION IN RECTAL CANCER: IMPACT OF TIME INTERVAL BETWEEN COMPLETION OF NEOADJUVANT TREATMENT AND SURGERY ON THE RATE OF PATHOLOGICAL COMPLETE RESPONSE

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Aims: To evaluate the impact, in terms of rate of pathological complete response (pCR), of the interval between the end of neoadjuvant chemo-radiotherapy (nCRT) and surgery in patients (pts) affected by locally advanced adenocarcinoma of the rectum.

Methods: From 2009 to 2017, a total of 78 pts with a diagnosis of locally advanced adenocarcinoma of the rectum (stage T3-4 N0-2) were managed at Niguarda Cancer Center along the whole diagnostic and therapeutic pathway. For this analysis we evaluated in all pts the time interval between the end of nCRT and surgical operation. The degree of correlation between this time interval and the rate of pCR was investigated stratifying pts into two six-week time interval groups: 4-9 weeks and 10-15 weeks.

Results: Out of a total of 78 pts, 38 underwent surgery within 9 weeks from the end of nCRT (interval 4-9 weeks). In this group 7 pCR were observed for a pCR rate of 18%. Forty pts underwent surgery after more than 9 weeks from the end of nCRT (interval 10-15 weeks). In this group 10 pCR were observed for a pCR rate of 25%. We also observed that among 18 pts submitted to surgery after more than 12 weeks from the end of nCRT (interval 13-15 weeks), 6 pCR were observed for a pCR rate of 33%. Conversely, the lowest rate of pCR (10.5%) was found in the group of patients operated early (week 4-8).

Conclusions: Our analysis confirms an increased rate of complete pathological response if the time interval between the end of nCRT and surgery is greater than 9 weeks. It also shows a peak of pCR if surgery is delayed until week 13 to 15. In the context of a possible strategy of organ preservation in the treatment of rectal cancer, and if these data will be confirmed by further analyses on greater numbers of cases, we can hypothesize that optimal delay for clinical restaging after completion of nCRT may be longer than 9 weeks. In case of a major clinical response on week 10, a second restaging could be performed on week 13 before leading pts to surgical intervention. A prospective trial (NOCUT trial- EUDRA CT-2017-003671-60) is in progress at our Center to carefully evaluate the safety of omitting surgery in case of clinical complete response.

CO071

TOXICITY PROFILE OF POSTOPERATIVE RADIOTHERAPY (PORT) AFTER TRANSORAL ROBOTIC SURGERY (TORS) IN OROPHARYNGEAL AND SUPRAGLOTTIC LARYNGEAL CANCER PATIENTS: EXPERIENCE OF AN ITALIAN TERTIARY CENTER

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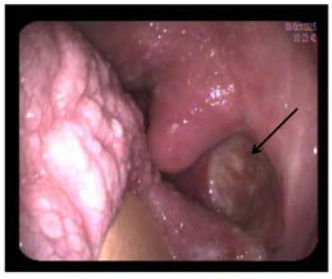
Aims: Postoperative radiotherapy (PORT) is indicated in almost two thirds of patients (pts) treated with transoral robotic surgery (TORS) for malignant head and neck tumors. Aim of the present analysis was to quantify the toxicity profile of pts treated with PORT after TORS for oropharyngeal and supraglottic neoplasms at our Institute. Methods We retrospectively reviewed all pts treated from July 2007 and June 2017 with TORS followed by PORT. Exclusion criteria were: 1) patients with flap reconstruction of the primary surgical site 2) benign diseases 3) recurrent disease 4) previous surgery and/or radiotherapy on head and neck region. Acute and late toxicity (at 12 months) were evaluated according to RTOG/EORTC. Need of enteral nutrition and tracheostomy were consider at any time during and after the course of treatments. Incidence and severity of soft tissue necrosis (STN) were correlated with clinical and dosimetric parameter. Results: Among the 140 patients treated with TORS in the considered period, a total of 28 pts (19 male, median age 63 years) met the inclusion criteria. Dosimetric data from the radiotherapy treatment plans were available for 26 patients: the median value of the prescribed dose was 66 Gy (mean 63.5Gy, range 50-70 Gy). Standard dose fractionation schedule was used for all patients. No patient experienced acute grade 3 skin or mucosal toxicity. One patient had grade 3 dysphagia. At 12 months from the end of treatment, no patient required enteral nutrition while two patients had tracheostomy. STN occurred was found in 4 (14%) pts. Figure 1 shows a typical clinical appearance of a benign ulcer classified as STN. All pts with STN had HPV-related oropharyngeal tumors. No correlation were found between incidence of STN and dosimetric parameters. Three out of 4 (75%) of pts with STN had diabetes whereas only 6 out of 13 (25%) patients without STN had diabetes and the difference was statistically significant (P=0.05). Patients with STN had also greater median depth of resection than patients without STN (2.05 versus 1 mm for STN and no STN, respectively, P=0.09). Conclusion We found a favorable acute and late toxicity profile of PORT performed after a TORS procedure in patients with oropharyngeal and supraglottic tumors. Diabetes results as a possible risk factors for STN. Further analysis on larger series of patients are required.



Clinical appearance of STN defined as persistent nohealing ulceration of the surgical bed > 6 weeks after completion of PORT, after recovery form the acute effects of adjuvant RT

Figure 1.

CO072

FUNCTIONAL OUTCOME OF POSTOPERATIVE IMRT AFTER LARYNGEAL CONSERVATIVE SURGERY: A PROSPECTIVE DATA COLLECTION ON 20 PATIENTS

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Aims: Historical data showed that postoperative radiotherapy performed by 3D conformal technique can worse functional outcome of patients (pts) treated with conservative surgery for laryngeal tumors. Aim of this prospective data collection was to evaluate whether the use of IMRT could ameliorate the toxicity profile of this combined treatment.

Methods: All patients treated with open or endoscopic conservative surgery for laryngeal tumors followed by postoperative IMRT have been prospectively evaluated. Exclusion criteria were: 1)recurrent tumors 2) previous treatment (both surgery and/or radiotherapy) on head and neck region 3) baseline swallowing or laryngeal dysfunction. Both acute and late toxicity have been evaluated according to Common Terminology Criteria

Adverse Event (CTCAE 4.03) scale. Long term functional outcome have been considered as presence of tracheostomy and/or need of enteral nutrition at any time after postoperative radiotherapy.

Results: Twenty pts (18 male, median age 63 yrs) were evaluated. The majority of them had advanced stage (III and IV in 17 pts) and supraglottic (12 pts) tumors. Surgical margins were negative, close and positive in 10, 5 and 5 pts, respectively. Concurrent chemotherapy was administered in 6 pts. Median radiotherapy dose prescription was 66 Gy (mean 63Gy, range 59.4-66 Gy). After a median follow up of 16 months, 12 pts were alive without disease, 1 patient was alive with local recurrence and 4 pts died (3 pts for disease progression). Data on acute toxicity (at the end of PORT) were available for 14 pts. No pts had grade 3 toxicity. Grade 1 and 2 functional mucositis and dysphagia were present in 11,2 and 8,5 pts, respectively. No patient had clinically significant dyspnea. Only one patient suffered from a grade 2 laryngeal edema and were submitted to a surgical removal of a mucosal laryngeal flap three months after the end of radiotherapy with symptoms amelioration. Late toxicity was available for 16 pts and were recorded after a median follow up of 11 months (range 2-32 months). One patient experienced a local recurrence with severe dysphagia (requiring enteral nutrition) and dyspnea. Five pts suffered of a grade 1 dysphagia. No patient required tracheostomy due to treatment-related toxicity.

Conclusions: Despite the short follow up, the toxicity profile of this cohort of pts treated with conservative surgery followed by postoperative IMRT seems to be very low. Further analyses are required to confirm this encouraging preliminary results.

CO073

DOSIMETRIC AND CLINICAL FACTORS AFFECTING TOXICITY IN LOCALIZED PROSTATE CANCER PATIENTS TREATED WITH HIGHLY CONFORMAL IMAGE-GUIDED RADIOTHERAPY

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Aims: to identify dosimetric and clinical factors influencing toxicity in patients affected by localized prostate cancer, treated with conformal (3DCRT, 4 mm micro-multileaf collimator) image-guided radiotherapy (IGRT, cone-beam CT).

Methods: we retrospectively analyzed 294 patients treated between December 2006 and April 2016. Patients received 76 Gy in 38 daily fractions (2 Gy per fraction) delivered to the target volume. X2 test was used to analyze associations between toxicity and dosimetric and clinical parameters. Multivariate analysis was performed using binary logistic regression. Kaplan-Meier method was used for survival analysis.

Results: Median age at diagnosis was 71 years. Median follow up was 62.9 months. Acute gastrointestinal toxicity (GI) grade ≥ 2 was 12.1%; 4 and 5 years late GI were 3% and 4% respectively. Acute genitourinary toxicity (GU) grade ≥ 2 was 33.9%; 4 and 5 years late GU were 6% and 10% respectively. Multivariate analysis showed a correlation between acute GI toxicity and rectal V70 ($p=0.01$, HR 2.73 CI 1.19-6.26), and between acute GU toxicity and smoking habit ($p < 0.01$, HR 2.50 CI 1.51-4.14). Late GI toxicity was correlated with rectal V70 ($p=0.04$, HR 4.76 CI 1.07-21.13), and late GU toxicity with pre-radiotherapy symptoms ($p=0.01$, HR 2.84 CI 1.29-6.22)

Conclusions: highly conformal image-guided radiotherapy shows low rates of acute and late toxicity. Besides the evaluation of high doses received by the organs at risk, comorbidities and lifestyle might have an impact on normal tissue complication risk. Smoking should be avoided during radiotherapy and baseline urinary function should be carefully evaluated.

CO074

CONTOURING OF CARDIAC SUBSTRUCTURES WITH DEFORMABLE NORMALIZED INTENSITY-BASED REGISTRATION

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Aims: Deformable image registration (DIR) is used to adapt organs at risk between two image set: we applied DIR between Contrast (cCT) and Simulation CT (sCT) for patients with mediastinal Lymphoma disease (mLD) treated with involved-site radiotherapy (IS-RT). Segmentation of cardiac substructures (CS) in sCT is time consuming and challenging because of image quality. On the other hand, contrast enhanced CT is routinely performed after Chemotherapy in Lymphomas and support delineation of cardiac vessels and chambers. We describe a fast method for transfer these contours in sCT for treatment planning. We report time required to contour, to perform DIR and verify deformation.

Methods: We selected 10 patients with stage II bulky mLD treated with total dose of 30Gy in 15 fractions IS-RT. Six patients were simulated with arms down and thermoplastic mask, 4 patients with arms up. All patient were with arms up during cCT. cCTs were imported in MIM Maestro (MIM Software, Inc) and the following CS were contoured: whole heart, right and left atrium, right and left ventricle, aortic and pulmonary vessels, left main, left anterior descending (LAD), left circumflex and right coronary arteries. We created a 2 steps workflow that transfers contours from cCT to sCT: the first step was an automatic rigid alignment focused on the upper-heart (vessels). The second step was an elastic alignment plus application of manual Reg-Refine tool focused of the lower-heart (chambers).

Results: Cardiac vessels moved different from chambers: position of the arms up and diaphragm seem

to stretch chambers from vessels. The site that shows major complications after RT for mLD is upper-heart. We focused on the alignment of aortic and pulmonary vessels and LAD. Figure 1 shows degree for DIR in sCT (1A with vectors, 1C with edges) and cCT (1B with vectors): deformation is bigger for chambers. Average time for contouring 11 CS in cCT was 30 min, while the average time to apply registration workflow and verify structures deformation was less than 10 min. Minimal manual intervention was required to adjust contours transferred special for chambers.

Conclusions: Delineation of CS during mLD IS-RT is feasible with cCT and DIR with normalized intensity registration. DIR accounts for different patient set-up, different respiratory and cardiac motion and morphological residual disease.

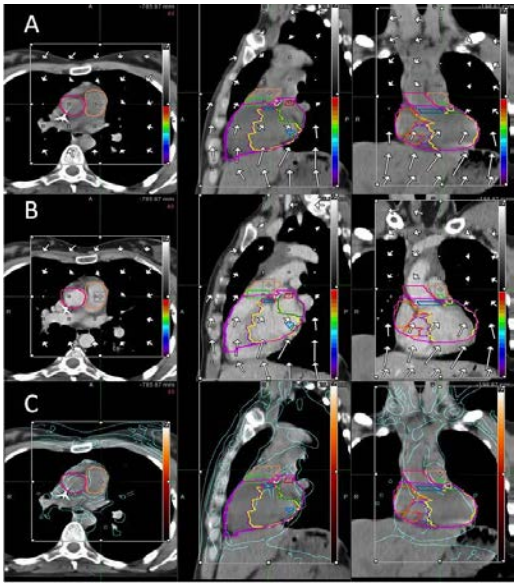

Figure 1.

CO075

10-YEAR CLINICAL AND COSMETIC OUTCOMES OF HIGH-DOSE-RATE BRACHYTHERAPY (HDR-BRT) FOR EARLY BREAST CANCER

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Aims: In GEC-ESTRO randomised trial accelerated partial breast irradiation (PBI) with HDR-BRT was not inferior to adjuvant whole breast irradiation at 5-year follow-up. The long-term results are lacking. We report long-term clinical and cosmetic outcomes of PBI with 192Ir HDR-BRT in early breast cancer patients (pts).

Methods: From May 2005 to February 2012, 124 early breast cancer pts were recruited in a phase II trial of exclusive 192Ir HDR-BRT. Inclusion criteria were: age >40, PS 0-2, unifocal invasive ductal cancer, intraductal cancer component <25%, negative axillary nodes and tumor size ≤2.5 cm. Treatment schedule was 4 Gy twice a day for 4-5 days, up to a total dose of 32 Gy in 8 fractions with a minimum interval between daily fractions of at least 6 hours. Late toxicity was graded at each follow-up visit according to RTOG/EORTC scoring criteria and cosmetic outcomes according to Harvard criteria and scored as excellent, good, fair and poor.

Results: Median age was 67 years (range, 42-85). There were 10 (8%) pT1a, 38 (31%) pT1b, 68 (55%) pT1c and 8 (6%) pT2. Estrogenic and progestinic receptors were positive in 113 (91%) and 104 (85%) cases,respectively. 110 (88%) and 15 (12%) pts received adjuvant hormonal therapy and chemotherapy, respectively. Median follow-up was 112 months (range, 8-156). 2 (1,6%) isolated in-field breast relapse occurred 123 and 129 months after HDR-BRT; 1 (0.8%) isolated out-field breast relapse occurred 107 months after HDR-BRT. 4 (3%) pts developed contralateral breast cancer and another one (0,8%) isolated regional relapse in axillary node. 10 (8%) pts reported a second primary cancer. 5- and 10-year overall survival and cancer specific survival were 95% and 88%, 100% and 98%, respectively. At last follow-up, 107 (86%) pts were alive without disease and 5 (4%) with systemic disease. 10 (8%) pts died: 1 (0,8%) for breast cancer, 4 (3%) for other cancers and 5 (4%) for other causes. Cosmetic outcomes were excellent in 102 (82%), good in 11 (9%), fair in 8 (6%) and unknown in 3 (2,5%) pts. Late skin toxicity was registered in 29 (23,4%) pts, grade 1-2 in 28 (22,5%), grade 3 in 1 (0,8%). Late toxicity was significantly related to the skin administered doses (≤ 55% vs. > 55%, P< 0.05).

Conclusions: PBI delivered with 192Ir HDR-BRT in selected early breast cancer pts was associated to high local control and survival with excellent cosmetic outcomes overall when skin dose was ≤ 55%.

CO076

ACCELERATED PARTIAL BREAST IRRADIATION WITH IOERT AFTER CONSERVATIVE SURGEY: CLINICAL RESULTS IN MONO ISTITUTIONAL EXPERIENCE AFTER LONG TERM FOLLOW UP

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Aims: Intra-Operative Electron Radiation Therapy (IOERT) in breast cancer is a suitable treatment option after lumpectomy, in appropriately selected early stage disease. In this mono institutional experience we eva-

luate local failure, overall survival and aesthetic results at a median follow up of 7,8 years in patients treated at Pisa University Hospital.

Methods: Between January 2003 and March 2013, 332 patients (pts) were submitted to breast conserving surgery followed by IOERT. Inclusion criteria were: invasive unifocal carcinoma without extensive intraductal component, negative margins upon intraoperative assessment, tumor size ≤2.3 cm; menopausal status. Median age of enrolled pts was 67,3 years (range 48 – 87,6). In all cases an informed consent was obtained by the pts, considering the non conventional treatment proposed. 21Gy radiotherapy total dose referred to isodose 90% was delivered by mobile electron accelerator Novac 7; electron energy ranged from 5 to 9 MeV according to breast thickness included in radiotherapy field and evaluated after lumpectomy; collimators diameter ranged between 5-8 cm depending on breast volume and tumor diameter. Univariate analysis was performed to identify predictors of local and distant failure, overall survival and also aesthetic result.

Table 1. Tumor characteristics.

Characteristics	N (%)
Median tumor size: 1,0 cm (range 0,1-2,3cm)	
Tumor grade	
Grade 1	25 (7,5)
Grade 2	163 (49,2)
Grade 3	112 (33,7)
n.d.	32 (9,6)
Histologic type	
Ductal invasive carcinoma	293 (88,3)
Ductal in situ carcinoma	6 (1,8)
Lobular invasive carcinoma	12 (3,6)
Other histologic type	21 (6,3)
Axillary nodes status	
N0	289 (87,1)
1 N+	34 (10,1)
> 1 N+	9 (2,8)
Hormone receptor status*	
ER-, PgR-	16 (4,8)
ER-, PgR+	2 (0,6)
ER+, PgR-	52 (15,7)
ER+, PgR+	258 (77,7)
n.d.	4 (1,2)
Her-2	
Negative	285 (85,8)
Positive	33 (9,9)
n.d.	14 (4,2)
Mib-1	
< 30%	285 (85,8)
30 – 60 %	34 (10,3)
> 60 %	4 (1,2)
n.d.	9 (2,7)
Medical treatments	
Hormone therapy	219 (66,0)
Chemotherapy	36 (10,8)

*ER- or PgR-: <10%

Results: At a median follow up of 7,8 years (range 0,1-14,7), 26 pts(7,8%) had an in-breast recurrence; 5 years local failure was 3,7%. A worse local control was significantly associated with tumor high grade and Mib-1>30%. We also observed 22 cases of distant metastasis (bone, liver, lung, axyllary nodes, brain). In February 2018, 295 pts were alive, 10 death by distant metastases and 27 death by other causes. We found a statistically significant relationship between breast cancer death, distant failure and some tumor characteristics: high grade, number of metastatic axillary nodes >1, negative or poor ER and PgR status and Mib-1>30%. Distant failure is also related to tumor size >1cm. Aesthetic result was good or excellent in the majority of pts treated; only in 9 cases was unsatisfactory but we didn't find any statistical relationship with specific tumor location in the breast (inferior or medial quadrant), tumor size or diameter of collimator used.

Conclusions: IOERT after breast-conserving surgery resulted in a good local control of early stage disease, excellent cosmetic outcome and could be considered an alternative to whole-breast external radiotherapy in properly selected pts.

CO077

CONSERVATIVE SURGICAL TREATMENT IN RECTAL CANCER AFTER NEOADJUVANT RADIOTHERAPY TREATMENT. PROSPECTIVE OBSERVATIONAL STUDY

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Aims: In 2012 we started a prospective observational protocol at the San Giovanni Addolorata Hospital in Rome for patients with rectal cancer with complete clinical response to neoadjuvant radiochemotherapy (nCRT).

Materials and methods: The radiotherapy schedule provides 41.9 Gy in 18 fractions of 2.75 Gy for fraction integrated with fluoropyrimidine (5Fluorouracil or Capecitabine). In our IRB approved protocol patients are evaluated at time 0 by objective, endoscopic, pathological and radiological examinations. 6 weeks after completion of nCRT they are reevaluated. In case of persistence or progression of disease patients undergo surgery with Total Mesorectal Excision. In case of complete or major clinical response they are reevaluated at 12 weeks and subjected to transanal surgical excision to confirm complete pathological response (pCR). Patients with pCR are followed up at 3 months interval whereas if tumor is found on the specimen the patient is operated upon.

Results: From May 2012 to December 2017, 33 patients were enrolled in our protocol. Mean age 64 years (range 54-78 y). Twenty-two men and eleven women; 5 dropped out of the protocol during the study. One patient (3%) was cT2N- stage; 3 patients (9%) cT2N +; 10 patients (30%) cT3N-; 18 patients (55%) cT3N +; 1 patient (3%) cT4N +. At the initial reevaluation (6weks) 15 patients (57%) had poor response to nCRT for which they underwent surgery. 3 patients (19.8%) experienced postoperative complications, according to the Dindo-Clavien classification of grades 1,2 and 5, respectively. One patient (6.6%) died from

postoperative respiratory complications. The remaining 13 patients (47%) had a complete or major clinical response at six weeks underwent transanal excision at 12 weeks. Three patients, who at six weeks had a good response, had a complete response at 12 week re-evaluation. In two of these cases complete response was confirmed to local excision. Of the patients undergoing macrobiopsy, three (23%) presented postoperative complications: two of grade 2 and one of grade 1. In 4 patients (30%) presence of residual disease was found in the specimen after local excision: 2 patients ypT1; 1 patient ypT2; 1 patient ypT3. All underwent LAR with TME.

Conclusions: Globally we found a complete pathological response in 32% of cases (9 patients). Patients were followed for an average of 43 months (range:9-67 mo). Overall survival is 92.9% and 85.8% disease-free survival with a local recurrence rate of 14.2% in the first group; there was no case of local recurrence or death in the second group.

CO078

MODERATE HYPOFRACTIONATED TREATMENT WITH VMAT-SIB TECHNIQUE IN PROSTATE CANCER. IMPACT AND USE OF CLARITY SISTEM IN REDUCTION OF PTV MARGINS AND SPARING OF BLADDER AND RECTAL WALL

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Aims: Clarity Autoscan is a system used for intrafractional prostate (P) motion management during radiotherapy. The system relies on soft tissue imaging of prostate with transperineal ultrasound without implanted fiducials or extra imaging dose. The Clarity system allows to correct the position of patient and the movement of P during treatment, it allows to reduce the margins of PTV. It performed a dosimetric assessment of patients treated with moderate hypofractionation and compares difference dose on bladder/rectal wall according two different ways of margin expansion. Methods: Six patients with P cancer limited to the organ with low-intermediate risk, were selected for treatment with VMAT-SIB. CTV included P in low/risk, prostate/seminal vesicles (SV) in intermediate. A 5 mm margin expansion was added to generate the planning target volumes except in the posterior direction (3 mm). OARs were bladder, rectum, bladder/rectal wall (internal and external to PTV), femoral heads, penile bulb, peritoneal cavity. All patients received 64.5/72 Gy/30 fractions to SV/P in intermediate risk, and 72Gy/30 fractions to P in low risk. The treatment PRV is automatically aligned with the reference PRV and thereafter manually by the operator. When alignment was appropriate, the system takes into account final target displacements with a couch translation alongside the 3 spatial vectors. We checked the intrafraction displacements, calculated average, median and shift ranges in all directions and visualized in a graphic box-plot. We performed dosimetric comparison between treatment-plans and ideal plans on PTV with expansion of 7 mm (5 posteriorly), which we would have carried out without the Clarity system.

Results: We have reported a box-plot with distribution of shift for each patients in IS, LR and AP directions. The target didn't deviate from limits defined in most of the sessions. In dosimetric evaluation between treatment plans and plans with higher margins of PTV we compared volumes of bladder/rectal wall portions included in the PTV, their Dmax and Dmean and we found a net gain in terms of volume and dose in the planes performed with reduction of the PTV margins allowed by the use of Clarity system. Conclusions: Clarity sistem is a non-invasive and non-ionizing treatment, its accuracy in intrafraction localization of target it allows to reduce the margins of the PTV and consequently the volume and the dose of OARS, in particular of the bladder and rectal wall.

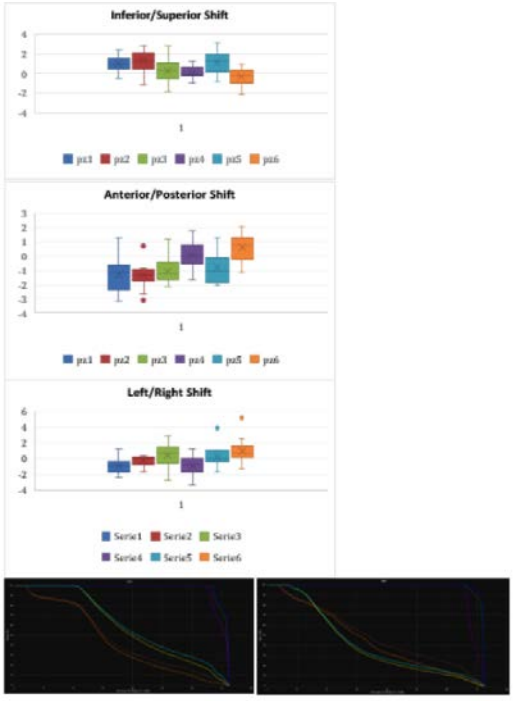

Figure 1.

CO079

CLINICAL OUTCOMES FOR CT-GUIDED HIGH-DOSE-RATE BRACHYTHERAPY IN WOMEN WITH LOCALLY ADVANCED CARCINOMA OF THE CERVIX (LACC)

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Aims: To evaluate the outcome and toxicity on LACC patients treated with radiochemotherapy and intracavitary brachyherapy.

Methods: This study includes 47 patients with LACC (range 30-83 years) treated between July 2010 an November 2016. The most represented stage was FIGO II B (22/47). The patients were consecutively treated with pelvic EBRT and boost to the cervix and parametrials, when indicated. Concomitant CHT with CDDP 40 mg/mq was planned. Subsequently, the patients underwent TC- based endouterine brachiterapy. The response was evaluated at 3 months with PET TC and/or pelvic RM with contrast medium. Since then the patients have been followed with clinical- instrumental controls every 4 months for the first 2 years and every 6 months for the following 3 years. Overall survival was defined from the diagnosis to the last follow-up and disease free survival from the complete response data to the relapse or/last follow-up. Outcome and acute toxicity (gastrointestinal and genitourinary within 6 month) were assessed for all these patients.

Results: The dose range of EBRT was 45-50.4 Gy. Thirty-five/47 underwent to boost to the cervix and parametrials up to 61.6-66 Gy . Concomitant CHT with CDDP 40 mg/mq was administred at 41/47 and all patients received intracavitary brachytherapy (dose range 10-28 Gy). We recorded 44/47 (93.6%) complete response. Three/47 (6.4%) showed a not respondent disease. We observed 8/44 (18%) relapses (one local and 7 sistemic) after a median time of 7 months (range 1-24 months) with a median DFS of 28 months (range 2-93 months). After a median follow up of 32 months (range 20-62 months). 32/47 (68%) patients were alive without disease. Fifteen patients were dead (10 for disease and 5 for other causes in absence of cervical cancer). The evaluation of the toxicity according to RTOG scale showed G1 genitourinary complications in 15/47 patients and G2 in 5/47, while only one patient complained of G3 toxicity. Gastrointestinal toxicity occurred in 11/47 patients for G1 grade and in 6/47 patients for G2 grade. 8/47 patients showed both genito-urinary and gastrointestinal toxicity at different stages of severity.

Conclusions: Our study confirms the efficacy on local control of RTCHT and intracavitary brachitherapy with an acceptable toxicity profile.

CO080

SURVEY AMONG SICILIAN CENTRES OF RADIATION ONCOLOGY ON THE USE OF COMBINED RADIO-CHEMOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER: STRATEGIES OF ORGAN PRESERVATION AND TOXICITY REPORT

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Aims: We conducted a survey among Sicilian centres of radiation oncology to record the different methods of integration of radio-chemotherapy for rectal cancer (RC) both in neoadjuvant and adjuvant settings, the evaluation of surgical procedures in relation to the sphincter preservation and to report the different toxicity profiles of the treatment strategies.

Methods: A questionnaire was sent at the end of 2017 to all the radiation oncology centres of Sicily region in order to collect the data retrospectively over the previous 5 years, from 2012 to 2016. The required data were collected from 12 centres out of 17 which correspond to about 80% of the Sicilian population.

Results: A total of 784 pts(M/F: 509/275) were treated between 2012 and 2016, with a median age of 67y (range 25-92). The majority of pts were treated in the neoadjuvant phase(NP, 62% of the total) compared to the adjuvant phase(AP, 31%) and to those treated radically(7%). The most used chemotherapy protocol was concomitant single-agent CAP(52% of patients) or 5-FU(14%), while 22% did not receive chemotherapy. Induction chemotherapy before concomitant phase was used in 14% of pts treated in NP, and in 64% of AP. In both cases, oxaliplatin-based protocols (FOLFOX/XELOX/CAPOX) were preferred (91% of pts). Information on the surgical treatment received is available for 88% of the sample. Of these, 93% received a surgical treatment. The overall rate of sphincter saving surgery (anterior resection) was 72%, but the contribution of neoadjuvant treatment allowed to reach a rate of 83% in this subgroup (against 65% found in the subgroup of patients treated in AP). Traditional radiotherapy schedule(45-50 Gy in 25-28 fr) was used in 76%

of patients, while an intensified treatment in NP(45 Gy + boost of 9-10 Gy) was used in 15% of patients. Short-course regimen(25 Gy in 5 fr) in NP had a limited use(6%). 3D-CRT technique was preferred over intensity-modulated ones(73% vs 27%). Toxicity was mainly of G I-II CTCAE(skin 23%, GI 39%, GU 14%) compared to G III(GI 4%, GU and haematological <1%). Interestingly, the toxicity rates were significantly higher in the adjuvant group compared to the neoadjuvant(GI: 58% vs 31%, GU: 21% vs 10%).

Conclusions: The survey shows that in the Sicily region integrated therapies for RC have allowed a neoadjuvant approach in the majority of patients, resulting in a greater use of sphincter conservative surgery. The toxicity is also significantly less in this treatment setting.

CO081

IMMUNOTHERAPY AND BREAST CANCER: PRELIMINARY TOXICITY DATA OF A COMBINED TREATMENT FOR TRIPLE NEGATIVE PATIENTS

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Aims: To evaluate the toxicity in triple negative breast cancer patients (pts) enrolled in Neotrip study at National Cancer Institute of Milan.

Methods: Neotrip is a randomized phase III study that evaluate the association of PDL1 direct antibody (atezolizumab) and neoadjuvant chemotherapy with nab paclitaxel plus carboplatin in triple negative breast cancer pts. After surgery pts received adjuvant chemotherapy with FEC schedule and subsequently radiotherapy (RT) if indicated. As part of this study we analyzed the toxicity data of these women. We collected data about haematological toxicity according to WHO criteria and we also reported acute toxicity of pts who received radiotherapy using RTOG criteria.

Results: At the time of this analysis, 6 pts were enrolled in this study. Three women had right and 3 left-side breast cancer, respectively. Pathological stage was IIB IIIA IIIB for 3, 2 and 1 pts, respectively. Median age was 48.5 (range 43-61). Three were randomized in the standard arm of neoadjuvant chemotherapy and the other three in the experimental group with anti-PDL1. In this group all pts received RT after surgery; one patient on chest wall and supra-infraclavicular lymph nodes and two patients on whole breast with boost on the tumor bed. Acute toxicity, assessed at the end of RT, consisted of G2 and G3 erythema in 2 and 1 patients, respectively. Only one patient of the standard group underwent radiotherapy on chest wall and supra-infraclavicular lymph nodes and had G1 skin toxicity. One patient of each group reported dysphagia G1. Haematological toxicities were neutropenia G3 in 3/3 pts, piastrinopenia G1 in 1/3, anemia G2 in 1/3 and leukopenia G3 in 2/3 pts of the group with neoadjuvant chemotherapy plus anti-PDL1. Maximum haematological toxicity in standar arm was anemia and piastrinopenia G2 in one pt and leukopenia and neutropenia G3 in one pt. One pt in the standard group had not any toxicity.

Conclusions: Haematological and acute RT related toxicities were acceptable in pts treated with PDL1 direct antibody. More pts need to be enrolled to confirm these preliminary data.

CO082

THE ROLE OF RADIOTHERAPY IN PATIENTS WITH ADVANCED NSCLC UNDERGOING IMMUNOTHERAPY WITH NIVOLUMAB

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Aims: Aim of the study is to perform a preliminary analysis investigating the role of Radiotherapy in patients with advanced NSCLC (stage IIIb o IV) undergoing Immunotherapy with Nivolumab.

Methods: We retrospectively analyzed 46 patients with advanced or metastatic NSCLC undergoing Nivolumab after platinum-based chemotherapy. All patients analyzed were treated between November 2015 and April 2018, and the indication to RT was assessed in a multidisciplinary setting, on the basis of symptoms, localization and extent of disease and performance status. RT was performed with 3D-CRT or IMRT, whereas the dose and fractionation were variable, based on the characteristics of the site to be irradiated. All patients performed a total body CT before Nivolumab and then every 3 months, or in case of worsening of the symptoms. Survival analysis was performed by Kaplan Meier analysis.

Results: 24/46 patients were treated with radiotherapy and Nivolumab. 7 patients were treated with RT on the primary site in 7 and 17 on metastatic ones. For treatments on the primitive were used conventional fractionations. For metastatic localizations, a conventional fractionation (300-400 cGy/day) was chosen in 10 cases, while an hypofractionation in 7 (> 400 cGy/day). Median follow up was 28 months. An advantage in PFS was observed in patients that were underwent RT on the primary tumor, compared to those

treated on secondary sites (p=0.030) and for patients treated with RT before immunotherapy, compared to those treated after (p=0.015). Better OS were observed in patients who received RT compared to those had never undergone RT (p=0.022) and for patients irradiated on primary lesions compared to patients irradiated on metastatic sites (p=0.02). Better OS was also observed in patients irradiated in metastatic sites, than those who had been subjected to daily fractions > 400 cGy/day (p=0.041).

Conclusions: The subgroup of patients undergoing RT has shown an advantage in terms of OS an PFS, with an acceptable safety profile. Prospective studies are needed to confirm these results and to optimally plan these therapeutic strategies.

Table 1.

Univariate analysis	PFS (months)	p value	OS (months)	p value
Sex				
Male Female	Median 6 (Mean 10+/- 1.5) Median 11 (Mean 12.9 +/-2.7)	*p-value= 0.46*	Mean 16 +/-1.9 Mean 19.5 +/-2.6	*p-value= 0.229*
Radiotherapy				
Yes Not	Median 11 (Mean 11.8 +/-1.7) Median 4 (Mean 9.9 +/-1.8)	*p-value=0.66*	Median 27 (mean 20 +/-1.8) Median 6 (mean 12 +/-2.2)	*p-value=0.022*
Site of RT				
Primitive site Mestastatic site	Median N/A (mean 18 +/-3.46) Median 3 (mean 8 +/-2)	*p-value=0.030*	Median 26 (mean 27 +/- 0.7) Median 11 (mean 14.8 +/- 2.6)	*p-value= 0.02*
Timing				
RT before Nivolumab RT after Nivolumab	Median 21 (mean 14.8 +/- 2.5) Median 3 (mean 5.7 +/- 1.5)	*p-value=0.015*	Median 26 (Mean 20.7 +/-2.6) Median 13 (Mean 16.8 +/-3)	*p-value= 0.67*
Fractionation				
300-400 cGy/die >400 cGy/die	Median 3 (mean 4.8 +/- 1.2) Median 10 (mean 10.6 +/- 2.2)	*p-value= 0.08*	Median 11 (mean 10.3 +/-2) Median 26 (mean 20.7 +/- 3.1)	*p-value= 0.041*

CO083

TRASTUZUMAB AND HYPOFRACTIONATED VMAT TREATMENT WITH CONCOMITANT BOOST FOR EARLY STAGE BREAST CANCER: ACUTE TOXICITY AND COSMETIC OUTCOME IN A PROSPECTIVE CASE SERIES

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Aims: To evaluate acute toxicity and cosmetic outcomes of hypofractionated simultaneous integrated boost (SIB) approach with Volumetric Modulated Arc Therapy (VMAT) as adjuvant treatment in patients with Her2 enriched early stage breast cancer .

Methods: Patients presenting early-stage breast cancer were enrolled in a phase II trial. Eligibility criteria were as follow: age >18 years, invasive cancer or DCIS, Stage I to II (T <3 cm and N ≤ 3), breast-conserving surgery, any systemic therapy was allowed. All patients underwent VMAT-SIB technique. Doses to whole breast and surgical bed were 40.5 Gy and 48 Gy respectively, delivered in 15 fractions over 3 weeks. All HER-2-positive breast cancers were treated with trastuzumab every 21 days for 1 year. Acute skin toxicities were recorded according to RTOG scoring criteria and late skin toxicities according to CTCAE v4.0. Cosmetic outcomes were assessed as excellent/good or fair/poor according to the Harvard scale.

Results: Between August 2010 and April 2016, 787 consecutive patients were treated. A subset of 175 patients underwent adjuvant chemotherapy. Of this subset, the median age was 55 years (range 27-78), the median follow up was 39 months (range 24-80). Seventy patients (40% of the chemotherapy group) had been given trastuzumab therapy. In this last subgroup, at the end of RT treatment, skin toxicity profile was G1, G2 and G3 in 51.1%, 9.7%, and 0% of patients, respectively. During the follow up no grade higher than G1 (13.5%) was reported and cosmetic outcome was good or excellent in 98.2% and 100% at 6 months and 2 years, respectively. We recorded no significant statistically differences compared to other patients. At 2 years, breast pain was recorded by 20.8% and 7.0% of the patients having received chemotherapy and immunotherapy, respectively, and this result was found significant (p=0.04).

Conclusions: Hypofractionated VMAT treatment with SIB after breast conservative surgery in patients undergone adjuvant systemic therapy and Tratuzumab was safe and well tolerated in terms of acute and early late settings. Cosmetic results were also good or excellent in the most of patients. Long-term follow-up data are needed to assess late toxicity and clinical outcomes.

CO084

ACUTE AND LATE TOXICITIES IN HER2-POSITIVE EARLY BREAST CANCER TREATED WITH CONCURRENT TRASTUZUMAB AND HYPOFRACTIONATED RADIOTHERAPY (RT)

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Aims: Trastuzumab combined with chemotherapy improves outcome in HER2-positive BC. However most important studies of hypofractionated RT did not include these patients (pts), usually receiving after chemotherapy concomitant trastuzumab and RT. The aim of our analyses was to evaluate acute and late toxicities of this combined treatment.

Methods: We retrospectively analysed 603 early

breast cancer patients consecutively treated in our Institute after breast-conserving surgery with hypofractionated RT (2.66 Gy x 16 or 2.25 Gy x 21, both schedule ± boost) from June 2014 to December 2017. Acute and late toxicities were assessed according to the CTCAE-v3 criteria. Breast erythema, moist desquamation, pain, fibrosis/induration, telangiectasia, hyperpigmentation, scar retraction, ulceration, breast/arm lymphedema, late mastitis were evaluated.

Results: Median follow-up was 27 (4-47) months. Hormonotherapy was administered in 513 (85%) cases, 161 (26.7%) pts received adjuvant chemotherapy and 62 (10.3%) pts received, after chemotherapy, concomitant trastuzumab and RT. The two cohorts (trastuzumab and non-trastuzumab group) were similar in comorbidity, postsurgical mastitis, RT technique, fractionation schedule, breast volume, menopausal status and clinical-pathologic stage. Hypofractionated RT was overall well tolerated with mild acute and late toxicity. No grade 3-4 side effects occurred. In the total group mainly factors significantly associated with acute and late toxicity were large breast size and maximum dose to the PTV, while the association of trastuzumab was not statistically significant.

Conclusions: In our experience, the association of hypofractionated RT with trastuzumab does not increase acute and late skin toxicity at a longer follow-up. Hypofractionated RT was generally well tolerated.

CO085

DOES COMBINED IMMUNE CHECKPOINT INHIBITOR WITH ENCEPHALIC RADIOTHERAPY INCREASE THE FREQUENCY OF TOXICITY AND ADVERSE EVENTS? EXPERIENCE OF A SINGLE CENTER

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Aims: Recently, immune checkpoint inhibitors (ICIs) have shown highly promising responses in solid tumors. Intracranial metastases are a common cause of morbidity and mortality in patients with tumor, and are frequently managed with radiation therapy (RT). The safety of cranial RT in the setting of treatment ICIs has not been established. We aimed to assess toxicity and adverse events (AEs) in a cohort of patients who received cranial RT and were treated with anti programmed cell death-1(PD-1).

Methods: We identified 12 patients with advanced solid tumors (10 Non Small Cell Lung Cancer (NSCLC) -83.3%-,1 melanoma-8.3%- and 1 renal cell carcinoma-8.3%-) with brain metastases, who received cranial RT and were treated with anti PD-1. RT-related AEs were retrospectively evaluated and analyzed according to ICI treatment status, cranial RT type, and timing of RT with respect to ICI.

Results: We enrolled 12 patients, between July 2017 and May 2018: 7 (58.3%), 2 (16.7%), and 3 (33.3%) patients received stereotactic RT, whole brain RT or both, respectively. 33.3% of patients received more than one stereotactic course . We observed seizures in one patient during whole brain RT who was symptomatic before treatment; Levitaceram dose escalation and mannitol were used to control seizures. We observed only one radionecrosis (8.33%) occurring 2 months after the end of stereotactic RT. We observed no significant difference in acute neurological toxicity between patients who received whole brain RT or stereotactic RT. Additionally, there was no difference in AE rates on the basis of timing of ICI administration with respect to RT. Cognitive evaluation is in full swing. The median follow up was 5 months, but 2 patients (16.7%) died before follow up and 2 (16.7%) haven't reassessed yet 6 patients (50%) had brain MRI after RT: 2 (33.3%) had brain progression after stereotactic RT , 3 (50%)complete response after stereotactic RT and 1(16.7%) partial response after whole brain RT. 2 patients(16.7%) died before MRI evaluation for extracranial disease progression and 4 patients (33.3%) will have MRI in the next few months .

Conclusions: Treatment with an ICI and cranial RT was not associated with a significant increase in RT-related AEs, suggesting that use of anti PD-1 in patients receiving cranial RT may have an acceptable safety profile. Nonetheless, additional studies are needed to validate this approach.

CO086

TOLERANCE AND SAFETY OF CYTOREDUCTIVE RADIOTHERAPY (RT) IN STAGE IV NON SMALL LUNG CANCER (NSCLC) PATIENTS DURING NIVOLUMAB: A RETROSPECTIVE SINGLE CENTRE ANALYSIS

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Aims: Immunotherapy (IT) has enhanced the treatment armamentarium for stage IV NSCLC. Radiobiological studies and initial clinical reports suggest a potential synergistic effect of RT and IT. Aim of the study is to investigate the safety of palliative RT during concurrent treatment with Nivolumab (NIVO) in metastatic NSCLC patients (pts).

Methods: 25 pts affected by stage IV NSCLC were treated with palliative RT given concurrently with NIVO from 2015 to 2018. Twenty-one pts were male, 4 pts female. Mean age was 65. Adenocarcinoma was diagnosed in 68% of pts, while squamous cell carcinoma in 32%. At diagnosis, 4 pts had Stage III NSCLC,while the other 21 pts stage IV. All pts were previously submitted to 1st line chemotherapy. NIVO was administered as 2nd line in 20 pts, as 3rd line in 3 and in the remaining 2 as 4th. Eight pts received RT immediately

before beginning NIVO, while 17 were irradiated during a previously initiated treatment. RT was delivered in 17pts to bone metastasis, in 5 to lung nodules, in 1 pt to lymph nodes and in 2 to soft tissue. Only 1 pt underwent whole brain RT.

Results: RT was always administered in a palliative setting:11pts received 30 Gy in 10 fractions(Fx), 10 pts 20 Gy in 5,2 pts 36 Gy in 12 Fx,1 pt 8 Gy in single session and another 1 pt 25 Gy in 5 Fx. In 40% of pts,treatment was planned with virtual simulation and post-hoc 3D dose calculation, in 56% 3D conformal RT was used a priori and in 4% a Volumetric Arc Therapy plan was prescribed. At a mean FUP of 18.7 months 11 pts were alive. During FUP 13 pts had disease progression (PD). Mean number of NIVO administrations was 14 and mean time to progression was 4 months.Seventy percent of pts had clinical benefit from RT in terms of clinical and/or radiological response. In 2 pts,RT seemed to enhance also systemic control in "out-field" metastatic sites, suggesting an "abscopal effect". No pt had to interrupt systemic therapies during/after RT and no severe RT-related toxicities were found. Known systemic side effects from NIVO were observed in 4 pts: 1 myocarditis, 1 liver toxicity, 1 pneumonitis and 1 intestinal subocclusion.

Conclusions: RT and IT with NIVO represent a safe and efficient multimodal treatment, with the available data suggesting also potential, synergystic effects on local and systemic disease in stage IV NSCLC pts even when palliative RT doses are used. Ongoing studies set out to understand the optimal timing, RT doses and ideal combination between RT and IT in advanced NSCLC.

CO087

A MONO-INSTITUTIONAL EXPERIENCE OF TRASTUZUMAB EMTANSINE (T-DM1) USE IN METASTATIC OR LOCALLY ADVANCED HER-2 POSITIVE BREAST CANCER PATIENTS

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Aims: The objective of our study was to evaluate safety and efficacy of T-DM1 in a cohort of metastatic or locally advanced HER-2 positive breast cancer (mBC) patients, in second-line setting and beyond.

Methods: analyzed patients were treated with T-DM1 and had to be affected by HER2-positive mBC having received prior therapy for mBC, or having developed disease recurrence during or within six months of completing adjuvant therapy. Data related to patients' characteristics, tumour status, and previous breast cancer-related treatments were recorded . We evaluated toxicity according to Common Terminology Criteria for Adverse Events (CTCAE) v4.03, and treatment response according to RECIST v1.1. Efficacy outcome was measured in terms of progression free survival (PFS), evaluated since the start of the T-DM1 to its interruption for progression of disease (PD), toxicity or death. Survival analysis was performed by Kaplan-Meier method. Moreover, univariate analysis was performed to correlate patients and disease-related parameters to outcome (e.g. age, inflammatory breast cancer, use of Trastuzumab-Pertuzumab, number of previous lines, best response).

Results: from July 2014 to May 2018, 34 patients were treated with T-DM1. Median age was 59 years. 3 (9%) patients were treated with T-DM1 in the first line, after a PD occurred during adjuvant Trastuzumab, 23 (68%) were treated in the second line, and 8 (23%) in a setting beyond. Treatment response assessment showed complete response in one patient (3%), partial response in 6 (17%), stable disease in 23 (68%), while 4 (12%) showed a PD. The main reason of T-DM1 interruption was PD (17, 50%); 6 (17%) patients interrupted drug due to severe toxicity (interstitial pneumonia), while 10 (29%) patients continued T-DM1 treatment at the time of analysis. At the last follow up 19 (56%) deaths occurred. The median PFS was 18 months. Univariate analysis showed adjuvant trastuzumab as the only variable significantly related to a better PFS (44 months vs 10 months, p .019). Overall survival, measured at the last follow-up, was 22 months. No parameter related with a better OS, with the exception of best response to treatment that showed a trend towards a better OS (20 months versus not reached, p .05).

Conclusions: our preliminary results in HER2-positive mBC confirm that T-DM1 is a well tolerated drug and offers a valid option in all subgroups of analyzed patients, even when heavily pretreated.

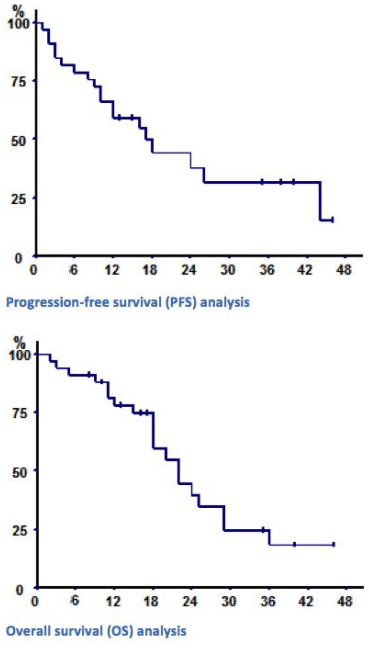

Figure 1.

CO088

IMPACT OF HEALTH-RELATED QUALITY OF LIFE AND SYMPTOMS SCALES IN IRRADIATED LUNG CANCERS TREATED WITH NIVOLUMAB IN OUR EXPERIENCE (YTHACA 1.1 LUNG)

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Aims: In the last decade, the prognosis of advanced non-small-cell lung cancer (NSCLC) has been improved by development of immune checkpoint inhibitors such as nivolumab. Patient-reported outcomes are increasingly used as a complement to biological data to inform patient-centred care and clinical decision-making. We here investigated the impact of patient-reported health-related quality of life and symptoms in NSCLC treated with nivolumab.

Methods: Consecutive patients with locally-advanced or metastatic NSCLC treated with nivolumab as second or third-line therapy for recurrent or progressive disease, between May 2017 and March 2018 were included. EORTC 30-item Core Quality of Life Questionnaire (EORTC QLC-C30) on general cancer symptoms, functioning, global health status and quality of life and the European Organisation for Research and Treatment of Cancer 13-item Quality of Life Questionnaire-Lung Cancer Module (EORTC QLQ-LC13) questionnaire on disease-specific symptoms, were administered before starting treatment (TP1) and at the time of the first revaluation (TP2). Raw scores were transformed to a linear scale ranging from 0 to 100, with higher scores representing better outcomes on the global health status/QoL and functioning scales and worse outcomes on the symptom and single-item scales.

Results: Seventeen patients were treated, mostly male (65%), current or former smokers (76.5%) with Eastern Cooperative Oncology Group (ECOG) PS score <2 (88%). Median age was 67 years (range: 49-79) and 53% were aged ≥65 years. Previously 15/17 (88.2%) patients had undergone radiotherapy on the thoracic disease or for metastatic sites. Mean number of nivolumab cycles was 12 (range: 1-26). The questionnaires were completed by 10/17 (59%) of the patients. The mean EORTC QLQ-30 scores at baseline were: 84.6 (range 72-100) for Functional scale; 15.83 (range 2.5-30.7) for Symptom scales and 68.2 (range 25-100) for Global health status/QoL. The mean EORTC QLQ-LC13 score at baseline was 17.7 (range 8.3-38.8). At TP2, patients experienced a mean improvement of 3.2 in Functional scale and 9.6 in Global health status/QoL and a mean reduction of 5.44 in Symptom scales and 1.5 in EORTC QLQ-LC13.

Conclusions: The use of health-related quality of life and symptoms questionnaire, favoured to its easy comprehension and patients high compliance, with other clinical and diagnostic factors, could be useful to help clinicians in the management of patients treated with nivolumab

CO089

CARBON ION RADIOTHERAPY IN THE TREATMENT OF MALIGNANT PERIPHERAL NERVE SHEATHS TUMORS: PRELIMINARY RESULTS

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Introduction: A malignant peripheral nerve sheaths tumors (MPNST) is a rare highly aggressive soft tissue sarcoma of ectomesenchymal origin. MPNSTs arise from peripheral nerve branches or sheath of peripheral nerve fibers and they are seen in 3 settings: sporadic, postradiation status and associated with neurofibromatosis type 1 (NF1), the latter is most important risk factor for MPNST. Radical surgical resection remains the mainstay of treatment, but it is not always technically possible for proximity to neurovascular structures and/or for tumor size or because it results in high unacceptable morbidity. Hence primary definitive radiotherapy (RT) can be considered and, due to their relatively radioresistance, carbon ions radiotherapy (CIRT) seems to be an attractive treatment option. CIRT offers increased biological effectiveness and very conformal dose distribution resulting in improved LC rates with a low toxicity profile.

Aims: To report our preliminary results (outcomes and toxicity) of CIRT in the treatment of MPNSTs.

Methods: We retrospectively analyzed 13 patients (pts) with MPNST treated with CIRT at CNAO between 2013 and 2016. Treatment planning was based on CT rigidly registered with contrast enhanced MRI. Toxicity was recorded according to CTCAE 4.0.

Results: Median age was 54 years (range 23-72). Two pts were NF1-associated, 1 pt had been previously irradiated for non-Hodgkin's lymphoma. Tumors were located in upper extremity (4 pts in brachial plexus), in pelvic region (1 pt), in head and neck (6 pts) and in trunk (2 pts). Median dose was 73.6 Gy[RBE] (70.4-76.8 Gy) in 16 fractions (4 fractions per week) with a median daily dose of 4.6 Gy[RBE] (range: 4.4-4.8 Gy) After a median follow-up of 24.6 months, we observed 6 local progressions with a median local progression free survival of 23.2 months (range: 2.2-45.4). Acute toxicities were mild, no grade > 2 side effects were observed and no treatment interruption was needed. G3 late toxicity was scored in 2 pts (brain radionecrosis in MPNST of the clivus, brachial neuropathy in MPNST involving the brachial plexus).

Conclusions: Despite some limitations of our study (namely the retrospective nature, the small sample size

and the short follow up), in our cohort CIRT yielded a good LC with a low rate of acute and late toxicities. CIRT for MPNSTs should be further investigated in a prospective trial.

CO090

CLINICAL OUTCOME IN PATIENTS WITH SKULL-BASE CHORDOMA TREATED WITH PROTON AND CARBON ION RADIOTHERAPY AT CNAO

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Aims: Chordomas are rare and locally aggressive tumors and treatment has proven to be challenging. Adjuvant radiotherapy (RT) is a predictor of improved progression-free survival and it is always recommended after surgery. Exclusive RT is the treatment of choice for unresectable chordomas. The aim of the study was to evaluate local control (LC) and toxicity profile of patients (pts) with skull-base chordoma treated with exclusive or adjuvant proton therapy -PT- and carbon ion therapy -CIRT-

Methods: Between September 2011 and December 2017, a total of 134 pts (79 men and 55 women) with a median age of 57 years (range 14-86) with histologically proven skull-base chordoma were treated with particle therapy. 102 (76%) pts had previous surgery and complete macroscopic resection was achieved only in 15 pts (20%). 61 pts were treated with PT and 73 with CIRT, the particle choice was based upon surgical treatment, toxicity risks related to patients' characteristics, surgical complications and the amount of residual disease after surgery. Median prescribed total dose was 70,4 Gy RBE (range, 35,2-70,4) in 8-22 fractions (median 16 fractions) of 3-4,4 Gy RBE (median 4,4 Gy RBE) for CIRT, and 74 Gy RBE (range, 70-74) in 27-37 fractions (median 37 fractions) of 2 Gy RBE for PT. Clinical outcome (LC, 3 year local relapse free- LRFS and overall -survival -OS-) and toxicity profile (according to Common Terminology Criteria Adverse Events -CTCAE V4.03- scale) were evaluated

Results: The median follow-up was 32 months (range, 2-64). LC was 83%. In pts that underwent complete macroscopic surgery followed by PT, LC was 100%, in pts with uncomplete resection/only biopsy and PT/CIRT, LC was 79%. In field recurrence occurred in 13% (18 pts). In 16 out of 18 cases the tumor was in close proximity to the brainstem. 6 pts (4%) developed distant metastasis after a mean interval of 12 months. The resulting 3-year LRFS and OS were 80% and 90% respectively. The toxicity profile was favorable. High grade (G3-G4) late toxicity occurred in 4% of pts: 1 case of complete visual loss (G4) expected because of optic nerve in field, 1 case of soft tissue necrosis, 2 cases of cranial nerve neuropathy and 2 cases of pituitary dysfunction

Conclusions: Particle therapy is the most innovative and conformal RT for treatment of skull base chordomas. It allows to deliver higher (biologically effective) dose levels and to obtain high tumor control rates, minimizing radiation-related side effects

CO091

PROTON THERAPY (PBRT) IN THE TREATMENT OF OCULAR AND ORBITAL DISEASES. THE EXPERIENCE OF THE CATANIA CENTRE

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Aims: The therapeutic possibilities of tumors of the eye and orbit are substantially two: surgical (eg resection, enucleation) or radiotherapy with proton beams (PBRT) or episcleral brachytherapy or SBRT with Gamma Knife. At CATANA centre (Centro di AdroTerapia ed Applicazioni Nucleari Avanzate) we use PBRT and to date we have a 16 years follow up.

Methods: From March 2002 to May 2018 a total of 376 patients (pts) suffering from eye or orbital tumors were treated with PBRT at our centre. 312 of these pts were affected by uveal melanoma in T1-T3 stage. 37 pts suffered by squamous or basal cell tumors of the eyelid and periorbital tissues, 27 pts were affected by other tumor types (eg conjunctival melanoma, orbital NHL, choroidal metastases). Treatment was carried out at CATANA facility by using a 62 MeV proton beam. Pts were treated with a total dose of 60 GyRBE in 4 daily fractions of 15 GyRBE (for melanoma isthologies), or 48-60 GyRBE (epithelial isthologies) or 36-44 GyRBE (NHL). Target volume was tumor as a whole with a margin of 2.5-3 mm.

Results: Pts were followed up every 6. Median follow-up was 9 years (range 0-16). Local control rate in pts with uveal and conjunctival melanoma was 98% and 96% respectively. Orbital lymphomas and periorbital skin cancers had a local control rate of 95%. OS in pts with uveal melanomas was 100%, 86%, 73%, 63% at 1, 5, 10 and 15 respectively. PFS was 92%, 82%, 75%, 61% at 1, 5, 10, 15 years respectively. Systemic metastases, mainly in liver (86%) and lung (13%), developed in 16% of pts after a median interval from treatment of 3.5 years. Radio-induced side effects such as neovascular glaucoma and madarosis developed in 23% and 33% of pts. Blepharitis, xerophthalmia, epithelial keratopathy, rubeosis iridis are rare. The maintenance of a good visual function was possible in 53% of pts. Eleven

percent of pts were subsequently subjected to enucleation following the appearance of radio-induced rethinal damage and rarely for local progression or corneal perforation (6 cases).

Conclusions: PBRT has been shown to be effective and safe in the conservative treatment of uveal melanomas, but also periorbital skin tumors and other rare orbital cancers can benefit from the treatment, thanks to the better dose distribution compared to the other radiotherapy methods.

CO092

QUALITY INDICATORS OF INTENSITY MODULATED-IMAGE GUIDED RADIOTHERAPY (IM-IGRT) CONCOMITANT TO CHEMOTHERAPY (CT): A BENCH-MARKING ANALYSIS FOR CLINICAL AND TECHNICAL GOVERNANCE

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Background: The introduction of new technologies of RT requires the analysis of complex quality and safety issue. Quality Indicators (QIs) may provide useful measures of workload, service and organization performances in order to compare sites with guidelines of 'best practice', in the field of accreditation/certification systems, to assess operative conditions and draw up plans of action to produce quality improvement.

Aims: 1) To administer a comprehensive indicator system on clinical, technical and organizational application of IM-IGRT combined with CT in the RT Unit of the Academic Hospital of Udine; 2) To compare the results with the data published by four italian RT Validation Centers (RT-VC); 3) To provide quality improvement for clinical and technical governance

Methods: Since 2014 to 2016, we studied the evolution of the technical and clinical application of IM-IGRT, related to the total courses of RT. Then, we analyzed the activity performed during a year, 2016, using a comprehensive indicator system published on Critical Reviews in Oncology/Hematology 108 (2016) 52–61, to compare our QIs with the data tested by four Italian RT-VC during a year, 2015, and with the International (European) Standards. QIs were divided into three types: two Structure QIs, ten Process QIs and two Outcome QIs

Results: We performed an upsizing of the technical and clinical application of IM-IGRT, related to the total courses of RT, from 13.31% (216/1622) in 2014, to 20.63% (299/1499) in 2015, to 30,04% (411/1367) during 2016. Regarding the QIs, the data are detailed in the Table 1. In Udine, the bench-marking analysis highlights seven QIs in the proposed standards, four above and three below the compared standards. The improving plan for clinical and technical governance includes the introduction of: 1) the elastic registration imaging and autoplanning softwares; 2) new prospective trials; 3) an adapted maintenance program of the LINACs; 4) the patients' opinion analysis; 5) the administration of QIs for pathology districts

Conclusions: The administration of a comprehensive QI system on the application of IM-IGRT + CT has offered a bench-marking analysis with the best practice of four Italian VC and the European standards. We provide a continuous quality improvement for clinical and technical governance in order to motivate and require additional resources. The next step is the validation and application of the Qis by a multi-institutional group of the AIRO

Table 1. Quality Indicators for IM-IGRT.

Quality indicators	Udine	Italian RT Validation Centers (VC)	International (European) Standards
Structure QIs: 1) Adequacy of equipment for IMRT/IGRT	3/3 LINACs (100%)	13/14 (92,8%)	72%
Structure QIs: 2. Workload	Total number of patients treated in 2016: 1367; Radiation Oncologist (MD): 8 (average 170,8), Medical Physicist (MP): 6 (average 227,83), Radiation Technologist (RTT): 16 (average 85,43)	In 2015, the number of patients treated per year, the number of MD, MP and RTT were 1040 patients, 7, 6, 12 for the Center 1; 1910 patients, 10,9,17 for the Center 2; 320 patients, 3,3,5 for the Center 3; 1936 patients, 8,6,20 for the Center 4	MD: 209, MP: 303, RTT: 77.
Process QIs: 1. Multidisciplinary approach to patient care	77%	81%	80%
Process QIs: 2. Adequacy of multi-parameter imaging	PET-CT: 12.5%; MRI: 47.5%	PET-CT: 27.9%; MRI: 25%	PET-CT + MRI: 15%
Process QIs: 3. Clinical record quality	100%	100%	100%
Process QIs: 4. Mean Waiting time	16 days per patient (pt)	22 days per pt	≤ 30 days per pt;
Process QIs: 5. Appropriateness of Quality Control programs (quality assurance QA)	100%	100%	100%
Process QIs: 6. Number of dosimetric controls on patients treated by IMRT/IGRT	100%	100%	100%
Process QIs: 7. Number of Megavolt(MV) or Cone Beam Computed Tomography (CBCT) controls versus number of RT fractions	1/3 fractions (off-line protocols are implemented)	100%	100%: at least once per fraction when off-line protocols are not implemented
Process QIs: 8. Number of clinical controls of patient during treatment	1 clinical examination every 5 RT sessions (1 per week) = 100%, even twice a week	100%	1 clinical examination every 5 RT sessions (1 per week) = 100%;
Process QIs: 9. Number of Adaptive radiotherapy	3%	10%	10%
Process QIs: 10. Total Treatment room occupation Time (called TTT) can be subdivided into the five intervals: URT (undressing room time), ST (set-up time), IT (imaging set-uptime), SAT (set-up approval time) and BOT (beam on time).	3 patients/hour	2.4-3 patients/hour	depending on the IMRT/IGRT machine, it should be at least 2.4 patients/hour.
Outcome QIs: 1. Number of patients treated in clinical studies	prospective studies: 0% retrospective studies: 81%	13% (range 3%-30%)	13%
Outcome QIs: 2. Machines uptime	96%	97.8% (range 93-99%)	range 90-97%.

CO093

REIRRADIATION OF SALIVARY GLAND TUMORS WITH CARBON ION RADIOTHERAPY (CIRT) AT CNAO

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Aims: To report oncologic and functional outcomes of carbon ion radiotherapy (CIRT) in re-radiation setting for recurrent salivary gland tumors at CNAO.

Methods: From november 2013 to december 2016 patients (pts) with recurrent salivary gland tumors were enrolled in a phase-II protocol (CNAO-S14) to evaluate outcome of CIRT in the setting of re-radiation in terms of toxicity and tumor control.

Results: A total of 51 pts met the criteria of the study and were enrolled on the protocol. Pts median age was 60 years (± 14.34), 53% males and 47% females. Majority of pts (74.5%) had adenoid cystic carcinoma, rcT4a (51%) and rcT4b (37%) stage, 90% without clinically diagnosed nodal disease. Median dose of prior photon based radiation was 60Gy (± SD: 10.4, range: 24-78Gy). Median time interval between prior radiation and recurrence was 6.33 years (SD: 3.67, range: 1.08 to 20 years). Median dose of CIRT at the time of re-radiation was 60GyE at 3 GyE per fraction. During re-radiation, 11 pts (21.6%) had G0 toxicity (no toxicity), 19 pts (37.3%) had G1, 19 pts (37.3%) had G2 and 2 pts (3.9%) had G3 toxicity. Median Follow-up was 19 months (SD: 14.42, range: 2-57). Twenty one (41.2%) pts had stable disease and 30 pts (58.8%) tumor progression at the time of last follow up. Furthermore, 14 pts (27.5%) had no late toxicity, 9 (18%) pts had G1, 19 pts (37%) had G2 and 9 pts (17.5%) had G3 . Using Kaplan Meier method, estimated progressione free survival PFS (actuarial) at one, two and three years were 80%, 65.1% and 43.5% respectively. Estimated overall survival OS (actuarial) at one, two and three years were 90.2%, 69.1% and 54.5% respectively. The estimated mean and median PFS was 28.89 (SD: 3.06) and 25.00 (5.95) months respectively. In receiver operating curve (ROC) analyses, there was significant difference of median survival time after CIRT between the cut-off value of 34 cc of gross tumor volume (GTV) in treated pts. The estimated median PFS in pts with GTV less than 34 cc and more than 34 cc were 34.00 (±3.37) and 13 months (±7.13) respectively (log rank test, p=0.038).

Conclusions: In re-radiation setting, CIRT is effective in controlling local progression of recurrent salivary gland tumors along with acceptable rates of acute and late toxicity. In this study Drs Hasegawa was supported by Associazione Italiana per la Ricerca sul Cancro (AIRC), project IG-14300.

CO094

EVALUATION OF OUTCOMES AFTER STEREOTACTIC HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER

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Aims: Several randomized trials support the use of high doses of radiation for prostate cancer in patients (pts) with localized prostate cancer. We retrospectively report collected data from a cohort of localized prostate cancer pts treated with Cyberknife (CK) Stereotactic Body Radiotherapy Treatment (SBRT) in our Center.

Methods: From July 2007 through June 2016 a retrospective analysis was carried out on 217 pts with a median age of 75 years (range 52 – 86), median prostate volume of 75.6 cc (range 37.03-163.16)and clinically localized prostate cancer. CK was used to deliver fiducials based image guided SBRT. The majority of pts 116 (53%) were low risk , 60 pts (28%) were intermediate risk and 41 patients (19%) were high risk (according to the NCCN criteria). Pre-treatment PSA ranged from 1.51 to 51 ng/ml (median 8.51 ng/ml). 17 (41%) of 41 high risk pts received Androgen Deprivation Therapy (ADT), that was not administered to any low – intermediate risk patient. The course of radiotherapy consisted of 38 Gy over 4 fractions (9.5 Gy per fraction) given daily to the PTV. Heterogenous dose planning was used, dose was normalized to the 75% isodose line in order for the prescription dose to cover at least 95% of PTV. Real-time intrafractional motion tracking was used.

Results: With a median follow up of 61 months (range 12 – 120), the six years actuarial PSA relapse free survival rate is 94.4% (CI: 90.8%-98.2%) with 98.2% for low risk, 94.5% for intermediate and 85.6% for high risk. In total 23 (10.5%) pts died during the follow up for unrelated causes, only one (0.5%) died for prostate cancer. The patterns of PSA response show a gradual decline with a PSA nadir below 1.0 ng/ml, 12 months after the treatment. The majority of pts did not reported any early genitourinary (GU) (53.5%) or gastrointestinal (GI) (79.3%) toxicities. Limited acute urinary symptoms(grade I or II) were common in 46.5% of pts, no one experienced grade III or worse symptoms. 20.3% reported grade I or II acute GI symptoms, while only one patient experienced a grade III acute proctitis. No grade IV rectal toxicity was observed. Regarding late toxicity the majority of pts (78.3%) experienced grade 0 GU toxicity, 39 (18%) pts experienced grade I or II symptoms, while 7 (3%) pts reported grade III toxicity. In one patient (0.5%) a grade IV bladder fistula was observed. The majority of pts (95%) did not experienced late GI toxicity, only Grade I or II

symptoms were observed in 10 patients (4.6%), while grade III or higher was not reported.

Conclusions: Our preliminary data confirm that Cyberknife SBRT represents a non invasive method for the definitive treatment of localized prostate cancer with results not inferior to standard fractionated radiotherapy in terms of biochemical control rates at up to 6 years and early and late toxicities. Long-term follow-up is needed in order to evaluate the maintenance of biochemical and clinicaloutcomes and late toxicity results.

CO095

ADENOID CYSTIC CARCINOMA OF THE HEAD AND NECK TREATED WITH CARBON ION RADIOTHERAPY AT CNAO ACCORDING TO PHASE II CLINICAL STUDY (CNAO S9/2012/C): PRELIMINARY RESULTS

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Aims: To evaluate preliminary results of carbon ion radiotherapy (RT) in patients (pts) with adenoid cystic carcinoma (ACC) of the head and neck (H&N) region treated with curative intent at the National Center for Oncological Hadrontherapy (CNAO) according to the phase II clinical study CNAO S9/2012/C.

Methods: Between March 2013 and September 2016, 135 patients (M/F = 61/74) with ACC of the H&N were treated with active scanning carbon ion RT. Pts average age was 54 (range 19 – 82). Tumour site was minor salivary gland in 90 (67%) and major salivary gland in 45 (33%) pts. In 20 pts (15%) treatment was at disease recurrence, 115 (85%) pts were treated after first diagnosis. Before carbon ion RT, 83 (62%) pts received surgery, of these 60 (45%) pts had positive margins (R1), 13 (10%) pts had no status of margins on histological report, and 9 (7%) pts receveid debulking surgery (R2). No pts received previous RT. In all the cases prescribedtotal dose was of 68.8 Gy(RBE) in 16 fractions, 4 fractions/week. Toxicity was evaluated according to the CTCAE v.4.0. Pts were followed up every three months after RT with clinical evaluation and MRI. For all patients C11 methionine PET-TC was used for target delineation.

Results: Median follow-up time was 23 months (range: 1 – 51 months). Local Control was reached in 101 out of 135 (75%) patients, with 12 and 24-months local control rates of 91% and 81% respectively. The Progression-Free Survival at 12 and 24 months was 81% and 67%, respectively. The Distant Metastasis Free Survival at 12 and 24 months was 86% and 81%, respectively. Median overall survival (OS) time was 24 months and the rates of OS were 95% and 85% at 12 and 24 months respectively. At the end of treatment toxicity was G0 in 2%, G1 in 20%, G2 in 52% and G3 in 26% of the patients. At 3 months toxicity was G0 in 36%, G1 in 43%, G2 in 19% and G3 in 2% of the patients. Acute G3 was always mucositis, in the long FU the late maximum toxicity was G3 for 20 (15%) pts and G4 for 2 (1%) pts. There were no G5 events.

Conclusions: CNAO preliminary data show encouraging outcome results and acceptable toxicities but longer follow-up is needed.

CO096

HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RECURRENCE GLIOBLASTOMA TREATED WITH ACTIVE BEAM PROTONTHERAPY

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Aims: Protontherapy (PT) could minimize the risk of side effects compared to conventional photon therapy and therefore reduce the possible detrimental effect on QoL of re-irradiation. We report the effect of re-irradiation with active scanning PT of recurrence GBM in terms of quality of life scored by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)—C30 and EORTC Quality of Life Questionnaire Brain Cancer Module (QLQ-BN20)

Methods: Between January 2015 and May 2018 twenty-eight patients with recurrence GBM were re-irradiated with active scanning PT. All patients had been previously treated with photon radiotherapy (60 Gy) with concomitant and adjuvant temozolomide (TMZ). Median age and Karnofsky performance status at re-irradiation were 53 years (range, 30-68 years) and 80%, (range, 60-100%), respectively. Target definition was based on CT, MR, and 18F-DOPA PET imaging. All patients received 36 GyRBE (RBE: relative biologic effectiveness) in 18 fractions, with concomitant TMZ in 7 patients (25%). Subscales within the EORTC QLQ-C30 include five functional scales (physical, role, emotional, cognitive, and social), three symptoms scales (nausea, vomiting, and fatigue), six single-item scales (insomnia, appetite loss, constipation, diarrhea, dyspnea, and financial effect of tumor/treatment) and global QoL. The BN20 is specifically developed for brain patients and assessed visual disorders, motor function, communication deficit, various disease symptoms, treatment, toxicity and future uncertainty. The patients completed the EORTC questionnaires before starting PT, the day of the end of PT and every follow-up consult (1-month, 3-months) until progression of disease.

Results: Twenty-six patients completed the questionnaires at baseline until progression of disease. The treatment was associated with improvement or stability

in most of the preselected HRQOL domains. Global health improved over time with a maximum difference of 6 points between baseline and 3-months follow-up. Social functioning and motor dysfunction improved over time with a maximum difference of 8 and 2 points, respectively. We showed only a small not significance decrease in cognitive and emotional functioning. Interestingly, fatigue remained stable during the analysis such as the other preselected domains.

Conclusions: Re-irradiation with PT is a safe treatment without a negative effect on HRQOL until the time of disease progression.

Poster

P001

TANGENTIAL BEAM IMRT VERSUS TANGENTIAL FIELD-IN-FIELD TECHNIQUE IN THE LEFT-SIDED BREAST HYPO-FRACTIONATED RADIOTHERAPY: A DOSIMETRIC COMPARISON

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Aims: A dosimetric comparison between tangential beam Intensity Modulation Radiation Therapy (IMRT) and 3D Conformal Radiation Therapy (3DCRT) in the left-sided breast hypo-fractionated treatment.

Methods: Twenty-four patients affected by left-sided breast cancer were selected. All of them underwent 3D conformal radiotherapy between March 2017 and March 2018 at our Radiation Oncology Therapy Unit. A total of 48 plans were developed for the 24 patients. Twenty-four 3DCRT plans were elaborated with tangential field-in-field technique. Twenty-four IMRT plans were elaborated with tangential beam IMRT technique. The same angles of medial and lateral fields of the 3DCRT plans were used for the corresponding IMRT plan. A dose prescription of 44Gy in 16 fractions has been chosen. A criterion of 95% of the target volume receiving the 95% of prescribed dose was satisfied for all plans. Statistical analysis was carried out using MedCalc Statistical Software version 17.9.6 (MedCalc Software bvba, Ostend, Belgium).

Results: IMRT and 3DCRT plans comparison demonstrated no significant difference in terms of organ sparing for heart and right breast. Instead mean dose, maximum dose and V(17) significantly decrease in IMRT compared with 3DCRT for descending coronary artery ($p = 0.0003$, $p = 0.004$, $p = 0.002$ respectively). For left lung, IMRT plans show statistically significant increase of V(17) compared with 3DCRT ($p = 0.003$). Differences in terms of conformity and homogeneity are not statistically significant. IMRT plans show a better with coverage compared with 3DCRT ($p=0.05$).

Conclusions: Tangential beam IMRT significantly reduces dose to descending coronary artery for left sided breast cancer. The addition of intensity modulation to the conventional 3DCRT tangent technique significantly reduce dose to descending coronary artery, with a delivery time similar to conventional 3DCRT.

P002

NEOADJUVANT CHEMOTHERAPY AND RADIOTHERPY FOR LOCALLY ADVANCED RECTAL CANCER. OUR EXPERIENCE

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Aims: To evaluate feasibility, tolerance and impact on local control in neoadjuvant chemotherapy and radiotherapy for locally advanced rectal cancer.

Methods: From January 2011 to December 2017, 85 Patients (pts) affected by locally advanced rectal cancer were treated with Neoadjuvant Chemotherapy (capecitabine) followed by radical surgery in our center. All patients had rectal adenocarcinomas, 50 G2 and 35 G3 at pretreatment biopsy. All patients had endoscopy and RM. The majority of patients had also an Endoscopic Ultrasound. At staging 20 patients had T3N0, 34 T3N1, 16 T3N2 and 15 T4aN1. All patients received 50.4 Gy

in 28 fraction on whole pelvis, 1,8 GY for fraction, All patients had radical surgery after a median of 79 days (range 68 – 118 days). 76 patients had radical anterior rectal resection, 9 pts a "Miles" surgery.

Results: After neoadjuvant treatment 61 pts had G0-1 rectal toxicity, 22 pts G2. In 2 cases treatment was interrupted. In one case per G3 local toxicity in a frail patient, In one case we founded lung progression during treatment. No genitourinary toxicity was recorded. At surgery 19 pts had a T0N0 (19/85 22%), 21 T1N0 (25%) 28 T2N0 (33%), 12 patient T2N1 (14%). 80/85 /94%) patients had a complete response on nodal site initially N+. During follow up one patient ad a gastric cancer (primary, total gastrectomy, NED after a total of 16 month). One patient T3N1 had a T1N0 at surgery but a local recurrence after 14 month. The patient with lung progression during treatment had also liver metastasis 6 month after initial treatment, and died after 17 month. No patients had post treatment permanent toxicity.

Conclusions: Our data suggests the feasibility of the treatment, because it results in a nonaggressive management, with good results in desease local control.

P003

VENEZIA: A NEW ADVANCED BRACHYTHERAPY GYNECOLOGICAL APPLICATOR FOR CERVICAL CANCER. OUR PRELIMINARY EXPERIENCE ON 8 PATIENTS

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Aims: The purpose of this work is to report our recent and preliminary experience with Elekta's Advanced Gynecological Applicator, Venezia™, a new applicator system that allows clinicians to treat different stages of cervical cancer as a hybrid brachytherapy (BT) applicator, combining characteristics of both ring and ovoid devices, with the possibility to perform interstitial BT.

Methods: Clinical data, BT parameters and acute toxicity (Radiation Therapy Oncology Group RTOG toxicity scale) of consecutive women treated in our institute with VeneziaTM were examined. Pulsed-dose-rate (PDR) was the technique chosen for all the patients. Clinical Target Volume (CTV) coverage and mean dose (D2 cm^3) to 2 cm^3 of bladder, rectum and bowel were assessed. The dosimetric parameters of a series of 10 consecutive patients treated previously at our center with interstitial PDR BT employing other applicators (MUPIT and Utrecht, unpublished data) served as a dosimetry benchmark for the VeneziaTM patients. Two-sided Wilcoxon rank sum test.was performed for statistical comparison.

Results: Since January 2018 to May 2018, 8 women, median age 51 years (27.2-64.2) affected by cervical cancer were treated with Venezia™. All but one underwent interstitial BT. Median dose prescribed to CTV was 30 Gy (range 30-35) with a median dose rate of 0.6 Gy/h (range 0.5 - 0.6). Coverage of CTV and dose to organ at risk (OAR) was reported in Table 1, along with the dosimetric parameters of PDR BT employing other applicators. Apart from manageable acute genitourinary and gastrointestinal toxicities (2 patients with RTOG grade 1), no complications grade > or = 2 were reported.

Conclusions: The initial experience revealed that BT treatment with VeneziaTM was well-tolerated and allows for adequate tumor coverage while satisfying the dose constraints for OARs. It also appears user friendly in positioning and removal time. A larger cohort of patients will be required for additional conclusions related to the long-term clinical benefits and late toxicity.

Table 1. Dosimetric parameters of VeneziaTM and benchmark applicator.

	Venezia™ applicator	Benchmark cohort	p-value
	Median (range)	*Median (range)*	
CTV90(%)	100 (90-108)	114 (102-128)	0.015
D2cm³ bladder (%)	73 (53-78)	82 (63-93)	<<0.01
D2cm³ rectum (%)	33 (23-53)	78 (28-90)	0.013
D2cm³ bowel (%)	66 (17-89)	59 (36-105)	0.9

P004

CLINICAL AND DOSIMETRIC PARAMETERS AFFECTING ACUTE SKIN TOXICITY IN WHOLE BREAST RADIOTHERAPY: A TWO INSTITUTION ANALYSIS

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Aims: To assess clinical and dosimetric predictive factors of radiation-induced acute skin toxicity in breast cancer patients

Methods: 180 patients treated between December 2015 and November 2016 are included in the present analysis. Whole breast irradiation was delivered with Conventional Radiotherapy (CR) (50 Gy, 2.0 Gy/day, 25 fractions) and moderate Hypofractionated Radiotherapy (HR) (44 Gy, 2.75 Gy/day, 16 fractions) followed by tumour bed boost. The impact of patients clinical features and dose inhomogeneities on the occurrence of skin reactions has been retrospectively evaluated.

Results: Acute grade ≥ G2 skin toxicities were registered in 37.7% (68/190) of the patients. The treatment plans analysis showed a strong correlation between dose inhomogeneities areas (V ≥ 105% of the prescribed dose) close to the skin surface and the presence of desquamation areas, as reported in the patients clinical records.The analysis of clinical and dosimetric factors showed that diabetes (p = 0.029 - Odds Ratio 5,076) and V ≥ 105 (p = 0.011 - Odds Ratio 1,008) significan-

tly correlate with acute skin toxicity.

Conclusions: In our experience dose inhomogeneities distribution and diabetes seem to represent the most important risk factors for radiation acute skin toxicity. In these patients, more complex treatment techniques should be considered to avoid skin damage.

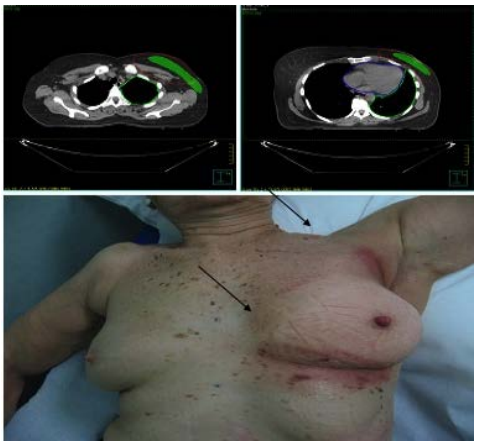

Figure 1. V≥ 105% dose distribution (green area) of a patient developing moist desquamation of the upper quadrant-axilla and infra-mammary fold (arrows).

P005

MODERATE HYPOFRACTIONACTION FOR EARLY-STAGE GLOTTIC CANCER BY MEANS OF VOLUMETRIC-MODULATED ARC THERAPY WITH IMAGE GUIDANCE

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Aims: To report feasibility and tolerability using volumetric-modulated arc therapy (VMAT) with image guidance (IGRT) for early-stage glottic cancer

Methods: From January 2012 to July 2017, forty-two patients affected by cT1-2N0 glottic cancer were treated. The prescription dose was 70 Gy/2.12 Gy (cT1N0) and 67.5 Gy/2.25 Gy (cT2N0). Organs at risk (OARs) were carotid arteries, pharyngeal mucosa and constrictors muscles. Adverse events were recorded during treatment and during follow-up, using the CTCAE 4.0. Acute toxicity was defined from the beginning of treatment until to 90 days; thereafter, toxicity was considered as late. Primary endpoint was the treatment-related toxicity. Secondary endpoints were LC and OS.

Results: Thirty cases (71%) were defined as T1N0 whereas the remaining cases (29%) were T2N0 tumors. The median age of patients was 73 years (range, 44-89 years). Overall treatment time was 6.5 weeks (range, 6-7 weeks). All patients completed treatment without interruption. The median follow-up was 24 months (range, 6-75). Before treatment, all patients referred dysphonia. In 5 out of 42 patients (12%), dysphonia got worse during and/or at the end of treatment. Interestingly, all patients recovered voice function within 6 months after irradiation. Concerning acute toxicity, no patient developed acute mucositis and/or swallowing disorders ≥G3. In 27/42 patients (64%) a G2 dysphagia was recorded. Lately, one patient experienced severe laryngeal edema 6 months post-therapy requiring tracheostomy and PEG positioning. For all the population of study, 1-year and 2-year LC were 97.6% and 92.9% respectively. One-year and 2-years OS were 92.3% and 85.6%. Cancer-specific survival was 98%. For T1N0 patients, 1-year and 2-years LC was 100% respectively. One-year and 2-years OS were 96.2% and 90.8%. Cancer-specific survival was 100%. For T2N0 patients, 1-year and 2-years LC were 90% and 72% respectively. One-year and 2-years OS were 81.8% and 68.2%. Cancer-specific survival was 98%.

Three patients, all in stage T2N0, developed in-field recurrence. These last patients underwent salvage surgery with complete remission.

Conclusions: In the present experience, moderate hypofractionaction for early-stage glottic cancer by means of VMAT-IGRT was feasible and safe, resulting in high rates of LC and acceptable toxicity. Long-term outcomes are needed.

P006

CONTACT HDR BRACHYTHERAPY IN EYELID CARCINOMA

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Purpose: To estimate the incidence of acute and late toxicity and to evaluate the clinical outcome after contact High Dose Rate brachytherapy (HDR-BT) for non melanoma skin cancer of eyelid.

Material and Methods: Between April 2010 and August 2017 10 patients with non-melanoma skin cancer of the eyelid underwent contact HDR-BT by custom-made surface mould. Every applicator was manually built using conventional thermoplastic material and standard plastic catheters. Dose was prescribed at the clinical target volume, defined on CT images acquired at 2.5 mm, represented by the visible tumour plus a safety margin of 5-10 mm. Median delivered dose was 42 Gy (range 30-48 Gy) with a median dose per fraction of 3.5 Gy (range 2.5-4.5 Gy) in a median of 12 fractions (range 10-17). In all cases an ocular shield was placed to reduce the dose to the eye. No procedural complications were recorded. Side effects were classified on the basis of RTOG toxicity criteria. Disease free survival was calculated from the end of HDR-BT till the last follow-up.

Results: The median patient age was 68 years (range, 31-88 years). According to TNM-UICC staging

system, 4, 2 and 4 patients were stage IA, IB and IC, respectively. Basal cell and sebaceous gland carcinoma were reported in 5 and 2 patients, respectively; other histologic types were Non-Hodgkin lymphoma, squamous cell carcinoma and plasmocytoma. After a median follow-up of 43 months (range, 9-90 months), all patients were alive. No patients were lost to follow up. No patients developed a clear evidence of local recurrence. No lymph node metastasis or distant metastases were documented. All patients developed some kind of acute reactions at the conjunctiva and at the adjacent skin. In all cases but one, the treatment tolerance were excellent without any severe complications. Only one patient required a temporary interruption of the treatment due to acute G2 conjunctivitis; after one year from the end of BRT she developed a corneal ulceration.

Conclusions: Our study confirms that contact HDR-BT can be considered a safe and effective treatment for eyelid carcinoma.

P007

LOCALLY ADVANCED OROPHARINX CANCER: PAROTID SPARING WITH OPTIMIZATION OF TREATMENT PLANS ON SUPERFICIAL PAROTID LOBES

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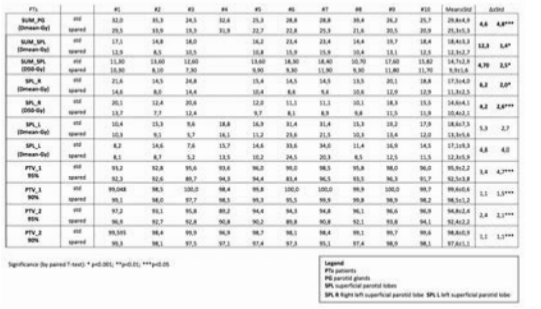
Aims: Radiation-induced xerostomia is a common side effect in patients (pts) affected by locally advanced (LA) head and neck cancer, treated with radical dose of radiation therapy with or without chemotherapy. Parotid glands (PG) sparing is a challenge to allow the organ preservation. In this study, we carried out a retrospective analysis on delivered intensity modulated radiation therapy (IMRT) plans, retrospectively optimized for superficial parotid lobes (SPL) according to PARSPORT II trial.

Methods: 10 pts affected by LA oropharynx cancer, treated from 2015 to 2017 at Radiation Unit of Cagliari, were analyzed. Median age was 60 years, 8 were male. 4 pts received induction chemotherapy with TPF schedule, all pts received concomitant chemotherapy, 9 CDDP-based and 1 cetuximab-based. All pts were planned using simultaneous integrated boost (SIB). Prescription dose was 69.3 Gy to planning target volume (PTV) of primary tumor and involved lymph nodes, 56.1 Gy to PTV of nodal levels at risk of microscopic disease, in concomitant 33 daily fractions. The treatment planning was performed by Pinnacle 9.10. Nine 6 MV coplanar photon beams at equispaced gantry angles were chosen for each patient. Step and shoot IMRT was calculated by direct machine parameter optimization (DMPO) and the maximum number of segment was limited to 80. Planning constraints of mean dose (MD) less than 26 Gy to either parotid gland were used. The parotid tissue lateral to the retromandibular vein was defined as the superficial lobe as PARSPORT II, and it was retrospectively contoured at the time of the study. SPL of each PG were combined as single structure. A new plan was obtained changing the "a-parameter" objective in the IMRT optimization. This parameter controls the sensitivity of the generalized Equivalent Uniform Dose (gEUD) computation of hot dose areas within the SPL.

Results: Both MD to sum PGs and to SPL were statistically lower after optimization. MD of sum of PGs decreased from 29.84 Gy ± 4.88 to 25.28 Gy ± 5.25 (p = 0.04); MD to SPL from 18.37 Gy ± 3.31 to 12.28 Gy ± 2.68 (p = 0.0004). Mean PTV D90% softly decreased respect to approved plan as seen in Table1, remaining within 1%.

Conclusions: SPL optimization plan is a valid option to reduce MD to PGs in oropharynx LA cancer, without compromising PTVs coverage.

Table 1. Dose parameters in delivered and optimized plans.



P008

CONCURRENT CHEMORADIATION WITH VOLUMETRIC MODULATED ARC THERAPY IN ANAL CANCER—ACUTE, PRELIMINARY LATE TOXICITY AND TREATMENT OUTCOMES

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Aims: To report the acute, late toxicity and clinical results in patients not HIV infected with anal cancer treated with volumetric modulated arc therapy (VMAT) concomitant with chemotherapy.

Methods: Since 2012 until 2016, a cohort of 30 consecutive patients (pts) with histologically confirmed squamous cell carcinoma of the anal canal ,TNM stage I- III ,was treated with VMAT with SIB in 25-30 fractions, combined with chemotherapy. Pts age ranged between 45 and 77 years. Dose prescription were: 42-46.2 Gy for inguinal/external iliac lymph nodes, 45-

50.4 Gy for internal iliac, perirectal and obturator lymph nodes, 50-54 Gy for involved lymphnodes and 54- 60 Gy for the gross tumor volume. Chemotherapy with MMC and 5-FU/Capecitabine was administered concomitantly. No gap for radiotherapy treatment was planned. End points were local control (LC), disease-free survival (DFS) and overall survival (OS).

Results: Median follow-up time was 35.5 months (range 13-70). Three year OS was 85%, DFS was 93% and LRC was 93%. Acute dermatological toxicity G3 was recorded in 10 patients, 10 patients experienced a G2 skin toxicity, while G1 toxicity was registered in ten patients. One patient developed Grade 3 acute gastrointestinal (GI) toxicity, 4 patients experienced grade 2 acute GI toxicity and 25 patients G1 toxicity. Acute genitourinary (GU) toxicity G1 was recorded in ten patients. All the pts except one were able to complete concomitant chemotherapy. We didn't find tumor related colostomy but one patient had a treatment related colostomy (fistula). No pelvic fracture was recorded. No late GI or GU toxicity >2 was found. All patients reported a satisfactory anorectal function at follow up.

Conclusions: Our results support VMAT as standard radiotherapy technique in the treatment of patients with anal cancer

P009

THE ROLE OF HIGH SENSITIVE CARDIAC TROPONIN T AND HIGH SENSITIVE C-REACTIVE PROTEIN FOR THE DETECTION OF CARDIAC TOXICITY DURING LEFT BREAST CANCER IRRADIATION: PRELIMINARY EXPERIENCE

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Aims: Whole Breast Radiotherapy (WBRT) in patients with left-sided breast cancer induces an increased risk of cardiac disease and mortality. Cardiac biomarkers may help in identifying patients with radiation cardiac dysfunctions following RT. High Sensitivity C-Reactive Protein (hs-CRP) and High Sensitive Cardiac Troponin T (hs-cTnT) are serum markers of myocardial damage. The aim of this study is to evaluate the early effect of WBRT on serum hs-CRP and hs-cTnT levels and their correlation with cardiac radiation dose and patients' clinical features.

Methods: A prospective study conducted between december 2017 to april 2018 included 31 patients with an early stage, left-sided breast cancer who underwent post-operative 3D-conformal WBRT without prior chemotherapy. Hypofractionated Radiotherapy (44 Gy, 2.75 Gy/day, 16 fractions) followed by tumour bed boost was administered. Serum levels were obtained before, weekly during RT and within one week of the end of treatment. Considering the physiological variations, a predefined increase >30% from the baseline values was considered to be significant for both markers. The main cardiovascular clinical factors are been recorded and dosimetric data were collected for the whole heart and left ventricle.

Results: hs-RCP levels during RT increased above the threshold value in only 5/31 patients (16%) ($p>0.05$). The hscTnT levels increased from baseline value in 25/31 patients (77,5%) and the increase at the fourth week was statistically significant (hscTnT=6.7±4 vs hscTnT =5.3±3, $p\leq0.05$). No significant correlation was found with respect to the analyzed data.

Conclusions: The increase in hscTnT levels during adjuvant WBRT suggested a correlation with the cardiac radiation doses in chemotherapy-naive breast cancer patients and confirms the data reported in the literature. A larger sample population is needed to exclude any correlation with the dose and patients' features.

P010

CHEMORADIOTHERAPY IN PATIENTS AFFECTED BY ANAL CANCER: A MONO-INSTITUTIONAL RETROSPECTIVE ANALYSIS

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Aims: The main goal of anal cancer management is to eradicate tumor and avoid permanent colostomy. The combination of radiotherapy and chemotherapy represents the standard approach of anal cancer to achieve loco-regional control and sphincter preservation. The aim of our retrospective study is to report acute and late toxicities, especially in terms of long-term effects on ano-rectal function, local control (LC), disease-free survival (DFS), overall survival (OS), in patients affected by anal cancer treated with chemoradiotherapy (CRT).

Methods: Between 2002 and 2018, 36 patients (median age = 65.75 years) affected by squamous cell anal cancer were treated in our Radiotherapy Department and were retrospectively analysed. Acute and late toxicities were assessed using the Radiation Therapy Oncology Group (RTOG) scale and the RTOG/European Organization for Research and Treatment of Cancer (EORTC) late radiation scoring system, respectively. The Memorial Sloan–Kettering Cancer Center (MSKCC) score was used for the evaluation of anal sphincter function. The overall survival (OS), the local control (LC) and disease-free survival (DFS) rates were obtained according to the Kaplan-Meier method.

Results: The median follow-up time was 63.25 months (range 1-190 months). The clinical stage distribution was: 3 patients in stage I (8.3%), 13 in stage II (36.1%), 7 in stage IIIA (19.5%), 13 in stage IIIB (36.1%). Then, 16 patients received a total dose between 4500 and 5400 cGy, 10 patients a total dose between 5500 and 6000 cGy, 10 patients >6000 cGy.

Concerning concomitant chemotherapy schedules, 7 patients received Platinum+5FU, 29 patients Mitomycin combined with 5FU or Capecitabine. Acute toxicities ≥G3 (skin and GI toxicities) were observed in 5 patients (13.9%). Regarding late side effects, 1 patient (2.8%) showed GI toxicity ≥G3. The MSKCC score is shown in Table1. Salvage surgery was performed in 6 patients (16.7%) due to a partial response or a progression disease in 5 patients (13.9%), or a recurrence in 3 patients (8.3%). The 5-year OS, DFS, and LC rates were 61.8% ±8.7%, 62.2% ±8.7%, and 88.7% ±10.4%, respectively.

Conclusions: In our study, CRT was associated with good results in terms of acute and late toxicities. According to literature data, CRT was correlated to a high rate of long-term LC, still preserving sphincter function. Radical surgery should be reserved for local recurrence or persistent disease after CRT.

Table 1. Memorial Sloan–Kettering Cancer Center sphincter functional score (n=30)

		No. (%)
Excellent	1–2 Bowel movements per day, no soilage	25 (83.3)
Good	3-4 Bowel movements per day, and/or mild soilage	2 (6.7)
Fair	Episodic >4 bowel movements per day, and/or moderate soilage	0 (0)
Poor	Incontinence	3 (10.0)

P011

APPLICATION OF A SMART 18F-FDG-PET ADAPTIVE THRESHOLD SEGMENTATION ALGORITHM FOR RADIOTHERAPY TUMOUR VOLUME DELINEATION IN HEAD AND NECK CANCER

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Aims: 18F-Fluorodeoxyglucose-positron emission tomography/computed tomography (18F-FDG-PET/CT) imaging is widely used in radiotherapy planning. However, a consensus on the best method for tumour segmentation is far to be reached. We studied an adaptive threshold segmentation (ATS) algorithm, previously validated in a preclinical setting on several scanners, in a clinical setting in order to evaluate its performance and clinical impact.

Methods: ATS algorithm was performed in 32 head and neck squamous cell carcinoma. Every biological tumour volume derived (BTVATS) was compared with the gross tumour volumes (GTVST) based on clinical examination, CT, Magnetic Resonance Imaging (MRI), and visual-based PET images used for the original radiotherapy treatment planning.

Results: elaboration of the ATS algorithm lasted no more than 5 minutes for every case. The median volume of GTVST was 14 (IQR 9-28) cm^3, while BTVATS was 11 (IQR 6-22) cm^3. The median Dice Similarity Coefficient was 0.72. The median volume and the median distance of the voxels over contoured by ATS were respectively 1 cm3 and 1 mm.

Conclusion: the ATS algorithm is easy to be used by physicians and physicists and might help physicians in target delineation of head and neck tumours. Moreover, it might be of great relevance in case of dose painting identifying the BTV. Finally, the ATS algorithm implies that PET volume data are comparable in a setting of a multicentre study. However, further studies are needed in order to assess the ATS algorithm performance of in other tumour sites.

P012

HOW A METAL ARTIFACTS TOOL CAN HELP DOSIMETRY IN H&N TREATMENT

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Aims: In radiotherapy process image artifacts can lead either a wrong definition of structure contours by the clinician either an erroneous computation of dose due to inaccuracies in the Hounsfield Unit (HU) values. Radiotherapy patients have often metal implants and this causes several image artifacts. This study is focused on the advantages using a commercial metal artifacts reduction algorithm, O-MAR (Philips Healthcare System, Cleveland, OH).

Methods: The study is performed on five head and neck cases with metal dental implants. Patients were scanned on a large bore CT Brilliance Philips. The scanned images were reconstructed with standard and O-MAR algorithm for each patient. The structures drawing by the clinicians on the O-MAR series were copied, on the originally CT images to evaluate the dose distribution on the same volume. The plans have been made on Pinnacle TPS in nine field steep and shoot intensity modulated radiation therapy (IMRT)). The treatment provided two or three PTVs, respectively with 54/66 Gy and 54/60/66 Gy and constraints were evaluated on different OARs, close to the artifacts region, such as bone marrow, parotids, mandibule. Hounsfield Units (HU) variation were analyzed also in additional region of interest (ROI) near the dental implant.

Results: In the OMAR images, noise values were generally reduced, standard deviation of HU is lower than standard images. Statistical analysis on HU values was performed, but without significant difference between the two data sets. Evaluating the dose distribution and the dose volume histogram (DVH) with the clinicians, no significant difference were detected.

Conclusions: In head and neck case, when patients have dental implants, the use of O-MAR improve the entire radiation treatment planning process, especially for contouring because increase the accuracy of CT HU and reduce the noise. No significant changes in dose calculation had been found.

P013

VOLUMETRIC MODULATED ARC THERAPY (VMAT) IN PATIENTS WITH ANAL CANCER

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Aims: To report preliminary clinical outcome of patients with anal cancer treated with volumetric-modulated arc therapy (VMAT) in our Institution.

Methods: We retrospectively review the records of all patients, from June 2015 to October 2017, with histological diagnosis of Squamous cell carcinoma of anal cancer who underwent VMAT. All patients underwent Endoscopic UltraSonography, pelvic MRI and 18F FDG PET/CT .The radiotherapy schedule was for T2 N0: 50.4 Gy in 28 fractions to the gross tumour volume; 45 Gy to the lymph nodes, T3 / 4 N0: 55.5 Gy in 30 fractions to GTV; 45 Gy to the lymph nodes. In 18F FDG PET/CT positive lymph nodes the dose delivered was 50.4 if less than 3 cm and 55.5 Gy if more than 3 cm. All patients with stage II or higher underwent concomitant chemotherapy (CT). The first end point was colostomy free survival (CFS).Second end point were disease free survival (DFS) and toxicity. We used Common Terminology Criteria for Adverse Events 4.03 scale for the acute and late toxicity. We included patients with at least 6 months follow up after VMAT.

Results: Twenty four patients with anal cancer where included. 21 Female and 3 male, median age was 65 years (range:35-83 years). Median follow-up was 11.5 months (range, 6-27 months). According the 8th TNM classification :4% of patients were stage I, 42% Stage IIA-IIC,46% stage IIIA-IIIC and 4% stage IV (liver metastases). Except 2 patients Nigro's regimen (Mytomicine and 5 Fluorurcile) was delivered as concomitant CT to RT. One patient underwent concurrent Capecitabine due to previously kidney transplant and in another one no CT was delivered due to comorbidity. All patients were alive at last follow up. Two year DFS and CFS were 75% and 80%,respectively. Maximum acute toxicities were: Skin-G2: 54%; gastrointestinal-G3: 4%; genitourinary-G3: 4%; Severe late toxicity (G3) was reported in only 2 patients (1 patient amenorrhea and another one rectovaginal fistula). Grade 2 toxicity was reported in 3 patients (10%) (2 patients reported vaginal toxicity and 1 patient diarrhea).

Conclusions: Although the follow up is short and the series is small our clinical results support the use of VMAT as a safe and effective intensity-modulated radiotherapy (IMRT) option in the combined modality treatment of anal cancer, with acceptable toxicity and promising sphincter preservation.

P014

GEOMETRIC CONFORMITY OF CHEST WALL AND HEART VOLUME AS CLINICAL PARAMETERS TO SELECT WOMEN FOR A TAILORED CARDIAC-DOSE SPARING APPROACH

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Aims: To evaluate the predictive role of chest wall geometric conformity on dose distribution to the left anterior descending coronary artery (LAD) and whole heart (WH) in patients with left-side breast cancer treated with adjuvant three-dimensional conformal radiation therapy (3DCRT).

Methods: We retrospectively reviewed the dosimetric parameters of 50 women with left-side breast cancer treated with adjuvant 3DCRT. For each patient LAD and WH were contoured according to Feng indications on a 3 mm CT scan acquired in supine position and in free breathing. The geometric conformity of chest wall was determined drawing a line between the posterior part of the sternum and the anterior part of the vertebral body (a distance). To more accurately define the whole thoracic conformity, three different a distances were determined at the most cranial part (the first CT slice where the manubrium appeared), at the middle and at the distal part (the CT slice were the body of sternum disappeared) of the sternum. A second distance named b was drawn between the insertion point of a distance on the anterior part of the vertebral body and the internal surface of the left chest wall with an angle of 45°. The ratio between a and b distances (a/b ratio) was determined on each of the aforementioned three thoracic wall level and the resulting median value was used as the parameter for the geometric conformity of chest wall. Dmax, Dmean, V5 and V20 for LAD and WH were chosen as dosimetric outcome measures. A partial correlation, weighted for WH and PTV volume, between a/b ratio and dosimetric parameters was determined. The a/b ratio cut-off point predictive of pre-specified dosimetric parameters was determined by the

sensitivity analysis.

Results: When WH and PTV volumes were used as covariates in the partial correlation, a significant association between the a/b ratio, heart Dmax (rp = 0,37 and p=0,008) and V5 (rp = 0,33 and p = 0,02) was found with a trend toward the significance for the V20 (rp = 0,26 and p = 0,07). Interestingly, heart Dmean as well any of the LAD dosimetric parameters did not significantly correlate with the a/b ratio. For an a/b ratio cut-off ≤ 0,91 and for a WH volume < 570 cm3 the probability of having a heart V5=0 was of 76,3% and 84%, respectively.

Conclusions: Geometric conformity of chest wall together with WH volume may be useful to assist clinicians and physicians in an individualized cardiac-dose sparing planning definition.

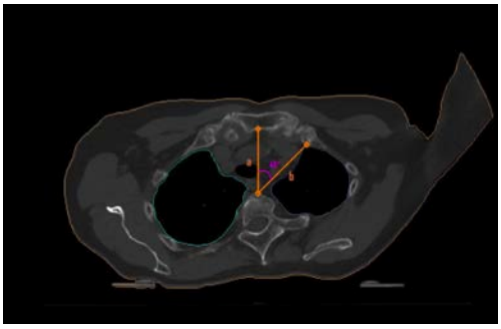

Figure 1.

P015

BRACHYTHERAPY FOR OCULAR MELANOMA AND METASTATIC UVEAL LESIONS WITH 106RUTHENIUM PLAQUE THERAPY: EXPERIENCE FROM THE AZIENDA OSPEDALIERO UNIVERSITARIA"SAN GIOVANNI DI DIO E RUGGI D'ARAGONA"

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Aims: Ocular melanoma is a rare disease and represents the most common intraocular malignant tumor in adults with an incidence of 6 cases in one million inhabitants. Conversely,metastatic lesions caused by other tumoral sites (e.g.lung,breast)are more rare. The current therapeutic approach is conservative and is based on laser therapies, applications of radioactive plaques or external beam therapies with heavy particles (adrotherapy). Enucleation, the only therapy in the past, is reserved for the most advanced cases. In our unit we use 106 Ruthenium (106Ru)episcleral plaque and the implementation of this technique is the result of a synergy between ophthalmologists,radiotherapists and physicists.

Methods: The implementation of this technique involved the drafting of an internal agreement protocol between the different professionals involved, concerning the management of both the radioactive plaque in compliance with the radiation protection standards (e.g.pre/post-operative sterilization, storage) and the patient's needs during hospitalization and in the postoperative period. The patients are referred to our center after ultrasound and/or angiographic examination that highlights the tumor location. To date, 3 patients have been treated in our center, 2 of them received diagnosis of choroidal melanoma and one of breast cancer metastasis.The first two were treated with a dose of 100 Gy and the other patient with a dose of 80 Gy. The treatment plans was performed with the TPS Plaque Simulator using a plate of 106 Ru with a diameter of about 2 cm. With the treatment plan the plaque implantation time,the dose that the critical structures received were evaluated, taking into account the lesion position.

Results/Conclusions: The 2 patients with choroidal melanoma had complete response with remission of the disease with a partial saving in terms of visual acuity.The patient with the breast cancer metastasis at the 3 months' follow up still showed signs of disease,we are waiting for the 6 months follow up to check for signs of remission.

P016

MRI-BASED VOLUMETRIC REGRESSION AFTER NEOADJUVANT CHEMORADIOTHERAPY FOR LOCALLY ADVANCED RECTAL CANCER: A CORRELATIVE ANALYSIS BETWEEN TUMOR VOLUME AND RADIOLOGICAL COMPLETE RESPONSE

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Aims: Several recently reported clinical data show that the strategy of organ preservation may be applied also to rectal cancer. One of the key points in this context is to identify, before treatment, the patients that have the highest probability of achieving a complete response after neoadjuvant chemo-radiotherapy (nCRT): in these patients omitting surgery should be most safe and effective. The aim of this analysis was to evaluate volumetric tumor regression using MRI before and after nCRT in order to correlate pre-treatment tumor volume with radiological response in patients (pts) with locally advanced rectal adenocarcinoma submitted to radical surgery.

Methods: Between 6/2013 and 12/2017, 27 pts (M/F 20/7) with a histological diagnosis of adenocarcinoma of the rectum staged T3-4 N0-2 were examined reviewing MRI studies perfomed before and after nCRT

at Niguarda Cancer Center. With the assistance of a dedicated radiologist we made the contouring of gross tumor volume (GTV) on axial-T2 MRI sequences in order to quantify the tumor volume (measured in cc) before and after nCRT.

Results: The median GTV pre-nCRT was 26.4 cc (range 2.41-195.26 cc). All pts had a tumor volume regression post-nCRT (range 38-100%, median 87%). In seven pts achieving complete radiological response (100% of volumetric reduction), the median GTV pre-nCRT was 8 cc (range 2.41-21.44cc). No complete radiological responses were observed in tumors greater than 21 cc.

Conclusions: Our analysis confirms the efficacy of n-CRT in rectal cancer, since all pts had a radiological response >66% at MRI. It also shows that in largest lesions (volume greater than 21.cc) a complete response could not be obtained. We can therefore assume that the volume of the tumor can be a significant predictor for a complete response after nCRT, regardless of the stage of T. If these data will be confirmed in further analyses, the volumetric parameter could become a useful factor to identify a more favorable group of pts to be managed with an organ preservation approach (i.e. omitting surgery). We could also assume that in larger tumors a program of dose escalation of nCRT is needed to increase the probability of achieving a complete respose.

P017

BIT-ART STUDY: COMPARISON OF BRACHYTHERAPY, INTENSITY MODULATED RADIOTHERAPY AND TOMOTHERAPY FOR ADVANCED RADIATION THERAPY IN PROSTATE CANCER

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Introduction: Aim of this study was to evaluate acute and late genitourinary (GU) and gastrointestinal (GI) toxicity in patients with prostate cancer treated with one fraction high dose rate-BT (HDR-BT) plus intensity modulated radiation therapy (IMRT), comparing to patients treated with exclusive IMRT or Helical Tomotherapy (HT).

Materials and Methods: This was a multicentric, retrospective study evaluating patients with prostate cancer treated in three European Radiation Oncology Departments (Rome, Lubeck and Perugia). Common selection criteria were high-risk or intermediate-risk features and no metastatic disease. Patients treated in Rome underwent IMRT alone or IMRT plus BT. Exclusive IMRT was performed in 40 daily fractions for a total dose of 80 Gy to whole prostate and 72 Gy to seminal vesicles. Combined treatment was performed with one fraction of HDR-BT (total dose 15 Gy) on high risk zone and, after two weeks, patients received IMRT (46 Gy/23 daily fractions). Patients treated in Lubeck underwent one fraction of HDR BT (total dose 15 Gy) plus IMRT with total dose delivered from 50 up to 70.4 Gy. In Perugia patients underwent HT (74.25 Gy/33 daily fractions or 67.50 Gy/25 daily fractions to whole prostate and 62 Gy or 56.25 Gy to seminal vesicles). All patients assumed androgen deprivation therapy. Acute and late toxicity (according to the Common Toxicity Criteria for Adverse Event Version 4.03) were collected.

Results: Data of 51 patients, from January 2013 to June 2017, were evaluated. Mean FUP time was 22 months. 17 patients underwent HT in Perugia; 17 patients were treated in Rome with IMRT and 17 patients underwent IMRT+BT in Lubeck (9 patients) and Rome (8 patients). No Late G2-3-4 GU toxicity was reported; G1 toxicity was showed in two patients treated with BT+IMRT and in one patient treated with IMRT alone. G3 GU acute toxicity occurred in one patient treated with HT; G1-2 toxicity occurred in 7 patients treated with BT+IMRT, 10 patients treated with IMRT and 13 patients treated with HT (see tab.1). One patient treated with IMRT alone showed G1 GI late toxicity. Acute G1-2 GI toxicity was showed in 4 patients treated with BT+IMRT, 7 patients treated with HT and 8 patients treated with IMRT. None of the 51 patients showed local recurrence (LR) at last FUP.

Conclusions: HDR-BT boost plus IMRT is comparable to HT and exclusive IMRT in terms of LR and tolerance. Patients undergoing HDR-BT boost seems to show less GU and GI acute toxicity.

Table 1. Toxicity (CTAE v4.03).

	Tomotherapy			IMRT			IMRT + HDR		
	G1	G2	G3	G1	G2	G3	G1	G2	G3
GU Acute	9	4	1	9	1	0	6	1	0
GU Late	0	0	0	1	0	0	2	0	0
GI Acute	5	2	0	6	2	0	4	0	0
GI Late	0	0	0	1	0	0	0	0	0

P018

PROPHYLACTIC WHOLE BRAIN IRRADIATION WITH HIPPOCAMPAL SPARING: A DOSIMETRIC STUDY

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Aims: Prophylactic Brain irradiation is common for small cell lung cancer (SCLC) patients. However whole brain irradiation even with lower doses may be associated with severe neurocognitive dysfunction. Several clinical studies found a relationship between hippocampus irradiation and deficit in the memory and in neurocognitive functions of patients treated with WBRT. The goal of this study is to investigate the feasibility of Hippocampal Sparing (HS) for prophylactic whole brain irradiation (WBRT), using Volumetric Modulated Arc Therapy (VMAT).

Methods: Fifteen patients were treated with a prescribed dose of 25Gy in fraction of 2.5Gy. The Hippocampus was contoured on T1-weighted MRI axial sequences by radiotherapist supervised by neuroradiologist. The Planning Target Volume (PTV) was defined as Brain minus hippocampus expanded volumetrically by 5mm, the Avoidance Region (AR). Several rings around hippocampus, were used as help volume to scale from prescribed target dose to hippocampus desired dose. The VMAT treatment plans were generated using four full 360° planar arc, two in clockwise direction e two in counter-clockwise direction. Plans were optimized with Eclipse Treatment Planning System (TPS) and calculated with Anisotropic Analytical Algorithm (version 10.0.28) for a True Beam Varian linac with 120-leaf millennium multi-leaf.

Results: A Dose-Volume Histograms (DVH) was generated for each treatment planning to evaluate target coverage and dose to Organs at Risk (OARs). About Target, mean Homogeneity Index is HI=0.13 ranging from 0.20 to 0.08, mean V95%=96.6% ranging from V95%= 98.1% and V95%=95.1%, mean Dmax=27.1Gy ranging from Dmax=27.3Gy and Dmax=26.9Gy. About hippocampus mean Dmax=14.2Gy ranging 15.4Gy and 12.7Gy, mean Dmean=10.8Gy ranging from 11.7Gy to 9.1Gy and mean D100%= 8.3Gy ranging from 9.2Gy to 7.3Gy. Mean value of ratio between Volume of avoidance region and the whole brain volume is VAR=2.35% ranging from 3.3% to 1.3%.

Conclusions: Proposed method allowed to obtain a low hippocampal Dmax, (RTOG 0933 protocol constraint recommended is Dmax<16Gy, D100%<9Gy) without compromising desired target coverage. Furthermore, using co-planar arc can reduce the treatment delivery respect non co-planar techniques used in other studies.

P019

DIFFERENT SURGICAL APPROACH FOR SELECTED GLOTTIC AND SUPRAGLOTTIC LARYNGEAL CANCER, WITH OR WITHOUT ADJUVANT RADIOTHERAPY: RETROSPECTIVE ANALISYS IN PATIENTS STADIATED PT3N0

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Aims: Aim of this study is to describe the results of management in patients (pts) surgically treated for squamocellular cancer (HNSCC) of larynx, stadiated pT3pN0 cM0, with or without adjuvant radiotherapy after different surgical approaches.

Methods: Between January 2006 and December 2017, 62 patients, with median age 66 (range36-84 years), clinically staged as cT3N0 in 47/62 pts, cT3N2c in 1/62, cT1-2 N0 in 11/62, 2/62 of pts was cT4N0 and 1/62 cT4N1. Twenty-eight patients underwent conservative surgery (group I) with open partial horizontal laryngectomies (OPHLs) or transoral laser microsurgery (TLM), while thirty-four (group II) underwent total laryngectomy (TL). Histologies were squamous cell carcinoma in 60 pts, or laryngeal localization of melanoma (1 pts) or mucoepidermoidal carcinoma (1 pts); 52/62 of patients underwent selective mono- (22/62) or bilateral (30/62) neck dissection (II-IV level). Location of disease was 37% and 63%, respectively for supraglottic and glottic site. All patients were staged as pT3pN0. In 4pts, 1 pt and 1 pt, margins were R1, R2, and Rclose, respectively. Based on presence of adverse risk factors, sixteen (25%) pts received adjuvant radiotherapy, delivered with intensity modulated technique in all cases, except one (3D-CRT), with a mean total dose to high risk volume of 60 Gy (2 Gy/fr) and 50 Gy (2Gy/fr) to elective neck.

Results: All pts completed adjuvant treatment, with an acute toxicity<G3 (CTCAE scale). At a median follow up of 15,6 months (4 - 87,6 mo). Loco-regional failure was observed 6,5% (4/62) of whom 2 pts in group I and 2 pts in group II, none in those subjected to RT. Overall survival was 92%. In patients who presented with recurrence or death, the median time to the event was 1 year. The relationship between site of tumor (supraglottic vs glottic) and recurrence or death is significant upon exploratory analysis (p=0.01), 7 pts of nine with event (recurrence or death) were supra-glottic.

Conclusions: A conservative surgical approach for laryngeal carcinoma could be a reasonable option in selected patients, having similar disease control when compared to total laryngectomy. These data seem to confirm the role of radiotherapy in patients with adverse risk factors.

P020

ORGAN PRESERVATION IN LOCALLY ADVANCED RECTAL CANCER AFTER CHEMORADIATION: VALUE OF HIGH RESOLUTION MRI AND PET IMAGING IN PREDICTING CLINICAL OUTCOMES

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Purpose: Correlation between imaging (High Resolution MRI and PET-TC) and pathological response after neoadjuvant concurrent radiochemotherapy, followed by surgery. We report our experience at S. M. Goretti Hospital in these last years.

Materials and Methods: From January 2007 to December 2017 we treated 60 patients diagnosed with locally advanced rectal cancer. 21 patients were females and 39 males. Median age at diagnosis was 65 years (range 47-83). Clinical stage was as follows: 18 pts stage IIA (T3N0) and 42 pts IIIB (T3-4 N1). All patients received a pre and post treatment staging including colonoscopy and computer tomography. Perfusion computer tomography was performed in the first 11 pts. A Magnetic Resonance and a PET-TC simulation was performed in the last 38 pts. All patients received a dose of 50-50.4 Gy in 1.8-2 Gy per fraction to the pelvic area. Concomitant chemotherapy was based on protracted intravenous infusion 5 FU (220 mg/mq) in 20 pts, capecitabine (825 mg/mq twice daily) throughout radiotherapy coursein 35 pts, and in 5 pts Cisplatin 60 mg/mq-5 FU 1000 mg/mq 1-4 days q28. Surgery was performed 6-8 weeks after radiotherapy course in 44 pts.

Results: After a median follow-up of 76 months (range 25-116 months), 55 patients are still alive and free of disease, 5 pts died of local progression of disease and systemic metastases, after 16, 18, 19, 28 and 36 months of follow-up. Sfincter saving surgery was performed in 57% of patients eligible for abdominal perineal resection. Complete pathological response was reported in 16 patients (pCR: 26.6%) and correspons to a clinical complete response, as assessed by MRI and PET-TC parameters. 6 pts who had achieved a cCR after radiochemotherapy did not undergo subsequent surgery. They are still alive and free of disease. The treatment was well tolerated, moderate acute and late toxicity (G1-2 according to RTOG scale) were reported. No patient suffered a performance status worsening during the scheduled treatment.

Conclusions. These results sugests that preoperative radiochemotherapy is a well tolerated and effective treatment and MRI and PET-TC parameters correlate clinical and pathological response.

P021

RADIOTHERAPY, IMMUNOTHERAPIES AND TARGETED THERAPIES IN ELDERLY PATIENTS: A SYSTEMATIC LITERATURE REVIEW

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Aims: In USA 53% of new cancer cases are diagnosed in people over 65 years, and in the next decade the incidence of cancer in elderly people will continue to grow up. Radiotherapy (RT), chemotherapy and more recently targeted therapy (TT) and immunotherapy have favorably changed the outcome of various cancers. Nevertheless, elderly people are under-represented in clinical trials. Aim of the present review is to assess the present data about the use of the association of Radiotherapy and new drugs in elderly people.

Methods: PubMed database was searched for English literature published up to December 2017 using keywords “radiotherapy” combined with “bevacizumab”, “cetuximab”, “trastuzumab”, “erlotinib”, “gefitinib”, “sorafenib”, “sunitinib”, “vismogenib”, “sonidegib”, “ipilimumab”, “pembrolizumab”, “nivolumab”. Studies performing radiotherapy and targeted/immunotherapy in people aged > 65 years were evaluated focusing on safety, toxicity and, if possible, efficacy. Studies eligible for inclusion in this review were: (a) case reports, retrospective or prospective studies in which RT and new drugs were used concomitantly or sequentially; (b) studies in which the evaluation of elderly sub-group was reported.

Results: The systematic search identified 626 records from PubMed. After exclusion of duplicates, full-text review, cross-referencing and paper that do not respect the inclusion criteria, 81 studies were included in this review. In elderly the combination of primary RT with cetuximab seems feasible in all patients with advanced HN cancer that are not eligible for cisplatin chemotherapy concomitant to RT with specific toxicities. In HER2 positive breast cancer there is a widespread use of trastuzumab associated to RT but limited study evaluated their combination, to date patients’ age should not be limited this association. The concurrent administration of EGFR targeting TKIs and RT might be associated with increased toxicity based on the irradiated volume. Regarding the Immune Check Point inhibitors and RT, tolerance seems similar among older and younger people but definitive data are lacking. Instead, the association of RT and HPI remains investigational and should be evaluated only in clinical trial.

Conclusions. TT/immunotherapies in association of RT seems to be safe, but in elderly patients data concerning safety and toxicity are limited, deriving mainly from trial in which the elderly patients enrolled were considered “fit”, which are not representative for all geriatric cancer patients. Specific clinical trials on this population are encouraged.

P022

INTENSITY MODULATED RADIOTHERAPY AND HYPOFRACTIONATED VOLUMETRIC MODULATED ARC THERAPY FOR ELDERLY PATIENTS WITH BREAST CANCER: COMPARISON OF ACUTE AND LATE TOXICITIES

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Purpose: To evaluate the differences between conventional fractionated intensity modulated radiotherapy (IMRT) and hypofractionated (HypoRT) volumetric modulated arc therapy (VMAT) in elderly women affected by early stage Breast Cancer (BC) in terms of RT-related acute/late side effect.

Materials and Methods: Between October 2011 and July 2015, 80 consecutive elderly BC patients were treated with IMRT for 5 weeks (40 patients) or HypoRT-VMAT for 3 weeks (40 patients). Inclusion criteria were: age ≥ 70 years, early BC (pT1-2 pN0-1), no prior neoadjuvant chemotherapy and non-metastatic disease. For patients receiving IMRT or HypoRT-VMAT, a total dose of 50Gy (25 fractions) or 40.5Gy (15 fractions) was prescribed to the whole ipsilateral breast, respectively. All patients received a simultaneously integrated boost (SIB) up to a total dose of 60Gy for IMRT and 48 Gy for HypoRT-VMAT. Acute and late side effects were evaluated using the RTOG/EORTC radiation morbidity scoring system.

Results: With a median follow-up of 45 months, acute skin toxicity was overall very low, with grade 1 in 25 cases (62.5%) of the IMRT group and 21 cases (52.5%) of the HypoRT-VMAT group; while grade 2 toxicity was reported in 10 IMRT patients (25%) and 1 HypoRT-VMAT patient (2.5%) (p=0.001). Regarding late adverse events, only grade 1 skin toxicity was recorded.

Conclusions: The present study showed that whole breast IMRT and HypoRT-VMAT are feasible and well tolerated in early stage BC elderly patients and that HypoRT-VMAT is affected by lower risk of acute and late RT-related side effects.

P023

HYPOFRACTIONATED RADIOTHERAPY FOR SKIN CANCER IN ELDERLY

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Aims: Non melanoma skin cancer(NMSC) is the most common cancer in deep old age(≥85 years) and long-lived persons(>95y.o). The first-choice treatment is surgery but the extension of the lesions or comorbidity of these patients(pts) often resort to radiotherapy. For this reason clinical trials rarely involve this population due to poor cooperation or general condition. In this cohort, hypofractionated radiotherapy(HRT), delivered either daily, alternative daily or once weekly is highly effective.

Materials and Methods: Between October 2013 and April 2018 in our Department 21 patients(pts) elderly, with median age 88 years old(range 75-97), were treated with Radiotherapy for skin cancer. All pts were staged with ultrasound of the soft tissues and biopsy of the lesions; only two have not been typified by age limits. The histologic exams showed 6/19 (32%) basal cell carcinoma, 11/19(58%) squamous cell skin and 2/19(10%) other subtypes of NMSC. Direct fields of 6 MeV electrons were utilized. Irradiated lesions were primary located on the head and neck (91%) and secondary on chest wall (9%). The intent of radiotherapy are two; to palliate cancer-associated symptoms such as pain, bleeding and ulceration in 13/21 pts(62%) and to cure advanced disease in 8/21pts(38%).

Results: We compared total dose, number of fraction, local control(LC), acute(AT) and late toxicity(LT). Common fractionation schemes include 2 to 20 fractions with dose per fraction sizes ranging from 250 to 800 cGy(Table1). At the end of radiotherapy pts were evaluated with clinical exam for the first time in a month, then after 3 months, followed every 6 months for 3 years and we obtained a median follow up of 11 moths(range 3;46). In tumors <4 cm(1;4 cm) are reported 89% of LC, only 3 pts(33%) had to suspend the treatment for max two days for cutaneous toxicity. The AT consists in skin erythema, according to RTOG Scale, and is records only in 4/9 pts(44%); G1 3/9 pts(33%), G2 1/9 pts(11%). No pts has experienced cutaneous LT. In larger tumors > 5 cm (5;16 cm) we have 8/12 pts(67%) LC and no one have suspended treatment. Skin AT: 2/12 pts(17%) G1, 2 /12 pts(17%) G2, 1/12 pts(8%) G3, 7/12 pts(58%) are negative instead LT is presents only in 1/12 pts(8%) G1.

Conclusions: HRT in elderly pts have excellent results with 89% of LC in early disease and 67% in advanced in according with international scientific literature. Furthermore is well tolerated with only 3/21 pts(14%) interruptions of treatment, >56% of pts with no AT and only 1/21 pts(4%) present LT.

Table 1.

Total Dose	Dose/ Fraction	N. Fraction	Weeks	N. patients
5000 cGy	250 cGy	20	4	3 (14%)
3000 cGy	300 cGy	10	2	3 (14%)
1500 cGy	300 cGy	15	3	5 (24%)
2000 cGy	400 cGy	5	1	2 (10%)
4000 cGy	400 cGy	10	2	4 (18%)
3000 cGy	600 cGy	5	1	2 (10%)
2100 cGy	700 cGy	3	2	1 (5%)
1600 c Gy	800 cGy	2	2	1 (5%)

P024

DISCONTINUATION OF HORMONE THERAPY FOR ELDERLY BREAST CANCER PATIENTS AFTER HYPOFRACTIONATED WHOLE-BREAST RADIOTHERAPY

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Aims: To examine adherence to hormone therapy (HT) in elderly breast cancer patients (≥65 years old) treated with hypofractionated radiotherapy.

Methods: We analyzed data on 550 ER-positive breast cancer patients given hypofractionated whole-breast radiotherapy from June 2009 to September 2016. Baseline comorbidities considered in the hypertension-augmented Charlson Comorbidity Index (hCCI) were retrospectively retrieved. Total hCCI scores were classified as no comorbidity (hCCI=0), low burden of comorbidity (hCCI=1), and high burden of comorbidity (hCCI≥2). Competing risk analysis was used to estimate the 5-year cumulative incidence of HT discontinuation. Fine and Gray models were used to estimate the adjusted subhazard ratio (SHR) of HT discontinuation by hCCI score.

Results: HT was initially prescribed for 85.6% of patients and almost all of them (468/471) took it for at least one month. It was subsequently discontinued by 45 patients (9.6%), for an overall 5-year cumulative incidence of 11.7%. The 5-year cumulative incidence of HT discontinuation rose from 3.9% in the youngest age group (65-69 years) to 23.3% in the oldest (≥80 years) (p=0.005). Baseline comorbidity had some effect on the likelihood of discontinuing HT, but only among patients with a low burden of comorbidity (hCCI=1, SHR 2.00, 95%CI 0.95-4.20)

Conclusions: Adherence to HT was better in our sample than in the literature, probably because patients were selected and motivated to continue HT. This confirms the importance of communication with patients to improve adherence to HT. We confirmed the association between HT discontinuation and older age, while comorbidity had a limited influence.

P025

FEASIBILITY AND COMPLIANCE OF HYPOFRACTIONATED ADJUVANT WHOLE BREAST RADIOTHERAPY IN ELDERLY

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In the last few years more and more breast cancers are diagnosed in old age and physicians often express some doubt about the opportunity to submit elderly patients (pts) to adjuvant radiotherapy, that forces them to many hospital accesses and can get worse comorbidities. In this subgroup of pts short-course RT can be a good option allowing completion of an adequate locoregional treatment without important quality of life implications. Review of our data has been realized to evaluate feasibility and compliance of an hypofractionated adjuvant whole breast radiotherapy (RT) in elderly. From January 2016 to December 2017 fifty pts older than 74 has been submitted to adjuvant RT after conserving surgery for breast cancer. Age range was 75-93. One of them received neoadjuvant chemotherapy (CT) and 4 neoadjuvant hormonal therapy (HT) before surgery. Five pts were submitted to adjuvant CT (4 cycles according to EC scheme followed by 12 weekly Paclitaxel) and in these cases RT started 3-4 weeks after last administration. Fortyfive pts received adjuvant HT: aromatase inhibitors in 41 cases and tamoxifen in 4. For them RT started within 12 weeks after surgery. Performance status was 0, 1 and 2 in 58%, 27% and 15% of pts respectively. Blood pressure hypertension was present in 50% of pts, arrhythmia in 12% (in 1 case treated with pacemaker) and diabetes in 38%. Other pts characteristics are reported on Table 1.

Table 1.

Histology		pT		ypT		pN		G		RROO		Her2	
Ductal	40	is	6			0	42	1	10	+	45	+	5
Lobular	3	1a	0			1	6	2	28	-	4	-	43
Mucinous	4	1b	6	1b	1	2	1	3	11	n.d.	1	n.d.	2
Others	3	1c	24	1c	1	x	1	x	1				
		2	9	2	3								
		3	0										

A 3D conformal RT was erogated with a total dose of 39Gy/13 fractions (frs), 4 frs a week, with a concomitant weekly photon boost of 3Gy/3 frs (or 4Gy/4 frs in

case of close margins). OAR dose constraints were as follows: omolateral lung V20<20%, heart V40<30% and V25<10%, mean dose to controlateral internal breast regions<4Gy. Skin damage topic prophylaxis was prescribed from RT beginning. All of pts completed RT without interruptions due to treatment side effects. Highest skin toxicity, determined within the last fr. and 1 month later, was: G0 10%,G1 60%, G2 25%, G3 5%. After 6 months: G0 52%, G1 36%, not evaluated 12%. No particular differences has been noted in disepithelization repair between diabetics and other pts. Mild or moderate fatigue was reported by 43% of pts, but none of them requests treatment interruption for this symptom. We can conclude that short-course adjuvant whole breast RT is possible and well tolerated by elderly pts and allows to improve local control without important impact on their quality of life.

P026

SKIN TOXICITY AND QUALITY OF LIFE IN ELDERLY WOMEN AFFECTED BY EARLY BREAST CANCER WHO RECEIVED HYPO-FRACTIONATED RADIOTHERAPY

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Skin toxicity and quality of life in elderly women affected by early breast cancer who received hypo-fractionated radiotherapy

Aims: The purpose of study cross-sectional is to evaluate skin toxicity, and quality of life of Short Course Hypo-fractionated Radiotherapy (HRT) in elderly patients affected by early breast cancer after breast-conserving surgery (BCS).

Methods: A total of 18 patients were treated with Short Course HRT between July 2015-May 2017. Eligibility criteria: age ≥ 60 years old, invasive cancer, stage I-II after breast conserving surgery. 28.5 Gy, in 5-fraction once-weekly, to the whole breast (WBI) were administred after breast-conserving surgery with "field and field" technique. The evaluation of toxicity was performed according to Radiation Therapy Oncology Group (RTOG toxicity scale) and the quality of life was evaluated by the Hospital Anxiety and Depression Scale (HADS). Patients were assessed as baseline, at the end of radiation therapy and after 3, 6 and 12 months of follow up.

Results: A cohort of 18 patients with a minimum follow-up of 12 months was evaluated. At the end of radiation therapy, the following results were obtained: G2 acute skin toxicity in 6/18 patients (33%) and G3 in 2/18 patients (11%) was recorded; depression and anxiety in 2/18 patients (11%) was recorded. After 3 months from the end of radiation therapy, G2 acute skin toxicity was found in 1/18 patients (5%) and G3 in 1/18 patients (5%); anxiety was found in 1/18 patients (5%). At 6 and 12 months from the end of radiation therapy, was recorded no skin toxicity. At 6 and 12 months from the end of radiation therapy, were recorded neither skin toxicity nor depression and anxiety. The only patient with G3 acute skin toxicity was the same one who experienced anxiety.

Conclusions: Data were analyzed after the Short Course Hypofractionated regimen on the whole breast following breast conserving surgery. This regimen was well tolerated with a good cosmesis results and quality of life. Additional follow-up with continued accrual is needed to assess late toxicity and cosmesis.

P027

EARLY SALVAGE RADIOTHERAPY AFTER RADICAL PROSTATECTOMY IN RECURRENT PROSTATE CANCER PATIENTS

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Aims: Early salvage radiotherapy (ESRT) following radical prostatectomy (RP) for prostate cancer is a potentially curative treatment for some men with a detectable prostate -specific antigen (PSA). The aim of this retrospective study is to evaluate the clinical outcome of 37 patients (pts) submitted to SRT between 2012 and 2016 at our institution. Outcomes included biochemical relapse-free (bRFS) distant metastases free (DMFS)and prostate cancer specific survival (PCSS).

Methods: From 2012 to 2016 60 pts underwent adjuvant radiotherapy after RP while salvage RT was administered in 37 pts. The characteristics of this second group of patients were analyzed. SRT was due to delayed rise in PSA in 24 pts (65%), in 13 (35%) also with clinical evidence. Median age was 70 years. 72% of pts had pT3a disease or greater, 45% of pts had Gleason score >/= 8 while 51% of pts had positive surgical margins. 56% of pts had undetectable postoperative PSA and median time from RP to SRT was 30 months (6-96). The RT dose was 70 Gy 3D technique. Men with high risk clinicophathological features were treated selectively to the pelvic lymph nodes at treating physician discretion. Adjuvant androgen ablation was associated in 29 pts (78%).

Results: Median follow up was 27 months (12-48). Biochemical recurrence was defined as posttreatment PSA 0.2 ng/mL or greater and occurred in 4 pts (16%). bRFS was 83% and stratified by PSA was 97%, 82% and 76% for PSA < 0.3 ng/mL, 0.3-0.7 ng/mL and > 0.7 ng/ml. All patients treated with early SRT are alive. Only 4 pts (30%) treated for clinical relapse are ned, metastasis-free survival was 92.5%, prostate cancerspecific survival 97%, and overall survival 94.9%.

Conclusions: Immediate Post operative RT is associated with an increased risk of acute and late side effects. Salvage radiotherapy administered at the first sign of biochemical recurrence might be associated with durable cancer control in selected patient.

According to recent trials there is an increasing hazard for biochemical failure , salvage androgen deprivation therapy, distant mts and prostate cancer mortality with increasing pre SRT values.

P028

BRACHYTHERAPY (BT) IN ELDERLY PATIENTS WITH UTERINE CANCER

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Aims: analyze the technical aspects, the role and feasibility of HDR intracavitary Brachytherapy in elderly patients with uterine tumors.

Methods: from January 2015 to December 2017, 8 females median aged 79 years old (range 71-91) with uterine cancer were treated with HDR Intracavitary Brachytherapy. Five patients were affected by carcinoma of the cervix and three by endometrial adenocarcinoma. All patients were staged with abdomen/pelvic CT and MRI and were discussed within our multidisciplinary group. Seven patients were previously treated with external beam radiotherapy (EXTRT) with a four-field (box) technique (6 with a dose of 45Gy in 25 fractions and 1 with a dose of 50.4Gy in 28 fractions) and one patient was treated with exclusive BT. The three patients younger than 75, were treated with concomitant chemotherapy. General anesthesia was not performed for brachytherapy insertions. The total number of insertions was 30, using Fletcher applicator with the High Dose-Rate MicroSelectron after-loader. After each insertion the applicator positioning was checked with IBU (Integrated Brachytherapy Unit) and then a CT scan was performed for 3D image-guided Treatment Planning with OncentraBrachy TPS.

Results: for all the patients the GEC-Estro constraints for organ at risk was respected: the total dose (EXTRT+BT) at 2cc of rectum was lower than 70 Gy, for the intestine the total dose at 2cc was lower than 70 Gy and the total dose at 2cc of the bladder was lower than 80 Gy. The EQD2 received from the CTV for the six patients treated with 45 Gy of EXTRT and 28 Gy of BT, was more than 80 Gy; for the patient who received only BT (38 Gy) the EQD2 to CTV was 51.8 Gy, and for the patient who received 50.4 Gy of EXTRT and 21 Gy of BT, the EQD2 to the CTV was 79.4 Gy. The median follow-up is 17 months: all patients are alive, 7 without signs of local recurrence and one with a recto-vaginal fistula at the site of the primary tumor (cT4)

Conclusions: although the follow-up is short we can say that curative radiotherapy should be considered in elderly patients. High Dose-Rate intracavitary Brachytherapy is a safe and technically viable procedure for women with uterine cancer.

P029

THE ROLE OF RADIOTHERAPY IN ELDERLY WOMEN WITH EARLY-STAGE BREAST CANCER TREATED WITH BREAST CONSERVING SURGERY

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Aims: The aim of this study was to analyse the impact of adjuvant radiotherapy (RT) on ipsilateral breast recurrence (IBR) and overall survival (OS) in early-stage breast cancer patients, older than 69 years.

Methods: From January 2007 to June 2015, we analysed retrospectively 137 women with T1-2 invasive breast cancer, negative axillary lymph nodes and estrogen receptor positive, dividing them into two subgroups: 70 to 79 years, older than 79 years.

Results: After a median follow-up of 43.2 months, the 3 years IBR free survival in patients treated with surgery plus radiotherapy (surgery + RT) was 98.8% and 92.1% in patients treated with surgery alone (surgery) with a significant difference ($p=0.01$). Radiotherapy did not impact overall survival ($p=0.10$). An higher percentage of patients aged between 70 and 79 years received RT after conservative surgery if compared with the older subgroup ($p<0.01$).

Conclusions: In elderly women adjuvant RT reduced the IBR, but did not improve OS.

P030

STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN EARLY STAGE LUNG CANCER (LC) ELDERLY PATIENTS (PTS)

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Aims: SBRT has emerged as a new technology in radiotherapy delivery, allowing for potentially curative treatment in early stage LC unfit for surgery. Several studies with SBRT have shown disease control and survival similar to that obtained with surgery. We present our experience on lung SBRT in elderly with early stage LC unsuitable for surgery.

Methods: Between March 2004 and April 2018, 58 early stage LC pts were irradiated with SBRT in 3-5 fractions. All pts had CT-PET 18-FDG before SBRT. Localization was obtained using a multi-slice computed tomography. Gross tumor volume (GTV) was defined as radiologically visible tumor using lung or mediastinal windows for peripherally and centrally disease, respectively. Clinical target volume (CTV) was coinci-

dent with GTV and planned target volume (PTV) was designed as GTV/CTV plus an additional 8 mm in the cranio-caudal and 5 mm in other directions. Response was assessed with CT-PET 18-FDG or CT 3 months after treatment and at 4 months interval thereafter with clinical evaluation and the same radiological exam.

Results: Median age was 71 (range 63-87); histology was adenocarcinoma, squamous carcinoma and small cell lung cancer in 36 (62%), 11 (18,9%) and 4 (6,8%) pts, respectively. 7 (12%) pts were submitted to SBRT without known histology because high risk of bioptic procedure. 40 (69%) pts had peripheral located disease while 18 (31%) pts had central located disease. 21 (36,2%), 32 (55,1%) and 5 (8,6%) pts received respectively 5 x 10Gy, 5 x 8Gy and 3 x12Gy. After a median follow-up of 18 months, 43 pts (74%) had radiological response: 18 (31%) pts complete response and 25 (43%) pts partial response; 7 (12%) pts obtained stable disease and 6 (10,3%) pts progression disease. 2 patients were lost to follow up. The median local recurrence free survival was 12 months (4-80 months). Neither acute nor late grade 2-4 toxicities were registered.

Conclusions: Our experience confirmed that SBRT for early stage LC in elderly pts unfit for surgery was an effective treatment with a high control rate of disease and low toxicity profile.

P031

MODERATE HYPOFRACTIONATED VOLUMETRIC MODULATED ARC THERAPY WITH DAILY IMAGE GUIDANCE FOR PROSTATE CANCER: MONOINSTITUTIONAL REPORT OF FEASIBILITY AND SAFETY IN ELDERLY PATIENTS

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Aims: To evaluate the feasibility and safety of moderated hypofractionated volumetric modulated arc therapy with daily image guidance (VMAT-IGRT) for prostate cancer (PCa) elderly patients

Methods: Between December 2016 and February 2018 thirty-one PCa elderly patients (≥70 years old) were treated by means of VMAT-IGRT. Dose prescription was 67.5 Gy in 25 fractions to prostate with or without seminal vesicles. Toxicities were assessed according to Common Terminology Criteria for Adverse Events (CTCAE) scales, version 4.02. Biochemical failure was defined as the nadir PSA level plus 2 ng/ml.

Results: Median age was 76 years (range 70-87 years). Median follow up was 12 months (range 4-17 months). According to risk category three patients out of thirty-one (10%) were low risk, 24/31 (77%) were intermediate risk and 4/31 (13%) were high risk. All patients completed the treatment as planned. No ≥ G2 acute genitourinary (GU) and rectal (GI) toxicity occurred. In 45% patients, G1-GU acute toxicity was recorded. Only a patient shown G1-GI acute toxicity. No G3 early late GU and GI toxicities were reported. G1-GU early late toxicity was developed by 16% of the patients. Only a patient reported G1-GI early late toxicity. G2-GU early late toxicity was observed in 6.4% and only one patient had G2-GI early late toxicity. No biochemical failure was recorded.

Conclusions: Moderate hypofractionated VMAT-IGRT for PCa elderly patients showed to be well tolerated and safe in terms of acute toxicity and early late toxicity. A longer follow-up is needed to define the efficacy on outcomes and late toxicity.

P032

FEASIBILITY OF SHORT COURSE PREOPERATIVE RADIOTHERAPY FOR RECTAL CANCER IN ELDERLY PATIENTS, UNFIT FOR CHEMOTERAPY

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Aims: Neoadjuvant therapy (chemo radiotherapy) is able to the improved local control, for locally advanced cancer patients, node-positive, with low-lying rectal tumors . In this study we investigated the feasibility and tolerance of short-course radiotherapy in elderly patients, unfit for chemotherapy.

Methods: A total of 94 patients with rectal cancer underwent neoadjuvant treatment at our center, between January 2006 and December 2016. 12 of these patients were unfit for chemotherapy. They were elderly and presented severe comorbidity. Patients showed distal or middle third, MRI diagnosed cT3-T4 or N+ rectal adenocarcinoma. So short course radiotherapy was performed with a total dose of 25 Gy, 5X5 fraction, with 3D conformal radiation therapy. The gross tumor volume (GTV) was the visible primary tumor and the visible pathological lymph nodes. The pelvic CTV included mesorectum and presacral space. Subsequently, a 0.8 cm margin was added to generate the 3D-PTV. To evaluate the tolerability of this treatment, the adverse events, we adopted the CTCAE scale. To define the pathological response we used Mandard classification.

Results: All patients completed the planned preoperative radiation short course and underwent surgery (6 low anterior resections and 6 abdominoperineal resections) after ten days. Acute proctitis G2 and 3 were seen in 2 (17%) and 1 (8%) patients, respectively. There were no G3 and 4 subacute hematologic and non-hematologic (genitourinary and peripheral neuropathy) toxicities and perioperative morbidities such as anastomose leakage. Grade 2 or higher late toxicities were not observed. T downstaging rate was 50% and in no case progression was recorded. Complete pathological response was never achieved. The 3-year overall survival and local control rates were 83% (no rectal cancer specific mortality) and 92%, respectively.

Conclusions: Shourt-course radiotherapy is well tolerated. Moreover, evidence showed that 5 × 5 Gy

with delayed surgery can be used routinely for the management of elderly patients who are unfit for chemotherapy in case of "unresectable" cancer or early cancer prior to local excision. This study showed that SRT followed by surgery is not only feasible and tolerable without significant toxicity but also, associated with promising pathological response rates.

P033

RADICAL RADIOTHERAPY IN OCTOGENARIANS PROSTATE CANCER PATIENTS: A MULTI-INSTITUTIONAL ANALYSIS

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Aims: Prostate cancer patients over 80 are considered frails, and generally managed conservatively either by means of androgen deprivation therapy (ADT) only or observation. The aim of present analysis is to determine the safety and efficacy of radical radiotherapy in octogenarians.

Methods: Records of 178 patients with prostate cancer treated with Radiation Therapy (RT) at six institutions. All patients were at least 80 years and received radical treatment with standard fraction or hypofractionation, according to their characteristics and IPSS score. ADT was allowed according to risk class or clinical conditions. Comorbidities were evaluated for all patients, and grouped into classes (cardiovascular, pulmonary, oncological, metabolic, neurological, renal, etc.), and the Charlson score was calculated accordingly. Toxicity was recorded according to CTC vers. 4.03 scale. Relapse free survival (RFS) was calculated using the Kaplan-Meier method.

Results: Median age was 81 years (range 80-89). Most patients received radiation therapy with conventional fractionation (144 pts; 81%). Treatment included pelvic lymph node area in 27 (15.1%) while 105 (59%) received ADT too. Comorbidity was none in 40 patients (22.4%), one in 89 patients (50%), two in 39 (21.9%) and three or more in 10 patients (5.7%). Charlson score was up to 6 in 153 (86%) patients. Cardiovascular comorbidity was recorded in 106 pts (59.6%), while 15 patients (8.4%) experienced additional cancer. Treatment was generally well tolerated: 152 patients (85.4%) completed treatment without any interruption. Acute toxicity was (all-grade): Gastro-intestinal (GI) in 77 patients (43.3%); Genito-urinary (GU) in 109 patients (61.2%). No grade 4 acute toxicity was recorded; 1 patient (0.6%) experienced grade 3 acute GI toxicity and 2 patients (1.2%) recorded grade 3 acute GU toxicity. Grade 2+ GI and GU late toxicity was recorded in 15 patients (8.4%) and 16 patients (9%), respectively. With a mean follow-up of 27.8 months, 3- and 5-years RFS was 85% and 76% respectively. For exploratory purpose only, a multivariate analysis was performed. Only low-intermediate risk disease seems related with RFS (HR: 0.27; 95% CI: 0.74-1.01).

Conclusions: Radiation therapy with radical intent in octogenarians patients with prostate cancer is safe and active, and should not be precluded in the decision making. Prospective data are needed to reinforce our findings.

P034

HYPOFRACTIONATED STEREOTACTIC RADIATION THERAPY WITH HELICAL TOMOTHERAPY FOR EARLY STAGE NON-SMALL CELL LUNG CANCER IN ELDERLY PATIENTS

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Aims: Surgery for early stage Non Small Cell Lung Cancer (es-NSCLC) in over 65 patients is often associated with a higher risk of perioperative complications. Stereotactic Body Radiotherapy (SBRT) represents a viable alternative for elderly patients unfit for resection. Here we report our single-center experience of SBRT delivered with Helical Tomotherapy for es-NSCLC in over 65 years patients.

Methods: From October 2014 to February 2018 we retrospectively evaluated 37 patients over 65-years with es-NSCLC. All patients were assessed using Charlson Comorbidity Index (CCI) and G8 screening tool; median age was 74 years (range, 65-91), 22 were stage I and 15 stage II. Most frequent histology was adenocarcinoma in 15 pts, squamous cell in 8, undifferentiated in 3; in 11 pts histological confirmation was not available and diagnosis was based on the evidence of pathological uptake detected on PET scan. Basing on tumor site we adopted different RT schedules: 60-70 Gy in 8-10 fractions for peripheral lesions (n=33), and 50-60 in 10 daily fractions for central (n=4). Median BED10 was 105 (75-119). Acute and late treatment-related toxicities were graded using CTCAE v4.0 scale, performing after RT chest CT scans every 3 months for the first year of follow-up. Fisher's exact test and

Kaplan-Meier method were employed to analyze any clinical correlation and Local Control and Overall Survival rates.

Results: Median CCI and G8 scores were 6 (4-11) and 14 (12-17). Median treatment time was 15 days (10-24), with 25 patients treated daily, and 12 every other day. Median GTV and PTV were respectively 6.64 cc (0.55-111.76) and 22.86 (5.15-181.33). With a median follow-up of 13 months (3-32) we observed 3 cases of acute G2 radiation pneumonitis, resolved after steroids therapy. As regards late toxicity, we reported only one case of G2 non cardiac chest pain and one case of G2 radiation pneumonitis requiring medical treatment. At the time of the analysis, we detected 4 local failures resulting in 1- and 2-yrs LC rates of 94% and 85%. 13 patients out of 37 died, 5 for non-cancer related causes, resulting in 1- and 2-yrs OS rates of 84% and 70%. No statistical correlation was found between clinical parameters and outcomes.

Conclusions: Our data support the use of SBRT via Helical Tomotherapy as a safe and effective treatment for elderly patients, reporting very low rates of toxicity with no G≥3 events occurred. LC and OS rates are comparable with other experiences in literature.

P035

PREOPERATIVE RADIO-CHEMOTHERAPY IN ELDERLY PATIENTS WITH RECTAL CANCER

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Aims: In studies of rectal cancer, the elderly have been frequently under-represented because comorbid conditions and functional status often lead to study exclusion. We performed a retrospective analysis in order to evaluate the tolerability of preoperative Radiotherapy in combination with oral fluoropyrimidine-based chemotherapy in patients aged>or=70 with locally advanced resectable T3-T4 N0-2 M0 rectal cancer, and to evaluate the influence of comorbidities (BPCO, cardiopathy, diabetes mellitus, hypertension, cerebrovascular diseases; IRC) on combinated treatment tolerance and on survival.

Methods: From January 2012 to April 2018, 63 patients (41 man and 22 woman), aged >or =70 with T3-T4 N0-2 M0 rectal cancer received a preoperative pelvic radiation therapy (3D-CRT 50.4Gy/28f/1.8 Gy/die) including tumor, entire mesorectum and pelvic lymph nodes. Performance status (KPS and ECOG score) and comorbidity (Charlson comorbidity index) were calculated. Neoadjuvant chemotherapy with concurrent capecitabine was administered in 51 "elderly fit" patients (80.95%), while 12 "frail "patients were not treated with oral fluoropyrimidine but only radiotherapy because comorbid conditions. During treatment, patients were monitored weekly for signs of acute toxic effects and evaluated using the National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE v3.0).

Results: 61 (96.8%) patients completed the planned RT, whereas 54 (85.7%) patients also completed the prescribed CT. Grade≥3 acute toxicity occurred in 12 patients. Radiation proctitis, fatigue, and diarrhea were reported in 35%, 48%, and 42% of the 63 patients, respectively. None of the patients in our series had grade 4 toxicities. The tumor and nodal down-staging was documented in 95% of patients; 42% of patients obtained a pathologic complete response. Surgical resection was performed in 61 patients. There were 2 post-operative deaths. After a median follow-up of 75 months, the 3, 5 and 6-year overall survival rates were 69%, 48% and 37% respectively. A significantly decreased of overall survival was observed in patients aged 80 or older. This negative influence on survival of cancer was due to the increased risk of death, correlated with comorbid conditions.

Conclusions: The results of the present study have shown that RT in combination with capecitabine is safe and well tolerated in older patients, especially in "elderly fit patients", with good results in terms of RC and OS.

P036

HYPO-FRACTIONATED STEREOTACTIC RADIOTHERAPY IN ELDERLY PATIENTS (> 75 YEARS OLD) WITH BRAIN METASTASES

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Aims: the main aim of our study was to evaluate the feasibility of a radiation treatment (hypo-fractionated stereotactic technique) in oligometastatic (< three lesions) elderly patients aged > 75 years old. Treatment compliance, acute toxicity and the response to the treatment at three months were analyzed

Methods: over the period 2013-2017, 27 patients (age ranging of 75-92) out of 250 patients affected by brain metastases (< three lesions and maximum diameter < 30 mm) underwent a stereotactic irradiation The male: female ratio in our 27 elderly cohort was 22:5. The primary tumors were as follows: 16 NSCLC, 1 breast, 3 gastro-enteric, 3 melanoma, 3 kidney, and 1 gynecological tumor. The most affected region was the right parietal lobe. In 9/27 patients, a neurological symptomatology occurred. Twelve patients showed extra cranial metastatic disease. All patients underwent a planning computed tomography (CT) and a treatment plans were development using by the Pinnacle ver.10 system. The total dose was 3200 cGy total dose in four 800 cGy session in twenty patients, and 4000 cGy in five 800 cGy session in seven patients. Initial and final KPS, acute toxicity and treatment compliance were monitored. Local control was assessed for each patient, at 3 months after the treatment, by brain MRI.

Results: All the patients completed the treatment without any interruptions. No change of the general conditions (KPS) and no neurological acute toxicity > G2 (CTCAE) were recorded. At 3 months disease progression was observed in 15/ 27 patients at MRI.

Conclusions: the stereotactic technique is a feasible and well-tolerated treatment for elderly patients (> 75 years) with a good local control to three months.

P037

TOTAL MARROW/TOTAL LYMPHOID IRRADIATION IN THE CONDITIONING REGIMEN FOR HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR THE ELDERLY WITH ACUTE MYELOID LEUKEMIA

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Aims: When a matched sibling donor is lacking for patients with intermediate-high risk acute myeloid leukemia (AML), a 1-haplotype mismatched (haploidentical) family member is usually immediately available. In elderly patients, myeloablative conditioning regimens, which may include total body irradiation, are associated with high toxicity and non-relapse mortality rates. Consequently, we designed a conditioning regimen for the haploidentical transplant setting with total marrow/total lymphoid irradiation (TMI/TLI) and low chemotherapy doses. The graft contained a ratio of conventional T cells (Tcons) and T regulatory cells (Tregs), which induce a Graft versus Leukemia effect with a low incidence of Graft versus Host Disease (GvHD).

Methods: July 2015-May 2018: 16 AML patients (median age 62 years, 8 in 1st and 7 in 2nd complete remission, 1 in partial remission) underwent haploidentical HSC transplantation. Composite comorbidity/age scores were 1/2 in 8 patients and 3/4 in 8. TMI/TLI target volumes were skeletal bones, major lymph node chains and spleen. TMI/TLI was delivered by Tomotherapy from day -7 to day -4, in 2 daily fractions of 1.5 Gy (TMI) and 1.3 Gy (TLI) (total doses 13.5Gy and 11.7Gy respectively). Chemotherapy included tiothepa 2.5 mg/kg (days -10 and -9), fludarabine 30 mg/m^2 (days -10 to -6) and cyclophosphamide 15 mg/kg (days -8 and -7). Haploidentical grafts consisted of 10x10^6/kg purified CD34+cells, 1x10^6/kg conventional T cells (Tcons) and 2 x10^6/kg freshly isolated T regulatory cells (Tregs). No post-transplant immunosuppression was given.

Results: G3 gastrointestinal toxicity in 2 patient was the worst TMI/TLI-related acute toxicity. All patients sustained primary full-donor type engraftment. Acute grade II-IV GvHD developed in 7 patients (44%) and chronic GvHD in none. Transplant-related causes of death were veno-occlusive disease (1 patient), sepsis (1), acute GvHD (1) and neurological toxicity (1). Immune reconstitution was good, with a rapid increase in peripheral blood T cells. Twelve patients are alive and relapse-free at a median follow-up of 22 months (4-34 months) for alive patients.

Conclusions: TMI/TLI and relatively low chemotherapy doses were safe in this conditioning regimen which was associated with low toxicity and mortality rates. The immunosuppressive effect of TLI ensured a high engraftment rate while the myeloablative effect of TMI, combined with Tcon/ Treg adoptive immunotherapy has, to date, prevented relapse.

P038

RADICAL RADIOTHERAPY IN ELDERLY PATIENTS AFFECTED BY FACE-LOCALIZED SKIN TUMORS

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Aims: We assess the effectiveness and feasibility of a curative radiation treatment for face-localized not operable skin tumors (basal cell and squamous cell carcinomas), in elderly patients (> 75 years old) reducing the symptoms while causing the least possible toxicity.

Methods: Over the period 2013-2017, we treated 15 not operable patients (75-93 y.o.) affected by face-localized skin tumors. Pathology showed: basal cell carcinomas (BCC) in six and squamous cell carcinoma (SCC) in nine. Periocular localization was the most frequent (14/15 patients). Total dose, ranging between 4000cGy, in 200 cGy session using electrons beams (BCC)) and 6000 cGy in 200 cGy session using photons beams (SCC), the latter patients were treated using IMRT technique, to minimize the dose to healthy organs, such as eyes and the conjunctival-lacrimal apparatus.

Results: All patients were followed up monthly with average follow up 18 months. Tolerance, skin acute toxicity and response rate were analyzed. Patients well tolerated the therapy, despite of the fact that three patients developed lung complications, which obliged to interrupt the treatment. No acute skin toxicity > G2 was reported. Six month overall response rate was 86, 6% (13/15) with pain resolution.

Conclusions: Elderly patients affected by face-localized skin tumors and characterized by algic symptomatology and disfigurement of facial symmetry can effectively undergo a curative radiation treatment. This option offers multiple advantages to patients as it is not invasive, easy to be performed, and allows the management of pain and the achievement of an excellent percentage of complete response with good tolerance.

P039

THE ROLE OF MRI AND CT/MRI FUSION IMAGING IN THE MANAGEMENT OF PATIENTS WITH PROSTATE CANCER CANDIDATE TO RADIOTHERAPY

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Purpose: To evaluate the accuracy of MRI in the local staging of prostate cancer. To demonstrate the clinical utility of MRI in the radiation therapy planning, particularly in the evaluation of target volume, risk organs assessment, radiation dose distribution and hormonal treatment association.

Materials and methods: Between January 2015 and December 2017 there were retrospectively identified 90 patients with prostate cancer treated by VMAT/IGRT. All patients underwent CT simulation and MRI using specific radiotherapy supports (kneefix and feetfix) to achieve CT/MRI fusion imaging. The correlation between biopsy stage and MRI stage was evaluated by Cohen's kappa and the differences in NCCN risk classes assignment were analysed using T parameter as independent variable. Differences between radiation volumes obtained by CT and radiation volumes obtained by CT/MRI fusion imaging have also been evaluated.

Results: The concordance between biopsy stage and MRI stage was moderate; particularly in 30/90 patients the T stage was upgraded on MRI and in 5/90 patients the T stage was downgraded. CT/MRI fusion imaging allowed a radiation volume reduction (mean CTV decrease of 30%) with consequent savings in dose to organs at risk and a toxicity improvement.

Conclusions: MRI has been proven as reliable and accurate technique in the management of patients with prostate cancer candidate to radiotherapy. The use of CT/MRI fusion imaging allowed a better evaluation of target volume and improved the radiation therapy efficacy.

P040

ELDERLY PATIENTS AFFECTED BY OLIGOMETASTATIC DISEASE: THE "BLITZKRIEG" RADIOTHERAPY APPROACH

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Aims: To evaluate, retrospectively, the outcome of stereotactic body radiation therapy (SBRT) in elderly patients with oligometastatic cancer from different primitive tumors.

Methods: We treated 70 patients with isolated body metastasis. Median age at diagnosis was 75 years (IQR 69-80). The most common SBRT fractionation schedule was 5x7 Gy, (total dose 35 Gy). The primary end points were Local Control (LC) and Toxicity. Secondary end points were Overall Survival (OS) and Disease Specific Survival (DSS). Response to radiotheraphy was evaluated according to RECIST criteria v1.1. Toxicity was determined according to Common Terminology Criteria for Adverse Events (CTCAE) v 4.0. Survival analysis was performed using the Kaplan-Meier method, and the correlation between time actuarial incidence and clinical parameters was investigated.

Results: Median follow-up was 26.5 months. Forty-four patients (62.8%) were alive at the time of analysis while twenty-two (31.4%) had died from the disease. Local control was 87% at 2 and 3 years. The 2 years OS and DSS were 84% and 71%, respectively, while the 3 year rates were 57% and 62%. PFS at 2 and 3 years was 41% and 25%. On univariate analysis, KPS $\geq$ 90 was correlated with improved OS and DSS ($p<0.05$). Acute toxicity $\geq$ G2 occurred in 4 patients (5.7%), while late toxicity $\geq$ G2 was reported in 6 patients (8.6%).

Conclusions: Ablative Radiotherapy is a safe, effective, and minimally invasive treatment for elderly patients with oligometastatic disease who are unfit for systemic therapy.

P041

CHEMO-RADIOTHERAPY FOR VERY ELDERLY ANAL CANCER PATIENTS: A MULTI-INSTITUTIONAL EXPERIENCE

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Aims: We retrospectively evaluated efficacy and toxicity of chemoradiotherapy (CRT) in the treatment of very elderly patients (pts) with anal carcinoma delivered using the radiotherapy schedule of the EORTC 22953 study.

Methods: Data of very elderly pts (80 years old or more) with a histological diagnosis of anal carcinoma treated in 4 Institutions were retrospectively reviewed. We analyzed and reported Local Control (LC), Disease Free Survival (DFS) and Overall Survival (OS) and the acute and late toxicity rates.

Results: From 01/2001 to 12/2015, 38 pts (M/F ratio: 10/28) were treated with curative RT with (n = 36 pts) or without (n = 2) chemotherapy. Median age was

83.6 years (range: 80.3 – 92.6). Four, 17, 8, and 9 tumors were staged as Stage I, II, IIIa and IIIb, respectively (2002 UICC TMN classification). Fifteen pts were N1-3 and 6 pts presented positive inguinal nodes. Median Charlson score was 9 (range, 6 -11). All the patients received the treatment using the EORTC 22953 RT schedule, i.e. 36 Gy (1.8 Gy/fraction) on the anal canal, on the rectum with the mesorectum, and on the inguinal and pelvic nodes, followed by a boost of 23.4 Gy on the initial anal and nodal sites of disease. The CTV to PTV margin was 1 cm. Thirty patients were treated using 3D-RT and 8 using different form of IMRT. Chemotherapy was delivered in 36 patients, usually with Mitomycine (n = 31) with 5-Fluorouracile (n = 4) or Capecitabine (n = 23). Four patients received Capecitabine alone. Two patients refused CT. The median follow-up was 79 months (95%Confidence interval, 95%CI: 66 - 109). Median LC time was not reached, while 5-year LC rates was 81% (95%CI: 80 - 82). Five-year DFS and OS rates were 68% (95%CI: 67% - 69%) and 79% (95%CI: 77.5% – 80.5%), respectively. Overall acute and late G3-4 toxicity rates were 20% (particularly skin G3 toxicity, 4/38 pts) and 2.5% (particularly rectal G3 toxicity, 1/38 pts), respectively. Eleven pts received a colostomy, but with only 2/38 pts received it to treat a G4 anal toxicity.

Conclusions: Standard CRT delivered using the radiotherapy schedule of the EORTC 22953 study is safe and achieves good LC and OS rates in very elderly anal canal cancer patients.

P042

RADIOTHERAPY IN OCTOGENARIAN AND NONAGENARIAN GYNECOLOGIC PATIENTS: A SINGLE INSTITUTIONAL EXPERIENCE

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Aims: The objective of this retrospective study was to evaluate the feasibility of radiotherapy (RT) in elderly patients with gynecologic cancers.

Material and methods: We retrospectively reviewed the outcomes of 26 consecutive ≥ 79 years old patients with gynecologic cancer (15 uterine cancers, 8 vulvar cancers and 2 vaginal cancers) who were consecutively treated with RT in our institution.

Results: Overall, patient median age was 83.5 years (range: 79- 98, DS: 5.47) and patient median Karnofsky performance status (KPS) was 70 (range: 50- 90, DS: 10.1) with a G8 score ranged from 4.5 to 12.5 (median 9.5, DS 2.0). External beam RT was performed in a palliative setting (n = 13; 50%), with a volumetric arc therapy (VMAT). The mainly VMAT schedule was 39 Gy/13 fractions that provides effective and efficient palliation of symptoms with an overall response rate for bleeding of 100% during the treatment and an overall response of pain and itch of 100% after 2 months from the end of RT. Early treatment interruptions were needed for 2 patients for cognitive and clinical deterioration. 13 patients underwent to brachytherapy (BT) for curative, palliative and adjuvant purpose with a median dose of 21 Gy (range: 14-42 Gy, DS: 7.2) and a median number of fractions of 3 (range: 2-7). Interruption of BT treatment was needed for a women affected by vaginal adenocarcinoma who developed surgical wound dehiscence. Overall, both for VMAT and BT were reported infrequent major acute or late toxicities (<G2 both for rectal, bladder and vaginal toxicity according to CTCAE4.02 score).

Conclusions: our experience showed radiotherapy as a safe and feasible treatment in elderly patients with gynecologic cancers. In particular the schedule of 39 Gy/13 fractions was mainly indicated in old women with a low Q8 score, providing low toxicity, both acute and late, and rapidity of local symptoms palliation.

P043

HYPOFRACTIONATED RADIATION THERAPY WITH MONO- AD BIWEEKLY FRACTIONATION FOR THE TREATMENT OF EPITHELIAL SKIN CANCER IN VERY ELDERLY PATIENTS

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Aims: Epithelial skin cancer are a common diagnosis of cancer in the elderly population. Radiotherapy is a well established treatment option of treatment with high response rates. Those tumors often occur in advanced stage, when intensive and, sometimes, disfiguring treatments are needed. The aim of our study is to evaluate the efficacy and tolerability of hypofractionated radiotherapy in a population of very elderly patients with early or locally advanced stage epithelial skin cancer. Primary endpoint were local control (LC) and compliance to treatment. Secondary endpoints were, socioeconomic impact, cosmetic result, overall survival (OS), cancer specific survival (CSS) and toxicity.

Methods: we treated 40 tumors in 32 patients with two different hypofractionated schedules: 6 Gy in 10 biweekly fractions and 5 Gy in 12 bi-weekly fractions (total dose 60 Gy). Median age at the treatment was 84.4 years (range 68-100); 21 (65.6%) patients had a PS(Ecog) of 1-2 and 11 (34.4%) patients had a PS(Ecog) of 3-4. Life expectancy according to the Charlson Comorbidity Index was ≤5 years in 90.5% patients.

Results: the overall response rate was 96.5% with a rate of complete response of 91.4%. Local recurrence occurred in 1 case after 20 months from primary treat-

ment. Five cases (12.5%) had a G3 acute local toxicity, while late toxicity occurred in 3 (7.5%) cases. All patients experienced an improvement of the symptoms and a reduction of pain and medications. Cosmetic outcome was good in 28 (70%) tumors, fair in 10 (25%) cases and poor in 2 cases (5%). Median OS in our series was 28 months (95% c.i. =4.7-51.2). At the time of analysis 56.25% patients are dead. Median CSS was not reached. One and 2 years CSS were 95%.

Conclusions: Hypofractionated RT is an effective option of treatment and can be safely administered also in elderly and comorbid patients, with low toxicity and optimal results. We suggest the use of the 6 Gy in 10 (biweekly) fractions schedule in this setting of elderly patients, mainly due to the shorter duration of the course and in the view of administer a treatment more sustainable by these frail patients and to reduce the costs.

P044

RADICAL RADIOTHERAPY IN ELDERLY PROSTATE CANCER PATIENTS: A MONOINSTITUTIONAL EXPERIENCE

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Aims: Continuous or intermittent androgen deprivation therapy (ADT) is generally prescribed in elderly prostate cancer (PCa) pts with under 10 years life expectancy. Unfortunately, 24-36 months later many pts become castration resistant and only palliative therapies are available. Here we report toxicity and outcomes obtained in elderly (≥80 years old at diagnosis) PCa (pts) treated with radical radiotherapy in a monoinstitutional experience.

Methods: From December 2006 to July 2014, 30 elderly PCa pts underwent radiotherapy with radical intent. Three pts, affected by a low risk cancer, were treated on prostate and seminal vesicles only, to 71.4 Gy in 28 fractions (EQD2 80.8 Gy, considering $\alpha/\beta=1.5$ for prostate cancer). Intermediate and high risk PCa pts underwent prophylactic irradiation on pelvic nodes to 51.8 Gy in 28 fractions (EQD2 52.2 Gy), with simultaneous integrated boost to seminal vescicles up to 65.5 Gy (77.7 Gy EQD2) and to prostate up to 74.2 Gy (88 Gy EQD2). Neoadjuvant and/or adjuvant androgen deprivation therapy (ADT) was prescribed in 24/30 pts for a median of 27.9 months (2-79 months). All patients were treated with helical IMRT (Tomotherapy®, Accuray, Wisconsin) and daily IGRT (MVCT). Patients' characteristics are reported in Table 1.

Results: Median follow up was 61.8 (41-127) months. Acute and late toxicity were mild, with only two late G3 rectal toxicity (6.67%) registered, eventually solved by Argon Plasma applications, and 1 G3 urinary stenosis (3.33%), solved with temporary catheterization. Late G2 toxicity were 16.67% (5 pts) for urinary tract and 6.67% (2 pts) for the rectum. Five pts were dead at the last follow up, only 1 due to prostate cancer progression. Five pts experienced biochemical and clinical relapse (1 intermediate, 3 high and 1 very high risk) , while 22 pts are free from biochemical progression. The median biochemical relapse-free survival (bRFS) and distant progression-free survival (calculated from the last day of RT) were both 61.1 months.

Conclusions: Radical radiotherapy with a curative intent even in elderly pts shows very good results in terms of both biochemical control and progression-free survival, with a good toxicity profile. In our opinion, radical treatment in elderly pts could improve their life expectation and quality of life.

Table 1.

Median (range) age at diagnosis	81 (80-85) years
Median (range) iPSA	7.6 (2.33-67.4) ng/ml
Median (range) Gleason Score	6: 8 7: 10 8: 6 9: 6
T Stage	cT1c: 12 cT2a: 5 cT2c: 11 cT3: 2

P045

FIVE YEAR OUTCOMES OF HYPOFRACTIONATED ADJUVANT RADIOTHERAPY IN ELDERLY PATIENTS WITH LOW RISK BREAST CANCER

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Aims: Several studies suggested that radiotherapy could be omitted in elderly patients(pts) with low risk breast cancer (LRBC). Despite a better 10-15 year local control, they present lower overall survival than younger pts, because of comorbidities and life expectancy. We report 5-year outcomes in elderly pts with LRBC treated with whole breast hypofractionated adjuvant radiotherapy(HRT).

Methods and Materials: One hundred forty five pts 70 years or older, Luminal A/Luminal B Her 2 neuwith pT1pN0-1a(<4+LN) tumor, without chemotherapy prescription, treated with 40 Gy/15 fractions forward planned IMRT without boost from 02/2009-05/2013 were analyzed. Median age was 73(70-90) years, 8 pts had ductal carcinoma in situ, 25 lobular invasive carcinoma or combination, 98 ductal invasive carcinoma and 14 other histology(mucinous, tubular, papillary); 70 were right sided and 75 left sided tumors. Hormonal therapy was prescribed in 133/145 pts. Our protocol

provides a 5 year follow up for possible side effects. Acute toxicity during HRT was evaluated with RTOG scale, late toxicity with SOMA-LENT score.

Results: A median number of 4(2-6) segments were used to obtain a homogeneous dose distribution. Acute toxicity was: 24.1% G0, 69,0% G1 and 24.1% G2. Half of G2 toxicities were delayed, 7-15 days after HRT, and concerned only the inframammary fold; 70% had breast volume> 600 cc. Two G2 toxicities were observed in low breast volume pts but with bolus for half therapy. Late toxicity was available for 131 pts: 16% were G1 edema/dyschromia, rarely persistent over three years, while 7.6% G1 fibrosis/teleangiectasia, starting generally from the third year after RT. Only one G2 fibrosis/teleangiectasia was observed. Four pts were dead at the last follow up: one of head and neck tumor, one of stroke and two of heart attack. The treatment plans of the two pts died of heart attack (one left sided tumor) were revised, but heart dosimetry was very good in both: V95%= 0 cc for both, V 20 Gy 0 for right sided, 0.76 cc for left sided pts and D 5 1.5 Gy for the right sided and 2.03 Gy for left sided pts. Two pts (1.52%) presented local relapse (4.4 and 7.9 years after HRT), 1 pts lymph-nodal relapse and 4 pts (3.02%) distant relapse.

Conclusions: Elderly pts with LRBC treated with HRT showed a good treatment tolerance and low local relapse (LR) rate, lower than the up to 9% reported without RT. Thus, a short, convenient HRT could improve quality of life by reducing the LR rate.

P046

CLINICAL OUTCOMES OF NEOADJUVANT TREATMENT FOR LOCALLY ADVANCED RECTAL CANCER IN ELDERLY PATIENTS

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Aims: Older patients with colo-rectal cancer are less likely to receive standard treatment than younger due to comorbidities and higher risk of toxicity. Aims of this study is to evaluate clinical outcome of neoadjuvant chemoradiation (nCRT) and the effect of surgical timing on pathological tumor response (pCR) after short or long course radiotherapy (RT) in elderly patients with locally advanced rectal cancer (LARC)

Methods: A retrospective analysis has been performed of 108 consecutive patients aged ≥ 70 years with LARC treated from May 2006 and September 2017 who underwent nCRT or short course RT followed by surgical rectal resection. RT was delivered with a 3-dimensional conformal multiple field technique at a total dose of 50.4 Gy in 28 fractions concomitantly with oral Capecitabine or 25 Gy in 5 fractions. Patients were divided into two groups according to the interval between the end of RT and surgery: < 8 wk (group A, 37pts) and ≥ 8 wk (group B, 59pts). pCR was defined as the absence of tumor cells in the surgical specimen, ypT0N0M0.

Results: Female were 47 (43.5%) and male were 61 (56.5%). Mean age was 77 years (range, 70- 94 years). Of 108 pts, 17 received short course RT and 91 nCRT. Chemotherapy has been interrupted only in 5 pts (6.3%): 2 due to haematological toxicity, 1 pt for diarrhea and 2 pts developed cardiotoxicity. 11/ 108 pts did not receive surgery (3 for complete clinical response and 8 for comorbidities or refuse of the pts), 1 pt was lost at follow up so 96/108 pts were considered suitable for pCR analysis. A total of 20/96 pts (21%) achieved pCR: 7(19%) in group A and 13(22%) in group B. At median FU 24 months, 3 year local control rate (LRC) was 98.5% [100% in group A and 97.4% in group B (p=0.624)].

Conclusions: In our experience neoadjuvant treatment in elderly patients (>70 years) was safe and well tolerated. Delaying surgical resection up to 8 weeks after radiotherapy +/- chemotherapy was not associated to a higher rate of pCR and LRC. Because decisions regarding eligibility for neoadjuvant treatment should not be based on age alone we need prospective studies to better select which patient aged > 70 years could benefit from preoperative approach.

P047

HIGH-DOSE-RATE INTERVENTIONAL RADIOTHERAPY TREATMENT FOR NON-MELANOMA SKIN CANCER IN VERY AGED PATIENTS

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Aims: non-melanoma skin cancer (NMSC) of the elderly has been rapidly increasing in incidence over the past 30 years. Therapeutic options like cryotherapy, laser therapy, topical treatments and photodynamic the-

rapy are usually reserved for early stage, low risk and superficial NMSC while the mainstays of treatment remain surgery and radiotherapy. Because surgical excision is known to be associated with < 5% recurrences, limited data are available on the effects of radiotherapy. High-dose-rate interventional radiotherapy (HDR-IRT) represent an excellent treatment option because of its high radiation dose conformity within the target volume, rapid dose fall off in adjacent organs at risk, short overall treatment time and excellent cosmetic and good functional outcomes.

Methods: Ten high-aged patients with advanced, biopsy proven basal cell carcinoma (BCC, n=6) or squamous cell carcinoma (SCC, n=4) were treated with exclusively HDR-IRT. After delineation of the Planning Target Volume (PTV= gross target volume (GTV) + 1.5cm in BCC and +2.0 cm in SCC) on each patient's skin, an individual double-layer mould of thermoplastic mask material was prepared and applied to the skin surface, ensuring at least 3mm distance from the skin to the plastic tubes which were fixed in appropriate geometry over the target area with an interspacing distance of 1.2 cm-1.4 cm. The PTV was marked on the mould surface by radiopaque material for visualization of the lesion on the native CT scan. Planning CT images were acquired with 2.5 mm slice thickness and transmitted to the planning system. Applicators were reconstructed and active/inactive lengths were defined. Individual dose volume optimization was added when required. Treatment intention was to deliver ≥ 95% of the prescribed dose to the PTV, accepting 90% as satisfactory. The dose was prescribed at 5mm from the skin surface in all patients. Acute toxicity was defined as occurring during HDR-IRT and/or within 90 days of its completion. Late toxicity was considered as developing > 90 days after completing HDR-IRT. Toxicities were assessed using the Common Terminology Criteria for Adverse Events scale (CTCAE) v. 4.0.

Results: Median age was 91 years (range 58-94 years). Acute toxicity: Grade 2 erythema appeared in all 10 patients. Towards the end of each treatment schedule, epidermolysis developed which was resolved within 6 weeks of completing HDR-IRT. Late toxicity: Grade 1 skin atrophy and pigmentation changes were observed in all patients as well alopecia in the field. At 5 months of median follow-up (range 4-38 months), all patients were disease free.

Conclusions: The use of customized moulds appears efficient, comfortable, simple and safe, and is associated with low toxicity and excellent cosmesis and represent a valid treatment choice for this cohort. A large data-base analysis of treatment results of these type of NMSC is advisory.

P048

EBRT FOR PROSTATE CANCER: TOLLERANCE IN ELDERLY

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Aims: Prostate cancer is a frequent pathology in the elderly. Radiation therapy represents an important resource for the treatment of these patients, mostly in patients with severe comorbidities that exclude surgical treatment. Radiotherapy, however, may decrease quality of life and it is considered less tolerated in elderly. Our aim was to evaluate the impact of EBRT for prostate cancer in our elderly patients.

Methods: We performed a retrospective analysis of elderly patients that underwent to radiation therapy for prostate cancer from April 2010 to September 2014. A total of 42 patients of age ≥ 75 years was treated, 39 of them on prostate with radical intent (70-78 Gy) and 3 of them on whole-pelvis with adjuvant intent (70-74 Gy to prostate bed and 54-60 Gy to pelvic lymph nodes). All treatments were performed using VMAT and IGRT. A total of 29 patients was treated with concomitant ADT. In this setting of patients we evaluated acute toxicity (appearing within six months from the start of the treatment). The toxicity was assessed using CTCAE grading scores. In particular we evaluated gastrointestinal and genitourinary toxicity.

Results: In our group of patients 11 were 75 years old, 9 patients were 76, 8 patients were 77, 9 patients were 78, 4 were 79 and one was 83 years old. The adverse events founded were distributed homogeneously in different age groups, this suggests that toxicity is not strictly related to age. No G4 and G5 events were recorded. Three patients developed G3 genitourinary toxicity (1 case of dysuria and 2 cases of nocturia) and no patients developed G3 gastrointestinal toxicity. G2 genitourinary toxicity was found in 17 cases and G2 gastrointestinal toxicity was found in 2 cases. The most common symptoms of G1 genitourinary toxicity were dysuria (25 cases; 59,5%) followed by nocturia (12 cases; 28,5%). The most common G1 symptom about gastrointestinal toxicity was tenesmus (5 cases, 11,9%).

Conclusions: In our experience there was no relevant major (G3-G5) acute toxicity in elderly population. We founded a fair amount of minor (G1-G2) acute toxicity cases. Moreover the toxicity detected seems not to be correlated with increasing age. This data shows that radiation therapy for prostate cancer in elderly is quite safe, but we need prospective studies with geriatric evaluation in order to have a better assessment of is impact in this kind of patients.

P049

EXCLUSIVE RADIOTHERAPY IN PAROTID GLAND CARCINOMA: A CASE REPORT OF AN ELDERLY FEMALE PATIENT

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Aims: The parotid gland carcinoma is a malignant neoplasm that comes from a pleomorf adenoma of the salivary gland. It is considered as a low grade tumor. Typically described as a tumor that rarely invades the adjacent tissues, it has a high rate of recurrence ranging. Mortality described in literature is low. The aim of this case report is to describe the story of an elderly female patient with locally advanced parotid gland carcinoma treated with radiotherapy.

Methods: We present an 89 years old female with a locally advanced carcinoma of left parotid gland, cT4a cN2b cM0. In CT the lesion appeared with unclear boundary, an important contrast enhancement, with axial measures 52x53x56 mm, that penetrated sternocleidomastoid muscle. Lymphonodal involvment in IIa left level. At MR we saw a solid lesion of 61x47x61 mm, heterogeneous with unclear margins and central necrosis. Two lymphonodes at IIa left level. She underwent to biopsy with diagnosis of malignant neoplasm. Clinically the lesion was hard and fixed, with a cutaneous fistula plentiful bleeding and patient reported left hear pain. Radiotherapy was the only treatment available for the patient because of her age and comorbidity. We performed radiotherapy using conventional schedule: 70 Gy to macroscopic lesion in 35 fractions with 6 MV photon beams with 3D technique. At 13rt and 27th fraction, after an awesome response of the lesion, we rescheduled patient. During the treatment she presented mucositis and dry mouth G1 and described dysphagia G1 and dysgeusia G2 at 22 Gy. A mild fatigue came at 36 Gy. Treatment was stopped for 3 days during 1st and 2nd week because lesion bled a lot. She was assisted by support therapy and treated with systemic and local antibiotics associated to tranexamic acid. Her weight body remained constant. After 30 days lesion was 30 vs 50 mm and not bleeding. Patient reported dysphagia, dysgeusia and dry mounth G1. After 53 days lesion was further reduced and she described only dysgeusia and dry mounth G1. Lesion produced a thick crust on cutaneus surface that patient treated with fibrinolytic lotion. We don't have follow up imaging because patient died with a cardiac attack after 50 days from radiotherapy.

Conclusions: The standard treatment for this cancer is surgery, but our elderly patient underwent only to radiotherapy and her clinical result was excellent with low toxicity. In our opinion age shouldn't be considered an absolute exclusion criteria for radical radiotherapy.

P050

THE IMPACT OF AGE ON THE PRESCIPTION AND OUTCOME OF STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR LUNG LESIONS: A COMPARISON OF "ELDERLY" E NON "ELDERLY" PATIENTS

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Aims: to investigate the impact of age on the delivery and outcome of SBRT for primary or secondary lesions located in the lungs.

Methods: clinical charts of all patients (pts) treated at Niguarda Cancer Center with SBRT for a lung lesion in the period 2015-2017 were retrospectively reviewed. Elderly pts were defined as those older than the median age of the series. Patient and tumour characteristics, as well as outcome information, were compared in the "elderly" group vs " non elderly" group. Median follow-up of surviving pts was 19 months (range 3-39).

Results: 60 patients were included in the analysis, with a median age of 75 years (range 46-92). Performance status was 0-1 in 83% of the pts and median Charlson Index was 3.7 (range 0-9).Overall, 66 lesions were treated with SBRT, 70% of them were lung primaries and 30% were secondary lesions. Histology was adenocarcinoma in 52%; squamous in 10%; other in 17%; unknown (PET positive) in 21%. Elderly pts >= 75 yrs old (n=33) were 55% of the series and non elderly pts (< 75 yrs old) were 46% (n=27). Tumour and treatment characteristics in elderly vs non elderly pts were as follows: Charlson Index 3,6 vs 3,9; secondary lesions were 18% vs 44% of the total number of targets treated in each group; average tumour volume (GTV) was 8,4 cc(range 1-22,9) vs 4,9 cc (range 0,2 - 11.5); average PTV was 62 cc(14,5-69) vs 39cc (5-91). Median fractional dose was 10 Gy (range 6-12Gy) in both groups, with total dose ranging 45-50 Gy vs 45-60 Gy. Biological Effective dose (BED) was >= 100 in 88% of elderly vs 74% in non elderly. As far as outcome is concerned, 11pts died of the disease after progression at distant sites, 1 patient died for other causes ; 4 pts are alive with distant progression, 1 patient is alive with local progression and 43 pts are alive without disease progression.

Conclusions: in our series we observed several differences in the characteristics of the patients and of the lesions in the "elderly" group as compared with "non elderly" group, but treatment prescription and outcome were similar in both groups, confirming SBRT as an effective, safe and manageable treatment modality in all groups of age.

P051

A SINGLE-INSTITUTIONAL ANALYSIS OF 1-YEAR DISEASE FREE SURVIVAL AND TOXICITY RELATED TO A RADICAL OR ADJUVANT RADIATION TREATMENT FOR ELDERLY PATIENTS WITH EPITELIAL HEAD AND NECK CANCER

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Aims: Elderly patients (pts) with head and neck cancer (EHNC) require a specific multidisciplinary approach because of their fragility that could prejudice the indication for radical treatments and could make them more susceptible to iatrogenic effects. We report our results on 1-year Disease Free Survival (DFS) and toxicity in HNC patients ≥ 70 years old (y.o) who underwent a tailored radical or adjuvant radiotherapy (RT) with or without combined chemotherapy (CT).

Methods: Between 2011 and 2016 56 EHNC pts (≥70 y.o) underwent a tailored radical or adjuvant RT in our Institute. Among them only 14 pts received a combined CT. We retrospectively analyzed from the medical charts the following clinical parameters: primary tumor site, stage (AJCC 7th edition), RT doses and volumes, acute and late toxicity (according to RTOG toxicity scale) and 1-year DFS.

Results: 21 female and 35 male pts with median age at diagnosis of 79 years (70-100; 11 pts ≥ 85 y.o) received RT for HNC. Primary tumor sites were: oral cavity (20 pts; 5 ≥85 y.o), nasopharynx (2), oropharynx (2), hypopharynx (1), glottic larynx (15 pts; 3 ≥ 85 y.o), rare histotypes (16 pts; 3 ≥ 85 y.o). 3 pts had stage 0 disease, 12 stage I, 2 stage II, 9 stage III, 30 stage IV. Radical dose of RT was 69,96-70 Gy (dose per fraction 2-2,12 Gy); for adjuvant treatments the median RT total dose was up to 66 Gy (range 54-66 Gy) with 1,8-2 Gy per fraction. 25 pts (of which 13 with glottic cancer) had RT only to macroscopic disease (T and N+); among them 8 pts (4 oral cavity, 3 glottic, 1 rare histotype) were ≥85 y.o; other pts received RT with standard volumes. Acute grade 3 toxicity affected 8 pts; no acute grade 4 toxicity was observed. 11 pts had RT interruptions (among them 5 completed RT course), 2 died for non specific cause. Median follow up is 16 months. 1-year DFS rate was 70%. During the first year post-RT no severe late toxicities were observed and the prevalent RT side effects were depending on the treatment volumes (skin fibrosis, low grade dysphagia or dysphonia).

Conclusions: Our experience supports the useful role of a tailored and multidisciplinary approach to E-HNC pts. Previous clinical, geriatric and performance status evaluations are necessary to select patients for treatments. A specific nutritional and psychological support may improve treatment tolerance. Future directions could include a limited RT volumes and tailored approaches during follow-up in order to improve quality of life.

P052

STEREOTACTIC BODY RADIOTHERAPY FOR ELDERLY PATIENTS (AGE ≥ 80 YEARS) WITH STAGE I NON-SMALL CELL LUNG CANCER

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Aims: Stereotactic body radiotherapy (SBRT) for non-small cell lung cancer (NSCLC) is primarily a treatment option for medically inoperable patients, who are often elderly. However, few studies report the effects of SBRT in elderly patients. We retrospectively analyzed clinical outcomes of elderly patients (age≥80 years) with stage I NSCLC treated with SBRT in our institution.

Methods: From February 2012 to December 2017, 80 patients aged ≥80 years with stage I NSCLC were treated with daily cone-beam computed tomography-guided SBRT. All patients were discussed in a multidisciplinary setting before SBRT. 18 F FDG PET/CT was performed in all patients before SBRT. A positive 18 F FDG PET/CT scan and an increase in the size of the lesion at CT scan were mandatory in patients in which an histological diagnosis was not available. Charlson Comorbidity index were defined in all patients. Acute and late toxicity were scored according to Common Terminology Criteria for Adverse Events version 4.0.

Results: Median age was 82.4 years (range, 80-90 years), 28 female and 52 male. Median Charlson comorbidity index was 3 (range, 2-6). Histological diagnoses was possible in 22.6% (6.3% Squamous cell carcinoma, 16.3% Adenocarcinoma). In the other 77.4% due to high risk of complication no biopsy was performed. 17 patients were T2 size and all the other were T1. Median dose/fractions was 55 Gy/5 fractions prescribed at 80% isodose (range,50-60 Gy/3-12 fractions), median BED:115.5 Gy. Median PTV:29.5 cc (range,3.7-147.9 cc). Median follow up was 14 months (range, 2-70 months). Two years Local control, Disease free survival, Overall survival were 86.9%,74% and 75%, respectively. No sever (≥ G3) acute and late toxicities were reported. No patients died within 30 days from SBRT.

Conclusions: SBRT is a safe and effective treatment for elderly patients with early stage NSCLC.

P053

OUR EXPERIENCE OF HYPOFRACTIONATED RADIOTHERAPY REGIMEN AFTER CONSERVING SURGERY FOR >70 YEARS BREAST CANCER WOMEN

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Aims: About 30% of breast cancer occur in women aged >70 years although elderly patients are often excluded from both retrospective and randomized trials and treated suboptimally, frequently without curative treatments. Hypofractionated radiotherapy appears to be a valid approach primarily for elderly women who are unable to undergo a longer radiotherapy regimen. The aim of this retrospective analysis is to evaluate outcome and toxicity in a group of breast-cancer elderly patients treated with a hypofractionated schedule with or without systemic therapy.

Methods: Between June 2005 and December 2013, one hundred twenty-four (124) breast cancer patients >70 years were treated at Radiotherapy Department in Taranto with adjuvant hypofractionated RT. The mean age was 75 years (range: 70-85 years). All patients underwent conservative surgery while axillary dissection was performed in 80% of patients. Fourteen patients had positive node and were excluded from this analysis leaving a total of one hundred ten (110) women. Pathological stage was pT1 in 45.5% and pT2 in 54.5% of patients. Most of patients (72.7%) received hormone therapy since they had positive estrogen and/or progesterone receptors while negative-receptor women received adjuvant chemotherapy. All the 110 patients received adjuvant RT with a hypofractionated regimen and a total dose of 42.56 Gy (2.66 Gy/die) without adding a boost. Acute and late toxicity were evaluated according to the RTOG-EORTC scale. Local recurrence rate, metastasis rate, overall and disease-free-survival were calculated.

Results: With a mean follow-up of 62 months (range: 6-132 months) no local recurrence was observed while only five patients (4.5%) experienced distant metastases and died (three with bone metastases, two with lung metastases). The disease-free-survival was 95% at 5 years and the overall survival was 91% at 5 years considering that five women died for cardiovascular disease (three patients irradiated for left breast and two irradiated for right breast). Acute skin toxicity was G1 for 77% of patients and G2 for 9% of patients while late skin toxicity was G1 for 10% of patients and G2 for 1.8% of women. No acute lung toxicity was observed while only one patient had late lung fibrosis.

Conclusions: The hypofractionated schedule with a total dose of 42.56 Gy (2.66 Gy per fraction) in woman >70 years old resulted in mild early and late toxicity with excellent local control and survival. It could be considered as a valid treatment option for elderly women who had indication for whole-breast radiotherapy.

P054

RADIOTHERAPY OF EARLY GLOTTIC CANCER IN THE ELDERLY: RETROSPECTIVE STUDY

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Aims. We performed a retrospective study in elderly patients with early glottic cancer treated with radiotherapy to evaluate tolerance, toxicity, local control, overall survival and specific disease survival.

Methods. From 2007 to 2017, 25 patients over 75s with early-stage glottic cancer (cT1cN0) were evaluated and treated with radiotherapy at our institute. Comorbidities of the patients were evaluated using the Charlson Comorbidity Index. All underwent external beam radiantion therapy with a total doses ranging between 66-70 Gy and standard fractionation.

Results. All patients completed the treatment with good tolerance. Only 3 patients needed to stop treatment for more than 3 days. Laryngeal toxicity occurred in 10 patients (6 with G1 and 4 G2). Pharyngeal toxicity occurred in 19 patients (10 with G1 and 9 G2). Candida infection was found in 12 patients. Three, five and nine-year local control was respectively to 86%, 86% and 42%. Corresponding values for overall survival were 83%. Corresponding values for disease specific survival were 87%. 10 of the 13 patients who had recurrence of disease were recovered with surgery, 2 refused surgery while 1 patient underwent palliative treatments.

Conclusions. Radiotherapy is feasible in elderly patients with early stage glottic cancer, providing good results in terms of survival and quality of life and radiotherapy may be considered a valid alternative to transoral laser surgery.

P055

ADVANTAGES OF INTRAOPERATIVE IMPLANT FOR INTERSTITIAL BRACHYTHERAPY FOR ACCELERATED PARTIAL BREAST IRRADIATION EITHER IN FRAIL PATIENTS WITH EARLY-STAGE DISEASE OR IN LOCALLY- RECURRENT BREAST CANCER

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Purpose: To describe the intraoperative multicatheter implantation technique for accelerated partial breast irradiation (APBI) delivered with high-dose rate brachytherapy (HDR-BT). Secondarily, to evaluate outcomes and toxicity in a series of 83 patients treated with this technique.

Materials and Methods: Retrospective analysis of a series of patients treated with HDR-BT APBI after

intraoperative multicatheter interstitial implant between November 2006 and June 2017 at Catalan Institute of Oncology (ICO-Barcelona). We assessed cosmesis, toxicity, overall survival (OS) and disease-free survival (DFS).

Results: Eighty-three patients were included: 59 patients (71.1%) presented primary early-stage breast cancer and 24(28.9%) locally-recurrent breast cancer. Tumorectomy was performed in all cases, with intraoperative tumour margin assessment and sentinel node biopsy. Median age was 82 years (range, 44-92). The total prescribed dose was 32 Gy (8 treatment fractions) in 60 patients (72.3%) and 34 Gy (10 fractions) in 23 patients (27.7%). Median follow-up was 40 months (range, 3-136 months). Three-year OS and DFS in the recurrent and primary cancer groups were, respectively, 87% vs. 89% and 96% vs. 97.8%. Five patients died from non-cancer related causes. No local relapses were observed. Rates of acute and late toxicity were low in both group. The cosmesis was good or excellent in most of patients treated for primary desease, in patients who underwent salvage brachytherapy for local recurrence, cosmesis was good in 49 pts, fair in 6.

Conclusions: This technique, although time-consuming, achieves good local disease control with a satisfactory toxicity profile in both early-stage and local recurrent breast cancer patients. It may be especially suitable for frail patients.

P056

NEOADJUVANT RADIOCHEMOTHERAPY IN ELDERLY LOCALLY ADVANCED RECTAL CANCER PATIENTS: A MONOINSTITUTIONAL EXPERIENCE

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Aims: The improving mean life expectancy increases the number of rectal cancer patients in good performance status (PS) than can be treated with curative intent. Moreover, modern radiotherapy (RT) permit a better coverage to the tumor, preserving the adjacent organs at risks, with a decrease in acute and late toxicities. The aim of this study was to evaluate the impact of neoadjuvant chemoradiotherapy (CRT) in elderly patients.

Methods: Between 2000 and 2018, 117 (M:80;W:37) locally advanced rectal cancer patients, with ≥70 years, were treated in our Radiotherapy Department and retrospectively analysed. They received concurrent chemotherapy with fluoropirimidine, associated or not with platinum based chemotherapy. RT was performed by 3D conformal technique, with a dose of 4500 cGy, on the pelvic nodes, followed by a sequential boost of 540 cGy (180 cGy/die) or a concomitant boost of 1000 cGy (100 cGy/die, 2 times/week). The pathologic response was evaluated according to Mandard tumor regression grade (TRG) score. The Memorial Sloan–Kettering Cancer Center score was used for the evaluation of anal sphincter function. Acute and late toxicities were assessed using the Radiation Therapy Oncology Group (RTOG) scale and the RTOG/European Organization for Research and Treatment of Cancer (EORTC) late radiation scoring system.

Results: Median follow-up was 45 months (range:1-163). The median age was 75 (range: 70-88). One hundred and three patients had ECOG PS 0. Thirty-four (29.1%) patients received a concomitant boost. A pathological complete response (TRG 1) was obtained in 23 patients (19.7%). Acute toxicities were reported in Table 1. Twenty-four patients (20.5%) were lost to the follow-up. Ninty-four (80.3%) patients were evaluated for late toxicities. Overall sphincter function resulted excellent in 23 (24.5%) patients, good in 3 (3.2%), fair in 6 (6.4%) and poor (incontinence) in 11 (11.7%) patients. Twenty-three (24.5%) patients presented stoma. One patient presented late skin toxicity ≥G3 and 2 late GI toxicity ≥G3. The 5-year local control (LC), disease-free-survival (DFS) and overall survival (OS) rates were 89.5%±3.9%, 73.3%±5.2%, 78.1%±5.0%, respectively.

Conclusions: Our results reported good tolerability and clinical outcomes of neoadjuvant CRT in patients ≥70 years. Also concomitant boost intensification can be considered in elderly patients with good PS.

Table 1. Acute toxicities.

Acute Toxicities	G0	G1	G2	G3
Skin Toxicity	63 (53.8%)	22 (18.8%)	31 (26.5%)	1 (0.9%)
GI Toxicity	37 (31.6%)	39 (33.3%)	39 (33.3%)	2 (1.8%)
GU Toxicity	88 (75.2%)	26 (22.2%)	3 (2.6%)	0 (0%)
Hematologic Toxicity	94 (80.4%)	10 (8.5%)	10 (8.5%)	3 (2.6%)

P057

LONG-TERM PROGRESSION-FREE AND OVERALL SURVIVAL IN ELDERLY MEN WITH POST-SURGERY NON-METASTATIC RADIOLOGICALLY OR HISTOLOGICALLY CONFIRMED MACROSCOPIC LOCOREGIONAL RELAPSED PROSTATE CANCER AND TREATED BY 3D-CONFORMAL OR VOLUMETRIC MODULATED ARC RADIOTHERAPY

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Aims: To report the fractionation schedules and the long-term oncological outcomes of men with post-surgery non-metastatic macroscopic locoregional relapsed prostate cancer (Pca) undergoing RT.

Methods: Forty-four patients with post-surgery non-metastatic radiologically or histologically confirmed macroscopic locoregional relapsed Pca were retrospectively reviewed. Progression free survival (PFS) defined as biochemical and/or radiological progression and Overall survival (OS) were used as main oncological measures.

Results: The mean age of studied population was 68,8 years (95%CI 67,2-70,5) and the mean pre-RT PSA was 2.1 ng/ml (95%CI 1,4-4,7). Thirty-two (72,7%) men received antiandrogen therapy before RT. Ten men (22,7%) were treated with VMAT and 25 (56,8%) also received IGRT. Macroscopically relapsed tumour was in prostate fossa and in the regional nodes in 39 (88,6%) and 5 (11,6%) patients, respectively. Eight (18,2%) men received the irradiation of the only prostate fossa (70-76 Gy in 35-37 fractions) and 3 patients (7%) received irradiation of the only macroscopic relapsed Pca within prostate fossa (36.25 Gy in 5 fractions). Twenty-six (59,1%) men received the irradiation of the prostate fossa (70-76 Gy in 35-37 fractions) with elective irradiation of regional nodes (45-50,4 Gy in 25-28 fractions). Two men (4,5%) received SIB-VMAT delivered to prostate fossa (68,4 Gy in 38 fractions) and macroscopically relapsed Pca (76 Gy in 38 fractions) and 3 men (7%) received SIB-VMAT delivered to elective locoregional lymph nodes (51-49,5 Gy in 30-33 fractions) and PET+ nodes (60-66 Gy in 30-33 fractions). Finally, two patients (4,5%) received VMAT delivered to PET+ lymph nodes (40 Gy in 5 fractions). The post-RT PSA nadir (0,082 ng/mL; CI95% 0-016) was achieved at a mean time of 11 months. The actuarial PFS and OS were 123.8 (103.97-143.7) and 138 months (121-154.4) with the rate of men free from progression and alive of 79,5% and 91%. Six men progressed in prostate fossa and 3 developed bone lesions. The mean PSA at the last follow-up was 3.75 ng/ml (0-10.1).

Conclusions: Radiation treatment of non-metastatic elderly men with macroscopic locoregional relapsed Pca poses a unique challenge for radiotherapists owing to the age related limited life expectancy and the high treatment effectiveness of multimodality treatment strategies. Tailored age-related defined treatment strategies should be identified to improve the quality of life of this population.

P058

CURATIVE RADIOTHERAPY IN THE TREATMENT OF INVASIVE BLADDER CANCER ELDERLY PATIENTS. IS SARCOPENIA A COMORBIDITY PREDICTOR OF SURVIVAL?

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Aims: Sarcopenia is a detrimental prognostic factor in elderly bladder cancer patients (EBCP) who underwent to radical cystectomy with elevated 90 days mortality. To evaluate if sarcopenia has any impact at 90 days in radiation therapy, we retrospectively analyzed it as predictor of clinical outcome in irradiated EBCP.

Methods: We reviewed clinical records of EBCP treated from March 2013 to April 2018 in two radiotherapy centers (Papardo Hospital and Policlinico G. Martino in Messina). All patients performed the CT-simulation (slice thickness: 2,5 mm); in the CT-simulation images fat (Vf) and muscle (Vm) were retrospectively contoured starting 3 cm below the lesser trochanter for a total of four consecutive slices (1 cm). The ratio Vf/VM (RV) has been calculated in cc; we considered two groups of patients: A) RV between 0,1-1; B) RV > 1 ("sarcopenic patients").

Results: 26 patients (3 female 23 male) were evaluated. The median age was 85.5 years (range 75-90). The patients received radical radiotherapy on bladder and clinically positive nodes. No efforts have been made to include negative nodes. The median delivered dose was 60Gy (range 36-66 Gy), with a fraction dose of 2-2.1Gy. 13 patients had a RV ≤ 1 (group A) and 13 >1 (group B). At 90 days 0/13 group A patients died, 0/13 group B died.

Conclusions: With respect to surgical series, 90 days mortality has not been observed in our small sample group. More data are necessary to confirm this hypothesis.

P059

RADIOTHERAPY OF EARLY BREAST CANCER IN ELDERLY WOMEN: TO DO OR NOT DO TO?

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Aims: The purpose of this study was to retrospectively report the balance between doing or not adiuvant radiotherapy in elderly patients(pts) with early breast cancer, according to health conditions and comorbidities.

Methods: Clinical end point was local control (LC). 30 pts has been chosen from 2015 and carefully analy-

zed: half of them were treated with whole breast hypofractionated radiotherapy(HRT), while the other half, according to severe comorbidities, low risk breast cancer, and obviously personal choice didn't underwent HRT. In the first group 15 pts were given 5.7 Gray (Gy) in 5 weekly fractions (total dose, 28.5Gy) plus/minus Simultaneous Boost (SIB) on tumor bed in "high risk" cases. SIB consisting in 0.5 Gy each fraction (total dose of 2.5 Gy) was added according to positive margins, high Ki67 index, High grading, and tumour size. In the second one, patients started a strictly follow up, with radiological examinations and clinical evaluations. Patients were aged over 70 years old (median age 84 y.o., range 72-90), pTis and pT1-2N0-1a, with different grading G1-G3, various biologic patterns all with positive hormonal receptors, different laterality and size (overall medium). Some of them underwent neoadjuvant hormonal therapy, most of them in adjuvant setting.

Results: Median follow-up for both groups was 2 years (range 1-3 years). At the last follow-up all pts were alive and disease-free without any recurrence. For those pts who did HRT, this schedule was well tolerated and a radiological follow-up showed a good response (15 negative mammography) and at a clinical evaluation all of them had a good aesthetic outcome. Also in the other pts, who didn't underwent HRT adjuvant treatment, final results (14 mammography and 1 breast ultrasound) were negative.

Conclusions: Despite the limited number of pts examined in our study, our results show that there is the possibility to avoid whole breast radiation therapy in selected pts, considering the risk of recurrence, general elderly-related health conditions, low life expectation and, last but not least, patient personal choice.

P060

HYPOFRACTIONATED RADIOTHERAPY IN THE ELDERLY: WHEN LESS IS MORE

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Aims: The aim of this study was to evaluate one weekly hypo-fractionated Adjuvant Radiotherapy (RT) in elderly patients affected by early breast cancer and to report clinical outcomes: acute and late skin toxicity profile and treatment feasibility.

Methods: Our study was conducted on 49 patients treated from October 2016 to July 2017. Patients underwent Adjuvant Radiotherapy with a hypo-fractionation regimen: 28,5 Gray(Gy) / 5 fractions / 1 fraction weekly plus/minus a 2.5 Gy Simultaneous Boost (SIB) on tumour bed in "high risk" cases. Patients were aged over 70 years old (median age 79 y.o., range 72-95), with no severe comorbidities, pT1-2N0-1a, with different biologic patterns, laterality and size (overall medium). Treatment was delivered in supine position, with tangential fields and constraints of conventional 3D-CRT for lungs and heart; V20=0 for Left Anterior Descending Artery (LADCA) was translated to V12 for radiobiological calculation. Field-in-field technique was used to increasing dose distribution homogeneity. Acute and late skin toxicity plus clinical outcomes were assessed based on RTOG scales and evaluated before, during each fraction, at the end of RT and at 2, 4 weeks, at 6 months and 1 year after treatment.

Results: The median follow-up was 10 months. Clinical outcome was good, no remarkable changes in breast appearance. Treatment was well tolerated in all cases except a 90 y.o. woman, who interrupted therapy after 3 fractions. Tangential fields were sufficient to achieve satisfactory distribution; SIB was added in 22 patients (45%). Severe grades of cutaneous toxicity (G3 and G4 RTOG) were no observed; grade 2 acute skin side-effects were significantly low: at the end of the treatment only 4 women (8%) needed topic cortisonic therapy for G2 dermatitis, which ameliorated within 3 weeks after irradiation. Furthermore 15 patients (30%) showed G1 erythema, spontaneously and quickly resolved. Late skin toxicity consisted in G2 fibrosis only 2 pts (4%), G1 5 pts (10%) and G0 41pts (85%), furthermore 1 patient (2%) develop hyperpigmentation. Aesthetic outcomes were good to excellent in 94% and fair to poor in 6%.

Conclusions: This hypo-fractionated schedule is proven to be a feasible treatment, with poor acute and late skin toxicity. Moreover, it represents facilitation to radiation treatment for elderly patients, who hardly acceed to the hospital, limiting the number of fractions and making this regimen safe.

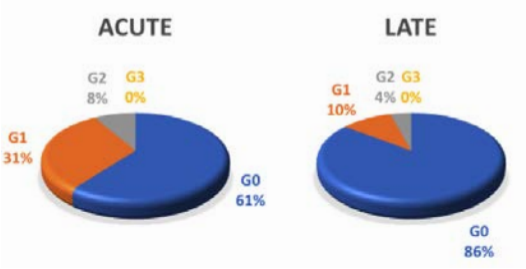

Figure 1.

P061

RADIOTHERAPY IN ELDERLY PATIENT: A CASE OF REPEATED ABLATIVE RADIOTHERAPY ON BRAIN METASTASES AND PALLIATIVE LUNG RE-IRRADIATION

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Aims: We report a case of elderly patient treated with brain repeated ablative radiotherapy and a palliative lung re-irradiation obtaining a benefit both in terms of local control and in the quality of life.

Methods and Results: 75-year-old patient, PS: 1, with lung adenocarcinoma (EGFR-, ROS-, ALK-) diagnosed in February 2016 in stage III B, treated with different chemotherapy lines. In February 2017 brain progression (one lesion in the right frontal lobe of 11x14 mm, and one in the left cerebral pedicle of 2-3 mm), was treated with stereotactic radiotherapy with 8 Gy x 3 fractions. Three months later MRI control demonstrates complete brain response in absence of neurological disorders. In June 2017 brain progression with two new lesions (one in the left cerebellar tonsil of 8 mm, and one in the right frontal lobe of 2 mm), the first was treated with stereotactic radiotherapy (8 Gy for 3 fractions) and the second was treated with 6.5 Gy for 3 fractions (reduced dose by proximity to the previous treatment). Three months later with MRI control appeared complete brain response in absence of neurological disorders. In September 2017 lung disease progression, the patient was treated with palliative radiotherapy on the lung with 3 Gy for 10 fractions. Two-months later the CT control reveals tumor mass reduction (40 x34 mm VS 64x64 mm, 16x7 mm VS 27x21 mm e 28 mm VS 70 mm) and a reduction of lung disorders. In February 2018, new brain progression (a lesion in the left frontal lobe of 5 mm) was treated with stereotactic radiotherapy with 7 Gy for 3 fractions (reduced dose due to previous treatments). In April 2018 another lung disease progression was treated with palliative re-irradiation with 5 Gy for 3 fractions. Follow up still in progress.

Conclusions: in this patient we highlight the important role of radiotherapy in the multidisciplinary treatment of tumors. Even in an elderly patient, we can think a more aggressive therapeutic attitude with benefit, both in terms of local control and in terms of quality of life. In this patient the lung palliative treatment obtained a reduction of the tumor mass and a reduction of lung disorders, while the brain repeated ablative treatments obtained a complete response without side effects, with an overall survival of 15 months and maintaining a PS: 1.

P062

HYPOFRACTIONATED WHOLE-BREAST RADIOTHERAPY: FIVE FRACTIONS ONCE-WEEKLY VERSUS TEN FRACTIONS 4-TIMES A WEEK

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Aims: The purpose was to compare 5 fractions(fx) one weekly hypo-fractionated Adjuvant Radiotherapy (RT) versus 10 fx 4weekly hypofractionation in elderly patients(pts) affected by early breast cancer and reporting clinical outcomes: skin toxicity profile and treatment feasibility.

Methods: This retrospective study was conducted on 96 pts, treated between 2016-2017. Patients underwent adjuvant radiotherapy with two different hypo-fractionation schedules. The first group (groupA) underwent 28,5 Gray(Gy)/5fractions/1 fraction weekly plus/minus a 2.5 Gy Simultaneous Boost (SIB) on tumour bed in "high risk" cases, the second one(groupB) 35Gy/10 fractions/4 times a week with a concomitant boost of 3 or 4 Gy once a week, according to risk factors. Pts in both groups were aged over 70 years old (median age 79 y.o., range 72-95), with no severe comorbidities, pT1-2N0-1a, with different biologic patterns, laterality and size. Treatment was delivered in supine position, with tangential fields. Regarding the saving of the organ at risk, conventional 3D-CRT lungs and heart constraints were used; V20=0 for Left Anterior Descending Artery (LADCA) was translated respectively to V12 and V14 for radiobiological calculation. Skin toxicity and clinical outcomes were assessed based on RTOG scales: at the end of RT, 6 months and 1 year after treatment.

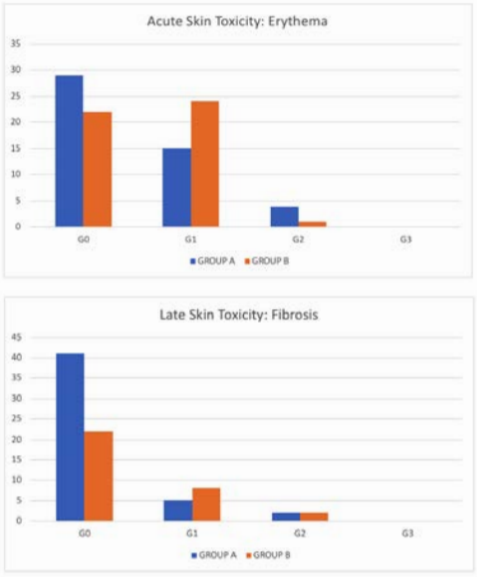

Figure 1.

Results: In groupA SIB was added in 22 pts(45%). In groupB a concomitant boost of 3 Gy was added in 31pts, 4Gy in the remaining 17. G3-G4 cutaneous toxicity were no observed in both groups; grade 2 acute side-effects were significantly low: at the end of the treatment only 4 women in groupA and just one in groupB needed topic cortisonic therapy for G2 dermatitis, which ameliorated within 3 weeks after irradiation. 15 pts(groupA) and 24pts(groupB) showed G1 erythema. Late skin toxicity (12 months) consisted in fibrosis groupA G2 2 pts, G1 5pts, G0 41pts; furthermore 1 patient developed hyperpigmentation. As regard group

B fibrosis G2 2 pts, G1 8 pts and G0 38pts, 2 patient showed skin retraction G1. Aesthetic outcomes were good to excellent in 94% and fair to poor in 6% in groupA, and respectively 96% and 4% in groupB.

Conclusions: Once weekly hypofractionated radiation therapy resulted comparable to ten fractions regimen without evidence of inferior treatment feasibility or higher adverse effects. Once weekly radiation therapy can be recommended as safe and effective alternatives for whole-breast adjuvant radiotherapy in elderly pts.

P063

RADIOTHERAPY IN VERY ELDERLY HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS

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Aims: To evaluate toxicities and clinical outcomes in very elderly patients with Head and Neck Squamous Cell Carcinoma (HNSCC) treated with radiotherapy (RT).

Methods: From January 2007 to December 2017 we retrospectively analysed all the patients affected by HNSCC treated with RT in our centre; among these we evaluated the records of > 75 years old patients irrespective to the purpose of the treatment (curative, palliative).

Results: A total of 308 HNSCC patients have been retrieved. 28/308 (9%) were >75 years old with a median age of 80 (range 75-92); 19 patients were male and 9 were female; primitive tumour sites were: oral cavity (8/28), larynx (11/28), oropharynx (2/28), parotid gland (5/28), nasopharynx (2/28). Comorbidities were present in 15/28 patients and were distributed as follow: cardiovascular diseases (5/15), chronic renal failure (1/15), metabolic diseases such as diabetes mellitus, hypercholesterolemia and dysthyroidism (6/15); 15/15 patients were affected by hypertension. Furthermore 1 patient had also a history of bladder cancer, 1 of gastric ulcer, 1 of benign prostatic hyperplasia, 1 chronic obstructive pulmonary disease. The treatment purpose was curative, palliative and adjuvant in 11, 7, 10 patients, respectively. The median dose prescribed was 62.8 Gy (range 30-70), with a median daily dose of 2.1 Gy (range 2-3 Gy). Only 2 patients underwent concurrent immunobiological therapy (cetuximab) with RT. None of the selected patients received CHT. All patients completed the planned RT treatment, apart a patient treated with Cetuximab and RT. G1-G2 dysphagia was observed in all patients. Other symptoms reported were dysgeusia (1 case), headache (1 case), xerostomia (1 case), dyspnea (1 case), skin erythema (2 cases), low grade fever (1 case); furthermore, one of the two patients undergone Cetuximab+RT developed hematologic toxicities needing hospitalization. At the last follow-up, 7 patients were still alive, 16 died (median OS: 12 months).

Conclusions: Our experience suggests RT is a valid and feasible therapeutic option in HNSCC very elderly individuals considering that it does not lead to severe toxicities in the majority of patients. Our reports demonstrate age is not an exclusion criteria for RT in HNSCC.

P064

HIGH-DOSE RATE BRACHYTHERAPY IN THE TREATMENT OF NON-MELANOMA SKIN CANCER: CLINICAL OUTCOME AND FEASIBILITY IN A SINGLE-CENTRE RETROSPECTIVE ANALYSIS

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Aims: Non-melanoma skin cancer (NMSC) is the most common malignancy in the white population, comprising about 2-3 million new diagnosis worldwide every year, with an increasing incidence observed in the last decades. High dose rate brachytherapy (HDR-BRT) is an advantageous treatment option both from dosimetric point of view and for patient convenience due to the small number of fractions. The purpose of this study was to evaluate tumor control and toxicity in elderly patients treated with HDR-BRT.

Methods: A total of 49 patients underwent skin HDR-BRT from October 2007 to April 2018 with Iridium-192 source. 30 lesions in 28 patients affected by NMSC were enrolled; lymphopoietic, breast and benign histology (keloids) were excluded from the analysis. The median age at diagnosis was 81,9 years. A surface flap was customized to the size of each target lesion and the catheters were embedded; every treatment was optimized with 3D planning using CT imaging. Different prescribed doses and fractionation have been chosen: 24-31.5 Gy in 8-12 fractions for palliative treatment (4 cases, 13%), 34-52 Gy in 10-20 fractions for adjuvant treatment (17 cases, 57%) and 36,75-60 Gy in 7-30 fractions for radical treatment (9 cases, 30%); the average biological effective dose (BED) was 36.2, 52.1 and 60.9, respectively. The treatment was mostly delivered with daily fraction and some schedules were accelerated with 2 fractions a day. Acute and late toxicity has been recorded according to CTCAE 4.0.

Results: At a median follow-up of 16 months (range 3-76 months), local control was 97%; in particular no patient treated with an adjuvant BRT HDR after radical surgery had local recurrence and seven of the nine lesions (78%) who received a radical dose showed a complete response. In only 5 lesions a partial response was observed, mostly in the palliative group, and just 1 case developed a progression. No severe acute toxicity was recorded; just 27% of the cases presented G2 acute toxicity, recovered within 2 months from the end of brachytherapy. Late G1 toxicity was showed in almost a

quarter of the lesions; no G2 or greater late toxicity was recorded. 70% lesions showed an excellent cosmetic impact and just one case resulted in a fair cosmetic outcome.

Conclusions: HDR-BRT represents an effective and safe solution for the treatment of NMSC, even in elderly population, with excellent clinical outcome and very low toxicity. More data with a longer follow-up are necessary.

P065

PANCREATIC CARCINOMA IN ELDERLY PATIENTS: OUTCOME REPORT AND COMPARISON IN A SERIES OF 47 RADIATION TREATED M0 PATIENTS

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Aims: Pancreatic cancer is the second cause of digestive cancer-related deaths. Aim of our study is to compare the outcome of elderly with younger patients affected by pancreatic adenocarcinoma, treated at the Radiotherapy Department of the University "Federico II" of Naples.

Methods: Forty-seven consecutive patients treated by radiotherapy for M0 pancreatic adenocarcinoma at the Radiotherapy Department of the University "Federico II" between January 2012 and January 2018 were analysed. Radiation treatment was delivered with a dose range between 45 and 56 Gy. Treatment was delivered after a neoadjuvant chemotherapy or after neoadjuvant chemotherapy and surgery, concurrently with radiosensitizing chemotherapy. Elderly group was defined as patients aged 65 years or over. Accordingly, the two groups, <65y and ≥65y, were compared with regard to recurrence rates (locoregional and /or distant), and for clinical and treatment features.

Results: Median age was 63 years (range 48-82). Elderly group included 21, while the <65y one included 26 patients. 4.3% of patients were stage I, 44.7% stage II and 34% stage III. Median tumor size was 32 mm (9-96 mm), and 31 patients were node positive. Thirty-one patients (66%) underwent surgery, and in 20 cases it was R0. Most patients had neoadjuvant (prior to surgery or definitive radiotherapy) and concurrent chemotherapy. No significant differences were observed in the distribution of patient clinical and treatment variables between the two groups. At a median follow up of 7 months (3-53), 28 (59.6%) patients were alive. The estimated 2-year recurrence rate was 70.2%. First site of recurrence was locoregional in 29.8%, locoregional and distant in 6.4% and distant in 34% of patients, respectively. No significant differences in recurrence rates were observed between the ≥65y group and the <65y one. Among the clinical and treatment variables the only significant impact on recurrence rate was given by the tumor size (p=0.001).

Conclusions: Our analysis confirms the poor outcome for pancreatic cancer patients, with high rate of recurrences in patients treated with surgery chemotherapy and radiotherapy, with no impact of older age, and clinical and treatment variables. The only factor that affected negatively the recurrence rate was the bigger tumor size. However a further study on a larger patients population is warranted.

P066

EARLY BREAST CANCER IN ELDERLY PATIENTS: OUTCOME REPORT IN AN HOMOGENEOUSLY RADIATION TREATED PATIENTS POPULATION

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Aims: The objective of this study was to compare the outcome of elderly with younger early breast cancer (BC) patients treated by conserving surgery and postoperative radiotherapy.

Methods: Four hundred nineteen consecutive early breast cancer patients treated by post-operative radiotherapy at the Radiotherapy Department of the University "Federico II" were analysed. All patients were at a stage between 0 and IIA. Radiation treatment was delivered with 50 Gy to the whole breast (2.0 Gy/25 fractions) followed by a boost dose of 10 Gy in 5 days delivered by electrons on the tumoral bed. Elderly group was selected as patients aged 65 years or over. Accordingly, the two groups, <65y and ≥65y, were compared with regard to loco-regional and distant recurrences (LRR and DR respectively), and for clinical, pathologi-cal and treatment features.

Results: Median age was 53 year (range 29-84). Elderly group included 73 patients, while the <65y one included 346 patents. At a median follow up of 73 months (2-219), 401 (95.7%) patients were alive and the estimated 5-year free of LRR rates were 98.5%, with no signifi-cant differences between the two groups. 5-years free of DR rates was 91.7% for ≥65y and 98.8% for <65 (p<0.001). No significant differences were observed in the distribution of pa-tient clinical and pathological variables between the two groups. The only difference was found in treatment with chemotherapy that was administered in a significant higher portion of patients in the <65y group compared with the elderly group (40.8% vs 18.1%, p<0.001).

Conclusions: Our analysis suggests an equivalent effect of radiotherapy in elderly and non-elderly patients in terms of loco-regional control. A higher rate of distant recurrences in the ≥65y group was observed. Moreover we found that chemotherapy was administered in a significantly lower portion of elderly patients.

P067

IMPACT OF PATIENTS' AGE ON PRESCRIPTION AND OUTCOME OF UPFRONT RADIOTHERAPY FOR HEAD AND NECK CANCER: EXPERIENCE AT NIGUARDA CANCER CENTER ON 171 CONSECUTIVE PATIENTS

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[1]SC Radioterapia, Niguarda Cancer Center, ASST Ospedale Niguarda, Milano; [2]Department of Oncology and Hemato-oncology, University of Milan; [3]SC Otorinolaringoiatria, Niguarda Cancer Center, ASST Ospedale Niguarda, Milano; [4]SC Oncologia Falck, Niguarda Cancer Center, ASST Ospedale Niguarda, Milano; [5]SC Medicina Nucleare, Niguarda Cancer Center, ASST Ospedale Niguarda, Milano; [6]SC Anatomia Patologica, Niguarda Cancer Center, ASST Ospedale Niguarda, Milano, Italy

Aims: To report our experience in the treatment of head and neck (H&N) cancer with upfront radiotherapy (RT), with or without chemotherapy (CT), focusing on the impact of age on prescription, compliance and clinical outcome.

Methods: We searched our prospective database including all patients (pts) treated at our Unit with RT for H&N cancer from 2009, with the following exclusion criteria: palliative or post-operative RT, diagnosis and follow-up at other centers, start of RT after 2015 (to ensure adequate length of follow-up). All time intervals were calculated starting from the first day of RT. One hundred seventy-one pts (N=171) were left for analysis, with the following characteristics: age- median 66 yrs, range 18-90; sex- male 81%; primary site- nasopharynx 17%, oropharynx 29%, hypopharynx 5%, larynx 37%, oral cavity 8%; stage- I, 29%, II, 11%, III, 17%, IV, 43%; chemotherapy- concomitant only 27%, induction and concomitant 29%, no CT 44%. To investigate the impact of age we separated the series into two age groups: "elderly" (>65 yrs) and "non-elderly" (<66 yrs). Elderly (E) pts were 53% (n=90) vs 47% (n=81) "non-elderly" (NE).

Results: Median follow-up of 113 pts alive at last contact is 55 months (range 25-110). Forty-seven pts died (30 due to the treated cancer, 15 due to a second tumor, 2 due to other causes), and 11 pts were lost to f-up at 4-70 months. Stage mix was more favorable in E pts, with 38% of pts in stage I (vs 20% in NE) and 36% in stage IV (vs 51% in NE). Total dose was similar in the two age groups: in NE median 70 Gy, range 66-70, in E median 69.3 Gy, range 64-76. Age had no impact on RT duration (median 50 days in both groups). As expected chemotherapy was prescribed more often in NE pts (76%) than in E pts (7%). Local-regional recurrence was detected in 27% of NE and in 23% of E pts. Severe late effects were uncommon, but tissue necrosis or need for tracheostomy/permanent feeding tube was recorded in 8 pts (3 NE vs 5 E).

Conclusions: In our series elderly pts were found to have lower stage disease compared to younger pts: this difference is explained by the higher number of stage I glottic cancer in this age group. Age had also a significant impact on CT prescription, but not on RT dose prescription and on compliance to treatment as measured by RT duration. Outcome of treatment, as measured by local-regional recurrence rate and by incidence of severe late effects, was also similar in the two age groups.

P068

ADVANCED LUNG CANCER IN ELDERLY PATIENTS: RESULTS OF A SHORT-COURSE ACCELERATED PALLIATIVE RADIOTHERAPY

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Aims: To assess the safety and efficacy of a SHort-course Accelerated RadiatiON therapy (SHARON) regimen in the palliative treatment of locally advanced or metastatic lung cancer in elderly patients.

Methods: Eligibility criteria for the analysis were: 1) histological confirmed lung cancers, 2) age ≥ 80 years, 3) expected survival > 3 months and 4) Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 3. A total dose of 20 Gy was delivered in 2 consecutive days with a twice daily fractionation (5 Gy per fraction) and at least 8 hour interval. Primary endpoint was the symptom response rate.

Results: Forty patients (male/female: 29/11; median age: 84.0 years; range: 80-96) were included in the analysis. ECOG performance status was < 3 in 36 patients (90%). Patients with different cancer histology were included in the analysis, in particular: adenocarcinomas (N°=22; 55%), squamous cells (N°=15; 37.5%), small cell lung cancer (N°=3; 7%). With a median follow-up time of 1.2 months (range, 1 to 20 months), no G3 acute toxicities were observed, 2 (5%) G2 acute lung toxicity, 2 (5%) G1-G2 acute skin toxicities and 2 (5%) G1 esophagus toxicities were recorded. Among overall 26 symptomatic patients, 25 showed an improvement or resolution of baseline symptoms (overall palliative response rate: 96%). With a median survival time of 10.8 months, the median symptom free survival was 8.5 months. No differences in terms of quality of life was recorded after the treatment. Two of 40 (5%)

patients required a retreatment that was performed in median after 5 months (range: 3-7 months) from the previous one.

Conclusions: Short-course accelerated radiotherapy in palliative setting of lung cancers is effective in terms of symptom relief and well tolerated even in elderly patients.

P069

COMBINATION OF RADIOTHERAPY AND CETUXIMAB FOR LOCALLY ADVANCED HEAD AND NECK CARCINOMA IN ELDERLY PATIENTS: A RETROSPECTIVE MULTICENTRE STUDY

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Objectives: Cetuximab-associated radiotherapy (CTX-RT) is an alternative treatment to platinum-based chemoradiotherapy in locally advanced head and neck carcinoma and the use of cetuximab is an interesting opportunity in unsuitable patients and / or with poor tolerance for standard chemotherapy as elderly patients.

Methods: We retrospectively analyzed 45 patients aged ≥ 65 years treated with CTX-RT for advanced head and neck carcinoma in Brescia and Florence in the last 10 years.

Results: Between February 2007 and February 2018, 45 patients were treated with CTX-RT. Treatment consisted of 66-70 Gy radiotherapy in conventional fractions or 69.3 Gy with a little hypofractionation (2.1 Gy) and a weekly cetuximab. 82.2% of patients were treated with IMRT. The Charlson comorbidity index (CCI) was more than 5 in 80%. Despite CCI, 82.2% of patients were ECOG 0-1. Median overall survival (OS) was 50 months and median disease-free survival (DFS) was 10 months. Grade 3-4 oral mucositis was observed in 44.4%, dysphagia in 42.2% and dermatitis in 33.3% of patients.

Conclusions: The objectives were treated population description, acute tolerance, progression-free survival (PFS), overall survival (OS). Forty-five patients were included. Treatment was completed without delay for 28 patients (62.2%). 3 patients died after treatment for toxicity. In our experience, acute G3-4 toxicities such as mucositis, dysphagia and dermatitis were common. We confirm that CTX-RT tolerance in elderly patients is relatively poor and patient fragility suggests that a balanced use of CTX-RT in this population is required.

P070

ADVANCED SKIN CANCER IN ELDERLY PATIENTS: RESULTS OF A SHORT-COURSE ACCELERATED PALLIATIVE RADIOTHERAPY SCHEDULE

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Aims: To assess the efficacy and safety of a SHort-course Accelerated RadiatiON therapy (SHARON) regimen in the palliative treatment of non-melanoma skin cancers in elderly patients.

Methods: Patients with histological confirmed non-melanoma skin cancers, age ≥ 80 years, expected survival > 3 months and Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 3 were considered eligible for this analysis. The primary endpoint was to evaluate the symptom response rate. Radiotherapy regimen was based on the delivery of 4 radiotherapy fractions (5 Gy per fraction) with a twice daily fractionation in two consecutive days. Three different level of dose were administered according to organ at risk constraints: 20 Gy (1 cycle), 40 Gy (2 cycles) and 60 Gy (3 cycles).

Results: Twenty-seven patients (male/female: 13/14; median age: 87.0 years; range: 80-98) were included in this analysis. ECOG performance status was < 3 in 18 patients (66.6%). Histology were squamous cell carcinoma (N°=21; 77.8%), basal cell carcinoma (N°=3; 11.1%), baso-squamous carcinoma (N°=2; 7.4%) and Bowen's Disease (N°=1; 3.7%). Among 14 patients who completed the 1 cycle, only one (7%) experimented acute G3 skin toxicity; two (14%) G2 skin toxicities were observed. Nine patients reported an improvement or resolution of baseline symptoms (overall palliative response rate: 64%). When more cycles were administered, mean time between cycles was 28 days. Six patients underwent to 2 RT cycles: of these, no G3 toxicities were recorded; four patients (66%) showed G2 mucosal toxicity and G2 skin toxicity. In this subset of patients the overall response rate was 100%. Six patients received 3 RT cycles: none of them experienced G3, but all of them showed G2 skin toxicity. Even in this case, overall response rate was 100%. With a median survival time of 17.4 months, the median symptom free survival was 12 months.

Conclusions: Short-course accelerated radiotherapy in palliative setting of non-melanoma skin cancers is effective in terms of symptom relief and well tolerated

even in elderly patients. High doses seem to be more effective in terms of response rate against a reasonable toxicity profile.

P071

INFLUENCE OF AGE AND SUBTYPE IN OUTCOME OF OPERABLE LIPOSARCOMA

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Aims: Liposarcomas (LPS) are rare tumors deriving from adypocytes. They can be classified in well-differentiated (WDLPS), de-differentiated (DDLPS), myxoid (MLPS) and pleomorphic liposarcomas (PLPS). In the current paper, we collected and reviewed data from a single institution cohort of patients in order to evaluate whether clinical characteristics, tumor- and treatment-related features affect clinical outcome in patients with non-metastatic LPS treated with curative intent.

Methods: Data of 186 patients with locally advanced, non-metastatic LPS treated between 1990-2015 and with at least 5 years follow up were retrospectively reviewed. Two patients subgroups were identified by setting a cutoff age of 65. Our major endpoints were Local Recurrence Free Survival (DFS-LR), Distant Metastasis Free Survival (DMFS) and Overall Survival (OS).

Results: At diagnosis 27.4% of patients were 65 years or older. At a median follow-up of 8.6 years, Kaplan-Meier (KM) survival analysis showed that LR, DM and OS were 75.5%, 76.6% and 48.1%, respectively. KM analysis showed that Age > 65, DDLPS and lower limb localization were related to LR (p=0,001, p=0,0001 and p=0,0001, respectively). Association between LR, Age and DDLPS persisted both at univariate (p=0,003 and p=0,0001, respectively) and multivariate Cox regression (CR) analysis (p=0,024 and p=0,002). Age, tumor depth and grading influenced distant recurrence, both at KM (p=0,023, p = 0.026 and p = 0.016) and univariate CR (p=0,026, p=0,042 and p=0,012). Age and grading were confirmed at multivariate analysis (p=0,009 and p 0,017). Patients with WDLPS and wide excision had significantly better OS (p=0,001 and p=0,03, respectively), while histologic G3 and age > 65 were related with worse OS (p=0,008 and p=0,0001, respectively). Age, DDLPS and Grade were related to OS at univariate (p=0,0001, p=0,0001 and p=0,03, respectively) and multivariate CR analysis (p=0,031, p=0,0001 and p=0,001, respectively). Analyzing the specific causes of death, elderly patients died more often due to other causes compared to younger population (p=0.006).

Conclusions: A tailored approach could be helpful in delineating therapeutic management of liposarcoma. Histotype-driven schedules of treatment should be developed to take into account biological heterogeneity of this disease. Further studies are needed to develop tailored treatment strategies in elderly STS, taking into account the frailty and peculiarity of this subgroup.

P072

FEASIBILITY OF ADJUVANT CHEMO-TMZ IN ELDERLY PATIENTS WITH GLIOBLASTOMA

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Aims: The present study was designed to evaluate the role of adjuvant therapy in a subset of elderly patients with glioblastoma.

Methods: We performed a retrospective analysis on 223 patients with glioblastoma undergone surgery and adjuvant chemo-radiotherapy (C-RT) between January 2010 and December 2017. We chose as cut-off an age>77 years and we analyzed progression free survival (PFS) and overall survival (OS) according to the age and the known prognosticators (surgery, KPS, MGMT status), with Kaplan Meier method (univariate) and Cox Regression Analysis (multivariate).

Results: A total of 223 patients were included in the analysis (mean age 61 years, median 64 years, range 35-84 years, 91 males and 49 females). Twenty-eight patients were older than 77 years (mean age 80 years, median 79 years, range 78-86 years, 18 males and 10 females). At univariate analysis the subset of older patients showed a worse OS (p:0,016, median 8 months for patients >77 years versus 13 months for the subset of younger patients) and a similar PFS (p:0,843). At multivariate analysis of OS, although, the only significant parameters were MGMT (p:0,001), KPS (p<0,001) and the radicality of surgery (p:0,015).

Conclusions: Our results suggest that older patients (>77 years) could theorically benefit from adjuvant therapy with both radiotherapy and temozolomide, as the lower survival in this subgroup seems to be correlated with the only known prognosticators (MGMT, KPS, surgery).

P073

VAGINAL-CUFF-BRACHYTHERAPY (VBT) ALONE HIGH-DOSE-RATE [HDR] 192IR-SOURCE POST-HYSTERECTOMY FOR ENDOMETRIAL CANCER IN ELDERLY PATIENTS

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Aims: To examine the tolerability, acute and late genitourinary (GU) toxicity of vaginal-cuff-brachytherapy (VBT) alone high-dose-rate [HDR] 192Ir-source post-

hysterectomy for endometrial cancer in elderly patients (pts).

Table 1.

No toxicity patients (n=17)	
Total dose (Gy)	
Mean	35.78
Range (min-max)	25.5 - 41
Dose per fraction	
Mean	6.46
Range (min-max)	5.5 - 7
D0.1 cc urethra (Gy)	
Mean	7.07
Range (min-max)	1.48 - 11.79
D2 cc bladder (Gy)	
Mean	4.34
Range (min-max)	1.1 - 6.7
Toxicity patients (n=4)	
Total dose (Gy)	
Mean	36
Range (min-max)	35 - 39
Dose per fraction	
Mean	6.86
Range (min-max)	6.5 - 7
D0.1 cc urethra (Gy)	
Mean	7.92
Range (min-max)	5.6 - 10.14
D2 cc bladder (Gy)	
Mean	4.55
Range (min-max)	2.05 - 6.3
Mann-Whitney test	
Urethra	p = 0.0459
Bladder	p = 0.5312

Methods: From July 2012 till April 2018, 21 consecutive pts mean age 73 years (range 66-86) with FIGO Stages IA(7pts) Ib(12pts) II(2pts) endometrioid endometrial adenocarcinoma were treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy plus lymph node sampling (2 pts) or bilateral pelvic lymphadenectomy (8 pts) or without lymph nodes pathological staging (11 pts), with laparotomy (6 pts) or laparoscopy (15pts) surgical approach followed by postoperative VBT HDR alone in 110 consecutive fractions. Pre-existing genitourinary disorders have been found in 4 pts (19%) (age range 70-86 years) as urinary urgency G1 and in 2 pts as urinary tract pain G1. At each fraction, all patients had a urinary catheter for bladder filling with physiological solution, rectal emptying and vaginal applicators (2,5 cm diameters) before undergoing planning CT. HDR Brachytherapy (MicroSelectron afterloading 192-Ir source) was completed using image-based planning with contouring of organs at risk (bladder, rectum, urethra) and optimization at each fraction; the dose was prescribed at 5 mm from the applicator surface. The dosimetric parameters for all pts (no toxicities/G1) were reported in Table 1. Toxicity scores were evaluated using the CTCAE 4.02 version at the end of VBT and at median f-up of 34 months (1-69).

Results: All patients completed the treatment with optimal tolerability and compliance. The GU toxicity at the end of VBT treatment was found in 4 pts as urinary urgency G1 without changes before and after treatment and in 7 pts as urinary tract pain G1. At median f-up of 34 months only urinary urgency G1 in the same 4 pts was found.

Conclusions: Although in a limited setting of patients, our data show that VBT-HDR as an exclusive post-operative treatment was a safe, well tolerated, non-detrimental treatment in terms of urinary toxicity in elderly patients, particularly in older than 70 years with pre-existing urinary disorders. Analysis of a larger patient series may confirm these preliminary results and help to find out further potentially predictive dosimetric parameters (cfr.Table 1).

P074

ACCELERATED HYPOFRACTIONATED RADIOTHERAPY TREATMENT IN ELDERLY PATIENTS WITH EARLY STAGE NON-MELANOMA SKIN CANCER: SAFETY AND EFFICACY RESULTS

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Aims: To assess the safety and efficacy of an accelerated radiotherapy schedule (Short Skin) in elderly patients with early stage non-melanoma skin cancer (NMSC).

Methods: Eligibility criteria for the analysis were: 1) Patients with NMSC ≤ 3 cm, without infiltration of deep structures; 2) aged ≥80 years; 3) Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 3. Exclusion criteria were as follows: T3–T4 disease stage, prior RT on the same anatomical site, and poor compliance. Radiotherapy was delivered using electrons (6-9-12 MeV) or megavoltage photons (6MV) depending on tumor site and characteristics. The field size choice depended on the lesion size and location. For basal cell tumors of stage T1, the field size included a 1.5-cm normal tissue margin, while for stage T2 and/or squamous cell carcinomas, a 2.5–3-cm margin was included. A total dose of 30 Gy was delivered in 5 Gy fractions throughout six consecutive days. Primary endpoint was the symptom response rate.

Results: Forty patients (male/female: 24/16; median age: 87.0 years; range: 80-98) were included in the analysis. ECOG performance status was < 3 in 37 patients (92,5%). The histology of skin cancer was squamous cell in 19 (47,5%) and basal cell in 19 (47,5%) patients, while 2 patients had mixed histology (5%). With a median follow-up time of 10 months (range, 2-66 months), no G3 acute skin toxicity was recorded, while G2 skin toxicity was recorded in 20 patients (50%) and G2 mucositis was recorded in one

patient (2,5%). The complete response of lesion was obtained in 18 (45%) patients , with a partial response in 9 (22,5%) patients. In 7 (17,5%) patients the response was not evaluable and in 6 (15%) patients was registered a stable disease. The 1-year actuarial local control was 82,5% with median local control not reached.

Conclusions: Short-course RT in elderly patients affected by early stage NMSC is able to produce more than 80% disease local control with excellent tolerability.

P075

A SINGLE INSTITUTION EXPERIENCE OF SBRT IN ELDERLY PATIENTS AFFECTED BY NSCLC

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Aims: Stereotactic body radiotherapy (SBRT) is the standard of care for medically inoperable early-stage non–small-cell lung cancer (NSCLC). Due to the aging of the oncological population, SBRT in patients with more than 65 years has become more and more explored. Aim of this retrospective study is to verify the outcome of SBRT in this population.

Methods: Clinical data of patients treated at our center between the 2004 and 2018 with radical lung SBRT were collected and retrospectively analyzed. All the patients were treated with VMAT technique. Acute and late pulmonary and esophageal toxicity were reported. Toxicities was classified in accordance to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Results: Demographic data are reported in Table 1. 76 patients with primary lung lesions and more than 65 years underwent radical SBRT treatment. Median follow up was 17.7 (range 3-65 months) The median age was 76 years (range 65-86 years old): 13 patients between 65-70 years, 15 patients between 71-75 years, 29 patients between 76-80 years and 19 over 80 years. 70/76 lesions were considered peripheral while 4 were central; 58/76 (76.3%) were stage I and 18 (23.7%) stage II. Citologic or histological confirm was available 61/76 cases: 28 were adenocarcinomas (46%), 22 squamous cell carcinomas (36%), 11 not otherwise specified NSCLC (18%). All patients underwent functional respiratory tests (classified with the Gold Scale) (Table 1). Median BED was 107 Gy (range 26.4-180 Gy). 4/76 patients experienced any form of toxicity: a G1 emotthisis and a G1 pyrosis, 2 cases of G1 thoracic pain and in one of them a G3 pneumonia were observed. First radiological evaluation was made at three months with a contrast enanched CT scan: stable disease was seen in 18 (29%) partial response in 29 (46%), complete rsponse in 12 (19%) and 4 (6%) a progression. At the time of the present analysis, 38 patients were still alive and 38 were dead. Median PFS was 10.0 months, median OS was 20.9 months.

Conclusions: In our experience, we assessed a satisfactory local control and low toxicity in this kind of setting. SBRT is confirmed as a reasonable option in elderly patients with early stage inoperable NSCLC.

Table 1.

	CLINICOLPHATOLOGIC CHARACTERISTIC (N = 76)
MEDIAN AGE	76.33 (years)
AGE CLASSES	
65-70	13 (17.1%)
71-75	15 (19%)
76-80	29 (38.6%)
>80	19 (25%)
SEX	
Men	60 (78.95%)
Women	16 (21%)
WHO PS	
0	12 (15.79%)
1	13 (17%)
2	45 (59.2%)
HISTOLOGY	
Squamous	22 (28.9%)
Non-Squamous	28 (36.8%)
NSCLL	11 (14.5%)
ND	15 (19%)
STAGE	
I	58 (76.3%)
II	18 (23.7%)
GOLD STAGE	
0	17 (22.4%)
1	13 (17.1%)
2	16 (21%)
3	24 (31.6%)
4	6 (7.9%)
cT	
1	43 (56.6%)
2	33 (43.4%)
cN	
1	74 (97.4%)
0	2 (2.6%)

P076

FEASIBILITY STUDY OF CHEMORADIOTHERAPY IN STAGE III NSCLC IN ELDERLY PATIENTS: RESULTS OF AN EXPERIENCE OF TWO ITALIAN ACADEMIC CENTRES

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Aims: To assess feasibility and safety of chemoradiotherapy (CRT) in elderly patients with locally advanced non small cell lung cancer (LA NSCLC). Concomitant (cCRT) and sequential (sCRT) are considered in stage III patients not suitable for surgery.

Methods: Retrospective data were collected from 2009 to 2017 in two Academic Italian Hospitals. All elderly (>65 years old) patients were treated with cCRT or sCRT. Demographic characteristics are shown in table 1. All of them received a platinum based doublet chemotherapy for a medium of 4 cycles (range 2-6). RT was delivered to tumor and lymphnode lesions avoiding elective nodal irradiation. Conventional fractionation or

moderate hypofractionation were used. The mean total dose was 61.9 Gy (range 44-70 Gy). GTV was delineated on CT scan, confirmed on PET/CT performed before or during planning procedure. 4DCT or active breathing control of motion were used in all patients. PTV was defined as ITV plus 1 cm. Acute and late toxicities were scored using the Common Terminology Criteria for Adverse Events 5.0.

Table 1.

Patients' Characteristics		
Age	Median	75
	Range	68-84
Gender	Male	54 (72%)
	Female	21 (28%)
Performance Status (ECOG)	0	32 (42,7%)
	1	42 (56%)
	2	1 (1,3%)
Histology	Adenocarcinoma	34 (45%)
	Squamous Cell Carcinoma	40 (54%)
	Large Cell Carcinoma	1 (1%)
Stage	IIIA	45 (60%)
	IIIB	30 (40%)
Chemotherapy	Concomitant	12 (16%)
	Sequential	63 (84%)
	Cycles: Median	4
	Cycles: Range	2-6
Radiotherapy	Mean Dose	61,9 Gy
	Moderate Hypofractionation	29 (38,7%)
	Conventional fractionation	46 (61,3%)

Results: We retrospectively analyzed 75 patients, of which 12 (16%) underwent cCRT and 63 (84%) received sCRT. 93% was evaluable for clinical response after a median follow-up of 10 months (range 2-50). Partial response (PR) was observed in 50% of the series, stable disease (SD) in 27,2%, progressive disease (PD) in 22,8% at first evaluation. Overall, PD occurred in 17 patients at primary tumor volume of RT and in 13 on nodal volume. Both nodal and tumor relapse appeared in 5 patients. 22 patients developed metastatic disease. One and 3-years PFS was 45.1% and 9.7% respectively; one and 3-years OS was 62.3% and 24.5% respectively. Univariate analysis proved tumor dimension as only negative prognostic factor for OS ($p<0.002$). Acute toxicity occurred in 45 patients: 21 developed esophagitis, 3 skin acute toxicity, 5 pneumonitis, 12 cough, 5 fatigue. Grade 1-2 acute toxicity was observed in 57.1% of sCRT and in 100% of cCRT. Acute Grade 1 esophagitis was main adverse event (60% of cases). No instances of Grade 3 or higher acute toxicity were reported.

Conclusions: Our experience seems to confirm the feasibility of CRT in elderly patients with LA NSCLC. Adequate selection of patients fit for CRT is compulsory in elderly patients. New integrated modality treatments (i.e. immunotherapy) are promising in therms of better PFS and OS.

P077

PROTONTHERAPY IN ELDERLY PATIENTS WITH BRAIN AND SKULL BASE TUMORS: EARLY OUTCOME, SAFETY AND HEALTH-RELATED QUALITY OF LIFE

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Aims: To report preliminary results of active beam scanning proton therapy (PT) for intracranical and skull base tumors in elderly patients, focusing also in the health-related quality of life analysis scored by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)––C30 and EORTC Quality of Life Questionnaire Brain Cancer Module (QLQ-BN20)

Methods: Thirty-nine elderly patients (age: ≥ 70 years) were treated with PT between January 2015 and May 2018. Median age was 77 years while KPS ranged between 60 and 100; 24 were female and 15 were male. Twenty-six patients were treated for a meningioma; three pts for a high grade glioma (HHG); three pts for a vestibular schwannoma (VS); two pts for a chordoma; one pts for a low grade glioma; one pts for a well-differentiated neuroendocrine carcinoma; one pts for a paragaglioma; one for cerebellar hemangioblastoma and one pts for an anaplastic hemangioperycitoma. All treatments but two were delivered at 1.8-2 GyRBE per fraction with a median total dose of 55 GyRBE (range 50-72 GyRBE). One meningioma and one VS were treated with radiosurgery with a single dose of 14 and 12 GyRBE, respectively. All pts were treated with active beam scanning PT using 3-4 fields with single field optimization technique. Toxicity was assessed according to CTCAE version 4.0. The patients completed the EORTC questionnaires before starting PT, the day of the end of PT and every follow-up consult until progression of disease.

Results: All pts completed the treatment without breaks. One pts discontinued the treatment because of tumor progression. There were no grade 3 or higher acute and late toxicities. Acute side effects include grade 1 (25%) and grade 2 (18%) skin erythema, grade 1 (2%) and grade 2 (30%) alopecia, grade 1 (54%) and grade 2 (13%) fatigue, grade 1 (5%) pain, grade 1 (30%) headache, grade 1 (2%) and grade 2 (2%) skin hyperpigmentation. Late side effects include grade 2 (23%) alopecia, grade 1 (25%) and grad2 2 (5%) fatigue, grade 1 (7%) headache, grade 1 memory loss (5%) and grade 1 (2%) skin hyperpigmentation. At the median FU of 10 months local control was 100% for all the lesions except for one HHG who progressed after a median time of 6 months. Regarding QoL analysis, the treatment was associated with stability or improvement in all of the preselected domains.

Conclusions: PT is feasible and safe treatment for elderly pts with intracranical and skull base tumors without a negative effect on QoL.

P078

CLINICAL PROTOCOL ON THE MANAGEMENT OF PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIEDS) UNDERGOING RADIOTHERAPY IN AZIENDA SANITARIA UNIVERSITARIA INTEGRATA DI TRIESTE (ASUITS)

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Aims: Italy is among the top countries for life expectancy. Although, there are numerous factors that can influence human lifespan, one indisputable reason to this can be a tremendous improvement in the survival rates of cardiovascular patients and correspondingly increasing use of CIEDs. On the other hand, it is no surprise that number of CIED patients encountered in radiation therapy is increasing. Therefore, the aim of this study is to discuss outcome of implementing our clinical protocol on the management of CIED patients receiving radiotherapy (RT).

Methods: The following main steps are followed in the protocol: 1) Identify CIED patients and inform cardiologist/electrophysiologist; 2) Classify patient according to the risk of malfunction and risk of adverse clinical events; 3) Evaluate RT plan and estimate CIED dose based on treatment planning and perform in-vivo dosimetry during first fractions whenever is required; 4) Inform patient about the risk associated with RT based on risk classification and obtain written consent from the patient; 5) Actions to be implemented based on the risk class (high, medium, or low); 6) Update patient database.

Table 1. The patient characteristics, and risk categories based on cumulative dose and pacing dependency.

Class of risk		LR	IR	HR
# patients	45	32	12	1
Fale	29	20	9	0
female	16	12	3	1
PM	38	28	9	1
ICD	7	4	3	0
Pacing-dependency	9	0	8	1
<2 Gy	42	32	10	0
2-10 Gy	3	0	2	1
>10 Gy	0	0	0	0

Results: Forty-five CIED patients (7 Implantable cardioverter defibrillators [ICDs] and 38 pacemakers [PMs]) were treated with RT in ASUITS between 2015 and 2017. The patient characteristics as well as risk categories based on cumulative dose and pacing dependency were summarized in table 1. As it can be seen from the table, the majority of patients 71.1% were categorized being at low risk, 22.2% were considered at moderate risk, and only one patient was classified as high risk. It should be noted that there was no patient receiving a CIED dose of 10 Gy or above.

Conclusions: According to our results, it can be concluded that our protocol, which is based on a multidisciplinary approach between radiation oncologist, cardiologist/electrophysiologist and medical physicist, ensures safe and effective management of patients with CIEDs. This is owing to the fact that no malfunction or failure due to RT has been reported in our department during these three years.

P079

TOXICITY AND TOLERANCE OF INTENSITY MODULATED RADIATION THERAPY IN ELDERLY SQUAMOUS HEAD AND NECK CANCER PATIENTS

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Aims: Use of intensity modulated radiation therapy (IMRT) in head and neck cancer patients aged >65 years old is increasing. The aim of this study is to evaluate the tolerance and side effects of IMRT in elderly patients treated with Tomotherapy with or without concomitant platinum-based chemotherapy.

Methods: 30 patients aged ≥65 years with locally advanced squamous head and neck cancer underwent IMRT with Tomotherapy in our institution from 2013 to 2017. 50% of patients received concomitant platinum based-chemotherapy. Median Performance Status (PS) was 2 according to ECOG scale. Patients had different comorbities: 33% hypertension, 13% diabetes, 10% ischemic cardiopathy, 10% chronic ostructive pulmonary disease, 10% hepatitis HCV-correlated, 6% other tumors.

Results: The median follow-up was 26 months (range 1-58 months). Median age of patients at the time of treatment was 75 years (range 65-89 years). RT interruptions greater than 3 days were needed in 37% of patients. Only 2 patients, treated with concomitant platinum-based chemotherapy, developed G3 toxicity according to CTCAE 4.0, both consisted in worsening anemia required unplanned hospitalization and blood transfusion. All patients completed treatment. Only three patients needed a new CT simulation because of changes in treatment volumes. 90% of patients were still alive at 1 year follow-up and achieved local control, without any >G2 side effects. 11 patients died during follow-up, 8 of these for disease progression with a median time to local-regional recurrence of 16 months.

Conclusions: Elderly patients with squamous locally advanced head and neck cancer appear to tolerate IMRT with Tomotherapy with acceptable toxicity and

good outcomes, also with concomitant chemotherapy, so they should not be denied curative treatment based solely on age. Further studies needed to optimize the best supportive therapies for this kind of population.

P080

RADIOCHEMOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER: AN AGED-BASED ANALYSIS

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Aims: The purpose of this analysis is to evaluate the feasibility and efficacy of concurrent radiochemotherapy (RCT) with or without induction chemotherapy for elderly patients with locally advanced pancreatic cancer (LAPC).

Methods: A total of 52 patients enrolled in mono-institutional prospective studies were included. All patients were treated with gemcitabine-based RCT. Of these, 31 patients were treated with induction chemotherapy (GemOx or FOLFIRINOX). The radiation therapy total dose was 54-59.4 Gy with conventional fractionation. We stratified population into two groups: the first included patients aged <70 years, the second one those aged ≥70 years. Overall survival (OS), progression-free survival (PFS), local control (LC) and toxicity rates were recorded.

Results: Thirty-seven patients aged <70 years (mean age 61 years) and 15 patients aged ≥70 years (mean age 74 years) were evaluated. Nineteen patients (51%) of the first group underwent radical surgery compared with five patients (33.3%) of the second group. Only 11 patients (57.9%) aged <70 years were treated with adjuvant chemotherapy. Median OS and 1-yr OS were 21.5 months and 83% in patients <70 years and 11.5 months and 40% in those ≥70 years ($p<0.01$). Median PFS was significantly higher in the younger group (19.4 months vs 9.9 months; $p<0.05$). LC was high in both groups (1-yr LC 87% vs 88%). For the entire cohort, the treatment protocol was well tolerated with no significant difference in grade 3 or 4 acute toxicities between the groups.

Conclusions: These data suggest that RCT has a role in the management of elderly patients with LAPC. Nevertheless, strategies to optimize local control and patients' selection for the combined approach may play an increasing role in improving outcomes.

P081

ADJUVANT RADIOTHERAPY IN HIGH RISK OPERATED SQUAMOUS CELL SKIN CANCER (SCC-C) OF THE HEAD AND NECK IN ELDERLY PATIENTS: SINGLE CENTER EXPERIENCE

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Aims: The aim of our work is to report a single institution experience on the impact of adjuvant radiotherapy in elderly patients with by high-risk operated head and neck squamous cell skin cancer (SCC-C).

Methods: This retrospective study analyzed the experience of our Centre (AOU Careggi Radiation Oncology Unit, Florence) between January 2000 and March 2018. Inclusion criteria were: patients with locally advanced or relapsed head and neck SCC-C undergoing radical surgery to the primary tumor and nodal basin for whom adjuvant radiotherapy was prescribed. By definition, were high-risk pathologic features: close/positive surgical margins, =>2 positive lymphnodes and extranodal extension (ENE). The burden of comorbidity was assessed according to Charlson Comorbidity Index (CCI). Until 2010, radiotherapy was delivered with a 3D conformal technique which was then replaced by IMRT radiotherapy.

Results: A cohort of 26 patients was identified. At time of adjuvant RT, the median age was 75.5 years (IQR: 67.5-82.5). A significant number of comorbidities was present, CCI was > 4 in 24 patients (92.3%). The primary disease site was the scalp in 17 cases (65.4%), followed by the lip in 7 cases (26.9%). Major surgery, consisting of primary tumor excision, neck dissection and parotidectomy, was performed in 14 patients (53.9%). The predominant high-risk feature was positive margins (6 cases, 23.1%), followed by the contemporary confirmation of margin involved, >2 nodes positives and extracapsular extension in 23.1% (6 cases). The majority of patients were treated with IMRT (14 cases, 53.9%). In terms of treatment volume, comprehensive unilateral neck irradiation + parotid lodge were treated in all patients. At a median follow-up of 14.5 months (range 1-195), 7 were alive. Notably, non-cancer related death was reported in 11 cases. In Regarding SCC-C outcome, 13 patients had a progression of disease. The median DFS was 8 months (range 0-77), the most common pattern of failure was loco-regional failure in 11/13 cases. Overall, the median OS was 21 months (range 1-197).

Conclusions: Prognosis is severe in case of high-risk features and loco-regional spread in SCC-C: adjuvant RT has a consolidated role, however long-term disease control is challenged by non-cancer related death in elderly population with multiple comorbidities. Prospective trials are warranted to define the benefit of adjuvant irradiation on survival in this subgroup of patients.

Table 1.

CHARACTERISTICS	No. PATIENTS (%) (n=26)
SEX	
M	19 (73,1%)
F	7 (26,9%)
MEDIAN AGE AT DIAGNOSIS (yrs-IQR)	75,5 (67,5-82,5)
CHARLSON COMORBIDITY INDEX (CCI-age unadjusted)	
<4	
>4	2 (7,7%)
	24 (92,3%)
LOCATION	
Skin	
Lip	17 (65,4%)
Ear	7 (26,9%)
	2 (7,7%)
HISTOPATHOLOGICAL RISK FACTORS	
Margin involved	6 (23,1%)
>2 N positives	1 (3,8%)
Extracapsular Extension	2 (7,7%)
Margin involved + >2 N positives	0 (0%)
Margin involved + Extracapsular Extension	2 (7,7%)
>2 N positives + Extracapsular Extension	2 (7,7%)
Margin involved + >2 N positives + Extracapsular Extension	6 (23,1%)
None	2 (7,7%)
Disease relapse	5 (19,2%)
SURGICAL PROCEDURE	5 (19,2%)
T Asportation	7 (26,9%)
T Asportation+Neck Dissection	14 (53,9%)
T Asportation+Neck Dissection+Parotidectomy	
TYPE OF RT	
3DCRT	12 (46.1%)
IMRT	14 (53,9%)
DTF (Median -IQR)	60 (54,5-66)
N. INTERRUPTION DAYS (Median-range)	0,5 (0-40)
ALIVE	
YES	7 (26,9%)
NOT	19 (73,1%)
END RT-LAST CLINICAL NEWS (Months-range)	14,5 (6-49,75)
GLOBAL SURVIVAL	
DEAD FOR H&N SCC	
DEAD FOR TOXICITY	8 (30,8%)
DEAD FOR OTHER CAUSE	1 (3,8%)
ALIVE WITH DISEASE	10 (38,5%)
ALIVE WITHOUT DISEASE	3 (11,5%)
	4 (15,4%)
DFS	
YES	13 (50%)
NOT	13 (50%)
END RT-DFS (Months-range)	8 (0-77)
DFS TYPE	
T RELAPSE	5 (38,5%)
N RELAPSE	2 (15,4%)
T+N RELAPSE	4 (30,8%)
MTS	2 (15,4%)
OVERALL SURVIVAL (Months-range)	21 (1-197)

P082

PREOPERATIVE SHORT COURSE RADIOTHERAPY (SCRT) IN ELDERLY PTS (≥70 YEARS) AFFECTED BY LOCALLY ADVANCED RECTAL CANCER (LARC)

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Aims: In patients (pts) with LARC, SCRT is an alternative cure to long course chemoradiotherapy (RTCT). Despite the overlap of results in terms of local control of the two schedules, there is a doubt to use SCRT regimen mainly due to the risk of toxicity and the uncertainty of pts selection. In this retrospective analysis we evaluated the safety of SCRT in elderly pts (≥70 years).

Methods: From June 2012 to January 2018, 47 pts (median age 79.8 years, range 70-86) affected by LARC were submitted to preoperative SCRT. All pts were staged by pelvic MR, total-body CT scan, UES, colonscopy and biopsy. 25Gy in five fractions were administered with DHX linac Varian System with 3DCRT or VMAT technique (20 and 27 pts, respectively), using 6 or 15 MV photons. CTV included GTV, mesorectal area and locoregional drainage nodes (obturatory, internal iliac and presacral). In 26 out 47 pts (55.3%) we utilized a belly-board system to reduce intestinal toxicity. To evaluate the performance status of these elderly pts we analyzed their cardiovascular comorbidity (diabetes, tia and stroke) and we retrospectively performed ADL (Activities of Dailiy Living) and IADL (Instrumental Activities of Dailiy Living) tests.

Results: 30 pts (63.8%) had at least one cardovascular comorbidity; only 3 of them (64%) resulted with a low score of initial ADL and IADL test. All pts completed the planned RT and underwent to surgery after a median time of 15 days (range 7-30). Sphyncter preservation was obtained in 36 pts (76.6%). The mean volume of small bowel that received 25Gy, 20Gy, 15Gy and 10Gy was 7cc, 74.3cc, 154.2cc and 400cc, respectively; the mean volume of PTV was 1068cc (range 470-1400). Postoperative gastrointestinal toxicities occurred in 18 pts (38.3%) and the only parameter associated with them was the initial cardiovascular comorbidities (p=0.028). After a median follow-up of 13.6 months (range 2.8-43.9), 9 pts (19%) developed distant metastases (6 are still alive) and 34 pts are alive without evidence of disease. No local recurrences were observed. The probability of survival at 2 years was 77%.

Conclusions: In elderly pts affected by LARC preoperative SCRT could be a safe regime of preoperative treatment. Based on our analysis, the only parameter related to late toxicities is the initial cardiovascular comorbidities, including diabetes; neither the dose delivered to the intestine, nor the use of belly-board system seem to influence postoperative gastrointestinal toxicities.

P083

SEQUENTIAL CHEMO-RADIOTHERAPY IN UNRESECTABLE STAGE III NON SMALL CELL LUNG CANCER IN THE ELDERLY

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Aims: Platinum based concurrent chemo-radiotherapy (CCRT) is superior to sequential chemo-radiotherapy (SCRT) and is the standard of treatment for patients (pts) with unresectable Stage III non small cell lung cancer (NSCLC). SCRT is recommended in pts who are unfit to receive CCRT or if treatment volume is too large. Most of elderly pts are not suitable for standard curative treatment and under-represented in clinical trials, therefore it is difficult to reach evidence-based clinical recommendations for them. We retrospectively analyzed elderly pts with diagnosis of unresectable Stage III NSCLC treated in our centre with SCRT to evaluate overall survival (OS), progression-free survival (PFS) and main toxicities.

Patients and Methods: We reviewed 18 pts with unresectable Stage III NSCLC, age >65 years, PS ECOG 0–1, who received SCRT from January 2013 to December 2017. Treatment consisted of 3-6 cycles of platinum based chemotherapy (CT) and sequential RT with a total dose of 59.4–61.4 Gy (1.8–2.0 Gy/fx, 5/w). To evaluate OS and PFS we used Kaplan Meier method. Treatment toxicities were assessed according the CTCAE v4 criteria.

Results: Pts were staged as IIIA (50%) and IIIB (50%). After CT partial responses (PR), stable disease (SD) and progression disease (PD) were achieved in 83.3%, 11.1% and 5.5% of pts, respectively. 3 month after RT, 50% of pts had PR, 22.2% of pts had SD and 27.7% of pts had PD. Median follow up was 14.25 months (2.9-36.6 months) and 72.2% pts had PD. Locoregional PD was more frequent than distant metastasis, 53.8% vs 46.1%. Median OS was 36.9 months (95% confidence interval; 15.4–58.4 months). The 2 years survival rate was 61.3%. Median PFS was 13.9 months (95% confidence interval; 9.1–18.7 months), 2 year PFSs rate was 15.4%. No grade 3 acute and late toxicity were registered. Grade 1 late radiation pneumonitis was observed in 61% of pts.

Conclusions: In the elderly pts, SCRT is a well-tolerated regimen with a good toxicity profile. Our results of survival are different from those reported in literature, and it could be explained by two main factors: the sample of pts small and highly selected (by treatment actually received); additional CT courses (a total of 3-6 cycles) before RT and subsequent systemic treatment at the time of PD. Further studies are necessary to establish the role of SCRT in elderly pts, to direct them to standard curative treatment.

P084

THE VALUE OF COMBINATION CHEMORADIOTHERAPY TO IMPROVE OVERALL SURVIVAL IN ELDERLY GLIOBLASTOMA PATIENTS

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Aims: To evaluate survival outcomes of elderly patients (pts), with newly diagnosed glioblastoma (GBM) treated with short course radical/adjuvant Image-Guided Intensity Modulated Radiotherapy (IG-IMRT) alone or combined with concomitant and/or adiuvant Temozolomide.

Methods: From April 2013 to October 2017, 26 newly diagnosed GBM in elderly pts with a median age of 72 (69-79) years, were treated with IG-IMRT in our Institution, 11/26 (42%) of the pts were female, while 15/26 (58%) was male. A total dose (TD) of 40 Gy/15 fractions was prescribed for all pts. One lesion was diagnosed in 17/26 pts (65.4%), while in 9/26 (34.6%) was multifocal GBM. Surgery was performed in 11/26 (42.3%) and biopsy in 15/26 (57.7%). Concomitant and adjuvant chemotherapy (CT) was prescribed in 14/26 (54%). All pts had a Karnofsky Performance Status ≥70 before beginning treatment, and glucocorticoids were prescribed in 24/26 (92%) pts. Median GTV was 58.4 cc (21.7- 162.4), while median PTV was 499.2 cc (243-793.2). GTV definition was based on contrast-enhanced magnetic resonance imaging in all pts. The radiation treatment was delivered with helical IMRT in 13/26 pts and with volumetric IMRT in 13/26 pts. Image guidance (kVCT/MVCT) was performed daily in all pts.

Results: Median overall survival (OS) of all pts was 6.5 months. Median OS was 7.8 months (0.9-15,9) in pts treated with surgery and adjuvant IG-IMRT and 3.3 months (2.2-19.2) in pts treated with radical IG-IMRT. When concomitant and adjuvant chemotherapy was added, median OS was 13.6 months in pts treated with adjuvant RT versus 5.3 months in pts treated with radical RT. Pts with only one lesion had a better median survival versus pts with multifocal GBM: 9.4 versus 5.4 months. Mean progression free survival was 5.6 months in adjuvant treatments and 3.9 months in radical treatments. No patients showed over G2 acute toxicity.

Conclusions: OS in elderly GBM pts is improved by surgery and combination chemoradiotherapy. Concomitant chemotherapy did not worsened the toxicity during treatment.

P085

GAMMA KNIFE RADIOSURGERY FOR ELDERLY PATIENTS WITH BRAIN METASTASES: MONOINSITUTIONAL EXPERIENCE

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Aims: We investigated the outcomes of gamma knife radiosurgery (GKRS) for elderly patients (≥65 years) with brain metastases, and identified survival-associated factors.

Methods: Between 2012 and 2017, we retrospecti-

vely analyzed data from 90 patients aged 65 years and older treated with GKRS for 1–10 brain metastases.Median age at the time of GKRS was 72.2 years (range, 65–87 years). A mean dose of 22.1 Gy (range, 15–24 Gy)was delivered to the mean 58.4% isodose line. At baseline, we assessed G8, Graded Prognostic Assessment (GPA) and Basic Score for Brain Metastases (BSBM) score for every patients.

Results: The median survival was 14.18 months. Most frequent primary tumors were NSCLC (n=67).At baseline, G8 score was <14 in 67% of cases, GPA was between 1.5 and 2 in 45% of patients and BSBM. A high score index for BSBM (score ≥ 3 p = <0.0001) and a high graded prognostic assessment (GPA score ≥ 2.5,p = 0.0069) were associated with longer survival. A multivariate analysis the scoring system evaluating survival duration showed that a low GPA score was a strong independent factor for predicting short survival (hazard ratio 1.756, 95% confidence interval 1.252–2.456, P = 0.001). Moreover, on multivariate analysis, a controlled primary tumor (p<0.001, HR 0.328, 95% CI 0.180–0.596) was a significantly favorable prognostic factors.

Conclusions: GKRS is a safe approach to treat brain metastases in elderly patients. In this group, our study identified GPA score at the time of GKRS as a strong prognostic factor for survival.

P086

PALLIATIVE RADIATION THERAPY AND BONE METASTASES IN ELDERLY: IMPACT OF RADIOTHERAPY SCHEDULES ON PAIN CONTROL

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Aims: To investigate the different types of palliative radiotherapy schedule for bone metastasis in patients ≥ 70 years old respecting our clinical experience by using numerical rating scale (NRS) pre- and post-radiotherapy (RT).

Methods: From January to December 2017, 88 elderly patients of 337 that underwent to palliative radiotherapy were treated for bone metastases. Twenty-nine of 88 were excluded (3 died before first re-evaluation and 26 were lost at follow-up); so 59 patients were retrospectively analyzed for a total of 162 bone lesions. RT schedule was chosen at the discretion of a radiation oncologist expert in palliative treatment considering lesion site and patient's clinical condition. We registered NRS pre- and post- treatment in order to evaluate pain reduction post-RT. Post RT NRS was evaluated within 3 months from end of treatment. Our endpoint was to evaluate if a RT schedules was related to better pain reduction post RT in elderly.

Results: Median age of patients was 76 years old (range:70 - 88). Of 162 treated lesions, 83 (51.2%) , 11 (6,8%), 30 (18,6%), 27 (16,6%) and 11 (6,8%) were localized in vertebral site, ribs, pelvic bones, coxofemoral joints and other, respectively. Moreover, treated metastases were from the following primary tumors: 47 breast (29%), 45 lung (27,8%), 26 prostate (16%), 4 pleura (2,5%), 4 kidney (2,5%), 8 gastroenteric (5%), 3 gynecological (2%), 1 larynx (0,6%), 4 rectum (2,5%), 4 bladder (2,5%), 15 hematological (9%) and 1 uknown primary (0,6%). As regards RT schedules: 53, 49, 58 and 2 lesions were treated with 8Gy/1fx, 16 Gy/2 fx, 20 Gy/4 fx and 30 Gy/10fx respectively. The median NRS pre-RT was 6 (range:0-10), median NRS post-RT was 0 (range:0-10). In 72,8% and 17,3% of treated lesions we registered an improvement and a stable NRS value, respectively. In 9,9% a worsening NRS. The median difference between NRS (ΔNRS) pre and post RT was of 3 points (range: -4 to 10). Using median ΔNRS as cut-off point, 87 and 75 lesions had a ΔNRS ≥3 (group A) and a ΔNRS<3 (Group B), respectively; the first group had a greater reduction of pain then the second one. No statistical significant difference was detected between Group A – B and RT schedule (16-8Gy/2-1 fx vs 30-20Gy/10-4 fx; p=0.088).

Conclusions: In our experience no difference in term of pain control was detected among different palliative radiotherapy schedule in elderly patients.

P087

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR UNRESECTABLE LOCALLY ADVANCED NON SMALL CELL LUNG CANCER (LA-NSCLC)

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Aims: Conventional fractionated radiotherapy (cRT) concurrent with chemotherapy (ChT) is the standard of care in unresectable LA-NSCLC. The majority of patients (pts) cannot tolerate this treatment due to its toxicity, so sequential ChT followed by cRT is the more frequent choice in clinical practice. Recently, SBRT has been used instead of cRT in NSCLC offering superior control with less toxicity. We present our experience with SBRT in LA-NSCLC.

Methods: Between June 2015 and January 2018, 12 LA-NSCLC pts who underwent SBRT were analyzed . 10/12 (85%) pts received neoadjuvant ChT before SBRT. All pts had CT-PET before SBRT. In pts submitted to neoadjuvant ChT the target volume was the residual disease defined on the basis of CT-PET images. The technique was intensity modulated arc therapy (IMAT) SBRT and volumetric modulated arc therapy (VMAT) SBRT in 9 (75%) and 3 (25%) pts, respectively. A specific treatment planning for primary tumor (T) and lymph-node/s (N) was done for 7 (59%) pts, while in remaining 5 (41%) the planning target volume (PTV) included both T and N. All pts repeated CT-PET 3 months after treatment and thereafter every 4-6 months. The toxicity was eva-

luated using CTCAE scale.

Results: Median age was 70 years (55-81). 7 (59%), 3(25%) and 2 (16%) pts had clinical N2, N1 and N3 stage at diagnosis, respectively. 7 (59%) and 5 (41%) had central and peripheral primary tumor. Median PTV for T and N separately treated were 16.7 cc (8.7-67.96) and 15.02cc (9.9-72.3), while for T and N treated in the same target was 81.23 cc (53.2-165.9). Median prescribed dose was 40 Gy (35-55) and 35 Gy (35-40) in 5 fractions to T and N, respectively. After a median follow-up of 12 months (4-35) 3 of 12 (25%) pts had local recurrence, 1 (8%) regional node recurrence and 1 (8%) distant progression. Median local recurrence free survival, regional node recurrence free survival and distant progression free survival were 8 months (4-35). Of note 2 patients who had hemoptysis before SBRT resolved the symptom after treatment. No patients developed > grade 2 toxicity.

Conclusions: IMAT and VMAT SBRT was a feasible, safe and effective treatment in selected unresectable LA-NSCLC pts. Although clinical outcomes were very promising in terms of results and toxicity, larger and more mature studies are needed to adopt this treatment in clinical practice.

P088

ACUTE AND LATE SKIN TOXICITY IN HYPOFRACTIONATED WHOLE BREAST RADIOTHERAPY AFTER CONSERVING SURGERY IN ELDERLY

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Aims: To evaluate acute and late toxicity in hypofractionated whole breast radiotherapy after conserving surgery.

Methods: Between 2012 and 2018 66 breast cancer patients (pts) were treated, median age 72 (range 65-76) undergoing breast conserving surgery and adjuvant 3-dimensional conformal hypofractionated radiotherapy. Quadrantectomy was performed in 58 pts (87,8%) and nodulectomy in remaining 8 pts (12,1%); axillary dissection was necessary in 4 pts (6%). Most frequent histology (81,8%) was invasive ductal carcinoma. The histological grading was 33,4% for G1, 43,9% for G2, and 22,7% for G3. 64 pts have been prescribed hormonal therapy. The basic course of radiotherapy (RT) consisted in a median prescription dose of 40,34 Gy (range 40,05-45,22) to the whole breast in 16 fractions (15-17) of 2,67 Gy daily, delivered over 3 weeks. No boost was delivered in any pts. Acute and late toxicity was weekly monitored during and after radioterapy, at every follow up visit, according to the RTOG /EORTC criteria.

Results: Median follow-up period was 20 months (range 2-71). Treatment was globally well tolerated. 66 pts were analyzed, by the end of RT, not reporting any G3 or more acute skin toxicity, while 3 pts (4,54%) and 22 pts (33,3%) developed G2 and G1 acute skin toxicity respectively. No worse late skin toxicity was observed excpet for 8 pts (12,1%) with G1. Skin toxicity was treated with moisturirizing cream, in daily applications, during the whole course of treatment. At last follow up, all the pts are alive without local recurrence except one patient died for non-cancer related causes.

Conclusions: Fractionated radiotherapy, according with current international guidelines, can be used as standard treatment after breast conservative surgery. Our results confirm the safety of this schedule treatment without adverse events for acute and late toxicity, offering a reduction of the total treatment time and optimal local control outcomes.

P089

HYPOFRACTIONATED VERSUS STANDARD FRACTIONATED RADIOTHERAPY IN DUCTAL INVASIVE BREAST CANCER IN ELDERLY

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Aims: To compare in a setting of patients (pts) with ductal invasive breast cancer (IDC), cosmetic outcomes, local control and overall survival between hypofractionated (HF-WB) and conventional (CRT) schedules.

Methods: Between 2012 and 2018 96 womens with IDC were retrospectively recruited; all pts included in this study were treated with adjuvant whole breast radiotherapy after breast conserving surgery. Median age 68,9 years (range 65 – 86). Inclusion criteria for both groups were early stage, conservative surgery, indication at hormonal therapy; presence of comorbidities like diabetes mellitus (present in to 13,5%) and hypertension (39,6%) was analyzed and correlated with toxicity, evaluated according RTOG/EORTC scale. We recruited 48 pts treated with HF-WB and a matched group of pts with CRT. CRT schedule was 52,86 Gy total dose (range 50-56Gy) using 2 Gy fractions; HF-WB schedule was 41,60 Gy total dose (range 40-45,22 Gy) 2,67 Gy per fraction. Both treatments were delivered with 3-dimensional conformal radiotherapy.

Results: Cosmetic outcomes where not significantly different between conventional and hypofractionated RT. No worse late and acute skin toxicity was observed except in acute for G2 in CRT and HF-WB (6,2%). Pts presented more frequently slight erithema or hyperchromia. After a median follow up of 24 months, there have not been local recurrences in both groups. In two pts in the CRT arm bone metastases occurred. At the last follow-up, all the pts are alive except one treated with HF-WB who died for other causes.

Conclusions: In this study, in agreement with large randomized trials results, hypofractionaction represents a suitable alternative for treating DCI in the vast of the majority of the breast cancer pts after conserving surgery. In our series the comparison between hypofractio-

nation and standard fractionation shows a substantial equivalence in terms of cosmetic outcomes, local control and overall survival.

P090

HYPOFRACTIONATED WHOLE BREAST IRRADIATION IN ELDERLY: A MONOISTITUTIONAL EXPERIENCE

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Aims: Breast cancer is the most common malignancy among elderly women and the main cause of mortality. A specific management for elderly woman is not clear because clinical trials are usually not customized for this subset of patients. The use of hypofractionated schedules changed the standard fractionation and has now been considered an advantageous option for the treatment of early breast cancer especially in elderly. The aim of this study is to report a monoistitutional experience with hypofractionated radiotherapy (hypo-RT) without boost to the tumor bed in the setting of elderly woman with early breast cancer.

Methods: Between January 2013 and December 2017, 868 patients (pts) were treated with 3D radiotherapy for breast cancer. In this analysis we included only the 98 pts received hypofractionated treatment according with national and international criteria. All patients were > 65 years old and all were treated with conservative surgery for early breast cancer. Among these 96 pts received 42.56 Gy in 16 fractions, 2 pts 40 Gy in 15 fractions on whole breast without boost. Acute and late toxicity was prospectively assessed during and after hypo-RT, every six months, based on the Radiation Therapy Oncology Group Scale (RTOG) scale.

Results: Median follow-up was 22 months. Median age was 73 years (65-87 years). All patients well tolerated the treatment. Among the 98 pts treated with hypo-RT, 83 pts (85%) were pT1, 85 pts (87%) were pN0, 56 pts (57%) was Luminal A, 31 pts (32%) Luminal B and 3 pts (3%) Triple Negative. Most pts (86%) had ductal invasive histology. Acute skin toxicity observed was G1 in 25% pts, G2 in 1% of pts and 66% didn't show acute skin toxicity (G0). No grade 4 toxicity was observed. Late toxicity was resolved in 96% of pts. Subcutaneous edema remained in 4 patients. 4.5% of patients developed systemic progression for bone (3%) and hepatic metastases (1%). No local recurrence has been found.

Conclusions: Hypo-RT represents a feasible and convenient option in elderly early breast cancer. It is a safe treatment modality with low skin toxicity rate and with acceptable local control of progression disease and local recurrence risk. The elderly patients' compliance were better with hypofractionation than standard RT.

P091

ELDERLY AND VERY ELDERLY PATIENTS WITH NON MELANOMA SKIN CANCER (NMSC) TREATED WITH HYPOFRACTIONATED ELECTRON BEAM RADIOTHERAPY: SEVEN YEARS EXPERIENCE AT AREZZO RADIOTHERAPY UNIT

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Aims: Epithelial skin cancer is a common neoplasm. Incidence is increasing probably as a result of increasing age and sun exposure of population. These tumors are more rapresented in elderly patients that usually require a multiprofessional approach to complete therapy and to maintain an adequate quality of life. The primary objective of this study was to assess the efficacy, feasibility and clinical outcome of primary hypofractionated electron beam radiotherapy treatment in 192 elderly, and very elderly patients with NMSC lesions.

Materials and methods: A retrospective chart review identified 192 elderly patients (81 females and 111 males) with no operated NMSC treated with radical hypofractionated electron beam radiotherapy from January 2010 to December 2017 at Arezzo Radiotherapy Unit. Patients age, gender, tumor histology (proven by biopsy), site, size (<2 cm; >2cm; >7 cm), presenting symptoms (pain and ulceration), and radiation treatment factors (dose and fraction) were recorded and analaysed. 59% of patients were > 85 years old. The majority of tumours were located at the face or scalp (73%), 27% at limb. In 41% of the lesions the histology was basal cell carcinoma, while in the 59% was squamous cell carcinoma. All the patients were treated with hypofractionated electron beam radiotherapy (55 Gy in 20 fractions; 50 Gy in 20 fractions; and 35 Gy in 7 fractions). Clinical outcome, overall survival (OS), disease specific survival (DSS), progession free survival (PFS) at 6 and 12 months, acute and late related toxicity were recorded.

Results: 79% of the patients achieved complete response (CR), while 17% partial response (PR) or stable disease (SD). OS at six and twelve months was respectively 96,8% and 83,5%; DSS at six and twelve months was 98.2%. PFS at six and twelve months was 97,1% and 80,8%. Histology, age, dose, fractionation and size of the lesions are resulted indipendent factors to OS, DSS and PFS. Total dose of 35Gy and 7 Gy fraction were related to a lower acute toxicity (p=0,024 and p=0,034). Acute toxicity was'nt related to the site and size of the lesions.

Conclusions: Hypofractionated electron beam radiotherapy is safe, effective and useful treatment modality for NMSC in elderly and very elderly patients. Patients age, caratheristics (size and ulceration) and critical site of the lesions (eylide; nose; ear) dont rapresent a limit to radical curative radiotherapy treatment.

P092

RADIO-CHEMOTHERAPY WITH TEMOZOLOMIDE IN ELDERLY PATIENTS WITH GLIOBLASTOMA: OUR EXPERIENCE

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Aims: Glioblastoma multiforme (GBM) is the most aggressive brain tumor in adults and the second most common brain cancer after meningioma with a peak of incidence on the fifthy decades of life. Due to the progressive ageing of the developed country population, more than a half of new cases occurs in patients older than 65 years. The aim of the present study was to evaluate the clinical outcome of radio-chemotherapy with temozolomide in patients with glioblastoma aged more than 65 years.

Materials and Methods: Sixty-three patients treated with radiotherapy and chemotherapy at Pisa University Hospital between September 2004 and November 2017 were enrolled in this retrospective analysis. All patients had a proven diagnosis of glioblastoma grade IV WHO, ECOG PS 0-2, age ≥ 65. Radiotherapy was delivered in daily fractions of 2 Gy given 5 days per week for 6 weeks, for a total of 60 Gy. During radiotherapy, temozolomide was administered at a dose of 75 mg per square meter of body-surface area per day from the first to the last day of radiotherapy. 5-6 weeks after the end of radiotherapy, adjuvant temozolomide was administered at 150-200 mg per square meter for five consecutive days, every 28 days. A maximum of 12 cycles were prescribed if MRI showed no disease progression and temozolomide was well tolerated.

Results: Data analysis was performed in April 2018. The present study was performed in 37 male and 26 female patients with a median age at diagnosis of 72,5 years (range=65-89 years). Fifty-seven patients underwent surgical resection, four patients stereotactic diagnostic biopsy, two patients had a radiologic diagnosis only. During follow up, we recorded 46 cases of disease progression with a median progression-free survival (PFS) of 12 months (range 1-88 months). Median overall survival (OS) were 25 months (range 1-107 months); at data analysis, 65 patients were died. After disease recurrence, based on ECOG, tumor burden and age, patients were treated with surgery (15 cases), chemotherapy (30 cases) and re-irradiation (11 cases).

Conclusions: In our experience, progression free survival and overall survival were similar to those reported in literature for younger patients. We think that radiochemotherapy is a good option for older patients with a good performance status in glioblastoma treatment.

P093

DOSIMETRIC FEATURES, SAFETY AND EFFICACY OF ELECTRONIC BRACHYTHERAPY FOR ELDERLY PATIENTS WITH NONMELANOMA SKIN CANCER

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Aims: Surface electronic brachytherapy (EBT) is a technique using miniaturized X-Rays source. It is gaining ground as an emerging alternative radiotherapy (RT) solution for small superficial skin cancers. It can also be used as an alternative treatment to surgery for selected patients (pts). This prospective, single-center, non-randomized, pilot trial shows the clinical implementation of a new EBT system named Esteya® evaluating dosimetric features, the clinical efficacy and safety of this approach. Preliminary results are presented.

Methods: Flatness and symmetry of X-Ray beams have been evaluated using a high definition 2D array equipped of liquid filled ionization chambers. Half Value Layer (HVL), PDD and absolute dose have been measured for each applicator with a soft x-ray parallel plate chamber and solid water. Dose distributions have been compared with the ones calculated for conventional electron treatments. Between November 2016 and March 2018, 24 pts > 70 years (median age: 88, range: 73-96) with nonmelanoma skin cancers (primary or recurrent squamous and basal cell carcinomas) have been enrolled and analyzed. Only lesions with a maximum diameter < 2,5 cm were treated with radiation dose of 40 Gy (5 Gy fraction, 2/week). Acute toxicity has been measured according to CTCAE v4.03 scales and cosmetic results assessed by RTOG-EORTC scales.

Results: Flatness, symmetry and penumbra showed excellent performance even if compared with eMC plans. Build up absence and PDDs slopes allow good homogeneity for coverage in superficial targets. No G3 or higher toxicity were scored. All pts presented erythema; moist desquamation and crusting were shown by 3 pts (G2 CTCAE in 78.3%). Slight pigmentation changes and moderate telangiectasia were recorded in 21.7% pts. Toxicity started after the 4thfraction and worsened between the end and 4 weeks after RT. A clinical complete response was observed in 91.4% of cases, 1 patient presented residual disease and 3 pts experienced marginal/in-field recurrence. Conclusions: Our preliminary results show that Esteya® is an effective, simple, safe, and comfortable treatment associated with good cosmetic outcomes for elderly pts with skin cancer. Even if a longer follow-up and a bigger sample size are needed to confirm these preliminary findings, shielding requirements, patient compliance and global

management of EBT make this treatment modality an attractive alternative solution for elderly pts.

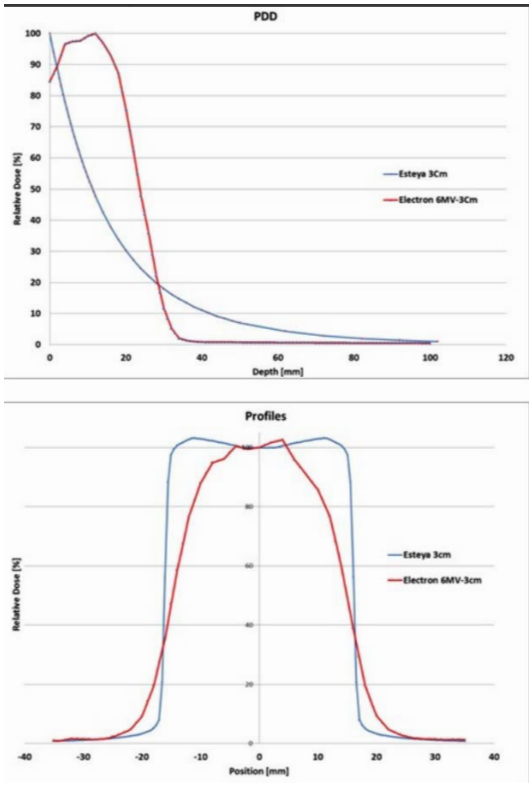

Figure 1.

P094

STEREOTACTIC BODY RADIOTHERAPY IN BONE OLIGOMETASTATIC PROSTATE CANCER PATIENTS

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Aims: The first line treatment of metastatic prostate cancer (PC) is androgen-deprivation therapy (ADT). A subgroup of patients (pts) presents with few lesions (i.e.,oligometastases). Stereotactic body radiotherapy (SBRT) can deliver high doses of radiotherapy while sparing adjacent tissues. We used SBRT in selected PC oligometastatic pts with bone metastases (BM) to improve local control.

Methods: Between October 2010 and December 2017, 11 oligometastatic PC pts with a total of 13 BM were evaluated regarding time to biochemical progression and initiation of ADT. Median age was 67 years (range, 62-73), median Gleason score at the primary diagnosis was 7 (range, 6-8). Median time from primary treatment to SBRT was 48 months (m) (range 9–108). Diagnosis of disease relapse was made with Choline-PET/CT. Median PSA value before SBRT was 2.2 ng/ml (range, 0.5-4.3). 9/11 pts underwent only SBRT, remaining 2 received also concomitant ADT. Two (18%) pts underwent SBRT for two synchronous BM. The BM sites were: pelvis in 8 (62%), spine and ribs in 3 (23%), and in 2 (15%) cases, respectively. Gross tumor volume (GTV) was delineated using Choline-uptake and planning target volume was defined as the GTV plus a 5 mm isotropic margin. Two different fractionation schemes were used: 5 × 8Gy in 7 (54%) lesions and 3 × 10Gy in others 6 (46%). Response was assessed with PSA evaluation scheduled every 3 m during the first year and then every 6 m. Pts with a reduction or a stability of PSA level were considered responders, Choline-PET-CT was done in case of a PSA level increase.

Results: With a median follow-up of 36 m (range 5-88), the median time of biochemical progression from the end of SBRT was 8 m (range 5-88). All patients had a decrease of PSA level after SBRT. Of responders, 6 (55%) pts remained biochemical relapse free, other 5 (45%) pts had a PSA increase due to an out-field progression confirmed by Choline-PET/CT. Of these last pts, 2 underwent SBRT on a new BM, and remaining 3 had a systemic progression of disease and were submitted to ADT. Median time to initiation of ADT was 7 m (range 2-8). No SBRT related acute or late toxicities were observed.

Conclusions: Our experience shows that SBRT of BM is a highly effective with an excellent risk-benefit profile. SBRT in PC bone oligometastases pts should be evaluated to improve response rate and delay ADT.

P095

LONG-TERM RESULTS OF STEREOTACTIC RADIOTHERAPY FOR RECURRENT MALIGNANT GLIOMA: UP-DATE OF A MONO-INSTITUTIONAL TRIAL

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Aims: To evaluate long-term results of recurrent Glioblastoma (GBM) and Anaplastic Astrocytoma (AA) treated with radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT), we present an up-date of our experience.

Methods: Between November 2001 and October 2017, 36 patients were re-irradiated for 36 recurrent GBM/AA, 19 (53%) with SRS and 17 (47%) with FSRT. SRS or FSRT were chosen according to lesion size and location. No concomitant chemotherapy was administered during re-irradiation. Follow-up was performed every 3 months with clinical visit and magnetic resonance imaging. Response was evaluated with RECIST/RANO criteria and toxicity with CTCAE

v4.03 scale.

Results: Male/female ratio was 23/13, median age 61 years (range, 30-78 years), median KPS 90% (range, 70-100%), histology GBM and AA in 35 and 1 patient, respectively. Median time between re-irradiation and primary radiotherapy was 14 months (range, 6-29 months), median doses were 16 Gy (range, 10-22 Gy) for SRS and 30 Gy in 10 fractions (range, 15-48 Gy) for FSRT. The median cumulative normalized total dose was 140 Gy and 98 Gy for SRS and FSRT, respectively. Median follow-up after re-irradiation was 11 months (range, 6-57 months), at the time of analysis all patients had died. After re-irradiation, 4 (11%) lesions had partial response, 22 (61%) stable disease, and 10 (28%) progression disease. Median duration of response was 6 months (range, 3-15 months) and median survival from re-irradiation was 11 months (range, 3-58 months). Acute toxicities recorded were 2 (6%) cases of headache and 2 (6%) other cases of nausea successful treated with medical therapy. Radionecrosis was registered in 4 (11%) cases, 3 asymptomatic and 1 symptomatic. The cumulative normalized total doses for the 4 patients with radionecrosis were 122 Gy, 124 Gy, 141 Gy and 140 Gy. In one case, the volume of the lesion was large (14 cc), and in the other 3 the interval between the first and second cycle of radiotherapy was rather short (5 months).

Conclusions: Re-irradiation with SRS and FSRT of recurrent malignant glioma patients was safety and effective. To avoid toxicity, an accurate patient selection is crucial as well an appropriate cumulative dose and a proper time to re-irradiation.

P096

HYPOFRACTIONATION, ABIRATERONE AND PREDNISONE IN THE TREATMENT OF BONE METASTASES IN PATIENTS WITH HORMONE REFRACTORY PROSTATE CANCER

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Aims: The hypofractionated radiotherapy plays a fundamental role in the treatment of bone metastases. At our center, we evaluated the feasibility and effectiveness of two schemes hypofractionation: 8 Gy single dose and 8 Gy in two fractions to be made within a week of each other. The two irradiation techniques have been associated with the new molecules used in medical therapy.

Methods: From July 2014 to March 2018 they were treated 36 patients with bone metastases from hormone refractory prostate cancer . The median age of patients studied was 71 years with bone metastasis respectively localized in the dorsal and lumbar spine in 50% of cases, 30% at the level of bilateral lower limbs and the remaining 20% at the level of the pelvis. Radiation therapy was by hand in a single dose in 60% of cases in patients with worse P.S. while in the remaining 40% it was backed bifractionation treatment. All patients were administered simultaneously, the abiraterone acetate 1 g / day, prednisone 10 mg/day in combination with LHRH analogue every three months.

Results: All patients were reassessed after 30-40 days of therapy. In no case were registered signs of toxicity. In 80% of cases there has been a reduction in their analgesic therapy administered dose.

Conclusions: In our experience, the radiotherapy hypofractionated 8 Gy in a single session or, alternatively, 8 Gy in two weekly sessions in conjunction with the abiraterone acetate was well tolerated and had a good impact both as regards the control of the pain is the improvement of quality of life.

P097

OUTCOME AND LOCAL CONTROL IN PATIENTS TREATED WITH BRAIN STEREOTACTIC RADIOTHERAPY FROM BREAST CANCER WITH CYBERKNIFE: A RETROSPECTIVE ANALISYS

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Aims: The objective of this study was to report our institutional experience with CyberKnife in the stereotactic radiation treatment (SRT) of patients with brain metastases.

Methods: One-hundred and two consecutive patients with brain metastases from breast cancer (199 lesions) were treated with brain SRT with CyberKnife from 02/2012 to 11/2017 as first brain radiation treatment and reviewed retrospectively for patient, tumor, and imaging characteristics. Parameters included demographics, histology and primary tumor characteristics, presence and control of extracranial disease, number of lesions and tumor volume. The imaging characteristics assessed were complete response (CR), partial response (PR), stable disease (SD), local (LF) and distant brain failure (DBF). Overall survival (OS) and local control (LC) at 2 years were evaluated.

Results: After a median follow-up of 11.6 months (range 2.6–65.6), at least one radiological evaluation was available for 152 brain metastases (76 patients, all women). Most of the lesions (41%) were treated with a single session of SRT with a total dose of 21 Gy, other fractionations (24 Gy in 2 or 3 sessions) were preferred in case of two or more concomitant metastases or in case of greater volume of the target. CR, PR and SD as best response were reported in 67 (44%), 56 (37%) and 26 (17%) of 152 lesions respectively, while 3 (2%) lesions had a progression disease at first control. Fifteen out of 149 (10%) lesions showed LF after a median of

12.5 months (range 1.2–63.4). Forty-seven (61%) women out of 76 developed DBF after a median of 7.0 months (range 1.0–39.6). Radionecrosis was radiologically (11c-methionine Positron Emission Tomography and/or Nuclear Magnetic Resonance with gadolinium) diagnosed for 14 lesions (13 patients, 17%) in a median time of 7.3 months (range 2–20.4). Seven (9%) women referred neurological symptoms (such as seizures), a neurosurgical treatment was needed for 3 of them in order to control symptoms. At the time of assessment, 36 (47%) patients are still alive, 32 (42%) died for tumor progression and 8 (11%) were lost to follow-up. OS after 2-years is 52%, LC after 2-years is 63%.

Conclusions: Our results showed the efficacy in the treatment of brain metastases from breast cancer with CyberKnife SRT. Correlation between clinical (volume of brain disease) and histological parameters with favorable outcome is under investigation.

P098

STEREOTACTIC ABLATIVE RADIOTHERAPY FOR OLIGOMETASTATIC PROSTATE CANCER

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Purpose: The aim of our retrospective study is to evaluate the feasible and outcomes of patients with oligometastatic prostate cancer (PCa) treated with stereotactic ablative radiotherapy (SABR).

Material and Method: 10 patients (pts) median age 69 years (range 62-77, mean 68) with 19 metastatic PCa lesions (11 lymph node, 5 bone, 2 prostate and 1 prostatic fossa) were treated with Varian Trilogy 6-15 MV. SBRT was delivered in 30 Gy in 5 fraction (fr) (80%), 25 Gy in 5 fr. (10%) and 15 Gy in 1 fr + 30 Gy in 10 fr (10%). Gross tumor volume (GTV) was defined as the sum of the abnormalities noted on PET, CT scan and/or MRI T2 sequences. Median follow-up was 11 months (mean 7.5, range 1-14) Androgen deprivation therapy (ADT) was administrated in all pts. In 3 pts was administrated Abiraterone after the SBRT. All the pts were clinically evaluated for urinary and rectal late complications according to CTC.AE 4.0 and RTOG/EORTC scale.

Results: Biochemical progression-free survival, distant progression-free survival, and overall survival were 40%, 20%, and 100%, respectively. Mean PSA at last follow-up was 2.6, median 3 (range 1-14). Acute toxicity: genitourinary (GU) $\geq$ G2 in no one pts and gastrointestinal (GI) $\geq$ G2 in 1 pts. Late toxicity: No GU and GI $\geq$ G2 were reported.

Conclusions: SABR for patients with oligometastatic prostate cancer provided optimal metastasis control, is feasible and well tolerated. The heterogeneity and small size of our series limits interpretation of clinically meaningful outcomes following, but our preliminary data suggests this approach is worthy of further prospective study. More definitive conclusions await the reporting of prospective randomized studies.

P099

RADIOTHERAPY FOR RECURRENT OLIGOMETASTATIC TRANSITIONAL CELL BLADDER CARCINOMA: SINGLE INSTITUTION SERIES OF 13 PATIENTS/21 LESIONS

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Objectives: The aim of our study was to retrospectively report on radiotherapy (RT) in the oligometastastic recurrence of bladder cancer. Thirteen patients treated for low-volume metastatic transitional cell urinary bladder carcinoma (TCC) were reviewed. The primary endpoint was to evaluate the safety and efficacy of RT, proposed as an alternative to systemic treatment and/or to defer the start of a second line chemotherapy.

Methods: Inclusion criteria for our retrospective study were as follows: adult oligometastatic TCC patients with lymph node, bone, lung or local recurrence that underwent RT but not other local/systemic therapy. Previous systemic therapy or surgery on the primary tumor were allowed. Toxicity and tumor response were evaluated. Progression free-survival was also evaluated.

Results: Thirteen patients for a total of 21 lesions were treated with CyberKnife (CK) or Vero System stereotactic body radiotherapy (SBRT) or conformal 3D radiotherapy (3D-CRT) between 2012 and 2017. All cases were discussed in a multisciplinary urologic board. Median age at RT was 71 years (range 50-84) and median Karnofsky performance status (KPS) was 90 (range 80-90). Mean interval between TCC diagnosis and the start of RT on oligometastasis was 2.5 years. The median treatment dose was 25 Gy (range 20-36 Gy) given over a median of 5 fractions (range 3-10 fractions). Median follow-up was 20.4 months (range 3.6-43.7 months). At the first imaging assessment, radiological response was complete response, partial response, local progression and not evaluable 11, 1, 8 and 1 lesions, respectively. The radiological progression of disease was registered in 9 patients at the median of 4.2 months (range 1.9-18.5 months) from RT; in 6 cases it was out-field and in-field progression, while in 3 patients only out-field progression was observed. At time of the analysis, 3 patients are alive with no evidence of disease (at median follow-up of 30 months from RT), 4 are alive with evidence of disease, 6 died of cancer-related disease and one was died for other disease. No severe acute and late toxicity were observed.

Conclusions: RT on lymph node or bone oligorecurrence from TCC offers a promising in-field tumor control with very low toxicity profile. Three patients out of 13 (20%) are free of disease at 30 months. Further studies are needed to establish a role of RT in the oligometastatic recurrent bladder cancer.

P100

HYPOFRACTIONATED STEREOTACTIC BODY RADIATION THERAPY BY MEANS OF HELICAL TOMOTHERAPY FOR THE TREATMENT OF OLIGO-METASTASES

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Aims: To report clinical outcomes and tolerability profile of hypofractionated stereotactic body radiation therapy (SBRT) performed with Helical Tomotherapy (HT) in the treatment of oligometastatic and oligorecurrent disease.

Methods: Between April 2014 and February 2018, 30 patients (37 lesions) with a median age of 72 years (range 44-85) were treated with HT-SBRT at our center. Only patients with ≤2 lesions were considered eligible for this treatment. Basing on tumor site and using a strategy of risk-adapted dose prescription, different treatment regimens were applied: 40-60 Gy in 4-10 fractions for lung metastases (median BED10=96 Gy, range 56-115.5 Gy), 25- 50 Gy in 5-10 fractions for nodal lesions (median BED10=57.6 Gy, range 37.5- 62.5 Gy) and 18-30 Gy in 5-6 fractions for bone metastases (median BED10=42.75 Gy, range 28.8-48 Gy). Acute and late toxicity were graded using CTCAE v4.0 criteria, during treatment and at every follow-up visit. Evaluation of tumor response was assessed by means of CT-scan every three months and/or 18FDG-PET/CT, if needed, after SBRT according to RECIST or PERCIST criteria. Kaplan–Meier method was used to generate Local Control (LC), Progression Free Survival (PFS) and Overall Survival (OS) rates.

Results: Only 7 patients had 2 lesions simultaneously treated, while 23 patients had a single site, for a total of 26 pulmonary metastases, 7 lymph nodal and 4 bony lesions. The most common primary tumor was Non-Small Cell Lung Cancer (n=11) followed by prostate (n=6), colorectal (n=5), bladder (n=2), and ovarian cancer (n=2); melanoma, larynx, pancreas and parotid gland tumor in the remaining 4 cases. With a median follow-up of 14 months (range 3-49), no acute or late toxicity ≥ G3 were observed, reporting only one case of acute G2 chest pain, and 2 patients experiencing late G2 dysphagia and chest pain fully recovered after short time steroid therapy. LC rates at 1- and 2-years were 65.3% and 53.8% for lung lesions, 57.1% and 42.8% for nodal lesions. For bone metastases we reported a 1-yr LC rate of 75%. 1-yr and 2-yrs PFS were 56.6% and 36.6%, respectively. The 1-yr and 2-yrs OS rates were 86.6% and 73.3%.

Conclusions: In our experience, SBRT in oligometastatic/oligorecurrence cancer has shown an acceptable rate of local control with encouraging survival rates and excellent toxicity profile. SBRT represents a safe, effective and minimally invasive treatment for oligometastatic/oligorecurrence disease.

P101

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR LUNG METASTASIS (MTS) TREATED WITH A FLATTENING FILTER-FREE BEAMS (FFF): EVALUATION EARLY RESPONSE AND ACUTE TOXICITY

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Aims: To report data on local control (LC) and acute toxicity for patients with pulmonary MTS treated with SBRT images guided (IGRT) using a FFF linac, compared with a group of patients with similar characteristics previously treated with SBRT conventional photon beams without IGRT.

Methods: From January 2017 to April 2018, were treated 57 patients (45-86 years) and 72 pulmonary MTS. Doses delivered were 39-60 Gy in 3/5 fractions alternate days or 20 Gy in single fraction with 10 MV photon beams flattening filter free with conformational DynamicArc (DynArc 43 lesions), HybridArc (HA 20 lesions) and RapidArc-VMAT (RA 9 lesions) tecniques. The control inter and intra-fractional positioning was achieved using the ExacTrac X-Ray and CBCT systems. All patients had 1-3 lesions ≤ 3 cm, life expectancy grater one year and received clinical instrumental evaluation (CT) at 45-60 days after the treatment. Response assessed: Complete (CR), Partial (PR), Stable Disease (SD) and Progression (P). The pulmonary dermatological and neurological toxicities were evaluated according to the CTCAE version 4.0 scales. The control group was of 116 patients (47-89 years) and 135 MTS treated with SBRT from January 2012 to December 2016 with 6 MV photon beams, conformational DynArc and HA techniques and MV-MV inter-fraction.

Results: We found: PR in 65 MTS (90%) and SD in 7 (10%); pulmonary toxicity G1 occurred in 55 patients (96.5%) and G2 in 2 patients (3.5%); 2 patients (3.5%) reported G2 neuralgia and radiculitis. No skin toxicity occurred. In the control group : 125 MTS (92.6%) presented PR, and 10 (7.4%) SD; pulmonary toxicity G1 reported in 60 patients (51.7%) and G2 in 56 patients (48.3%); 12 patients (13.9%) developed G2 neuralgia and radiculitis. No patients showed skin toxicity.

Conclusions: In our short clinical experience of pulmonary SBRT with FFF beams, we found very good disease control and low acute toxicity profiles, futhermore is a safe and effective therapy. However, greater follow-up is needed to assess long-term disease control, possible relapse time and late toxicity.

P102

STEREOTACTIC BODY RADIATION THERAPY IN OLIGOMETASTATIC COLORECTAL CANCER: A SINGLE-CENTER EXPERIENCE

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Aims: Patients with oligometastatic colorectal cancer (CRC) are considered candidates for curative treatment because long-term survival can be expected. Recent studies have shown that stereotactic body radiation therapy (SBRT) in oligometastatic CRC is an excellent option for the local treatment of metastases with a good outcome and low toxicity profile. The primary aim of our retrospective analysis was to evaluate feasibility, local control, progression free survival (PFS), survival outcome and toxicity of SBRT in oligometastatic CRC patients in a single institution.

Methods: Inclusion criteria were: histologically-proven colorectal adenocarcinoma; oligometastatic disease, (up to 5 metastases, both synchronous and metachronous, in an otherwise well-controlled disease state); written informed consent. All metastatic locations were included in this study. Treatments were performed using VERO® and CyberKnife systems. The SBRT prescribed dose was related to the volume of the lesions and their locations. Tumor response and toxicity were evaluated using the Response Evaluation Criteria in Solid Tumors (RECIST) and the Common Terminology Criteria for Adverse Events (CTCAE) v4.03, respectively. Computed tomography (CT) or positron emission tomography (PET) were performed at 2-3 months after RT treatment. Local progression free survival (LPFS), PFS, overall survival (OS) were calculated via Kaplan-Meier method.

Results: Between January 2012 and December 2015, 102 oligometastatic CRC patients (179 lesions) underwent SBRT with a median dose of 45 Gy and 15 Gy dose/fraction. Median follow up was 11 months. Progression disease occurred in 38 (24%) of the treated lesions out of 161 evaluable lesions. Pattern of failure was predominantly out-field. No G3-G4 acute or late toxicities were observed. Actuarial 2-year LPFS, PFS and OS rates were 55%, 15%, and 90%, respectively.

Conclusions: Our study showed that SBRT is a high compliance, non-invasive treatment modality in oligometastatic CRC. It offers good local control with very low toxicity rate. Further studies should be focused to clarify which patient subgroup will benefit most from this treatment modality and the appropriate dose for a better LC with low toxicity profile.

P103

THE THERAPEUTIC HORIZON OF STEREOTACTIC BODY RADIATION THERAPY FOR NON-SPINE BONE OLIGOMETASTASES: OPTIMAL DISEASE CONTROL ACROSS EARLY PAIN RELIEF AND HIGH TOLERABILITY

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Aims: Bone is one of the most common sites of metastatic disease in cancer patients and can cause debilitating effects including pain, hypercalcemia and pathological fracture. The use of SBRT may benefit patients with bone metastases by extending duration of pain control, delaying disease progression and subsequently the need for reirradiation. However, there are few studies examining the toxicity and outcomes of SBRT for non-spine bone metastases, and the increased dose may put the patient at risk for fracture, which could negate any benefits. The aim of this study is to evaluate outcomes, toxicity and the risk of fracture related to SBRT for non-spine bone metastases.

Methods: Between 2012 and 2017, 20 patients and 23 non-spine bone oligometastases were treated with Stereotactic Body Radiation Therapy (SBRT) at the Radiotherapy Unit of San Donato Hospital, Arezzo, and retrospectively reviewed. CT/PET was fused on simulation CT and used to outline the target volume in order to reduce inter-observer variation. Acute and late toxicity were reported and graded as per standardized Common Toxicity Criteria for Adverse Events 4.0 criteria. Local control (LC), overall survival (OS), and progression-free survival (PFS) were evaluated and predictive factors for LC were examined.

Results: The median age of patients treated was 72 years (range 49-85). The most common histology was prostate cancer (50%), followed by breast (25%), bladder (10%), lung (5%), kidney (5%), and rectal cancer (5%). Most of the non-spine bone metastases laid within the pelvis (80%). Pain was present before SBRT in 50% of cases and assessed according to the Numerical Rating Scale (NRS). Median SBRT dose used was 30 Gy (range 25-36) in 3-5 fractions. Early pain relief was observed in all symptomatic patients. After a median follow up of 27 months (range 5-60), 1-year LC, OS and PFS rates were 90%, 95% and 72%, respectively. Local progression occurred in 9 patients with a median time to local failure of 22.5 months. Three patients developed acute toxicity (grade 1 fatigue in 1 case and grade 1 acute pain flare in 2); no late toxicities were observed and SBRT-related fractures did not occur. Predictive factor of better LC was smaller PTV (<40 cc, $p = 0.03$). No patients required reirradiation.

Conclusions: Even across non-spine bone metastases and multiple histologies, SBRT is a feasible treatment and yields high rates of long-term LC with low acute toxicity and no long term side effects.

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STEREOTACTIC RADIOTHERAPY FOR LUNG METASTASES: OUR EXPERIENCE

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Aims: The gold standard in treatment of metastatic tumors is represented by systemic therapy. However, in selected patients with low tumor burden, local metastasis treatment may be useful to improve local disease control.

Methods: We analyzed data of 15 patients (8 female and 7 male) with lung metastases treated with Stereotactic Ablative Radiotherapy (SABRT) in our Institution from March 2016 to February 2018. Median age was 69.1 years (range 43-88 years). The primitive tumor was sarcoma (5.6%), breast (11.2%), uterus (22%), rectum (16.7%), colon (11.2%), kidney (11.2%), anus (16.6%), prostate (5.5%) carcinoma. The number of total treated lesions was 18. The treatment was administered with Linear Accelerator 6MV with Volumetric Modulated Arc Therapy (VMAT) technique for a total dose of 50 Gy in 5 daily fractions. All patients were subjected to MDC-free TC simulation and with an image fusion software we merged TC and PET images for the contouring of the lesions. We added a margin of 0.5 mm in the lateral-side and 0.8 mm in the cranial-caudal direction to GTV (Gross Tumor Volume) to prevent any geographical missing due to respiratory acts. It was calculated that average dose delivered to GTV was 51.12 Gy, while maximum dispensed dose to GTV was 54.53 Gy. Only in one case was administered concomitant chemotherapy with target therapy. Dose constraints of the Quantitative Analysis of Normal Tissue Effect in Clinic (QUANTEC) model have been used for inverse planning.

Results At the median follow up of 16 months (3-26 months), 4 pts have died for systemic progression of disease, 4 pts have achieved a partial response (RP) to SABRT,5 pts obtained complete response(RC) but with lung progression that consisted of a new pulmonary lesion, and in 2 pts was observed RC with no progression at the time of the last detection. Analyzing the values of the registered SUV before and after the treatment we detected an average reduction in the value of the SUV of 8 (0-15.1). In patients with complete response the imaging showed signs of fibrosis and flogosis. Acute toxicity observed during the treatment was grade 1 fatigue experienced in 48% of cases.

Conclusions: The observed data showed that SABR is a safe and feasible treatment, well tolerated even by older patients and has good local control even if is systemic progression is predictable.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN RENAL CELL CARCINOMA (RCC) LUNG METASTASES

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Aims: RCC is generally considered a low radioresponsive tumor. Hypofractionated high dose SBRT can theoretically improve response rates. Limited data exist regarding the role of SBRT in the treatment of RCC lung metastases. However, SBRT is an attractive treatment option for metastatic RCC tumors in which effective long-term palliation of symptoms or local control in oligoprogressive disease is desired. Our experience in this field is reported.

Method and Materials: 11 pts with 13 metastases from RCC were treated. Male/female ratio was 9/2, median age was 73y (range, 56-79), median KPS was 100% (range, 80-100). At the time of irradiation 5 and 3 pts were receiving target therapy with tyrosine-kinase inhibitor (TKI) and nivolumab, respectively. Systemic therapy was stopped 7 days before and started again 7 days after SBRT. Patients with synchronous diagnosis of metastatic RCC received SBRT after nephrectomy and before to start targeted/immunological therapy. The majority of lesions were treated with a median of 5 fractions (range, 3-5) at a median single dose of 10Gy (range, 6-13) and a median total biologically effective dose BEDα/β10 of 100Gy (range, 48-132). In 2 patients were treated 2 lesions at the same time, in the others 1 lesion for each patient.

Results: At a median follow-up of 24 months (range, 6-118), all patients were evaluable. Computed tomography response using RECIST criteria 3 months after treatment was obtained in 100% of treated lesions (TL), 4 TL were stable, 3 TL were in partial response and 6 in complete remission (CR). Systemic therapy was started again without delay 7 days after SBRT. None patients experienced progression in the irradiated sites. Every patient with CR received a BEDα/β10 of 100Gy. 4 patients had out-field lung progression after a median time of 24 months, 2 were treated with SBRT, 1 received second line target therapy and 1 received nivolumab. 1 patient had systemic progression and received nivolumab. No G3-G4 toxicity was registered.

Conclusions: SBRT for RCC lung metastases was associated with low treatment-associated toxicity and an excellent LC, especially in those patients receiving a BEDα/β10 ≥100 Gy. In patients who develop oligoprogression, SBRT may delay the start of systemic therapy and the shift from a first line to a second line medical therapy.

P106

SURVIVAL AND TOXICITY EVALUATION OF HYPO-FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR PATIENTS WITH LIMITED BRAIN METASTASES

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Aims: Evaluation of response, local control (LC) and toxicity in patients with limited brain metastases (BM) after hypo-fractionated stereotactic radiotherapy (HFSRT).

Methods: Nineteen patients (10 women, 9 men) presenting 1-4 BM treated with HFSRT between 2015 and 2018 were analyzed; age, status of primary tumor, systemic disease, Performance Status (PS) were considered as inclusion criteria to HFSRT and according to DS-GPA scale. Patients received a total dose of 20-24 Gy administered in 3-5 fractions (5-8 Gy/fraction) with a VMAT (Volumetric Modulated Arc Therapy) technique. A baseline MRI was performed before starting HFSRT and co-registered with planning-TC. During follow-up, brain MRI was performed at 3 months after the end of HFSRT, every 3 months during the first year, thereafter annually. Toxicity was recorded at each follow-up visit and graded using CTCAE v.4.3 scale.

Results: A total of 29 BM from melanoma, lung, breast, kidney and colorectal cancer were treated; patients had received biological therapies (5/19) and chemotherapy (1/19). Median follow-up duration was 8 months (range 3-24); crude local control rate (LC) and 1-year LC rate were 84.2% and 64%, respectively, mean overall survival (OS) was 11.8 months (median: 8; range 3-24) and 1-year OS was 42%; to date 17/19 patients (89.5%) are still living. Maximum response was: complete response (CR, in 7 patients, 36.8%), partial response (PR) in 5 patients (2.3%), stable disease (SD) in 4 patients (21%) and no response in 3 patients (15.8%). Median duration of response was 12 weeks (mean: 18.3 weeks; range 10-36 weeks). During follow-up 7 patients (36.8%) experienced a recurrence of disease (4 local and 3 distant), 5 patients (26.3%) received a recovery whole brain radiotherapy. Median progression free survival (PFS) was 16 weeks (mean: 26.7 weeks; range 12-52). Patients receiving a total dose of 24 Gy showed better results in respect to those receiving 20 Gy (CL 87.5% vs 81.8% and 87.5%, 1-year CL was 66% vs 45%, 1-year OS 37.5% vs 36.4%) with a response rate (CR+PR) of 75% vs 54.6% in patients receiving 24 Gy and 20 Gy respectively. Regarding toxicity, no severe (G3-G4) acute and late toxicities occurred; radionecrosis rate was 7.7%.

Conclusions: Although on a small sample, the results from our study showed OS, DFS, LC and response rates similar to literature with better trend in patients receiving 24 Gy. Prospectively, we need to recruit more patients in order to confirm these results.

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ROLE OF EXCLUSIVE STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC HORMONE-SENSITIVE PROSTATE CANCER (MHSPC) PATIENTS: A PRELIMINARY EXPERIENCE

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Aims: SBRT represent a widely treatment option in oligometastatic prostate cancer. This analysis describes our preliminary experience with treating mHSPC patients with SBRT alone.

Methods: Between January 2016 and March 2018 eleven mHSPC patients were treated with exclusive SBRT, delivered using LINAC with daily cone beam CT. All patients underwent [(11)C] choline or [(64)Cu] positron emission tomography(PET) for biochemical relapse after local primary treatment (RT or surgery): eight patients had isolated abdominal or pelvic nodal disease and three patients had single bone metastases. Prescribed dose was 30 or 35 Gy in 5 fractions. We did not prescribe concomitant androgen deprivation therapy (ADT) in all these patients who had PSA doubling time > 6 months Response to treatment was assessed with periodical PSA evaluation and a further PET in patients with biochemical increase.Toxicity was evaluated according to CTCAE vers.4.02.

Results: The median age was 71 years; the median follow-up was of 10 months (range 3-26) and the median PSA pre-SBRT was 1.1 ng/ml (0.43-2.8). A significant and persistent reduction of PSA was observed in 7/11 (63%) patients; 2 patients started with ADT for multimetastatic disease progression after SBRT; other 2 patients required a second salvage SBRT for metachronous nodal relapse after 8 and 12 months of biochemical control but one of them started palliative ADT for further disease progression. All patients with biochemical and clinical control disease had a pre-SBRT doubling time > 10 months. Acute and late toxicities greater than G1 were not recorded.

Conclusions: Despite the small number of patients and the short follow-up, our experience shows that salvage PET-guided SBRT is safe and effective in deferring the start of palliative ADT in selected low-volume and low biochemical kinetics mHSPC patients.

P108

STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN OLIGOMETASTATIC PATIENTS WITH CANCER OF THE PROSTATE

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Aims: To evaluate the outcome of patients (pts) treated with SBRT with or without androgen deprivation therapy (ADT) for nodal or bone recurrence after primary local treatment with External Beam Radiotherapy (EBRT) or surgery.

Methods: We retrospectively analyzed data of patients treated with SBRT for oligometastases at Niguarda Cancer Center between 2010 and 2017. All patients showed less than 3 lesions detected with choline PET-CT or MRI. Biochemical response was evaluated with PSA level variation between pre-RT and post-RT. Biochemical failure was defined as a PSA rising beyond pre-RT levels. PET imaging was performed only in case of biochemical failure to differentiate local from systemic failures.

Results: Thirty-six pts were treated on 45 metastatic sites: 27 pts (60%) on nodal metastases (NM) and 18 pts (40%) on bone metastases (BM). Median age was 76 years. Median PSA before SBRT was 2.48 ng/ml. Initial NCCN class risk was intermediate in 7 pts (19%) and high in 29 (81%). Androgen deprivation was added in 8 pts (22%) before SBRT, 18 pts (50%) were already receiving hormonal therapy and ten pts (28%) were without systemic treatment. Median dose was 30 Gy/3-5 fractions for BM and 36 Gy/3-4 fractions for NM, lower doses being delivered in previously irradiated volumes. All treatments were image guided (IGRT). Median follow-up was 44 months (range 4-86 months), with two pts (5%) lost to follow up. No significant acute or late toxicity was reported. A complete PET response was observed in 39 treated sites (87%), while in field progression or no response occurred at 6 sites (13%). Twenty pts (51%) showed a biochemical progression of disease, confirmed by PET imaging in all cases. Median time to biochemical progression was 12 months (range 3-85 months). Three pts (8%) died: two (5%) for systemic disease progression and one (3%) for other causes.

Conclusions: SBRT for oligometastatic disease due to prostate cancer is a safe treatment modality associated with a high local control rate (88% in our series). Further data are needed to identify patients who could benefit most from this treatment.

P109

STRONGLY HYPOFRACTIONATED RADIOTHERAPY TREATMENT FOR NON SPINAL BONE METASTASES: FEASIBILITY AND PRELIMINARY RESULTS

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Aims: To evaluate the feasibility, toxicity and preliminary results of strongly hypofractionated radiotherapy for non-spinal bone metastases

Methods: Patients with non-spinal bone metastases from different primary tumours were treated at our institution with a prescribed dose of 21 Gy with 7 Gy per fraction. For all patient the treatment was delivered using 3D conformal radiotherapy or intensity modulated radiotherapy with almost 5 coplanar fields or volumetric arc radiotherapy. Patients were treated in supine position using vacuum-locked or other customized devices. Local control was evaluated at least after three months after treatment completion by means of radiological exams, while pain responses assessed at the end of treatment and every three months thereafter. Acute toxicity (defined as toxicity <90 days) were reported and graded as per standardized Common Toxicity Criteria for Adverse Events 4.0 criteria.

Results: Between May 2016 and May 2018, 29 subjects (for 29 treated lesions) with non-spine bone metastases were treated. The mean age of patients at the time of RT was 62.7 years. The most common primary sites were lung cancer, breast cancer, prostate cancer and renal cancer (27.6%, 20.7%, 19.2% for both renal and prostate cancer respectively). The most common treated sites were the pelvic bones (89.6%). All patients with pain before RT, experienced a complete pain response. Among them, only 14/29 patients (48.3%) have been evaluated at follow up (median follow up 6.57months). Only 2 local failures were observed, with a local control rate of 85.7%. 6 patients (42.8%) experienced a complete response at the first imaging (PET/MRI), 4 patients (28.6%) a partial response and 2 (14.3) a stable disease. None patient developed acute toxicity in terms of pain flare up and nobody developed pathologic fractures.

Conclusions: Strongly hypofractionated radiation therapy is a feasible and tolerable treatment for non-spinal bony metastases. Longer follow-up and a better selection of patients will be needed to accurately determine response and late effects.

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IMAGE GUIDED STEREOTACTIC BODY RADIOTHERAPY IN METASTATIC PROSTATE CANCER

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Aims. In the last years the use of stereotactic body radiotherapy (SBRT) has increased in patients with oligo-metastatic prostatic cancer. The advent of image-guided radiotherapy (IGRT) makes possible to obtain tumour control and adequate safe profile, whereas the use of systemic therapy (hormonal or chemo-therapy) makes difficult to evaluate the effect of radiotherapy on local control. In this prospective observational monocentric study, avoiding any influence of systemic therapy, we assessed the role of IGRT in terms of local control and safety.

Materials and Methods: From April 2011 to June 2017, 51 patients with oligometastatic prostate cancer were selectionated; all the lesions were detected using choline PET/CT and no systemic therapy was administrated after SBRT. 6 weeks after SBRT and thereafter every 3 months patients were assessed measuring total PSA value; to identify relapse of illness a new Choline PET/CT was performed after PSA increase. The SBRT treatments were performed using 6-MV photons with flattening filter-free beams; the CT image slice was set of 1.25-mm. Target lesions (GTV) were identified using choline PET/CT images and Planning Target Volume (PTV) consisted of an isotropic 3 mm expansion of the Clinical Target Volume (CTV). Metastatic lesions were treated with 24 Gy as a single fraction or 27 Gy in 3 fractions (depending on tumour volume and proximity to critical structures as bowel or vessels). Before each fraction a cone-beam CT was performed for patient's set-up. Task group 101 of the American Association of Physicists in Medicine constraints were used. Primary and secondary endpoints of this prospective observational study were local control and safety related to IG-SBRT.

Results: 79 metastatic lesions were treated (33 bones and 46 nodes) from 51 patients; 29 were treated with 24 Gy as a single fraction whereas 50 with 27 Gy in 3 fractions. After a median follow-up of 18.5 months (range 3-103), only 2 lesions (1,58%) relapsed inside the radiation field (all located on the bone). The tolerance at the treatment was optimal (toxicities less than G2), excepted for one vertebral fracture.

Conclusions. IGRT is safe and can be considered as a valid therapy in patients with metastatic prostate cancer needing a long-lasting metastases control.

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN THE MANAGEMENT OF OLIGOMETASTATIC OVARIAN CANCER

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Aims: The objective of this study was to assess the role of stereotactic body radiotherapy (SBRT) in the treatment of distantly recurrent, oligometastatic ovarian cancer.

Methods: The hospital records of 40 patients with18 F-fluorodeoxyglucose [18F-FDG] positron emission tomography [PET] positive, distantly recurrent, oligometastatic ovarian cancer were reviewed. All these patients had a number of target lesions < 5, with largest diameter <6 cm. The treatment was delivered with a TrueBeam™ LINAC and RapidArc® technique, using 10 or 6 MV FFF beams. A total of 60 lesions were treated and lymph nodes represented the most common site of metastases, followed by liver, lung and soft tissues. Nineteen lesions were treated with one-single fraction of 24Gy and fourty one lesions received 27Gy, delivered in three fractions, depending on the ability to fulfill adequate target coverage and safe dose/volume constraints for the organ at risk with either regimen. Systemic chemotherapy before and/or after SBRTwas given to all patients.

Results: PET scan three months after SBRT showed a complete response [CR] in 33 lesions (55.0%), a partial response in 22 (36.7%), a stable disease in 3 (5.0%) and a progressive disease in 2 (3.3%). No lesions in CR following SBRT subsequently progressed. Overall acute toxicity occurred in 8 (20.0%) patients. The most common grade 1-2 adverse event was pain (n.10, 16.7%), followed by nausea and vomiting (n. 7, 11.7%). No grade 3-4 acute toxicities occurred, and no late toxicities were observed. Lesions with pretreatment mean PTV <15 mm3 had a higher CR probability when compared with those with higher uptake, (HR, 3.244; 95% CI,1.304-8.071; p = 0.011). Patients with lesions received 27Gy delivered in 3 fractions had a 2.234-fold higher risk of death compared with patients with lesions treated with a single-dose of 24Gy (p = 0.049).

Conclusions: SBRT seems to be a safe, effective, and minimally invasive approach for selected cases of oligometastatic ovarian cancer. The single-dose approach seems to be the preferred regimen, improving survival together with multiagent-chemotherapy. Further clinical investigations are necessary to determine dosing and fractionation schedules and selecting ideal patient to maximize efficacy and limit toxicity.

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CYBERKNIFE STEREOTACTIC RADIOTHERAPY FOR SPINAL METASTASES FROM RENAL CELL CARCINOMA. A RETROSPECTIVE EXPERIENCE

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Aims: Renal Cell Carcinoma (RCC) is usually considered a radio-resistant tumor. Data from literature demonstrated that alpha-beta ratio for specific RCC cell lines is low, confirming only a moderate sensitivity to RT. In this setting, use of Stereotactic Radiotherapy (SRT) to deliver high doses per fraction could increase tumor cell killing and improve local control of metastatic lesions located in critical sites. The primary objective of this study is to evaluate the efficacy of SRT performed with CyberKnifeR in terms of local control in patients affected by spinal metastases from RCC. Moreover, data about Pain relief in symptomatic patients and radiation-associated toxicity are reported.

Methods: Data about 21 patients with 39 spinal metastases from RCC, treated with CyberKnifeR robotic system radiotherapy between January 2015 and June 2017, were retrospectively reviewed. The total dose delivered ranged between 18 Gy and 30 Gy in in 3-5 fractions. Disease control was evaluated through CT scan performed every 3 months. Data about pain relief in symptomatic patients and radiation-associated toxicity according to CTCAE v 4.03 scale were collected and reported.

Results: Median follow up was 9.8 months (SD: 10.7; range 3-36.6 months). The mean age at RT was 63.5 years (range: 35–83 years). Sixteen out of 21 patients (16.2%) were symptomatic for pain at baseline. Local control was achieved in 19 patients (90%). Distant progression (defined as progression out of irradiated volume) occurred in 11 patients (52%). Average progression-free survival time after radiotherapy was 6.1 months (SD 6.1; range: 0.8-16.2). Pain relief was achieved in all symptomatic patients. Only one patient reported G2 acute gastrointestinal toxicity.

Conclusions: CyberknifeR robotic radiotherapy showed excellent results in terms of local control and pain relief in this population. Prospective data are needed to compare this treatment strategy with conventional radiotherapy.

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TYROSINE KINASE INHIBITORS AND SEQUENTIAL HYPO-FRACTIONED STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH LIMITED BRAIN METASTASES: SAFETY AND EFFICACY

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Aims: Hypo-fractioned stereotactic radiotherapy (HFSRT) and target therapies, like tyrosine kinase inhibitors (TKI), show an increasing role for treatment of brain metastases (BM) despite a limited literature. Association TKI-radiotherapy for BM is controversial; some studies showed efficacy and safety, while others failed to confirm that. In this study we analyzed toxicity and clinical outcomes in patients with BM treated with TKI followed by HFSRT.

Methods: From a sample of 34 patients (pts) with 1-4 BM treated with HFSRT between 2015 and 2018, a subsample of 6 patients who had received TKI were analyzed. HFSRT was delivered with 20-24 Gy (5-8 Gy/day) using Volumetric Modulated Arc Therapy technique. All 6 pts received TKI therapy before HFSRT. Timing between TKI suspension and start of HFSRT was registered. Toxicity using CTCAE v.4.3 scale was recorded at each follow-up visit; radio-necrosis and BM response were evaluated on brain MRI performed at 3 months after the end of HFSRT, every 3 months during the first year, thereafter annually. Progression free survival (PFS) and overall survival (OS) were calculated.

Results: A total of 10 BM from melanoma (4 pts), kidney (1 pts) and lung (1 pts) cancer were treated. Melanoma BM patients had received: Vemurafenib (3 pts) and Dabrafenib+Trametinib (1 pts); Gefitinib was administered in patient with lung cancer, Sunitinib in patient having BM from kidney cancer. Median time lapse TKI-HSFRT was 7 days (range 3-37); median follow-up was 4 months (range 3-23) and to date 5/6 pts (83.3%) are still alive. Maximum acute grade 3 toxicity was ataxia (1/6 pts). Thus far no severe late toxicity occurred; radio-necrosis was observed in 1 patient (16.7%) receiving Gefitinib and HSFRT. Three complete responses (CR, 50%), 1 partial response (PR, 16.7%), 1 stable disease (SD, 16.7%) and 1 local progression (LP, 16.7%) were observed. From the original sample of 34 pts, no-TKI patients presented: RC 13.7%, RP 31.8%, SD 22.7%, LP 31.8%. Mean PFS in TKI group was 12 weeks vs 22.8 (median 16, range 7-52) in no-TKI group; mean OS were 8 months (median 4, 3-23) and 11.8 (median 12, 3-28), respectively. No significant acute toxicity occurred in both no-TKI and TKI patients.

Conclusions: Our study seems to show good response, without increased toxicity in patients treated with HFSRT after TKI. Longer follow-up and larger sample are necessary in order to confirm this favorable trend.

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STEREOTACTIC–BODY RADIATION THERAPY (SBRT) IN OLIGOMETASTATIC OVARIAN CANCER: A PROMISING THERAPEUTIC APPROACH

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Aims: SBRT has been successfully used to treat oligometastases of several primary tumors, but few experiences have been described in patients with gynecological oligometastatic cancer, particularly in ovarian neoplasm. The aim of this study was to evaluate the role of this new radiotherapy modality in a series of oligometastatic ovarian cancer patients.

Methods: We retrospectively analyzed the outcome of patients affected by oligometastatic ovarian carcinoma of any histology and treated with SBRT in our Institution. Toxicities were graded according to Common Terminology Criteria for Adverse Events version 4.0. Tumor response was evaluated by CT/ PET and/or MRI, according to Response Evaluation Criteria in Solid Tumors (version 1.1).

Results: Twenty-six patients with 44 metastatic lesions (lymph nodes 63.6%, liver 31.8% and lung 4.5%) treated with SBRT between January 2011 and May 2017 were analyzed. Complete radiologic response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) were observed in 26 (59.1%), 9 (20.5%), 6 (13.6%) and 3 cases (6.8%), respectively. An objective clinical response (CR+PR) was observed in 35 (79.6%). The overall clinical benefit (CR+PR+SD) was 93.2%. After a median follow-up period of 28.5 months (range 6-86), 17 patients (65.4%) were still alive at time of analysis: 6 are without evidence of disease, 11 experienced a disease progression. Eight patients died of disease, one died because of an heart attack while being disease free. The median LC was not reached. One year- two year- and 5year-LC were 92.9%. Median PFS was 19 months, with one year- PFS of 69.3% and 38% at two year, 19% at 5 years. Median OS was 64.5 months, with all patients alive after one year, 92.7% at two year, 61.7% at 5 years. Five cases (11.3%) experienced G2 toxicity; most common adverse effect was nausea and vomiting (3 cases, 6.8%) followed by abdominal pain (2 cases, 4.5%). None of the patients had grade 3 /4 acute or late toxicity.

Conclusions: In conclusion, SBRT is a feasible and safe approach for selected cases of oligometastatic ovarian cancer, with satisfactory results in terms of LC and PFS.

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OLIGO-METASTASES AND OLIGO-RECURRENCES IN PROSTATE CANCER: WHAT TO TREAT?

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Aims: Oligo-metastatic/oligo-recurrences in prostate cancer (PC) can show al good response to local therapies delaying the use of systemic treatment, thanks to new imaging techniques (as multiparametric MRI and choline/PSMA- CT-PET) that have allowed to early detect it. In this study we compared two different philosophies of RT treatment for this setting of patients (pts) experienced in our Institute.

Methods: From October 2010 to April 2018, we treated 53 patients (pts) with node and/or bone recurrences from PC highlighted by functional imaging (by PSMA /CT-PET in 7 pts, choline /CT-PET in 40 pts, multiparametric MRI in 6 pts).Thirty five pts (8 in group1 and 7 in group 2) were hormonal escape. The recurrence site were: bone in 2 pts, nodal in 45 (pelvic in 24 pts, lumbar aortic in 8 pts, both in 13 pts) and both in 6. The number of metastases (mts) ranged between 1 and 7 (mean 2.5) for group 1 and between 1 and 2 lesion for group 2.Thirty-eight pts (group 1) were treated by IMRT-SIB-IGRT with Tomotherapy on regional node with prophylactic doses (range 51-54 Gy) and on positive nodes (range 66 to 70,5 Gy). Fifteen pts (group 2) were treated with targeted radiation therapy on lesions: 14 received IMRT -IGRT with Tomotherapy (Doses: 24-30 Gy/4-5 fractions) and 1 pt received LINAC based SBRT with TrueBream STx (Dose 18 Gy in single fraction).

Results: No toxicity > G2 (RTOG scale) was observed in both groups. All constraints for normal tissue were respected according to QUANTEC. The mean follow up was 38 mths (range 10-69) in the group 1 and 6,4 mths (range 5-17) in the group 2. In the group 1, 3 pts dead for progression disease and 2 were lost at follow up; loco-regional control (LRC) was 80%, LC was 95% and average time to recurrence was 16,7 mths (range 6-43); the site of recurrence was loco-regional in 5 pts, bone in 2 pts, both in 2 pts; 1pt developed liver and nodal mts, 1pt lung and nodal mts. In the group 2, LC was 100% and average time to recurrence was 3,71 months (range 1-8). The site of mts in this group was loco regional (pelvic) in 4 pz, 3 patient showed only a biochemical relapse.

Conclusions: Our preliminary data show better results in terms of time to recurrence adding extended volumes RT to only targeted recurrence RT, despite a similar LC and tolerance, suggesting that ablative treatments do not always turn in positive oncological results and that each case nedds a multidisciplinary evaluation

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STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR METASTATIC LIVER TUMORS IN OLIGOMETASTATIC OR OLIGOPROGRESSIVE PATIENTS

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Aims: It is still widely debated which is the ideal treatment for patients affected by liver metastasis, especially for patients not candidates for surgery. With the main objective to assess local control and toxicities after SBRT for secondary liver tumors, 12 patients treated from October 2013 to December 2017 were retrospectively analyzed.

Methods: Patients were evaluated at 1-3-6-9-12-18-24 months after the end of the treatment to assess local control and toxicity (according to CTCAE scale 4.03). Abdomen CT (21% of cases) and MRI with Gd-EOB-DTPA (79% of cases) were used to prospectively define the extent of Focal Liver Reaction (FLR). FLR was analyzed in relation to toxicities (AST, ALT, GGT, PLT) and dosimetric data in terms of isodose to better Conformality Index (CI).

Results: Patients and treatment characteristics were reported in Table 1. After a median follow-up of 21 months (6-32 months) the local control rate was 100% and median Progression Free Survival was 15 months (2-32 months). Recorded toxicity was mostly Grade 1-2 for all evaluated parameters, only 1 case of G4 GGT was registered at 6 and 9 months. FLR decreased in the follow up and sometimes disappeared. FLR resulted related to a mean isodose of 26 Gy (CI 70%), 35 Gy (CI 63%), 40 Gy (CI 54%) and 42,5 Gy (CI 54%) at 3, 6, 9 and 12 month, respectively.

Conclusions: Liver SBRT is an effective treatment, able to ensure high local control rates. Toxicity is acceptable in most cases. Extension of FLR decreases during follow up and is related to increasing isodose with a CI ranging between 70% - 54%. These data should be confirmed in larger series before using it to predict toxicities.

Table 1.

Patient	Age	IK	Primary	Volume PTV (cc)	Volume LIVER (cc)	DOSE (Gy)	FU (mesi)
1M	63	70	Oropharynx	36,14	1788	60 Gy, 3fr	20
2Ma	71	90	Colon-Rectum	12,26	1630	60 Gy, 3fr	21
2Mb				16,46		60 Gy, 3fr	
3M	71	70	Colon-Rectum	134,97	1806	48 Gy, 3fr	26
4M	73	80	Pancreas	27,33	1003	60 Gy, 3fr	24
5M	65	90	Colon-Rectum	15,17	1450	60 Gy, 3fr	24
6M	52	90	Lung	9,13	2337	48 Gy, 3fr	32
7M	63	90	Oropharynx	10,76	1189	60 Gy, 3fr	26
8M	85	70	Colon-Rectum	28,29	1297	60 Gy, 3fr	23
9M	77	80	Kidney	8,3	1035	60 Gy, 3fr	19
10M	61	90	Ovary	20,3	1331	60 Gy, 3fr	17
11M	84	80	Colon-Rectum	27,5	1450	48 Gy, 3fr	12
12M	54	90	GIST	35	1089	60 Gy, 3fr	6

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STEREOTACTIC BODY RADIATION THERAPY FOR THE MANAGEMENT OF LUNG METASTASES FROM SOFT TISSUE SARCOMA: LONG TERM RESULTS

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Purpose: Patients with lung metastases (LM) from soft-tissue sarcomas (STS) have been treated with surgery and/or chemotherapy in the last decades. With the improvement of the radiation therapy techniques, Stereotactic body radiation therapy (SBRT) has been included in the management of oligometastatic disease. Aim of the present study was to evaluate the outcome of patients with LM from STS treated with SBRT.

Methods: Endpoints of the present study were local control of treated metastases (LC), progression free survival (PFS), and overall survival (OS). We included in the analysis patients with ECOG Performance status 0-2, a maximum of 4 lung metastases unsuitable for surgical resection, resected or controlled primary tumor. Lesions were treated with a risk adaptive scheme and prescription doses were: 30Gy/1fr, 60Gy/3fr, 60Gy/8fr and 48Gy/4fr. All treatments were delivered with Volumetric Modulated Arc Therapy. Tumour response was classified according to EORTC-RECIST criteria version 1.16. Toxicity was reported according to Common Terminology Criteria for Adverse Events scale version 4.0.

Results: From February 2007 to December 2017 a total of 59 patients with 74 lesions was treated. The most common histologies were leiomyosarcoma (43%) and synovial sarcoma (25%). Nine patients (15%) were diagnosed with synchronoyus LM. Fifty patients had metachronous LM and median time to diagnosis of metastases was 36 months (range 6-86 months). With a median follow-up of 31 months (2-92 months), the 5-years LC rate was 96%. Rates of OS at 2- and 5-years were 70% and 63.8%, respectively. At last follow-up 37 patients (62.7%) were alive. No severe toxicity of grades III-IV was observed both in acute and late setting.

Conclusions: According to our results, SBRT can be considered an effective and safe approach for the management of LM in patients affected by STS. Prospective trials are necessary to clarify the selection of patients who can benefit from SBRT.

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STEREOTACTIC RADIOTHERAPY IN OLIGOPROGRESSIVE AND OLIGORECURRENT UROTHELIAL CANCER PATIENTS: A RETROSPECTIVE EXPERIENCE

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Aims: Patients affected by urothelial cancer often recur after local surgery, with distant metastases representing up to 90% of relapses. Metastatic disease is detected at diagnosis in 4% of patients. After relapse, few therapeutic options are available, with a median overall survival of 9 to 15 months. Highly selected patients with low burden of disease may benefit from local treatment of metastatic sites. In this setting Stereotactic Body Radiation Therapy (SBRT) could increase local control and improve patients outcome. We retrospectively reviewed data from patients treated with SBRT in our institution for metastases from urothelial cancer, to analyze efficacy and toxicity of this approach.

Methods: Data from clinical records of 19 patients treated in our institution since May 2011 to October 2017 with SBRT for oligometastatic recurrence after local surgery or oligoprogression during systemic therapy for urothelial carcinoma (< 3 metastatic lesions) were retrospectively collected. Simple descriptive statistics were used to analyze local control (LC), response rate, symptoms control, progression free and overall survival (PFS and OS), measured from the start of treatment to progression or death from any cause. Acute and late adverse events were reported according to CTCAE v 4.03.

Results: Nineteen patients were treated on 25 metastatic lesions; 5 of them received treatment on multiple sites. Median age at treatment time was 71 years. Primary tumor sites were bladder (78,9%), kidney pelvis (15,8%) or urethra (5,3%). Majority of patients had received radical surgical treatment of primary tumor. Only one patient was metastatic at diagnosis, and received surgery as a primary treatment. After an average follow up of 11.5 months, LC was achieved in 17 lesions (68%). Complete response, partial response and stable disease was reported 2 (8%),8 (32%) and 7 (28%) treated lesions, with an overall response rate of 40%. Of note, no local recurrence or progression was noticed during follow up in lesions with complete or partial response. Average overall survival (OS), was 13.8 months. Only 3 patients reported <G2 adverse events, consisting of asthenia, disphagia and nausea.

Conclusions: SBRT for local treatment of oligometastatic or oligoprogressive disease can be effective and safe in selected patients. Prospective studies are needed to find correct selection criteria and optimal dose and fractionation.

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ROLE OF ABLATIVE RADIOTHERAPY IN CRANIAL AND EXTRACRANIAL METASTATIC MALIGNANT MELANOMA

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Aims: Malignant melanoma (MM) is known to be a relatively radioresistant cancer. Systemic therapy and recently immune therapy have the main role in metastatic setting. For patients with advanced stage and metastatic disease, RT is highly effective in providing symptom palliation. In this study, we evaluated the SBRT/SRS and hypofractionated RT results in terms of local control (LC), and toxicity for metastatic melanoma patients.

Methods: Between September 2011 and April 2018, 24 pts (12 male, 12 female) with MM was treated by SBRT, SRS or hypofractionated RT on 84 metastatic lesions. Secondary tumor site was brain in 63% , bone in 6,5%, abdominal in 16,8%, lung in 7,8% and other in 5.9%. The median age was 52 years (range 27–81). 8 pts received immune therapy. Doses were selected based on tumor size and location, however it was prescribed in one up to 3 fractions to 70% isodose in 81% of lesions (68 lesions), in 3 fractions to isocenter in 7.1% (6 lesions) and in more of 3 fractions in 11.9% (10 lesions) . BED10 was greater than 110Gy and in only three case the BED10 was lower than 110Gy for tumor volume. PTV volume ranged between 1.3cc and 130cc (median 27.6cc). The VMAT treatment was delivered by 6MV Linac with multiple planar and co-planar arcs. Pts set-up and isocenter position were controlled before each fraction by CBCT. Clinical and radiological follow-up after treatment occurred at 3-month intervals. Toxicity was assessed by CTCAE score.

Results: The median follow-up was 6 months (range 1–24 months). Local control for MM was 89% at 3 months. Particularly, 10% of lesions had RC, 75% of lesions had RP with a reduction of 35% on size and 4% of lesions was stable but appeared necrotic. Nevertheless, 76.5% of pts had a PD in other sites. Local control was 84% at 6 months and 68% at 24 months. The pts who received immune therapy had the greatest overall survival. Treatment was well tolerated.

Conclusions: SRS,SBRT and hypofractionated RT achieved high local control with very limited toxicity, melanoma appears responsive to high Hypofractionated RT. In our study, the impact on OS was lowly because multi-metastatic state of treated pts. The interaction between radiotherapy and systemic therapy can improve the OS. Therefore, a multidisciplinary approach, with optimal systemic therapy combination, timing and schedule of RT fractionation, is necessary.

The results needed to be confirmed with a greater number of case and longer period of follow up.

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SALVAGE ELECTIVE PELVIC NODAL IRRADIATION (ENRT) COMBINED WITH FOCAL NODAL STEREOTACTIC BODY RADIOTHERAPY (SBRT) IN THE NODAL METACHRONOUS OLIGOMETASTATIC CASTRATION-NAIVE PROSTATE CANCER: A TWO-INSTITUTION EXPERIENCE

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Objective: Radiation therapy (RT) as salvage treatment for oligometastatic (≤5 metastases) pelvic nodal (OPN) relapses of prostate cancer (PCa) is promising in terms of local control with low treatment-related toxicity. In this report, we present our preliminary results in terms of early outcomes and toxicity data adopting the combination SBRT+ENRT on the pelvic nodal relapses after primary treatment for PCa. Methods:From May 2016 to April 2018, 12 patients (pts) with 15 isolated lymph nodes of recurrent prostate cancer were treated combining ENRT with SBRT on pelvic nodal relapses in two Italian Centers. pts features are summarized in Table 1. All pts underwent Choline-PET or PSMA PET/ CT to assess local failure. SIB schedula were designed to deliver 54 Gy (1.8 Gy/fraction(fr)) to the pelvic lymph nodals, 60 Gy (2 Gy/fr) to the positive nodes and, in six pts, 69 Gy (2.3 Gy/ fr) to the prostate bed too. The boost dose to positive nodes was designed to deliver in one session 10 Gy, according to a purely SBRT approach. The delivery technique employed was IMRT. The most critical organ at risk was the bowel bag (BB). To evaluate the total dose received by the BB, we converted to EQD2(alfa-beta 3Gy) the dose distributions of the single treatment phases and then summed them. For the resultant dose, we requested that the dose maximum (dose to a volume of 1 cc) was inferior to 63 Gy.For 9 pts, neoadjuvant ADT was administered for a median time of 3 months. Only 2 pts received adjuvant ADT for 6 and 12 months respectively. Routine Image-based patient position verification protocols foresaw daily online matching by CBCT. The acute and late toxicities were recorded using the RTOG/EORTC scale. Restaging with PET/CT was performed 3 months after the end of treatment.

Results: The median follow-up duration was 12 months (range: 3 to 24 months). The incidence of acute gastrointestinal (GI) toxicity of any grade were 18.2%, no late toxicity ≥ 2 was noticed. Biochemical response seems to be complete 3 months after the end of treatment, 8 patients underwent a restaging with PET-CT imaging with complete metabolic response.

Conclusions: Combined treatment modalities looks to be safe and effective in the treatment for OPN prostate cancer. These results may provide a basis for a larger phase II study to examine the role of the elective pelvic nodal irradiation combined with focal nodal SBRT in this population currently treated only with focal nodal SBRT.

Table 1. Patient characteristics.

Characteristic	Value
Age, yr	
Mean ± DS	71 ± 6
Median (range)	72 (67-80)
Primary treatment	
EBRT	1
Surgery	6
Surgery + EBRT	5
stage - *N*	
T2b-T2c	7
T3a-T3b	5
Gleason score	
6 - *N*	2
7 – *N*	6
≥8 – *N*	3
Progression-free survival mo	
<12	0
>12	12
PET imaging	
PSMA - N	3
Colina - N	9
Baseline PSA, ng/ml	
Median	0.9
≥ 0,5-1 - *N*	6
≥ 1 - *N*	6
Number of treated nodes	
1	9
2	3
≥3	0

SD = standard deviation; PSA = prostate –specific antigen, Yr=years; mo= months; N = number of patients, PSMA = prostate-specific membrane antigen.

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LOCAL CONTROL WITH STEREOTACTIC BODY RADIATION THERAPY FOR LIVER METASTASES

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Aims: Liver is common site of metastases. Recently the prevalence of oligometastatic patients is increasing. Surgical resection is the standard of care in metastatic liver tumors, however, the resecability rate is only 10-20%. Otherwise, radiofrequency ablation (RFA) or transarterial chemoembolization (TACE) may be adopted. Stereotactic ablative body radiotherapy (SABRT) allows to deliver curative radiation dose without radiation injury to the healthy liver tissue. The aims of this study is to report our experience with SBRT in secondary liver tumors.

Materials and Methods: In this retrospective study a cohort of 49 patients with 58 liver metastases were treated with SBRT at our institution. All patients had not been eligible for other local treatment options. The prescribed

doses were 22 to 54 Gy in 3 to 8 fractions, but these were modified according to the localization and size of lesions and tolerance of the adjacent normal tissue. To allow for dose comparisons, a biological equivalent dose was calculated. Local control and disease free survival were evaluated using Kaplan Meier analysis.

Results: The study included 49 patients with 58 liver metastases. Median age was 70 years (39-84 years). Colorectal adenocarcinoma (CRC) was the most common primary cancer (56.9%), followed by breast cancer and lung cancer (13.8% respectively) and other (15.5%). 79.6% of patients received prior chemotherapy. Median tumor volume was 20.5 mm (6-45 mm), median SBRT dose was 45 Gy (22-54 Gy) delivered in a median of 3 fractions [3-8]. At a median follow-up of 14.3 months (3-99 months) LC rates at 1-3 and 5 years was 72.3%, 69.6% and 55.7% respectively. Hepatic PFS at 1-3-5 years was 53.7%, 43% and 36% respectively. Extrahepatic PFS at 1-3 was 59.6% and 15.3%. There was no difference in LC based on histology of the primary tumor. The major pattern of failure was distant metastasis. There was no grade ≥3 toxicity.

Conclusions: Stereotactic body radiation therapy of liver metastases offers a locally effective treatment without significant complications.Further studies will be needed to compare the efficacies of SBRT with those of surgical resection or radiofrequency ablation.

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IMPROVED OVERALL SURVIVAL IN SELECTED COHORTS OF OLIGOMETASTATIC HNSCC PATIENTS TREATED WITH LUNG SBRT

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Aims: Our analysis aim to explore if SBRT to metastatic sites of head and neck squamous cell carcinoma (HNSCC) might improve the progression-free survival (PFS) in oligometastatic HNSCC patients. Secondary endpoints were local control (LC), overall survival (OS) and toxicity.

Methods: We retrospectively selected 17 patients affected by oligo-metastatic HNSCC treated between April 2013 and February 2017, at the Unit of Radiation Oncology. Inclusion criteria were the following: oligometastatic HNSCC with ≤5 metastatic sites,PS <= 2, FDG-PET/CT staging, histology confirmed through FNAB. Radiotherapy has be delivered using stereotactic body radiotherapy (SBRT) technique consisted of 45-60 Gy in 3-7 fractions. Primary end points was progression-free survival (PFS) in oligometastatic HNSCC patients. Secondary endpoints were local control (LC), overall survival (OS) and toxicity.

Results: Among the 17 HNSCC patients (1 women and 16 men; mean age 66,1 years) with lung metastatic lesion, 4 had larynx carcinoma (23,5%), 4 oropharyngeal carcinoma (23,5%), 4 hypopharyngeal carcinoma (23,5%), 2 oral cavity carcinoma (11,8%), 1 nasopharyngeal carcinoma (5,9%), 1 CUP (5,9%) and 1 squamous cell carcinoma of salivary glands (5,9%). p16/HPV status was tested only on 6 patients (4 negative and 2 positive). 5 patients were metastatic "ab initio", 7 patients presented an oligoprogressive disease while the remaining 5 patients had an oligorecurrent pulmonary disease. After a median follow-up of 33 months (range, 6-60 months),mean PFS after SBRT was 13 months. One-year after SBRT LC and OS were 90% and 100%, respectively. One-year LC after SBRT and OS were 71,5% and 92,3%, respectively. At Univariate analysis Overall survival (OS) was higher for patients without "ab initio" metastatic disease (P = 0,0019, 95% CI 44,380- 59,398), but this was not confirmed at multivariate analysis. PFS post SBRT was longer both at univariate and multivariate analysis for non smoker (p=0,04 and p=0,0438, respectively) and for patients who had primitive cancer of larynx (p=0,0007 and p=0,0263). SBRT was well tolerated, and no Grade ≥3 toxicity was documented. Grade 2 acute toxicity were fatigue in 2 cases and Grade 1 dyspnea in 1 case. We recorded only 1 case of late toxicity dyspnea G1.

Conclusions: Lung SBRT for selected cohorts of HNSCC oligometastatic patients is safe and feasible treatment providing an OS benefit.

P123

STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN OLIGOMETASTATIC PATIENTS WITH LUNG LESIONS

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Aims: Pulmonary parenchimal tissue represents a common site for metastatic seeding in most solid tumors. Surgical resection has been for several years the standard choice for patients with oligometastatic lung cancer. At present time, SBRT represents an alternative therapeutic option with low toxicity profile and high local control rate. The aims of this retrospective study was to evaluate efficacy and feasibility of SBRT in patients with pulmonary metastasis treated between 2009 and 2017 at our institution.

Methods: Oligometastatic patients with documented lung lesions were evaluated at our institution for SBRT. Sites of primary tumor, histology, size, and prescribed dose for each lesion was recorded. The prescribed dose was modulated according to location of the lesion and tolerance of the surrounding organs at risk: 54 Gy in 3 fractions for peripheral lesions, 60 Gy in 4 fractions for lesions near to the chest wall, 60 Gy in 8 fractions for central lesions. Treatment-related toxicity was recorded according to criteria of National Cancer

Institute (CTCAE v.4.03). Local control and metastasis free survival were evaluated using Kaplan Meier analysis.

Results: Between 2010 and 2017, 119 oligometastatic patients were treated at our institution, for 161 total lung lesions. The number of lesions treated for each patient ranged from 1 to 4. Median age was 71 years (38-88 years). Primary tumor was lung cancer in 40.4%, colon-rectum cancer in 33%, head and neck cancer in 8%, breast cancer in 6.2%, and other in 12.4% of cases. Median tumor volume was 12 mm (6-33 mm), The median value of BED was 140 Gy (range 80- 157). Treatment was well tolerated. Grade 1 pulmonary toxicity without clinical symptoms was recorded in 12.4% of cases. 2.4% of cases developed Grade 2 symptomatic pulmonary toxicity. No pulmonary toxicity of grade 3-4 were recorded. At a median follow-up of 14.8 months (3-93 months) Local Control rates at 1-2 and 5 years was 92.5%, 85.1% and 77.6% respectively. Most common pattern of failure was distant metastasis. MFS at 1-2 years was 51% and 31% respectively with a median of 10.2 months.

Conclusions: Stereotactic body radiotherapy is an effective therapeutic option in the treatment of patients with oligomestatic lung disease, with a high local control rate and low treatment–related toxicity profile.

P124

TREATING NODAL METASTASIS WITH CURATIVE INTENT: STEREOTACTIC BODY RADIOTHERAPY (SBRT) BOOST TO POSITIVE CHOLINE PET / CT LYMPH NODES BEFORE WHOLE PELVIS LYMPH-NODAL IRRADIATION (WPRT) FOR OLIGOMETASTASIZED PROSTATE CANCER (PCA) PATIENTS

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Aims: The purpose of this study is to evaluate the feasibility and toxicity of linear accelerator (LINAC)-based stereotactic body radiotherapy (SBRT) boost before whole-pelvic radiotherapy (WPRT) for oligometastatic prostate cancer (PCa) patients.

Methods: In this prospective, pilot study, consecutive oligometastasized PCa patients with nodal and bone metastasis (≤ 5 lesions) were treated using SBRT boost before WPRT in association with androgen-deprivation therapy. All patients were studied with Choline PET /CT before RT. The prescribed SBRT boost dose to pathologic lymph nodes was 10 Gray (Gy) , delivered in single fraction to have a better control of organ motion (bowel above all) and normalized so that the 80% isodose covers 100% of the PTV. Prescribed external pelvic RT dose was 50Gy in 2 Gy daily fractions. Prescribed dose to prostate was 80Gy with standard fractionation. Bone metastasis were treated with a dose of 3 x 7-10Gy. Biological effective dose (BED) to pathologic lymph nodes was 126 Gy (alpha/beta value=3). Gastrointestinal and genitourinary toxicity was assessed using the Common Terminology Criteria for Adverse Events version 4 (CTCAE v 4).

Results: Between June 2017 and May 2018, nine oligometastasized PCa patients with a total of 29 nodal metastasis were treated with whole pelvis lymph-nodal irradiation plus stereotactic boost on positive choline PET / CT lymph nodes. At a median follow-up of 4 (1-10) months , no grade 3-5 toxicity was observed. Acute toxicity was low and mainly associated to normofractionated treatment of prostate (rectal and/or urinary urge symptoms).

Conclusions: LINAC-based SBRT boost to positive choline PET / CT lymph nodes before WPRT for oligometastic prostate cancer is a feasible treatment modality with minimal toxicity . Further studies with a longer follow-up are needed to better evaluate late toxicity and local control.

P125

RADIOCHEMOTHERAPY AS A MULTIMODALITY APPROACH IN THE TREATMENT OF UNRESECTABLE CARDIAC ANGIOSARCOMA

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Aims: Angiosarcoma is the most common primary cardiac malignant tumor. Diagnosis can be delayed and, in most cases, distant metastases can be found at presentation. Prognosis is very poor, even after surgery and despite adjuvant treatment. However, radiochemotherapy (RTCT) can still play a very important role even in the unresectable disease, as we aim to show with the following clinical case.

Methods: We herein present the case of a 49-years-old man, good performance status, with a diagnosis of right atrial and ventricular angiosarcoma with multiple lung and liver metastases. The patient received 11 cycles of Gemcitabine (1000 mg/m^2) 1-8 q21, as first line therapy, with good response. Then, he underwent concurrent RTCT with weekly Paclitaxel 80 mg/m^2. For a better target definition, our simulation CT was associated with a cardiac MRI. Our CTV (Clinical Target Volume) included all the detectable mass; a further margin of 5 mm was added to obtain the PTV (Planning Target Volume). Dose was 50.4 Gy (1.8 Gy/fr in 28 fractions). We used VMAT (volumetric modulated arc therapy) in order to better spare the surrounding normal tissues and the uninvolved myocardium. Mean PTV dose was 50.1 Gy (D2% 102.2%, D98% 95.7% D95% 98.7%), with a mean dose to the heart of 26.7 Gy (mean heart – CTV dose was 20.6 Gy); left lung V5, V20 and mean dose were, respectively, 21.6%, 2%, 4.1 Gy; right lung V5, V20 and mean dose were, respectively, 55%,

12%, 9.9 Gy; liver V30 was 3% and oesophagus mean dose was 9.3 Gy; the maximum dose to the spinal cord was 17 Gy. RTCT was well tolerated, and we did not registered any significant acute toxicity. After that, the patient underwent further 6 cycles of Gemcitabine.

Results: In the follow-up, the patient had cardiac MRI at 3 and 8 months that showed, a reduction of the cardiac lesion and a local stable disease respectively. Despite the achieved local control, he had an early systemic disease progression. The patient died of respiratory failure 10 months after the end of RTCT (22 months after histological diagnosis).

Conclusions: According to our experience, RTCT with weekly Paclitaxel for patient with unresectable cardiac angiosarcoma, is a safe and effective multimodality approach, in order to achieve a good local control or at least to slow down the growth of the disease.

P126

PRIMARY BREAST DIFFUSE LARGE B-CELL LYMPHOMA (PB-DLCBL): A CASE REPORT

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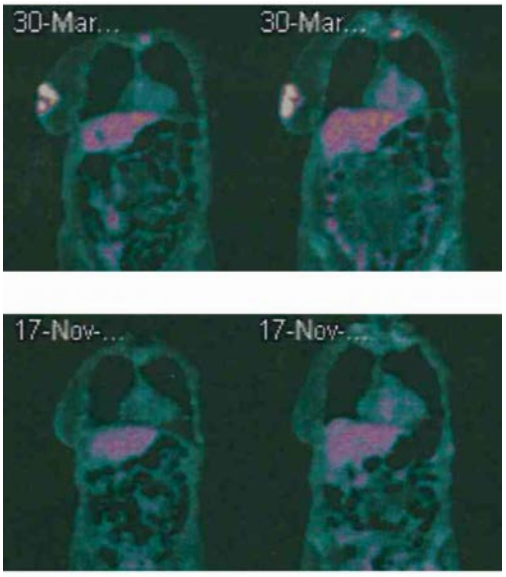
Aims: Primary breast lymphoma is a rare form of extranodal lymphoma, defined by the presence of a primary lesion within the breast with or without regional nodal involvement but no other extra-mammary sites of involvement. Extranodal lymphoma represents fewer than 0.5% of all malignant female breast tumors. It comprises different histologic subtypes, but diffuse large B-cell lymphoma is the most common. This type of extranodal lymphoma has a high risk of contralateral breast and central nervous system (CNS). Treatment of primary breast lymphomas does not include surgery, but is typically based on systemic chemotherapy with anthracycline-containing regimens, followed by consolidative radiation therapy to add therapeutic benefits. The introduction of anti-CD20 antibody Rituximab for the treatment of B-cell non-Hodgkin lymphoma has significantly improved the clinical outcome of these malignant diseases.

Methods: We are describing a case of patient affected by primary breast diffuse large B-cell lymphoma treated with radiotherapy in our institute. An 87 years old patient presented mass of the right breast discovered during her annual mammography. The needle biopsy of nodule showed the presence of diffuse large B-cell non-Hodgkin lymphoma. Clinical evaluation and staging workup by mammography, ultrasonography,TC total body, PET-CT (Figure 1), bone marrow biopsy and immunohistochemical biomarkers, showed limited right breast disease. The patient started on chemotherapy (R-CHOP protocol: Cyclophosphamide, Doxorubicin, Vincristine, Prednisone and Rituximab)) for a total of 8 cycles. Also, she had 4 intrathecal methotrexate (MTX) chemotherapy. PET-CT restaging confirms a complete metabolic remission (Figure 2). After chemotherapy she was treated with consolidative radiation therapy of mammary gland. Radiotherapy treatment was performed with LINAC 6-10 MV x-Rays, with three-dimensional conformal technique at doses of 3600 cGy, 200 cGy daily.

Results: She's alive and with no-evidence of disease 12 months after the completion of therapy. Restaging exams confirm complete remission of disease.

Conclusions: Primary breast lymphoma is a rare non-Hodgkin's lymphoma with limited data. The main clinical manifestation is painless mass, which is difficult to distinguish from breast carcinoma. The most common type is DLBCL. The introduction of Rituximab seems to improve the outcome of breast DLBCL. RT still adds significant therapeutic benefits for patients with primary breast diffuse large B-cell lymphoma in the Rituximab era. Further studies are needed to advance our understanding of breast DLBCL and optimise the treatment strategy.



Figures 1 and 2.

P127

LONG TERM FOLLOW UP IN A RARE CASE OF INTRACRANIAL CHONDROSARCOMA

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Aims: Chondrosarcoma is a malignant cartilage tumor that usually affects the axial skeleton, but in rare cases it may arise from the sella turcica. Only a few cases are described in the literature and there is no univocal consensus on the efficacy and safety of adjuvant radiation

treatment after surgery. This report presents a rare case of chondrosarcoma treated with craniotomy and adjuvant radiotherapy.

Materials and Methods: In February 1989 a 35-year-old man came to the emergency room for visual field disturbances with right hemianopia. Brain CT showed multinodular expansive lesion of 2 cm at the left suprasellar region. In March he performed craniotomy with macroscopic total excision. Histopathological examination revealed areas of cartilaginous differentiation with binucleated chondrocytes and large abnormal chondrocytes exhibiting nuclear atypia, nuclear hyperchromatism, nuclear and cellular pleomorphism within lacunae in a highly cellular connective tissue stroma. In view of these findings, the histopathological diagnosis was "Grade II Chondrosarcoma". Diagnosis was confirmed by a second opinion from a reference center. In consideration of the site of the disease that does not allow a safe microscopic eradication and of the young age of the patient, in May 1989 an adjuvant radiotherapy was performed with 2DRT 60 Gy in 30 fractions. Treatment was delivered by A10 Philips linac with 10 MV photon beam with two opposite lateral fields of 4 x 5 cm.

Results: Regular subsequent negative neuroradiological checks followed. Late sequelae were psychomotor retardation, mnesic disorders, hemianopia and right hemiparesis. Last Brain MRI with contrast and pituitary study (October 2017) compared with previous of September 2015 showed that the findings are stable and unchanged, outcomes of previous intervention in the left fronto-temporal site with parasellar and hypothalamic degenerative area, the peduncle appears thickened. Last neurological visit, on May 2018, shows attention deficit, Mini Mental State Examination 25.9 / 30, autonomous in the activities of daily living and low grade hearing loss.

Conclusions: The long (29 years) follow up shows that adjuvant radiotherapy, following tumour resection is effective and well tolerated allowing long-term local control of grade II chondrosarcoma. To our knowledge, in the literature no cases with such a long follow-up are reported.

P128

A RARE CASE OF PRIMARY INTRACRANIAL FIBROSARCOMA

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Aims: Primary central nervous system fibrosarcomas are rare tumors either deriving from sarcomatous transformation of a meningioma or arising de novo within the brain parenchyma. To our knowledge, only <50 cases have been reported or described in the literature until now and there is no clear consensus about treatment as well as outcome. This is a very rare case of primary intracranial fibrosarcoma with long-term follow up.

Materials and Methods: In February 2001, a 21-years old man entered the emergency room for loss of consciousness preceded by headache and vomiting. A brain MRI with contrast showed massive left frontal intraparenchymal hematoma with blood spread of the ventricular system, with no signs of ventricular tension. He performed, on urgency, craniotomy with hematoma evacuation, external ventricular derivation and removal of a bloody tumor mass. Histopathological examination revealed multiple tissue fragments consisting partly of spindle cell tumour with parallel beam distribution and high mitotic index and marked proliferative activity (70%). The immunophenotypic image showed unique positivity for vimentin and negativity for myogenic, glial, neuronal, epithelial, vascular and germinal markers. During post-operative re-evaluation the Tomo-PET with F18-FDG found a lesion in the right occipital region but no metastases or extracranial primary, the brain CT scan showed small hyperdense lesion after contrast in the left occipital region, and the brain RMI with contrast showed no lesion. In the hypothesis of cerebral metastases from sarcoma, in April 2001, the patient was submitted to a whole brain radiotherapy (WBRT) treatment with 50 Gy in 25 fractions. A second opinion of a center of reference (Mayo Clinic of Rochester) confirmed that the cerebral lesion was a primary tumor, modifying the therapeutic program. Therefore, after the first 46 Gy on the whole brain, in May 2001, 14 Gy were delivered in 7 fractions on the surgical bed using 3DCRT, followed by chemotherapy with Epirubicin and Ifosfamide.

Results: During the follow up, only post-RT panpituitarism with good clinical conditions were reported until May 2013, when progressive decay of cognitive conditions, with epileptic seizures and space / time disorientation occurred. Last brain MRI with contrast, performed in April 2017, is negative in terms of progression of disease.

Conclusions: Fibrosarcoma is a rare disease, surgery remains the primary treatment but local adjuvant radiotherapy confers long-term disease control and survival.

P129

RADIOTHERAPY (RT) AND CONCOMITANT TEMOZOLAMIDE (TMZ) IN RESECTED PATIENTS WITH GLIOBLASTOMA MULTIFORME (GBM): THE EXPERIENCE OF OUR INSTITUTION

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Aims: GBM is the most frequent neoplasm of central nervous system; surgery followed by cranial irradiation still remains the standard treatment. However, the outcome of patients (Pts) treated with such approach is

dismal with most of them having a survival time of less than 2 years. Temozolamide has shown to be effective and manageable when given to Pts with advanced stage of disease.

Methods: To assess efficacy and toxicity of TMZ given as concomitant treatment to 60 Gy and as maintenance therapy after RT in Pts with completely surgically resected GBM. From 1997 to 2017 295 Pts (male 180, female 115) with a median age of 59 years (range 24 – 75) were enrolled in this observational study. All Pts received cranial RT 60 Gy with daily fraction of 2 Gy and concurrent TMZ at dose of 75 mg/m² daily. Six weeks after the end of treatment, Pts underwent cranial MRI. The Pts that were still in CR received TMZ at dose off 200 mg/m²/daily for 5 days every 4 weeks for 4 courses.

Results: None of Pts enrolled progressed during RT and all received TMZ also al maintenance therapy. 25% Pts had progression disease during the maintenance therapy and died. After a median follow-up of 18 months the overall and progression-free survival rates were 70% and 55% respectively. Four patients had a survival of more than four years without progression of disease. Main toxicities were WHO grade 3 leukopenia and thrombocytopenia recorde in 10% of courses and WHO grade 2 nausea and vomiting occurred in 25% of courses.

Conclusions: TMZ given as concomitant to RT and as maintenance treatment in Pts with GBM has shown to be effective and well tolerated in adjuvant setting. Further follow-up and larger number of Pts will be required to define its concrete advantage on survival.

P130

ROLE OF BRACHYTHERAPY BOOST AFTER COMBINED CHEMORADIATION TREATMENT IN ANAL CANCER: A SYSTEMATIC REVIEW

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Aims. Chemoradiation is the primary treatment in anal cancer. However the optimal total dose and the role of a radiation boost is still unclear. No randomized trial nor systematic review have been performed to investigate the role of brachytherapy (BCT) as boost in anal cancer. Therefore, we performed this systematic review in attempt to define the role of BCT as a boost in anal cancer.

Methods. A systematic search of the bibliographic databases PubMed, Scopus and Cochrane library from the earliest possible date through August 31, 2017 was performed. The primary outcome was loco-regional control (LRC). The secondary outcome were colostomy free survival (CFS), overall survival (OS), disease free survival (DFS), and toxicity.

Results. Ten articles fulfilled the inclusion criteria. All the studies had retrospective design. All studies were classified to provide a level of evidence graded as 3 according to SIGN classification. Five year LCR, OS, CFS and DSF ranged: 70-98%,66-85%,61-86%,63-82%, respectively. The toxicity was acceptable. Acute toxicity ≥ G3 ranged from 2% to 42%. The most frequent were proctitis (range 15% - 42%), skin toxicity (range 1.4%-2%), and diarrhea (range 1.4%- 6%). Severe late (≥ G3) toxicity ranged from 1.1% to 8%. The most frequent toxicities were radionecrosis (range 2%-8%), incontinence (4%) and rectal bleeding (2.6%).

Conclusions. Chemoradiation is the cornerstone of treatment in anal cancer. Evidences from studies regarding the role of BCT boost in anal cancer is low. Further studies should investigate the optimal radiation dose and the number of fractions.

P131

AN EXTERNALLY VALIDATED (TRIPOD TYPE 3) NOMOGRAM FOR RESPONSE PREDICTION USING IMMUNE INFLAMMATION INDICATORS IN ANAL CANCER PATIENTS TREATED WITH CONCURRENT CHEMO-RADIATION

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Department of Radiation Oncology, University of Turin, Italy; Department of Medical Oncology, ASL Biella, Italy; Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRST IRCCS, Meldola, Italy; Department of Radiation Oncology, Centre Hospitalier Régional Universitaire 'Jean Minjoz, Besancon, France; Modena Cancer Center, Department of Oncology/Hematology, University of Modena and Reggio Emilia, Italy

Aims: In anal cancer, there are no markers nor other laboratory indexes able to predict prognosis and guide clinical practice for patients treated with concurrent chemo-radiation (CT-RT). In the present study, we retrospectively investigated the influence of immune inflammation indicators on treatment outcome of anal cancer patients undergoing concurrent (CT-RT).

Methods: All patients had a histologically proven

diagnosis of squamous cell carcinoma of the anal canal/margin treated with CT-RT according to the Nigro's regimen. Impact on prognosis of pre-treatment systemic index of inflammation (SII) (platelet x neutrophil/lymphocyte), neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were analysed. A nomogram was created to predict for response/non-response to treatment based on immune inflammatory indicators and clinical factors. The nomogram was then externally validated on a different set of anal cancer patients, treated at different Institutions.

Results: A total of 161 consecutive patients treated at 3 Italian Institutions was available for the analysis. Response to treatment was the single most important factor for progression-free survival (PFS) and overall survival (OS). At univariate analysis, a higher SII level was significantly correlated to lower PFS ($p<0.01$) and OS ($p=0.046$). NLR level was significantly correlated to PFS ($p=0.05$), but not to OS ($p=0.06$). PLR level significantly affected both PFS ($p<0.01$) and OS ($p=0.02$). On multivariate analysis pre-treatment SII level was significantly correlated to PFS ($p=0.0079$), but not to OS ($p=0.15$). We developed a logistic nomogram using SII, nodal status and pre-treatment haemoglobin levels as variables to predict the chance to respond/not respond to treatment. The nomogram was then externally validated on a cohort of 147 anal cancer patients treated in Italy and France. Results showed a good predictive ability with a C-index of 0.74. An online available calculator (ARC: Anal cancer Response Classifier) was also created.

Conclusions: The low cost and easy profile in terms of determination and reproducibility make SII a promising tool for prognostic assessment in anal cancer patients treated with concurrent CT-RT.

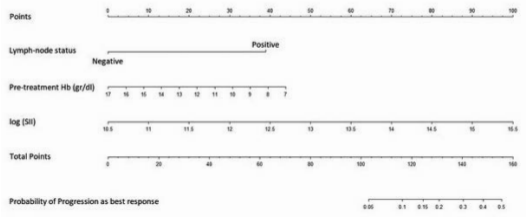

Figure 1.

P132

POSTOPERATIVE RADIOTHERAPY IN HIGH RISK THYMOMAS: SAFETY AND OUTCOMES AT 5 YEARS MEAN FOLLOW –UP. OUR EXPERIENCE

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Aims: To date the role of adjuvant radiotherapy (ART) in the treatment of resected thymomas remains still controversial. Stage , histology and margin status are the most important prognostic factors to advise ART although there is a cost to pay in toxicity. Herein we report our single institution retrospective experience .

Materials and Methods: From 2004-2017 34 consecutive patients (pts) with histologically proven thymoma were treated by ART at our institution.ART was prescribed in pts with at least one of these unfavourable prognostic factors: pathological stage III, IVA (Modified Masaoka staging system) , margins status (R close, R1 , R2), histology as B3 and C. Neoadjuvant chemotherapy (CT) was given to 6 pts in order to achieve an optimal resection while adjuvant CT in 4 pts was advised. All pts were treated with three dimensional conformal radiotherapy (3D-CRT). The mean delivered dose was 50 Gy (45-60 Gy) to the surgical bed or residual mass . Statistical analysis with log rank test and Kaplan-Mayer to evaluate Overall Survival (OS), Distant Metastasis Free Survival (DMFS) and Local Relapse Free Survival (LRFS) were applied. Pearson's covariance for multivariate analysis was conducted.

Results: Median follow-up time was 5 years (1-10 yrs). The 5 yrs OS was 87%; DMFS was 90.3% with the DMFS mean time of 8.8 yrs .LRFS was 90% with the LRFS mean time of 9.1yrs .At χ^2 test analysis, OS was related to R2 resection ($p = 0,02$),neoadiuvant and adiuvant CT ($p = 0,003$). For local relapse predicitve factors were stage T3/T4 ($p =0,03$), dose < 50 Gy ($p =0, 03$), R2 resection ($p = 0,002$) and neoadiuvant and adiuvant CT ($p < 0,001$) For distance relapse, predictive factor were neoadiuvant and adiuvant CT ($p = 0,03$). The multivariate analysis confirmed the results of univariate analysis for OS: R2 resection ($p = 0,022$), neoadiuvant and adiuvant CT ($p = 0,002$). For local relapse predictive factors were stage ($p=0,025$), dose < 50 Gy ($p=0,025$) and R2 resection ($p = 0,02$). Acute toxicity was dysphagia in 70% of pts mainly as G1 according to the CTCAE v.4.03. Late toxicity was an asymptomatic pulmonary fibrosis radiologically detected in 50% of pts, 1 pt developed a cardiac toxicity.

Conclusions: Adjuvant radiotherapy achieved good local control and showed an acceptable toxicity prophile in high risk resected thymomas.

P133

ADJUVANT RADIATION THERAPY (RT) HAS A ROLE IN PATIENTS AFFECTED WITH PRIMARY G2 INTRATESTICULAR LEYOMIOSARCOMAS?

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Aims: Primary intermediate grade intratesticular leyomiosarcomas, are extremely rare infact in the last 20 years at our institution we have only 1 case. The therapeutic approach usually is radical ochiectomy;however, the optimal local and systemic treatment remains debated. Our purpose was to evaluate efficacy and tolerability of radiotherapy (RT) after surgery in a patients trea-

ted at our Institution.

Methods: A 80-year old-man, with a history of resected testicular carcinoma, presented a right testicular mass (8,3x7,5 cm in size). Biopsy showed a primary G2 intratesticular leyomiosarcoma. He undergone a right radical inguinal orchiectomy and adjuvant RT was performed with a conformal technique. The patient received a total dose (DTF) of 50,4 Gy in 28 fractions,and boost of a DTF of 10Gy in 5 fractions in October 2012. The primary endpoint was local control,secondary endpoints were disease free survival(DFS), overal survival (OS) and toxicity.

Results: During RT toxicity profiles was good, no acute skin toxixity in the inguinal fold. No metastasis or recurrence was observed in the 13 months follow-up of the patient. No late toxicity were noted. The patient died of other causes.

Conclusions: The optimal adjuvant management of paratesticular leyomiosarcoma is still uncertain. Looking at the literature, it seems that adjuvant Rt can improve locoregional control and DFS without additional late toxicity.

P134

CHEMORADIATION IN UNRESECTABLE BILIARY TRACT CANCER: A SYSTEMATIC REVIEW

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Aims. To present a systematic review on efficacy and toxicity from concurrent chemoradiation (CCRT) in unresectable biliary tract cancers (BTC).

Methods. A systematic review of literature published within the last ten years (1 January 2007- 31 December 2017), based on PRISMA methodology and using PubMed was performed. Only articles reporting patients outcome in terms of toxicity and/or overall survival (OS) or progression-free survival (PFS) after external beam radiotherapy (EBRT) plus CCRT, with or without other treatments, were analyzed. Only studies of patients with diagnosis of unresectable cholangiocarcinoma, including intrahepatic, extrahepatic, and gallbladder neoplasm were considered.

Results. Six eligible studies were included reporting data on 195 patients. Median follow-up ranged between 9.4 and 27.7 months (median: 16 months). Four studies were prospective phase II trials and 2 had a retrospective design. Different EBRT techniques and CT schedules were used while only in one study a brachytherapy boost was delivered. Tumor Response evaluation was reported in 3 studies using the RECIST criteria in 2 studies. Grade ≥ 3 acute toxicity (hematological or gastrointestinal) ranged between 0.0 and 55.6% (median: 37.0%). One study reported 30.0% gastrointestinal grade ≥ 2 late toxicity. PFS ranged between 6.8 and 10.5 months (median: 7.5 months) in 5 studies. OS ranged between 9.6 and 13.5 months (median: 13 months) in 5 studies.

Conclusions. CCRT remains a reasonable treatment option for locally advanced BTC, providing results comparable with the ones of standard CT, particularly in terms of OS. Considering the progressive advance of modern EBRT techniques, further improvement of these results can be expected. Therefore, clinical trials aimed at CCRT optimization and improvement of combined modality treatments based on CCRT plus systemic therapies are warranted.

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A POOLED ANALYSIS OF COMBINED CHEMORADIOTHERAPY FOR UNRESECTABLE BILIARY CANCER

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Aims: To retrospectively evaluate the outcome of a combined modality treatment based on chemoradiation (CRT) +/- brachytherapy (BRT) in a pooled analysis of 3 series from different institutions of patients with unresectable biliary cholangiocarcinoma (CC).

Methods: Data of patients with intrahepatic CC (ICC), Klatskin's Tumor (KT), distal extrahepatic CC (ECC), and gallbladder cancer (GBC) diagnosed from 1991 to 2017 were retrospectively analyzed. The treatment was mainly based on concurrent chemotherapy (CT) plus external beam radiotherapy (EBRT), +/- BRT

boost. The Kaplan-Meier method was used to calculate survival curves in terms of overall survival (OS). Log-rank test was used to compare survival curves.

Results: Seventy-eight patients were included in this analysis (59%: males; 41%: female; median age: 67 years). A minority of patients (7.7%) were treated for disease recurrence after surgery. According to TNM, 77.6% of patients had a T stage > 3 and 79% of patients were treated with CRT while 21% received EBRT followed by sequential CT. Median EBRT dose was 50 Gy (range: 16-75 Gy) delivered with conventional fractionation. CT was based on Gemcitabine or 5-Fluorouracil. BRT was prescribed to 50% of patient with a median dose of 7 Gy. Reported Grade ≥ 3 acute GI and hematological toxicity were 13.0% and 7.9%, respectively. No other severe acute toxicities were reported. One- and 2-year OS were 60.1% and 29.2%, respectively (median: 15 months), while 1- and 2-year PFS were 42.4% and 7.8%, respectively. Analyzing the impact of BRT on OS, 24-month OS was 22.9% for the BRT group, and 36.2% for EBRT alone, while at 48-months, OS was 9.8% for the BRT group, and 0.0% for the group without BRT (p = 0.68).

Conclusions: Combined modality treatment (CRT + BRT) in unresectable biliary cancer was associated with acceptable toxicity and OS almost comparable to the actual standard (CT). Further prospective studies are needed to improve outcome by using advanced treatment techniques and innovative combined modality therapies.

P136

VMAT-BASED STEREOTACTIC RADIOTHERAPY IN A PATIENT AFFECTED BY ADRENAL CARCINOMA LOCORE-GIONAL RELAPSE AND PERITONEAL MULTIPLE LOCALIZATIONS

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Aims: Evaluation of feasibility of radiotherapy treatment in a pararenal relapse of mixoid adrenal carcinoma and peritoneal metastasis.

Methods: A 44 years-old patient with a diagnosis of adrenal carcinoma of the left adrenal gland, in February 2017 underwent surgical resection of the adrenal lesion. In august 2017 18FDG CT-PET examination showed hy-perfixation of surgical bed, plus left pararenal nodules, close the square of the loins and psoas left muscles. In november 2017 new surgical procedure was performed to remove recurrence in the adrenal loggia. A CT scan of the abdomen with a re-evaluation score, performed in December 2017, documented an increase in peritoneal lesions. The patient came to our observation in February 2018 for radiotherapy evaluation. Indication has been given to treat the tumor-bed recurrence and the three peritoneal nodules by stereotactic radiatiotherapy, using VMAT technique, with a total dose of 25 Gy in 5 fractions to each lesion. A treatment plan using a volumetric modulated arc therapy technique was developed using TPS Monaco 5.11.02, by two 360° arcs with a single isocenter and photon-beam energy of 6 MV. The total dose was prescribed at the mean dose of PTV. The treatment was delivered using a VERSA HD linear accelerator equipped with multi leaf collimator Agility. Daily IGRT control was performed during treatment. OARs were represented by stomach, liver, right kidney, left kidney, small bowel, spinal cord.

Results: In the treatment planning evaluation, the coverage of the PTV and the dose constraints for the OAR were taken into account and all the established criteria were met. The only criticality found in the small bowel, because its mobility, could have received a higher dose than the one calculated. Daily IGRT execution was allowed to evaluate the correct dose distribution to the four PTVs, and particular attention has been turned to the position of the small bowel within the 12 Gy's isodose.

Conclusions: Thanks to the VMAT technique used for treatment with stereotactic radiotherapy, it has been possible to treat the tumor bed recurrence and the three peritoneal lesions simultaneously. During treatment, the patient presented no acute toxicity and the therapy proved to be safe.

P137

A LONG TERM ANALYSIS ON A LARGE PATIENT POPULATION WITH HIGH GRADE SOFT TISSUE SARCOMAS

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Aims: To evaluate clinical outcome of patients and to assess efficacy and safety of perioperative brachytherapy (BRT) plus postoperative external beam radiation therapy (EBRT) in a large population with high grade primary, recurrent or re-excised soft tissue sarcomas (STS) of extremities or trunk.

Methods. Two hundred eighty-nine patients treated

with surgery and perioperative BRT followed by adjuvant EBRT +/- chemotherapy (CHT) were retrospectively analyzed. One hundred and seven patients (37.02%) were treated for primary STS, sixty-six (22.84%) for recurrent STS, while one hundred and sixteen patients (40.14%) underwent BRT + EBRT after unplanned surgery and re-excision of the scar (radicalization) within a maximum of 3-6 months from the previous surgery. All patients underwent the same radiotherapy treatment. At the time of surgical excision, the Clinical Target Volume of BRT was defined by surgical, pathological and imaging findings. The delivered dose was 20 Gy. EBRT was delivered with 3D-technique using multiple beams, the median prescribed dose was 46 Gy to the Planning Target Volume, conventionally fractionated. Neoadjuvant and adjuvant CHT was used in patients with potentially chemosensitive histological subtypes. Univariate analysis was estimated according to Kaplan-Meier method and the log-rank test.

Results. 289 patients (median age 53 years, range: 9-86), treated from January 2000 to January 2011 for high grade primary, recurrent or re-excised STS were included in this retrospective analysis. Median follow-up was 81 months (range: 4-176). Thirty-nine patients (13.49%) developed local recurrences during FU and 36 (12.46%) died. Late (>3 years) local recurrences were recorded in 11 patients. A higher LC was recorded in patients treated for re-excised STS, compared to primary or recurrent tumors: 5-year LC were 94.3% vs 80.9% vs 78.7%, respectively, while 10-year LC were 94.3%, 77.2% and 65.6%, respectively; p: 0.002. Statistical significance was also achieved for overall survival: 5-year OS were 91.7%, 87.4% and 75.1% respectively for re-excised, primary and recurrent STS; p: 0.015.

Conclusions. The results of this analysis confirm those observed in literature showing that a combination of BRT and EBRT is able to produce high LC and OS rates. Prospective studies on the use of BRT/EBRT with uniform radiation doses and large patient population in the adjuvant setting of STS are still needed to define the optimal treatment schedule.

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BRACHYTHERAPY AND EXTERNAL BEAM RADIATION THERAPY FOR HIGH GRADE LATE RECURRENT SOFT TISSUE SARCOMAS

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Aims: To evaluate clinical outcome in patients presenting high grade late recurrent soft tissue sarcomas (STS) of extremities or trunk treated with surgery, perioperative BRT and adjuvant external radiation therapy (EBRT) +/- chemotherapy (CHT).

Methods: Sixty patients were retrospectively analyzed. Local recurrences occurred after a median of 41.3 months after the first surgery (range: 5-268 months). BRT delivered dose was 20 Gy (LDR or PDR technique). EBRT was delivered with 3D-technique using multiple beams. The prescribed dose was 46 Gy to the planning target volume (PTV), delivered over 23 daily fractions. Neoadjuvant and adjuvant chemotherapy was used in patients with potentially chemosensitive histological subtypes. Patient outcomes during FU as well as prognostic factors of patients outcome in terms of local control (LC), metastasis-free survival (MFS), disease-free survival (DFS) and overall survival (OS) were investigated. Univariate analysis was estimated according to Kaplan-Meier method and the log-rank test.

Results: Sixty patients (median age 53.5 years, range: 9-79), treated from January 2000 to January 2011 for high grade recurrent STS were included in this retrospective analysis. Median follow-up was 60.9 months (range: 15-114), starting from the second surgery, performed for the late local recurrence. Thirteen patients out of 60 (21.7%) relapsed during FU, fifteen (25.0%) developed metastases and thirteen (21.7%) died. One-year LC, MFS, DFS and OS were 93.2%, 90.0%, 86.4% and 100.0%, respectively. 5-year LC, MFS, DFS and OS were 76.7%, 74.3%, 62.2% and 74.6%. An improved 5-year DFS was recorded in patients with lower arm versus upper arm and trunk tumors: 82.2% versus 53.8% and 66.7%, respectively; p: 0.034. The worse results recorded in upper limb STS may depend on the greater difficulty of radical surgery in this dimensionally smaller and richer of neurovascular bundles district. No statistical difference according to histology was detected. Patients not receiving CHT showed an higher 5-year MFS, DFS and OS (p: 0.055, 0.091 and 0.070, respectively).

Conclusions: The combination of BRT and EBRT is able to obtain satisfactory results and should therefore be taken into consideration in case of recurrent tumors to ensure a greater local control compared to surgery alone. Prospective studies on combination treatment modalities in the adjuvant treatment setting of relapsing STS are still necessary to improve these results.

P139

PRIMARY MEDIASTINAL SEMINOMA: A CASE REPORT

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Aims: The Primary Mediastinal Seminoma (PMS) is a rare extragonadal germ cell tumour (EGCTs). EGCTs is mostly present in the medial side of the body including mediastinum and retroperitoneum. These tumors are considered to arise from the abnormal migration of germ cells during embryogenesis; a primary malignant mediastinal germ cell tumor is defined as occurring in a mediastinum location without evidence of gonadal mass detectable by diagnostic imaging examination. The incidence rate of these malignant diseases accounts for 1-4% of mediastinal tumours. Usually these tumours are slow growing and have limited potential to metastasis. This abstract presents a case of PMS investigating the role of radiation therapy .

Methods: A 43 year old male presented a history of progressive dyspnea, cough and dysphagia. On clinical examination there were signs and symptoms of superior vena cava syndrome. CT scan showed heterogeneously enhancing large mass (11 x 11,5 x 10 cm) involving the anterior superior portion of the mediastinum (Figure 1).

The ultrasound of scrotum was negative. PET-CT scan revealed unique abnormal uptake in the anterior mediastinum with cortical sternum erosion (Figure 2).

A biopsy was performed and the histological examination revealed a primary seminoma. The patient received chemotherapy comprising of bleomycin, etoposide and cisplatin once every 3 weeks for four cycles until May 2017. The patient tolerated chemotherapy well with no dose reductions. Restaging CT showed a good response with residual disease of 5,2 x 6,3 cm. The patient was treated with intensity modulated radiotherapy (VMAT) from June to July 2017. Radiotherapy treatment was performed with LINAC 6 MV X-rays at dose of 40 Gy in 20 fractions to the anterior mediastinum. Clinical target volume (CTV) included original tumour as seen on diagnostic PET-CT with 5 mm margin.Planning target volume (PTV) included CTV with a margin of 5 mm for set-up error.

Results: The post radiation PET–CT showed complete metabolic regression of the disease (Figure 3). Tolerance was good. For 10 months subsequent to treatment, to the present time, there has been no relapse of the tumour and the patient is leading a normal life.

Conclusions: The treatment course and a preliminary clinical-radiological follow up confirm radiation therapy in association with chemotherapy as a therapeutic option for PMS. Further follow up is needed to confirm local and distant control disease.

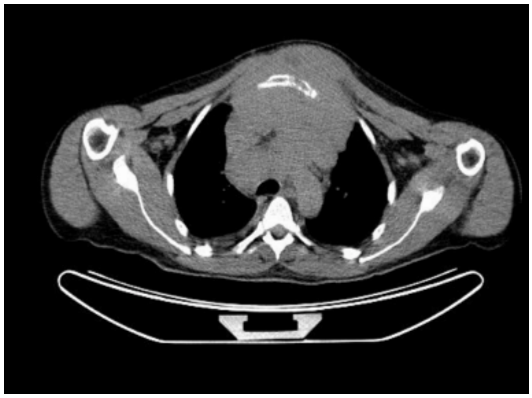

Figure 1.

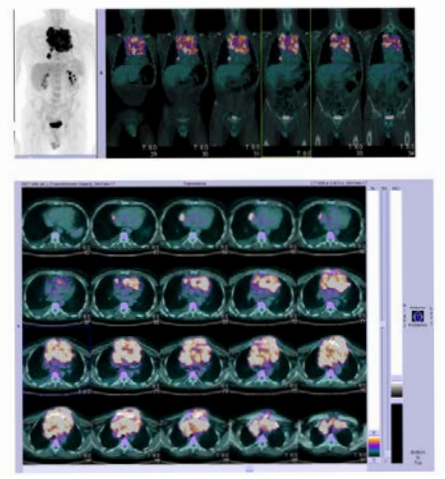

Figure 2.

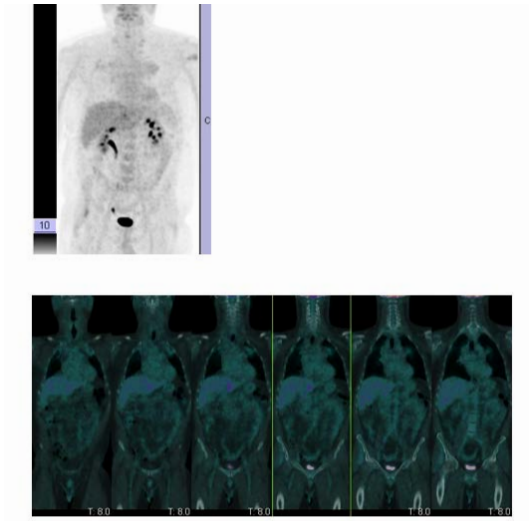

Figure 3.

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THE PROGNOSTIC ROLE OF HEMOGLOBIN LEVELS IN PATIENTS UNDERGOING CONCURRENT CHEMO-RADIATION FOR ANAL CANCER

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Aims: Concurrent chemo-radiation (CT-RT) is a standard therapy for squamous cell carcinoma of anal canal. Different clinical and biological factors may potentially affect outcome. We investigated the prognostic role of baseline hemoglobin (Hb) in a cohort of anal cancer patients submitted to CT-RT with 5-fluorouracil and mitomycin C.

Methods: Up to 161 patients with clinical stage T1-T4/N0-N3/M0 were treated. Response was assessed at 6 weeks and thereafter at 3, 6 and 12 months. Two different approaches were used:a)simultaneous integrated boost following RTOG 05-29 indications;b)first sequence of 45Gy/25 fractions to the pelvis followed by 9–14.4 Gy/5–8 fractions to the macroscopic disease. Primary endpoints were progression-free survival (PFS) and overall survival (OS).

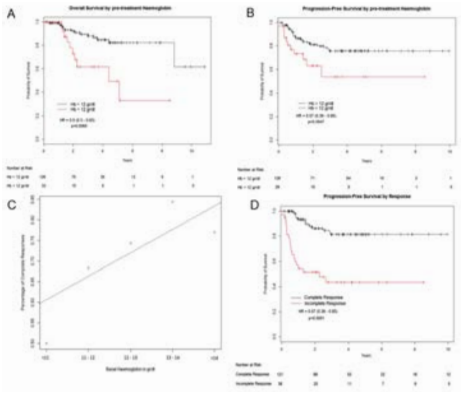

Figure 1.

Results: On multivariate analysis, pre-treatment Hb level had a significant correlation to OS (HR:0.53;95% CI:0.33–0.87; p=0.001), but not to PFS (HR:0.78;95% CI:0.53–1.15; p=0.12) Patients with pre-treatment Hb≥12 g/dl had 5-year PFS and OS of 82.2%, compared to 29.3% and 32.8% for those below the threshold (Figure 1A-B). The likelihood to achieve a complete remission increased by 5.6% for every single-unit (g/dl) increase in baseline Hb level over 11 g/dl (Figure 1C). Comparing outcomes according to response to treatment, both the 3- and 5-year PFS were 81.5% for patients achieving a CR compared to 43% for patients with incomplete response (Figure 1D). Three- and 5-year OS rates for the same response stratification were 93.1% and 85. 4%, 56.6% and 51.4%, respectively. On multivariate analysis, response to treatment had a significant correlation to PFS (incomplete vs complete response – HR:5.43;95% CI: 2.75–10.7; p<0.0001) and OS (HR: 6.96;95% CI:2.96–16.5; p<0.0001).

Conclusions: We showed that baseline Hb level is a strong indicator for poor response to CT-RT in anal cancer patients. A close clinical monitoring for incomplete response to treatment should be advised in patients with low pretreatment Hb. The hypothesis that the preservation of adequate Hb level during treatment may lead to a better outcome needs prospective evaluation.

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NEOADJUVANT RADIOTHERAPY IN SOFT TISSUE SARCOMAS: TIMING AND OUTCOMES

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Aims. The purpose of this retrospective study was to investigate a possible correlation between timing of radiation therapy (RT) and outcome in patients treated for primary or recurrent localized soft tissue sarcomas (STS) of extremities.

Methods. Sixty-one patients (median age 52 years), affected by primary (88.5%) or recurrent (11.5%), G1 (8.2%), G2 (6.6%) or G3(85.2%) grade STS (according to FNCLCC classification), were treated with pre-operative RT, limb-sparing surgery +/- chemotherapy (CHT). Patients received a dose of 4400-5000cGy to the target, delivered in 22-25 daily fractions. Only one patient received a dose of 4480 cGy/28 twice a day.

Treatment was delivered with multiple photons beams technique. Neoadjuvant and adjuvant CHT was used in patients with potentially chemosensitive histological subtypes. The study evaluated the impact of RT duration (range: 22-64 days, median: 35 days, with delays due to both clinical or technical reasons) and the time interval between end of RT and surgery (range 10-52 days, median 29 days).

Results. Median follow-up was 60.8 months (range 12-116). Two patients had local relapse after surgery and 5-year local control (LC) was 95.8%. Fifteen patients developed metastases with 72.9% 5-year MFS and 71.6% 5-year DFS. Six out of the 61 patients died, with 90.8% 5-year OS. No statistically significant correlation was found between RT duration and the interval between end of RT and surgery in terms of patients outcomes.

Conclusions. The management of non-metastatic STS involves the use of potentially curative surgery associated with RT to improve LC rates. In this series no correlations were found between RT duration and timing of surgery and LC rates, possibility to perform limb-sparing surgery, and patients outcomes.

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UNUSUAL SITE OF MALIGNANT PERIPHERAL NERVE SHEATH TUMOR (MPNST): A CLINICAL CASE REPORT

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Aims. This case analyzes the management of a Malignant Peripheral Nerve Sheath Tumor (MPNST) of head and neck (H&N). MPNST are very rare tumors with incidents of 0.001%in the population; H&N site is very uncommon with only 2-9% of all cases. Typically affect middle age people. Based on historically high rates of local recurrence and rapid disease progression, the prognosis for MPNSTs is generally poor despite aggressive therapy. MPNST were diagnosed based on a thorough history, physical and radiological examination and confirmed through biopsy or histopathological analysis. Usually the treatment method consisted of a combined-modality approach of wide-local surgical excision and adjuvant radiation therapy (RT) to aid in local control.

Methods: In April 2017,a55-years-old man,with no relevant past medical history,presented a retromandibular mass. Following the appearance of dyspnea the patient(pt) has performed checks;endoscopic examination revealed the presence of a mass extended from oropharynx to supraglottic larynx.In December 2017MRI scan confirmed the presence of mass 50x32x70mm extended from tonsillar pillar to cricoid and the presence of a right laterocervical nodes 12x6mm at II level. 18F-FDG-Pet-scan confirmed MRI findings with pathologic uptake only at oropharynx and supraglottic larynx, no pathologic uptake in lymphnodes. Pt was underwent to surgical resection and pathological examination showed MPNST grading 3 with positive margin. Adiuvant RT started after surgery.A simulation CT-scan was performed in the supine position with a thermoplastic mask.The radiation was delivered with arc-therapy. The clinical target volume (CTV) including the area of surgical resection.The planning target volume were defined adding 5mm to CTV. The doses prescribed were 66Gy in 33fractions(fr), 5fr/week from march to april 2018. At the end of RT Pt showed dysgeusia and grade 2 xerostomia.

Results. The first clinical follow-up was performed 20 days after the end of RT to evaluated acute toxicity,based on CTCAE scale. Pt presented only grade1 xerostomia and an improvement of dysgeusia.At the clinical evalutation there are not palpable lymph nodes. It was scheduled a reevaluation MRI after 2 months from the end of RT.

Conclusions. Based on literature review, our treatment raccomandations are:surgical strategy remains the mainstay of management of Pt with MPNST;adjuvant RT are recommended according to the risk of local and distant relapse based on residual disease after surgery, tumor size, grade.

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VERTEBRAL HEMANGIOPERYCITOMA: A CASE REPORT

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Introduction: Psueudomyogenic hemangioperycitoma (PHPC) is a soft tissue tumor, rare with aggressive biologic behavior found in adults, predominantly males. The tumor has been reported in various locations in the body, including the head, neck, chest wall, extremities, bones. In this report we present a case of PHPC localized in the L3-L4 vertebral body, not usual side.

Methods: A 64 year old man presented with history of fever, anaemia (hemoglobin 10.2) and lumbar pain during february 2017 to our Department of radiotherapy. Diagnostic workup including thoracolumbar Magnetic Risonance Imaging (MRI) and positron emission thomography (PET) has revealed L3-L4 lesions. In May 2017 he underwent to vertebral biopsy. Histopatologycal finding revealed PHPC. From 7 June 2017 to 19 July 2017 he underwent to radiotherapy (RT) on the vertebral bodies as above mentionated, with 6 MV-LINAC (total dose 55.94 Gy and daily dose 1.8 Gy).

Results: During the radiotherapy the patient had pain relief, absence of fever and hemoglobin level increased but two months later, new PET showed

uptake right emithorax, left iliac ala, left femur with progression disease, without uptake in vertebral bodies treated and he underwent to 2 cycles of chemotherapy (CT) with gemcytabina. After CT, the PET performed in October 2017 showed hot uptake to the sacrum, so the patient underwent to palliative treatment on this side, from 16 October 2017 to 20 October 2017 (total dose 12 Gy and daily dose 4 Gy) with partial reduction sacral pain but RT was stopped early for performance status decreased . The patient was lost to follow up.

Conclusions: In our case report the RT appeared to be of benefit in controlling of local pain.

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PRIMARY SQUAMOUS CELL CARCINOMA OF BREAST (PSCC): A CASE REPORT

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Aims: Primary Squamous cell carcinoma(PsCC) are normally not found inside the breast. Therefore PsCC of the breast is an exceptional phenomenon and the management of this type of desease is still debated. Aim of this report is clinical outcome assessment of a patient(pt) with PsCC.

Methods: We report a case of a 69 years pt with history of chronic thyroiditis, seizures, diabetis and hypertension that had mastostodynia and edema of right breast on December 2016. On January 2017 a mammography presented an irregular abnormality in a lower-inner quadrant in right breast which was classified as BI-RADS 4 and breast ultrasound releaved an hypoechoic lump of 8mm and adenopaty in right axilla of 17mm. Then a biopsy was performed with evidence of metaplastic squamous cell carcinoma G2 B5. The diagnostic work up to rule out other primary sites of SqCC included whole body CT and bone scan. On February 2017 the pt underwent to right quadrantectomy with lymphnode biopsy. Microscopic examinatation showed an irregular lesion of 8mm with negative margins. The tumor was classified as stage I according to TNM staging system (AJCC, 8thedition2017).Biological evaluation was negative for estrogen, progesterone receptors and HER2neu;Ki67was15%.Then the pt received 6 cycles of CMF. On July 2017 the pt was evaluated to our Department and underwent adjuvant RT. The dose prescribed to PTV was 50 Gy with 2 Gy daily and a boost of 10 Gy.The DVH for the lung was V20<13% for the right lung. The pt had acute G2 skin toxicity, according the RTOG scoring system. No late skin or respiratory toxicity was observed.

Results: Follow-up(F-U) evaluations consisted of history and physical examination approximately 3 months after completion of RT and then 3-6 months .F-U imaging typically involved a mammography. Tumor marker including CEA ,CA 15-3 and SqCC antigen were assessed during the fu, always staying in the normal range.

Conclusions: PsCC of the breast is a rare and aggressive disease often reported as treatment refractory.Rates of local failure after surgery for such patients have been reported to be as high as 30%. Our case shows that addition of RT after lumpectomy, allows to achieve a high local control without adding severe toxicity. The dose of RT used was the standard. After fu of 22 months, the pt is with no evidence of local or distant recurrence.

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PLEOMORPHIC XANTHOASTROCYTOMA IN ADULT OF THE PINEAL GLAND: CASE REPORT

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Aims: Pleomorphic xanthoastrocytoma(PXA) is a rare brain tumour (<1% of all astrocytic neoplasms) classified as a low grade(WHO II).It is tipically located in the temporal lobe and is exceptionally rare in the pineal gland(PG). Most PXAs have a good prognosis although an anaplastic variant and malignant potential have been described.Total resection is the treatment of first choice but subtotal resection(SR) has been associated with good long-term outcome.Radiotherapy(RT) and chemotherapy(CT) are reserved for recurrent disease(RD).We describe a rare case of PXA of the PG treated with RT for RD.

Methods: A 41-year-old woman presented a hystory of sudden onset of headache gradually worsened and subnormal visual acuity. MRI revealed a lesion localized to the PG extended to the quadrigeminal lamina and the midbrain and associated hydrocephalus. It was suggestive of pineoblastoma.Patient(Pt) underwent to endoscopic third ventriculostomy and SR. The hystological diagnosis was PXA WHOII (mitotic activity low: 1/20HPF,no necrosis, ki67:2%, BRAFv600mutation,no anaplastic features). Two months after SR,Pt presented urinary retention and visus reduction.MRI showed residual tumor. Following worsening of symptoms and hearing loss, MRI revealed increase in tumor size and RT was prompted. Pt underwent to RT with concomitant Temozolomide(TMZ). To improve the accuracy of tumor delineation, Planning CT (pCT) images were co-registration with MRI. Total dose delivered was 54 Gy in 27 fractions.Technique used was 3DCRT with energy of 15MV photons. Dose–volume histogram was examinated and target coverage was V95 95%. Constraints to organs at risk were respected.

Results: The treatment was well tolerated .Two months after RT,RMI showed slight increase of the lesion so TMZ (3 cycles) was resumed with dose dense scheduling.The further slight increase in tumor size was treated with Fotemustine interrupted after 2 cycles for severe toxicity. Currently Pt undergoes to radiological follow up and residual tumor remains stationary.

Conclusions: Our experience adds to literature a case of malignant evolution outlining once again the

potential malignancy of PXA.PXA has been demonstrated to manifest the V600E BRAF mutation in nearly 70% of all tumors.This discovery suggests a potential target with currently available BRAF inhibitors (vemurafenib) for recurrent PXA that is surgery, RT and CT refractory, as in the case of our PT.

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ADJUVANT RADIOTHERAPY IN RETROPERITONEAL SARCOMA A CASE REPORT USING MR-GUIDED IMRT

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Aims: This report wants analyse safety of new technology in radiotherapy (RT) for adjuvant treatment of retroperitoneal sarcoma (RPS). Surgery is the mainstay of treatment but adjuvant strategies are needed to decrease the risk of local recurrence. For RPS adjuvant radiotherapy is a challenge to adjacent radiosensitive normal tissues. MR guided IMRT can reduced the risk of radiation-induced side effects. This technique let to us make the Adaptive Radiation Therapy (ART).

Material and Methods: We report a case of a 62 years old woman presented with a mass in the space between inferior vena cava (ICV) and portal vein identified by CT. This mass measured 90 mm in the axial scan with a plentiful contrast enhancement in the arterial phase. The adjacent structures were compressed and displaced. The patient underwent to surgery and the histological exam described a Leimiosarcoma FNCLCC 2 pT2b. After multidisciplinary discussion no adjuvant treatment were proposed and the patient started an imaging follow up. Six years later CT performed a new mass in the same region measuring 70 mm in the axial scan, with a deep contact on ICV but a new surgery was impossible. So she underwent to RT. We prescribed 62.5 Gy in 25 fractions using static intensity modulated radiotherapy step and shoot with Cobalto photon beem MR guided. During treatment there were no gastrointestinal toxicity. After 45 days the lesion was 40 mm. So despite the high risk of near vesseles rupture she accepted a boost on the residual mass and received 15 Gy in 3 fractions, by the same technique. Relevated toxicity was G0. The calculated BED was (78+22.5) Gy with a/b 10. After 60 days the lesion was 34 mm and the patient started with systemic therapy. After 3 months she executed a CT and a PET and the lesion was 28 mm with a light positive storage of FDG. So she continued with only follow up.

Conclusions: New technology like RM guided IMRT in adjuvant treatment of RP sarcoma can decrease the risk of local recurrence and reduce inoperable mass, with a paltry acute toxicity to adjacent radiosensitive normal tissues. Using ART the treatment plan can be modified using a systematic feedback of measurements. ART intends to improve radiation treatment by systematically monitoring treatment variations and incorporating them to re-optimize the treatment plan early on during the course of treatment. So toxicity is low and efficacy is maxim.

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UNDIFFERENTIATED EMBRIONAL SARCOMA OF THE LIVER: A CASE REPORT OF A CHILD

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Aim and background: We describe a case of undifferentiated embryonal sarcoma of the liver (UELS) in a 7 years old girl treated with trimodality therapy in complete response after 2 years since surgery. UELS is an aggressive high-grade primary liver sarcoma with high metastatic potential. It found predominantly in the pediatric age group. It was first identified as an independent clinico-pathologic type of sarcoma in 1978. Abdominal pain is the usual presenting symptom. Radiographic examination demonstrates a big lesion of the liver. The tumors are large, single, globular, well demarcated and have multiple cystic areas of hemorrhage. Histologic examination shows a pseudocapsule. There is no standardized treatment except complete surgical resection for local control. Actually the introduction of modern therapy and multimodal treatment, including adjuvant chemotherapy and radiotherapy, have improved the long term survival rate.

Methods: We present a case of a child arrived in hospital with abdominal pain. Ultrasonography (US) showed an hypoechoic polisepted mass of 14x14 cm similar to a large cystic hepatic mass. CT scan evidenced an ipodense lesion of 12x12x15 cm with a rich contrast enancement. PET showed increased uptake of the metabolic tracer only in periferical zone of the lesion. Biopsy demonstred an UELS and followed CT evidenced a communication between the lesion and abdomen cavity. So she underwent to surgery with radical escission and histologic exam confermed diagnosis and Ki67 was 40%. Adjuvant chemotherapy was performed for 9 cycles (Ifosfamide, Vincristine and Adriamicina for 6 cycles and Ifosfamide, Vincristine and Actinomycin D for 3 cycles). In agree with AIEOP protocol she underwent to radiotherapy of whole abdomen. We prescribed 30 Gy in 20 fractions by 1.5 Gy using 6 MV photon beams with VMAT and IGRT. All dose constraints of thoracic and abdominal organs were respected. Kidneys median dose was maintained under 8 Gy,

heart V20 < 20% and lungs V20 < 10%.

Results and Conclusions: She reported vomit and diarrea G1 in treatment. During clinical follow up she was in healthy and periodic CT showed no evidence of recurrence from 2 years. In this case, postoperative RT seem have a role to prevent local recurrence with low toxicity. It should be necessary have more literature data to consolidate our experience.

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A CASE OF ANAPLASTIC GANGLIOGLIOMA IN A 62 YEARS WOMAN

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Aims: Anaplastic Ganglioglioma (AGG) is a rare central nervous tumor, representing approximately 1% of brain tumors. In literature there are no treatment guidelines due to the rarity of the disease. Histopathological grading criteria are still ill-defined. Surgery is considered the mainstay, but many patients experience recurrence or persistence and adjuvant treatments both chemotherapy and radiotherapy (RT) can be considered. No clear statements about radiotherapy indication, dose and volumes are reported in literature.

Methods: A 62 years woman underwent to brain MRI after 3 weeks history of episodic loss of memory and anxious status. The MRI showed a large lesion localized in deep temporo-occipital position involving the trigone wall and occipital horn. The lesion extended caudally and posteriorly to reach the calcarine convolution. Performance was ECOG 2/3. Surgery was performed and the pathological examination reported an AGG; immunohistochemical pattern was GFAP, ATRX, CD34 positive; MAP-2, p53, SMI32 partially positive; IDH1 and BRAF negative. A 1-month post-surgery MRI was performed for planning purpose and showed a contrast enhancement at the surgical cave and a non-univocal diffuse signal alteration on T2 sequences with no contrast enhancement but high CBV values at the perfusion study. The latter, after an extensive multidisciplinary evaluation, was interpreted more likely to be a residual low grade infiltrative component of the operated lesion then edema. Adjuvant radio-chemotherapy was indicated and started 6 weeks after surgery. GTV was defined as the contrast enhancement on T1 MRI sequence plus the iperintensity on T2 sequences (CTV volume 98 cc). A CTV=PTV was defined as GTV plus 3 mm. The prescribed dose was 56 Gy (2 Gy/die). Concurrently, temozolomide (75 mg/mq/die) was prescribed. An image guided radiotherapy protocol with daily cone beam CT was carried out.

Results: The patient has well tolerated the treatment, without breaks, and with CTCAE neurotoxicity G1. A reduction of the presenting symptoms was observed one month to the end of RT course, ECOG 2. A 2 months control MRI was scheduled.

Conclusions: In AGG the role of adjuvant therapy remains unclear because of its rarity. A gross total resection remains the aim of surgery adjuvant RT and chemotherapy should be employed to improve the outcome especially in no clear situation of surgical radicality. Functional MRI imaging can be crucial for the definition of the target delineation.

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TAILORED CHEMORADIATION FOR A CASE OF LOCALLY ADVANCED ANGIOSARCOMA OF THE NASAL VESTIBULE

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Aims: Angiosarcoma of the face is a rare neoplasm of soft tissues with no standard treatment established, which requires a multidisciplinary evaluation and tailored multimodal treatments. We report our results after a tailored chemoradiation (CTRT) approach for a patient with a locally advanced angiosarcoma of the nasal vestibule.

Methods: In February 2018 we evaluated a 76 years old male patient with a locally advanced and ulcerated angiosarcoma of the nasal vestibule. After first diagnosis in December 2015, patient started chemotherapy (CT) with Gemcitabine and obtained a partial remission of disease (May 2016) until deterioration of general status and local progression of disease, with the neoplastic mass externalized from the upper lip region. A multidisciplinary evaluation did not indicate radical surgery as local treatment. For this reason patient started CT with Epirubicin and a subsequent/concomitant palliative radiotherapy (RT). Imaging pre-RT showed the presence of an heterologous tissue with larger diameter of 30 mm in upper lip region, which involved nasal cavities; the neoplastic lesion was contiguous to the alveolar processes of maxillary bone with initial cortical erosion. After the simulation procedures, using a thermoplastic mask as custom immobilization system, RT planning was perfomed using Varian Treatment Planning System. RT total dose to PTV (Macroscopic disease + margins) was 32 Gy, with dose per fraction of 4 Gy.

Results: An adequate dose-sparing for normal tissues was obtained. No severe acute toxicity was observed during RT course. At clinical examination after RT we observed a sensitive reduction (>75%) of lesion's dimensions. Currently, patient continues Epirubicin with good tolerance, no RT-related toxicity and improved quality of life. A computed tomography of head and neck performed 3 months after RT reports the necrosis of central area of the treated lesion (current diameters: 25x15 mm).

Conclusions: Our experience confirms the great

importance of the multidisciplinary evaluation and tailored treatments for rare cancers. The proposed RT fractionation schedule, combined with systemic treatments, was well-tolerated and allowed to obtain a great improvement of patient's quality of life, which was the first aim of our multimodal approach. We need an extended follow up to consider the efficacy of our treatment on tumor local control.

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POSTOPERATIVE RADIOTHERAPY IN THE TREATMENT OF MALE BREAST CARCINOMA: A SINGLE INSTITUTE EXPERIENCE

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Aims: Reported single institution experience in rare disease.

Methods: We retrospectively reviewed clinical records of male patients, from November 2010 to February 2017, with invasive ductal or lobular carcinoma breast cancer who underwent postoperative radiotherapy.

Results: Nine patients fulfilled the criteria and were included in the study. Median age was 63 years (range, 50-81 years). Luminal A: 33.3% Luminal B HER 2 negative: 44.4%, Luminal B HER 2 positive: 11.1%, HER2 positive: 11.1%. All the patients received surgical treatment, and the surgical procedures were in : 66.7% mastectomy and lymph node sentinel biopsy and in 33.3% mastectomy and axillary dissection. The were staged : 33%pT1pN0, 56%pT2pN0, 11% pT4bpN1. Chemotherapy was delivered in 88.8% of patients. Hormone therapy was prescribed in all patients with positive hormonal receptor, Tamoxifene was the most common drug. The volume of radiotherapy treatment were 55.6% thoracic wall and clavear lymph nodes, and in 44.4% thoracic wall. The median dose/fractions was 46 Gy/23 fractions (range, 40.05 -50 Gy). Median follow up from surgery was 56 months (range,10-86 months). One patient relapsed distantly in liver and bone metastases and 1 patient relapsed in axillary nodes after axillary dissection and radiotherapy. Five year OS: 75%, DFS:73%,LRC: 88%. No acute and late ≥ Grade 3 toxicity was reported.

Conclusions: The incidence of male breast cancer is rare. This malignancy is mainly seen after 50 years, with relatively long disease course. Biological characteristics and clinical outcome are not different from those observed in females. Surgery followed by adjuvant chemotherapy, radiotherapy and hormone therapy are also in males the main therapeutics options.

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IS IT POSSIBLE TO OPTIMIZE THE PRESCRIPTION OF PET/CT AND MRI IN ANAL CANCER PATIENTS FOLLOW-UP?

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Aims: To analyze the pattern of prescription and the impact of PET/CT and MRI on the detection of local and distant relapse compared to physical examination alone during the follow-up of anal cancer patients (pts)

Methods: From 2007 to 2015, 104 pts received curative chemo-radiotherapy (CRT) (with the EORTC 22953 schedule). Of them, 68 received at least one PET/CT (n = 62, 91.17%) and/or MRI (n = 40, 58.82%) during their follow-up, and were included in this analysis. 30, 20, 17 and 1 pts were initially staged as Stage II, IIIA, IIIB and IV respectively (2002 UICC TMN classification). PET/CT or MRI were prescribed because of a suspicion of clinical relapse or because considered indicated in the follow-up. A total of 108 PET/CT, 55 IRM have been prescribed.

Results: Data obtained from a total of 535 follow-up visits were available (median follow-up: 39 months, range 5-120). Data about discordance between PET/CT or MRI and the clinical physical examination are expressed as number of exams. PET/TC: 74/108 (68.5%) PET were prescribed in pts with negative DRE. 6/74 (8.1%) PET/TC showed a distant relapse (Stage II and IIIB- median time of relapse 20.5 months). The CT of the PET was positive in all these 6 pts. 34/108 (31.5%) exams PET were prescribed because of a suspicious (n=13) or a positive clinical examination (n=21).Seven/34 (20.5%) pts showed signs of distant relapse, 5/34 (14.7%) of local relapse and 3/34 (8.8%) showed no response to CRT. MRI: 34/55(31.8%) exams were prescribed in negative DRE pts. 1/34 (5.8%) was positive (pt stage IV). 21/55 (38.2%) IRM were prescribed because suspicious (n=15) or positive clinical findings (n =6). All these pts presenting a positive DRE presented positive MRI.

Conclusions: In our experience, PET/CT and MRI

only rarely add useful information in the follow-up of anal cancer patients should not be always prescribed in the follow-up but should be reserved only to pts with more initial advanced T and/or N disease or with suspicious clinical findings.

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TOMOTHERAPY FOR EWING'S SARCOMA OF THE SPINE. MANAGEMENT OF A COMPLEX CASE

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Aims: Sarcomas that arise within the spinal canal are rare, especially within the pediatric population. We report a case of Ewing's sarcoma of the spine in an 8-year-old boy.

Methods: The patient presented at the end of June 2014 with back pain and paresthesia of the lower limbs Spinal MRI revealed an intra- and extra- spinal mass at D12-L1, extradural extending to the perivertebral tissues and vertebra and touching reaching the pleura and renal capsule. On 30/6/14 the patient was submitted to laminotomy, with removal of the endocanal component of the lesion. The initial histological diagnosis was poorly differentiated sarcoma, but was subsequently confirmed as Ewing's sarcoma. Chemotherapy was administered according to the ISG / AIEOP EW-1 protocol, the patient undergoing the first 4 cycles. During the 4th treatment cycle, he developed an allergic reaction to ifosfamide and then to cyclophosphamide. Restaging con RMN (10/10/14) e TC (16/10/14) with MRI (10/10/14) and CT (16/10/14) after the first 4 cycles revealed a significant reduction in the residual tumor in the right posterolateral part of the vertebra, pedicle and D12 lamina extending through the conjugate foramen between D11 and D12. Ruling out further surgery to remove the residual tumor, the patient was referred to us for radiation treatment to be followed by further intensified CT and autologous hematopoietic stem cell transplantation. He underwent RT from 3/12/2014 to 15/1/2015. A dose of 54 Gy in 27 fractions was delivered by TomoTherapy to the site of disease and dose constraints for all organs at risk were respected, with the exception of nausea and vomiting during the first few sessions resolved with Zofran 4 mg before treatment, tolerance to RT was very good.

Results: Following RT and subsequent CT, the patient underwent further surgery and is currently in complete remssion.

Conclusions: In this particular case, the use of TomoTherapy proved invaluable in delivering a dose of 54 Gy around the spinal cord, the maximum dose to the spinal cord did not exceed the established dose limit of 45 Gy

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PERIOPERATIVE RADIOTHERAPY FOR SOLITARY FIBROUS TUMORS

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Introduction: Solitary Fibrous Tumor (SFT) is very rare, may arise anywhere in the body, and can run an indolent as well as a malignant clinical course. Surgery is potentially curative, but the role of (neo)adjuvant radiotherapy (RT) is less well described.

Patients and Methods. A retrospective study was performed in our center, retrieving clinical data on patients (pts) receiving perioperative RT. Local control (LC) and overall survival (OS) were calculated from start of RT until local progression or death.

Results: Perioperative RT was prescribed to 11 pts (5 pre- and 6 postoperative, median total dose of 50.4 Gy in 1.8 Gy fractions, mitotic count >4 in 41%). Median FU was 60 months (up to 168 months). Resection status in the preoperative group was R0 in 3 pts, R1 in 1 pt and in 1 pt no surgery was performed for progression disease. LC rates after 1, 2 and 5 years were 96,4%, 92,1% and 87,1%, while OS was 96,4%, 92,1% and 82,1% respectively. The chance of an R0 resection after preoperative RT was much higher in the preoperative subgroup. Also the 5-year OS rate tended to be higher in the subgroup with R0 resection as compared to R1 resections.

Conclusions: While acknowledging all the caveats of retrospective cohort patterns of care analysis, this study with prolonged follow up suggests that, in resectable patients the addition of (neoadjuvant-)RT, is associated with a LC probability of 87,1% at 5 years. There is a significant higher rate of R0 resections after preoperative RT associated with a non-significant increase in LC rates. Prospective studies are warranted, but they are hampered by the extremely low incidence rates of SFT.

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PROGNOSTIC ROLE OF PRIMARY TUMOR AND RETROPHARYNGEAL NODAL GTVS FOR UNRESECTABLE NON-GLANDULAR EPITHELIAL SINONASAL CANCERS TREATED WITH IMRT AND CHEMOTHERAPY

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Aims: Malignant epithelial sinonasal cancers (SNCs) represent a very rare disease, with a wide heterogeneity of histology and prognosis. Among these, a group of non-glandular epithelial SNCs with similar outcome and challenging management can be identified. Although some clinical and radiological prognostic factors have been established, it is still unclear whether tumor volume (TV) and retropharyngeal nodes (RPN) metastasis could play a prognostic role in SNCs. Aim of this paper is to assess the impact of tumor and nodal volume on the outcome of a cohort of consecutive patients with inoperable epithelial non-glandular SNCs treated with definitive IMRT.

Methods: Primary tumour GTV (GTV-T), pathological neck nodes GTV (GTV-N), positive retropharyngeal nodes GTV (GTV-RPN) of 34 patients with epithelial non-glandular SNCs receiving IMRT to a total dose of 70 Gy with or without chemotherapy were retrospectively measured. We defined Total GTV (t-GTV) as sum of the three aforementioned GTVs, while GTV total-nodes (GTV-TN) included GTV-RPN and GTV-N. The GTV variables were analyzed in relation with Overall survival (OS) and Progression free survival (PFS). Survival curves were estimated by the Kaplan-Meier method and compared with the Log-rank test. We also estimated the crude cumulative incidence (CCI) of locoregional relapses (LR) only and CCI of distant metastasis (DM). The optimal volumetric cut-off points for OS or PFS were determined according to Hothorn et al. (statistically significant whenever a p-value below 5%).

Table 1. Survival endpoints for all population.

Endpoint	2-year estimate (%)	95% CI	5-year estimate (%)	95% CI
OS	55.9	41.5-75.3	42.9	28.9-63.8
PFS	47.1	32.9-67.2	37.3	24.0-58.2
*LR-CCI**	26.5	15.0-46.7	33.3	20.3-54.6
DM-CCI	26.5	15.0-46.8	29.4	17.3-49.9

OS: overall survival, PFS: progression free survival; LR: local relapse; DM: distant metastasis. CCI: crude cumulative incidence. * 3 dead patients who had developed the relapse at an unknown date were included in the LR-CCI estimation using their survival time in place of the relapse time.

Results: 13 patients had positive neck nodes, 9 patients had positive RPNs, 16 patients had neck and/or RFN involvement. The 2- and 5-year OS, PFS, LR-CCI and DM-CCI are reported in Table 1. GTV-T was significantly associated with decreased OS (p=0.003) and PFS (p=0.003). Moreover, patients with t-GTV smaller than 149.44 cm^3 had better OS and PFS than patients with higher volumes (p<0.0001 for both). Neck nodal metastasis impacted on OS and PFS (p=0.030 and p=0.033, respectively), but GTV-N did not (p=0.961; p=0.958). Retropharyngeal nodes metastasis was not associated with prognosis (OS: p=0.400; PFS: p=0.104). When GTV-RPN was added to GTV-N (GTV-TN), a relation with PFS (p=0.041) and a trend toward significance for OS (p=0.075) were found.

Conclusions: Our results show that tumor volume is a powerful predictor of outcome in SNCs. It could be useful to identify patients with worse prognosis deserving different treatment strategies.

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PROTON BEAM RADIOTHERAPY (PBRT) FOR EYELID POROCARCINOMA

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Aims: Porocarcinoma is a rare sort of skin cancer developing from sweat glands, specifically, it is a malignancy of the eccrine sweat glands. We use proton beam radiotherapy (PBRT) for a case of a old man who suffered from a porocarcinoma at the level of the left inferior eyelid. The prescribed total dose is 60 GyEBR with fraction of 15 GyEBR. No relevant effects have been reported and visual function is maintained. We believe that PBRT can become a valid alternative to surgery for this type of cancer for surgery.

Methods: We report the case of a 98 years old man who suffered from a histologically proven porocarcinoma at the level of the left inferior eyelid. The lesion showed a rapid growth in a two-month period. Because of his age and the cardiac comorbidities, surgery was excluded. There was no involvement of ocular structures and patient retained a good visual acuity. The objective of treatment was to reduce the eyelid swelling that produced a major discomfort, a moderate-severe painful symptomatology to the patient and some bleeding episode. Moreover, the rather tumultuous growth of the tumor mass would shortly cause a loss of visual function to the patient. PBRT was delivered at CATANA (Centro di AdroTerapia ed Applicazioni Nucleari Avanzate) Centre. Patient fixation is allowed by a thermoplastic mask fixed on a frame. We use a customized collimator packaged to take the entire lesion in its shape. We invited the patient to look at a point to create an optimal beam angle, in order to avoid unnecessary irradiation to organs at risk, and gaze angle to treat the tumor, while sparing as much as possible the cornea. The treatment is carried out in 4 fractions on 4 consecutive days. The prescribed total dose is 60 GyEBR with fraction of 15 GyEBR.

Results: At follow-up after 4 weeks the lesion was completely disappeared, with an acute conjunctivitis and eye swelling as unique acute side effects. The complete response was maintained after 14 months from the end of treatment. No relevant late side effects have been reported, except for an eyelashes loss and eyelid telean-

gectasia, visual function is maintained.

Conclusions: Sweat gland carcinomas are a rare cutaneous adnexal tumor with confusing histopathology and uncertain clinical behavior We believe that our experience can allow other patients to benefit from PBRT for the treatment of orbital and periorbital malignant tumors

P156

RADIOTHERAPY FOR EXTRACRANIAL SOLITARY FIBROUS TUMOR: STUDY FROM THE RARE CANCER NETWORK

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Aims: The aim of this study was to investigate the role of radiotherapy (RT) and of other potential prognostic factors in the management of extracranial solitary fibrous tumor (SFT).

Methods: Clinical records of 143 patients (pts) with SFT, treated from 1982 to 2012, were retrospectively reviewed in the framework of the Rare Cancer Network. Patients who had surgery (S) alone were compared to patients who received S and RT. Local control (LC), disease-free survival (DFS), metastasis-free survival (MFS) and overall survival (OS) were calculated with Kaplan-Meyer method and patient and tumor parameters were analyzed by univariate and multivariate analysis.

Results: In total 143/151 collected cases were suitable for statistical analysis: 82 females (57.3%) and 61 males (42.7%) with median age of 57 years (range: 18-87 years). Tumor sites included: 46 abdomen/pelvis (32.1%), 40 thorax (28.0%), 28 head and neck (19.6%), 17 spine (11.9%), and 12 extremities (8.4%). Eighty-nine out of 143 patients (62.2%) underwent surgery (S) alone, 41 patients (28.7%) S with pRT, 9 patients (6.3%) RT alone, and 4 patients (2.8%) received best supportive care. In the group of 130 operated patients (90.9%), S consisted of gross total resection in 108/130 cases (83.1%) and subtotal resection in 22 cases (16.9%); gross total resection was significantly more frequent in the group treated by S alone ($p=0.04$). RT was administered to a median total dose of 60 Gy (range 12-68.4 Gy) with daily fractionation of 1.6-12 Gy. In the group of 130 patients treated by S or S+RT, the actuarial LC rates at 5 and 10 years were 64.4%, and 30.17% after S alone and 82.9% and 71.8 after S+RT, respectively ($p<0.01$). DFS rates at 5 and 10 years were 56.5% and 23.8% after S alone and 74.8 and 49.9 after S+RT, respectively ($p=0.02$) and OS rates were and 90.5% and 69.7% after S alone and 82.5% and 61.6% after S+RT, respectively ($p=0.25$). The addiction of RT to S resulted in better LC and DSF at multivariate analysis. Other significant prognostic factors at multivariate analysis were: maximum tumor diameter for OS and MFS, and age for MFS. In the group of 41 patients treated with S+RT, total dose did not significantly correlate with LC or survival.

Conclusions: Surgery has the main role and was used in most of the patients. Despite of the unfavorable case distribution in terms of radicality of surgical resection, RT in addiction to S was able to significantly improve LC and DFS rates compared S alone.

P157

A VERY RARE CASE OF SCC OF THE TONSIL AND MIXED (SCC AND NEUROENDOCRINE SMALL CELL) METASTASES OF THE CERVICAL LYMPH NODES

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Aims: Report of a very rare case of SCC of tonsil and mixed SCC and neuroendocrine small cell metastases in the neck.

Methods: A 62-year-old male with right tonsil mass. In February 2014 the patient underwent right tonsillectomy and ipsilateral lymph node dissection. Histology revealed tonsil moderately differentiated (G2) squamous cell carcinoma, with very close margin pT1; 1/46 lymph nodes was interested by mixed squamous cell carcinoma (p16+, p63+) and small cell high grade neuroendocrine tumor (sinaptofisine +,CK7+, CK20-, p16+, p63-, Ki 67: 80%). Histology was revisited and confirmed by a reference centre. The patient underwent FDG PET/CT scan for staging that was negative. For the presence of the 'very close' margin, he was treated with radiotherapy on T and ipsilateral latero cervical lymph nodes and concomitant chemotherapy with Cisplatin (100 mg/m^2 every 3 weeks). Radiotherapy was performed with IMRT technique and 64 Gy were administered on tonsillar region (2 Gy/die) and 60.8 Gy (1.9 Gy /die) on ipsilateral cervical lymph nodes regions (level II-V). At the end of the treatment, he was followed with clinical exam every three months and PET/CT every year.

Results: After 4 years of follow up with no evidence of cancer, it was decided to perform a biopsy of a small abdominal mass (1.5 cm width), visible on CT scan near aortic carrefour, PET negative. Histology revealed the presence of low grade neuroendocrine tumor. The patient will perform in few days time a Dotanoc PET/CT for staging.

Conclusions: Even if in head and neck region rare cases of mixed, squamous and neuroendocrine tumor, were observed, mainly of the larynx, it was never described mixed tumors in metastatic lesions. Positivity of p16 in primary and metastatic lesions suggests that probably also primary lesion is of oropharynx, but, after 4 years of follow up, no evidence of loco regional relapse is present. It is difficult to hypothesize a relation-

ship between the metastatic cervical latero lymph nodes and the small abdominal mass, considering the sites (neck and abdomen) and of the histology (high grade the first, low the second).

P158

INTENSITY MODULATED RADIOTHERAPY WITH SIMULTANEOUS INTEGRATED BOOST IN CAPECITABINE-BASED CHEMORADIATION FOR ANAL CANCER

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Aims: To assess acute and late toxicity, and efficacy of intensity modulated radiotherapy (IMRT) with hypofractionated simultaneous integrated boost (h-SIB) in anal cancer (AC) patients (pts) undergoing definitive chemoradiation (CRT).

Methods: We retrospectively analyzed data of pts with histologically confirmed AC treated with IMRT 45 Gy in 25 daily fractions on elective pelvic and inguinal lymph node areas and h-SIB on primary tumor and macroscopically involved lymph nodes. Capecitabine was given orally (650 mg/m^2 twice daily) seven days a week and associated with either Mitomycin-C (10 mg/m^2) on day 1 or weekly Carboplatin (AUC2). Acute and late toxicities were evaluated according to the CTC-AE 4.0 scale. Sphincter function was clinically evaluated. Treatment response was clinically and radiologically assessed at 8 and 24 weeks.

Results: Fourty-eight consecutive pts were treated from January 2011 and October 2017. Median age was 60 years (range 38-85). Six pts HIV positive (HIV+) undergoing HAART were also included. All pts had adequate anorectal function. Fourty-five pts (94%) had squamous AC, 2(4%) adenocarcinoma and 1(2%) adeno-squamous. Stage I, II, III and IV was reported in 3(6%), 13(27%), 29(61%) and 3(6%) pts respectively. All pts received Capecitabine. Fourty-one pts (85%) received Mitomycin-C and 7(15%) Carboplatin (frail pts). Median h-SIB dose was 54 Gy (range 52.5-55.2) to primary tumor and 52.5 Gy (range 52.5-54) to positive nodes. 45 pts (96%) completed the planned IMRT-hSIB. Grade 2 or 3 acute hematologic toxicity was reported in 15 pts(31%), grade 2 or 3 gastro-enteric in 23(48%) and grade 3 dermatitis in 16(33%). A discontinuation of capecitabine for more than 7 days was required in 13 pts(27%), 2 of them were HIV+. Late grade 2 proctitis was reported in 2 pts (4%) and late grade 2 dermatitis in 1 (2%); late mild reduction in sphincter control was observed in 6 pts (12%). Response was evaluated in 47 pts. At 8 weeks from CRT, 32 pts (68%) had a complete response (CR) and 7(15%) a major response. At 24 weeks, 37 pts (79%) had a CR. Salvage surgery was required in 6 pts (13%) for persistent-progressive local disease.

Conclusions: IMRT with h-SIB and concurrent Capecitabine-based chemotherapy appears feasible and effective with no increase in late toxicity or function impairment in pts with AC. HIV+ pts could also receive this treatment safely. We will continue the evaluation of this intensified approach in a larger number of pts.

P159

IMPACT OF RADIOTHERAPY IN ANAPLASTIC THYROID CANCER

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Aims: To evaluate clinical outcomes in anaplastic thyroid cancer patients treated with radiotherapy.

Patients and Methods: we reviewed clinical records of anaplastic thyroid cancer patients submitted to radiotherapy in our center from January 2011 to April 2018.

Results: Four patients treated with radiation therapy have been evaluated. Four had previous surgery with thyroidectomy and central lymphadenectomy. At the time of primary diagnosis staging was pT3 (3 patients), pT4 (1 patient), pN0 (1 patient), pN1 (2 patients), cM0 (2 patients), cM1 (2 patients with pulmonary metastases). All patients have been treated with hypo-fractionated radiotherapy delivering a median total dose of 35.75 Gy (range 30-50 Gy) . One patient had primary chemotherapy with ADM+CDDP (1 course) followed by CBDCA concomitant with radiotherapy (4 courses). A local recurrent disease has been observed in one patient 4 months after the end of the concomitant radio-chemotherapy. The median overall survival was 2.8 months (range 1-12 months).

Conclusions: Due to the poor prognosis with scarce survival profile, in anaplastic thyroid cancer patients radiotherapy could be omitted.

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PATTERNS OF FAILURES AND CLINICAL OUTCOME OF PATIENTS WITH LOCALLY ADVANCED ADENOCARCINOMA OF THE UTERINE CERVIX, TREATED WITH TAILORED INTEGRATED APPROACH

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Aims: Aim of this study was to assess the clinical outcome of patients treated with neoadjuvant chemotherapy prior to surgery followed by radiotherapy+/-chemotherapy or with concurrent chemo-radiotherapy (CCRT) for locally advanced adenocarcinoma of the uterine cervix.

Methods: The hospital records of 35 patients: 9 mucinous (25.7%),15 endocervical usual type (42.9%), 2 endometrioid (5.7%), 3 villoglandular (8.6%) and 6 clear cell (17.1%), histological subtypes of adenocarcinoma of uterine cervix (stage Ib2-IIIb) were reviewed. Thirty-one patients (88.6%) received combined chemotherapy of taxane and platinum, with or without anthracycline, followed by type II-III radical hysterectomy with pelvic lymphadenectomy and underwent adjuvant RT 45-50.4Gy (in 25-28 fractions) +/- high-dose rate (HDR) vaginal brachitherapy (BT) boost 10Gy (in 2 fractions). Sixteen women (51.6%) received concurrent CDDP 40 mg/m^2 weekly. The 4 patients scheduled for definitive CCRT received weekly paclitaxel (80 mg/m^2) plus carboplatin (AUC2) for 6 cycles followed by external beam RT 45-50.4Gy (in 25-28 fractions) concurrent with CDDP 40 mg/m^2 weekly; a boost irradiation was used on the involved pelvic nodes. External RT was performed with a 6-15 MV beam and a four-field conformal technique or with Volumetric Modulated Arc Therapy (VMAT) using 6MV beam. Subsequently, a HDR intracavitary BT was delivered as a boost with a three-way Fletcher-Williamson applicator set; the prescribed dose to the target volume was 21-28 Gy (in 3-4 fractions).

Results: Five-years DFS and OS were 71% and 83%, respectively. Patient aged ≤ 50 years at univariate analysis had a significant lower risk of death (p=0.048).There was a trend for a higher risk of progression and death (p=0.097 and p=0.095 respectively) for patients with clear cell histology. The nodal status and the number of metastatic nodes were relevant for prognosis; there was a trend for worse OS (p=0.085) in node-positive compared with node-negative patients and in women with ≥ 4 affected nodes at primary surgery (p=0.078).

Conclusions: Only age and nodal status are prognostic variables for locally advanced adenocarcinoma of the uterine cervix treated with neoadjuvant chemotherapy, radical surgery and adjuvant RT or CCRT, that improved survival. Clear cell histology is associated with poor survival outcomes. Future prospective studies are needed to provide more information about this malignancy.

P161

MULTIFOCAL GLIOBLASTOMA MULTIFORME INVOLVING BOTH HEMISFERES: A CASE REPORT

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Introduction: Multifocal glioblastoma (GBM) is uncommon and refractory type of glioblastoma with multiple and synchronously foci, often localized in the same hemisphere. The incidence of multifocal glioblastoma is reported between 0.5 and 20% of all GBMs and are associated with worse outcome and poorer overall survival times compared with single focus GBMs. Currently there are no clear guidelines regarding optimal management of multifocal GBM. The role of surgery, radiotherapy intent, target volume and dose definition is controversial.

Patients and Methods: We reported a case of 54 years-old woman presented with neck and headaches associated with dizziness since about 3 months. The MRI images showed an insular glioma on the left extending to the temporal-mesial lobe and into the uncus and parahippocampal gyrus. The second smaller focus was located mainly in the splenium on the right . The neurological status before surgery was evaluated: patient was awake, alert and oriented with right sided hemiparesis G4. After being judged inoperable by a first center, the patient underwent RMI-guided fronto-temporal craniotomy to remove the main lesion in a second center. Immunohistopathology was consistent with multifocal glioblastoma, IDH-wild type, MGMT unmethylated. At neurological evaluation post-surgery the patient was alert and oriented, no cranial nerve and visual field deficits are reported with improvement of right sided hemiparesis.

Results: At three weeks after surgery, the patient underwent a simulation-computed tomography (CT). The gross tumor volumes (GTVs) was defined according to the ESTRO-ACROP guidelines on post-operative MRI fused with simulation-CT. The clinical target volumes derived from the addition of a 2 cm margin to GTVs. CTVs were expanded of 5 mm to originate PTVs. A 3D conformal treatment plan with non-coplanar beams was performed. A total dose of 40.05 Gy (2.67 Gy/fraction) plus concomitant daily Temozolomide (75 mg/mq) was administered followed by adjuvant Temozolomide (150 mg/m² for 5 days every 28 days). The patient has well tolerated treatment reporting only asthenia and muscle weakness. EEG tracing is normal, right sided hemiparesis is G0. We scheduleded a follow up MRI at 1, 2 and 3 months after radiotherapy.

Conclusions: Currently, there is no specific treatment protocol for multifocal GMB and these patients are often excluded from clinical trials. The treatment choice is frequently based on case-related clinical evaluation.

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CLINICAL OUTCOMES AND TOXICITY FOLLOWING EXCLUSIVE RADIOTHERAPY OF UNRESECTABLE JUGULOTYMPANIC PARAGANGLIOMA. BENEFIT/COST RATIO IN 2 REPRESENTATIVE CASES

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Aims: Jugulotympanic Paragangliomas (JPs) are rare locally aggressive tumors. Surgery is the primary definitive treatment but affected by morbidity rates not acceptable considering the benign nature of disease. However, JPs are often unresectable because of intracranial extension and Fisher stage; in these cases, conventional or stereotactic radiotherapy (RT) can obtain disease control or growth inhibition, but not without radiation-induced sequels. We present 2 cases of unresectable JP treated with exclusive RT.

Methods: 1st case: 68-year-old woman with tinnitus and paresis of right hemi-tongue, hyperaemia of lower quadrants of tympanic membrane and peripheral paralysis of XII cranial nerve. Head CT and MRI revealed a right-sided JP of 4 cm. 2nd case: 73-year-old woman with worsening dysphonia, dysphagia and otodinia. A left JP measuring 2 cm was detected on diagnostic CT and MRI. RT was administered using IMRT and VMAT technique. Prescription dose was 50-50.4 Gy (1,8-2 Gy/fx) in both cases. GTV was defined as macroscopic disease, CTV was obtained adding a 1.5 cm isotropic margin around GTV and a geometric 3 mm expansion was applied to obtain PTV. Acute and late toxicities were recorded according to CTCAE v4.0 scale; clinical and radiologic follow-up was performed every 3 months during the first year.

Results: Radiation treatment was completed without interruption in both cases. Acute toxicity consisted in G1 radiodermatitis, oral mucositis and dysphagia for the 1st case, while G1 radiodermatitis, oral mucositis, dysphagia and G2 otodinia in the 2nd case. After a follow-up of 2 years 1st patient presented disease stability, without any radiological response, late mastoiditis, dysphagia G1, persistent tinnitus after a temporary resolution. In the 2nd patient at the first clinical and radiological follow-up partial response and mild toxicity were observed. Particularly G2 otodinia persists currently complicated by bacterial otitis.

Conclusions: Despite it is known a role of RT in local control of JP, the real LC and disease response after RT course is not clear. RT can achieve a local control for unresectable JP, without severe radiation induced toxicity. IMRT and VMAT techniques can contribute to minimize related-toxicity but low RT-sequels, in addition to the symptoms of persistent disease are disabling and affecting quality of life. Very long follow up and large databases are necessary to evaluate the real benefit and cost/benefit ratio of RT in JP.

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SAFETY AND EFFICACY OF ACTIVE BEAM SCANNING PROTON THERAPY FOR VESTIBULAR SCHWANNOMAS: EARLY OUTCOMES

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Aims: To report preliminary outcomes and toxicity of active beam scanning proton therapy (PT) for vestibular schwannomas (VS).

Methods: Between October 2014 and February 2018 fourteen patients (pts) with unilateral VS were treated with PT. Median age was 51 years (range, 43-82) while KPS ranged between 90 and 100 (median 90); three were female (21%), and 11 were male (79%). Facial nerve function (House-Brackmann [HB] Grade 1) and trigeminal nerve function were normal in all pts. Four pts (27%) had good or excellent hearing (Gardner-Robertson [GR] Grade 1), and one pt (7%) had serviceable hearing (GR Grade 2). Standard fractionated PT was used at daily dose of 1.8 Gy(relative biologic effectiveness [RBE]); all but three pts received 50.4 GyRBE in 28 fractions. Three pts (21%) were treated with PT radiosurgery: 12 GyRBE in one fraction. All pts were treated with active beam scanning PT using 3-4 fields with single field optimization technique. GTV ranged from 0,2 to 13.3 cc (median 2.4 cc). Toxicity was assessed according to Common Terminology Criteria for Adverse Events version 4.0. Minimum follow-up (FU) was 3 months. Median FU time was 9 months (range, 3-40).

Results: All pts completed the treatment without breaks. Registered acute side effects include grade 1 (10%) fatigue, grade 1 (14%) muffled, grade 2 (14%) headache, grade 2 (7%) nausea. There were no grade 3 or higher acute toxicities. Registered late side effects include grade 1 (7%) and grade 2 (14%) dizziness, grade 2 (7%) vertigo, grade 2 (7%) nausea, facial nerve deficit (HB grade 2) (7%). During follow-up one pt (7%) with the largest VS (13.3 cc) and brainstem compression (Koos 4) developed hydrocephalus that needed ventriculoperitoneal drain; the same patient developed also brainstem radionecrosis with facial and trigeminal cranial nerve palsy, gait deficit and imbalance. This pt was treated with steroids and hyperbaric oxygen therapy. There were no further grade 3 or higher late toxicities. Currently, absolute tumor control is 100%. Despite the short follow-up radiological reduction was registered in 21% of pts. Of the five pts (36%) with functional hearing (GR Grade 1 or 2), all (100%) retained serviceable hearing ability. Absolute normal facial and trigeminal nerve function preservation rates were 86% and 93%.

Conclusions: Active beam scanning PT is feasible and safe treatment for pts with untreated VS. Longer FU is necessary to assess definitive efficacy and toxicity.

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CASE REPORT OF A POLY-TREATED PARTIALLY RESECTED GLIOBLASTOMA MULTIFORME: WHAT IS THE BOUNDARY BETWEEN BENEFIT AND TOXICITY?

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Aims: Gliobastoma multiforme (GBM) is the most common and aggressive malignant brain tumor in adults. The standard multimodal approach includes surgery, adjuvant radiotherapy (RT) with concomitant/sequential temozolomide (TMZ), sec. Stupp schedule. However, prognosis of GBM patients remains poor, especially in unresectable or partially resected tumors where the standard treatment, if applied, cannot obtain the same survival benefit reported in literature. We describe the complex multimodal management in a case of partially-resected bifocal GBM.

Methods: A 56-year-old male presenting clonic seizures interesting the right side of the face, dysarthria and aphasia. Cranial MRI showed 2 brain lesions, the largest one in the left frontal lobe (LF, 2.5 cm) and the other in the right occipital lobe (RO, 1 cm). In December 2016, the patient underwent a partial resection of the only LF lesion. Histopathological examination showed a diagnosis of GBM, IDH wild type, MGMT positive. Concurrent RT (60 Gy/30 fractions) and TMZ 75 mg/m^2/day for 42 days was administered 4 weeks after surgery, with good tolerance (G1 nausea and G1 legs astenia, sec. CTCAE v.4) and followed by 10 cycles of sequential TMZ (150-200 mg/m2, days 1-5 every 28 days), until November 2017. Cranial MRI performed after 4 cycles of adiuvant TMZ, showed good response of the partially resected lesion and stability of the RO lesion. In July 2017, after a new neurosurgical evaluation, the patient underwent a resection of the RO lesion and 2-months after surgery, brain MRI showed a residual of 7 mm of the resected RO lesion, while stability of the LF lesion. Following a further evaluation for protontherapy (PT), the patient received reirradiation with PT of the right occipital lesion (36 Gy/18 fractions, relative biological effectiveness) and TMZ 75 mg/m^2/day for 18 days.

Results: No severe sequels occurred. Steroid intake was not required. During all treatment course and at 17 month-follow up the patient presented KPS score 70, mild dysarthria, left hemianopia and he started taking 4 mg of dexamethasone/day after PT. The patient is attending a new MRI follow up.

Conclusions: Despite a very poor prognosis, some unresectable or partially resected patients could have a certain life expectancy, independently from received therapy. Lacking standard of care in this setting without any survival estimation, combing different treatments seems questionable because the uncertain benefit-toxicity boundary.

P165

SURVIVAL OUTCOMES AND PROGNOSTIC FACTORS IN HIGH GRADE GLIOMAS: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Aims: To analyze the role of possible prognostic factors that may influence survival outcomes of patients affected by high grade gliomas treated with RT +/- CT

Methods: From July 2014 to December 2017 fifty-one patients (median age 60 years; range 27-88, SD 13.32 years) affected by histologically confirmed diagnoses of high grade gliomas were treated in our institution. Forty patients (pts) were GBM at the diagnosis and 11 resulted anaplastic astrocytoma and anaplastic oligodendroglioma (Grade III WHO). Of them 41 patients underwent Stupp regimen and 10 pts were treated with hypo-fractionated RT course (40 Gy in 15-16 fractions) due to low KPS (unfit at Stupp protocol) according to international guidelines. The treatment was performed with LINAC Synergy of Elekta company using 3DCRT of VMAT technique.

Results: At analysis 32 pts (62,7%) were male and 19 (37.3%) female. The median KPS was 80 (range 60-100). The patients with KPS > 80 had one advantage in terms of OS compared to pts with KPS ≤ 70 (p-value 0,003; IC 1,166-6,915; HR 3,042). Equally, the OS in pts with total resection compared to pts who had partial tumor resection or biopsy was longer (p-value 0,001; IC,191-1,60; HR 4,905). Moreover, the survival resulted longer in pts who received a total dose ≥ 54 Gy compared to pts which received TD < 54 Gy (p-value 0,004; IC 0,166-0,928; HR 3,235); pts which received > 54 Gy had an advantage in terms of survival of 7 mnths (median survival 18 vs 11 mnths). One other prognostic factor influencing the OS was the response/absence of tumor at RM evaluation (according to RANO criteria) after RT; the pts with complete response/absence of tumor had a longer OS compared to pts with SD, PD or PR (p-value 0,001; HR 3,159; IC 1,275-0,783). Pts ≤ 70 years old reported a trend in terms of longer survival in confront of patients older than 70 years old (p-value 0,078; HR 1,904, IC 0,992-1,052). Finally, pts treated with VMAT had one advantage in terms of OS compared with pts treated with 3DCRT.The OS in all patients treated resulted 16 months and at the moment of abstract submission 19 patients are still alive.

Conclusions: The results of our retrospective study showed that young age, total dose, VMAT, high KPS, total tumor resection and CR after radiotherapy treatment were prognostic factors regarding the OS in patients with high grade gliomas. Nevertheless, our study with higher number of patients and longer follow-up are necessary to confirm our results

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HIGH-DOSE-RATE BRACHYTHERAPY FOR PRIMARY VAGINAL MELANOMA TREATMENT: A CASE REPORT

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Aims: Malignant melanoma of the vagina is a rare, aggressive malignancy with poor prognosis. The incidence is higher in post-menopausal women, ranging between 2.08/100,000 for 60- to 69-year-old women and 4.43/100,000 for 80- to 89-year-old women. We present a clinical case report of primary malignant vaginal melanoma in a 90 year old woman successfully treated with High-Dose-Rate Brachytherapy (HDR-BT).

Methods: A 90-year-old woman referred postmenopausal vaginal bleeding. On gynecological examination, two raised lesions, which bled easily on contact, were seen on the right third-inferior of vaginal wall, and melanosis of right vaginal fornix was also observed. The lesions were biopsied and diagnosed as vaginal melanoma with a maximum tumor thickness of 3 mm. Staging by PET/CT did not show lymphadenopathy nor distant metastases. Considering the age and the anesthesiological risk, patient was not suitable for surgery and has been candidate for HDR-BT. A vaginal multichannel applicator was used and treatment planning was performed on CT images acquired for each treatment fraction. The prescription dose was 25 Gy in 5 fractions to whole vagina, followed by a boost of 10 Gy in 2 fractions to the third-inferior of vaginal wall. The treatment was delivered at our Department with an HDR remote after loading device provided with an Iridium-192 source.

Results: Patient completed the treatment with no interruptions. After the second treatment fraction (10 Gy) we clinically observed a dimensional reduction of the two lesions. After five fractions there was no bleeding. At the end of treatment, G1 vaginal substenosis and dysuria were the main adverse effects. PET at first follow-up did not show local nor distance progression of disease.

Conclusions: The current treatment approach for primary vaginal melanoma includes wide local excision (WLE), radical surgery, chemotherapy and immunotherapy, alone or in combination, whereas radiotherapy is mainly used as adjuvant therapy. However, as shown with this experience, in particular conditions as in elderly women, HDR-BT can represent an interesting alternative treatment that produces local tumor control and low morbidity.

P167

COMPREHENSIVE ANALYSIS OF HEMATOLOGICAL TOXICITY IN PEDIATRIC STANDARD RISK (SR) AND HIGH RISK (HR) MEDULLOBLASTOMA (MB) PATIENTS TREATED WITH 3DCRT AND VMAT CRANIOSPINAL IRRADIATION (CSI)

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Aims: CSI is a mainstay of postoperative treatment of pediatric SR and HR MB. VMAT technique for CSI has proven to be superior to 3DCRT in term of target coverage, homogeneity and organ sparing, but it causes exposure of red bone marrow to low doses, that may increases acute hematological toxicity. Aim of the study was the evaluation of hematological changes observed in pediatric SR and HR MB pts treated with 3DCRT and VMAT-CSI.

Methods: Clinical records of SR and HR MB children treated in our Institution were collected. A dose of 23.4 Gy/1.8 Gy daily was prescribed to SR pts to craniospinal axis, followed by a 54 Gy/1.8 Gy boost to the tumor bed. HR children received hyperfractionated accelerated RT (HART) with CSI doses of 39 Gy or 31.2 Gy/1.3 Gy twice daily depending on age and a boost to the tumor bed (59.8 Gy) when indicated. Before HART all HR pts received high dose sequential chemotherapy (CT). HR pts with persistent disease, or M4, were consolidated with 2 courses of myeloablative CT and autologous hematopoietic progenitor cell rescue (ASCT) before RT, while the remaining received standard maintenance CT. Hematological changes were recorded weekly during RT and scored according to RTOG system. Mean RT dose to iliac bones was collected to evaluate dose to the red bone marrow.

Results: Data from 26 pts (SR: 11,HR: 15) were collected (median age 10 y,4-33): 10 pts received 3DCRT-CSI (SR: 5,HR: 5), 16 pts were treated with VMAT(SR: 6,HR: 10). 4 HR pts were consolidated with 2 ASCT before HART (3DCRT: 1,VMAT:3). Within SR groups no hematological toxicity differences were observed (4 G3 leuko-neutropenia,3DCRT: 2/5,VMAT: 2/6).G3 toxicity occurred in all HR pts. G4 (leuko-neutropenia, thrombocytopenia) was recorded only in 4 VMAT pts, 3 of whom received ASCT before HART. Within ASCT-VMAT group more use of G-CSF and transfusions during and after RT was required and 1 child stopped earlier HART due to hematological toxicity. In ASCT-VMAT children leukopenia and thrombocytopenia worsened of 20% and 5%,respectively, compared to other HR pts, and they recovered slower (Figure 1).

Mean RT dose to the iliac bones was 0.9 Gy for 3DCRT and 5.8 Gy for VMAT.

Conclusions: Exposition of red bone marrow to low doses during VMAT-CSI decreases hematopoiesis and is responsible for more severe hematological toxicities in HR pts who received ASCT before HART. Hence, to reduce toxicity during VMAT-CSI for these children a planning effort is strongly recommended to lower mean dose to iliac bones as much as possible.

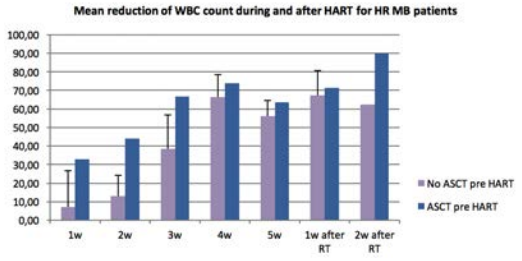

Figure 1.

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ADJUVANT AND PALLIATIVE RADIOTHERAPY IN MERKEL CELL CARCINOMA: EXPERIENCE OF RADIATION ONCOLOGY OF SAN LUIGI AND MAURIZIANO HOSPITAL

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Aims: Merkel cell carcinoma (MCC) is an uncommon neuroendocrine cutaneous tumour malignancy with a high propensity for local recurrence, regional spread and distant metastasis. The treatment for localized MCC is wide excision and lymph node dissection, radiotherapy (RT) play an important role as adjuvant therapy after surgery and as exclusive therapy in the inoperable disease. We report the results of postoperative and palliative RT in patients with MCC treated at Radiation Oncology (RO) Department of San Luigi and Mauriziano Hospitals.

Methods: In this small retrospective analysis eight patients with localized MCC have been treated between April 2011 and March 2018, six in RO of San Luigi Hospital and two with advanced inoperable MCC in RO of Mauriziano Hospital. Tumours were located on face (two patients), gluteus (two patients), lower third of the leg (one patient), hand (one patient) and inguinal region (two patients) respectively. The median age was 75,1 years (range 73-87). Adjuvant RT was performed after surgery on the primary tumour and regional lymph nodes in five patients; in one patient surgery and adjuvant RT was carried out only on primary tumour. Two patients with inoperable localized MCC were treated with exclusive high dose RT. RT was delivered to the primary site and regional lymph nodes with dose ranging between 54 to 60 Gy. Treatment was performed using Three-Dimensional Conformal Radiotherapy (3DCRT) and Volumetric Arc Therapy (VMAT) with 6-10 MV photon beam. Seven patients received concomitant boost using 6-18 MeV electrons.

Results: With median follow-up of 32,9 months (range 0-83), in the adjuvant setting three patients were alive with no evidence of disease (NED), one patient died for distant metastasis but locally NED, two old patients died for progression disease. In the RT alone setting a partial response (>80%) was obtained in both treated patients. No several cutaneous radioinduced complications were observed in all patients.

Conclusions: Our results, based on a small number of patients, show that postoperative RT plays an important role in the treatment of MCC, increasing loco regional and distant control and palliative RT produces excellent in-field disease control suggesting that high dose RT may be able to provide reasonable results for MCC patients who are unable to undergo surgery.

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A MATCHED COHORT STUDY OF ADJUVANT RADIO-CHEMOTHERAPY VERSUS RADIOTHERAPY ALONE IN SOFT TISSUE SARCOMA PATIENTS

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Aims: Adjuvant radiotherapy is the standard postoperative treatment after conservative surgery in high risk soft tissue sarcoma. The role of adjuvant chemotherapy is still debated. Therefore, a matched cohort analysis was performed in high risk soft tissue patients to analyse differences in terms of clinical outcome and toxicity between patients treated with concomitant radio-chemotherapy (RTCT) and radiotherapy (RT) alone.

Methods: Ninety patients were selected, a half of patients underwent radio-chemotherapy and a half received radiotherapy alone. For each patient in RT group was selected a patient in the RTCT group matching for age, T stage and grading. Acute and late toxicity were recorded, overall survival, recurrence free survival and distant metastases free survival were analyzed and compared between the two groups.

Results: During the treatment Grade 3 dermatitis was recorded in 15 (16.7%) patients, 6 (6.7%) patients associated chemotherapy and during follow up 12 (13.3%) patients developed grade 2 late fibrosis, 3 (3.3%) joint stiffness and 1 (1.1%) patient experienced

a bone fracture. There were no differences in the rate of acute and late toxicity between RTCT and RT alone group. Nineteen (21.1%) patients developed local recurrence, overall 5-year local relapse free survival was 83%. There were no differences between the two groups. 29 patients developed distant metastases, 14 (15.6%) patients in the RTCT group and 15 (16.7%) patients in the RT group. The 5-year distant metastases free survival was 67%. Age >65 years was the only independent factor affecting distant recurrence (HR=5.7,95% CI 2.7-11.9; p=0.001). At the time of analysis 15(16.7%) patients were dead, 6 (6.7%) patients in the RTCT group and 9 (10%) patients in the RT group. 5-years overall survival was: 88%. At multivariate analysis age > 65 years was an independent prognostic factor of overall survival (HR=3.7, 95% CI 1.2-12.1, p=0.037).

Conclusions: Prospective randomized study with large size population and with subgroup analysis for histological subtypes are necessary to clarify the role of adjuvant chemotherapy in soft tissue sarcoma patients. Tailored treatment has to be considered in elderly soft tissue patients to guarantee a better outcome in this high risk and fragile population.

Keywords: soft tissue sarcoma, radio-chemotherapy, radiotherapy, chemotherapy, toxicity

Acknowledgments: none

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GAMMA KNIFE RADIOSURGERY IN RECURRENT HIGH GRADE GLIOMAS: EXPERIENCE AT NIGUARDA CANCER CENTER

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Aims: To report our experience in the salvage treatment of recurrent high grade gliomas (HGG) with single-fraction Gamma Knife (GK) radiosurgery (Elekta Leksell Perfection) at Niguarda Cancer Center. Current standard of care in newly diagnosed HGG is maximal safe surgical resection followed by adjuvant Radiotherapy (RT) and concomitant Temozolamide (TMZ) (Stupp protocol). Recurrences are mostly (80-90%) within 2 cm of the resection cavity. For patients with recurrent HGG there is no standard of care. Stereotactic radiosurgery is a viable approach in case of small volume recurrent HGG, but the role of single-fraction radiosurgery with Gamma Knife is still to be defined.

Methods: Clinical charts of 38 patients with a small volume recurrence of HGG (glioblastoma or anaplastic astrocitoma) treated with GK radiosurgery from May 2009 to June 2017 were retrospectively reviewed. The series includes 25 males and 13 females with a median age of 57 years (range 28-75) and a relatively good Performance Status (0-2). Primary treatment at first diagnosis was surgery followed by adjuvant RT (60 Gy in 30 fractions) and concomitant TMZ. Median time to recurrence after primary treatment was 12.3 months (range 4.3-92 months). The recurrent lesion was treated with single fraction GK radiosurgery at doses ranging from 11 to 20 Gy (median 16 Gy) delivered at the 50% prescription isodose. Median volume of treatment was 9 cc (range 0.02-52.9 cc). TMZ was ongoing at the time of relapse in 35 pts, and 16 pts were also treated with second line chemotherapy (Fotemustine) after treatment with GK. In 5 patients a second re-irradiation was performed (GK radiosurgery or conventional RT).

Results: Median overall survival (OS) after primary treatment was 28.5 months (range 11.7-134.6 months). Median OS after GK treatment was 9 months (range 0.9-110.2 months). Survival rates at 6 months and 12 months from GK treatment were 73.6% and 34%, respectively. Five patients are alive at the last follow up (May 2018), including two pts without any sign of progression. Median survival of these 5 pts after GK treatment is 27.6 months (range 6.3-110.2 months). We stratified pts into two groups based on tumor volume (TV) at MRI performed during GK procedures: in 21 pts TV was equal or smaller and in 17 pts TV was larger than 9 cc, respectively. Median survival was 13.2 months (range 2.4-110.2) in the first group and 5.4 m (range 0.9-13.4) in the second group.

Conclusions: GK radiosurgery is a feasible treatment in selected cases of recurrent HGG, achieving significant survival results in smaller volume lesions. Based on our data, we suggest a cutoff value for tumor volume of 9 cc.

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TUMOR RESPONSE AND TOXICITY IN PATIENTS WITH A DIAGNOSIS OF PRIMARY OR RELAPSES OF RETROPERITONEAL SARCOMA TREATED WITH VMAT OR TOMOTHERAPY

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Background: Retroperitoneal sarcoma (RPS) is a rare disease accounting for 0.1%-0.2% of all malignancies. Extended surgery is the standard treatment of RPS, but there remains a significant need for additional therapies capable of reducing the risk of local or distant disease recurrence, and potentially downstage locally advanced tumours. Aim of the study is to evaluate the tumor response and toxicity of radiotherapy (RT) concomitant with chemotherapy (CT) in the neoadjuvant setting for

primitive tumours, and RT alone or with CT for relapses.

Methods and Materials: From 2008 to 2016, 37 patients (pts) with RPS (26 primary tumours and 11 relapses) were treated with VMAT or Helical-Tomotherapy. Mean follow-up was 55 months (range 16-178 months). The most frequent histological variants were liposarcoma and leiomyosarcoma. Prescription dose was in the range 30-60 Gy. Acute toxicity was scored with RTOG/ EORTC scale, haematologic toxicity was scored according to CTCAE version 4.3. Tumor response was evaluated with RECIST parameter, and necrosis rate with FNCLCC grade system. Kaplan-Meier analysis was used for overall survival (OS) and progression free survival (PFS).

Results: OS was 143 months (95% CI: 120 to 166) from diagnosis. PFS was 91 months (95% CI: 63 to 119). 7 pts died but only 4 pts died for progression disease (PD). 13 pts completed the planned preoperative RT-CT and underwent R0 or R1 resection with curative intent. Necrosis rate was G2 and G3 in 11 pts. During follow-up, 20 pts had a complete response, 9 pts had PD, 3 pts had a partial response, and 5 pts had stable disease. Fifteen pts had a PD with a new lesion in a different site. Two pts interrupted radiotherapy for haematologic toxicity G4. Only one patient reported gastrointestinal acute toxicity grade G4.

Conclusions: Despite the few cases we recorded, our experience showed encouraging local control rate (67% of cases) with few cases of toxicity G4. Furthermore, pre-operative RT-CT improved tumor resectability. The main pitfall of the study is the small number of patients enrolled. Greater number of cases may be reached in a context of network or alliance between other sarcoma centres thus establishing more powerful conclusions regarding the management of these complex disease.

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LOCAL CONTROL IN ANAL CANAL NODULAR MELANOMA: CASE REPORT OF POSTOPERATIVE BRACHYTHERAPY

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Purpose: Melanoma is traditionally considered to be a radioresistant tumor. However radiotherapy and immunotherapy latest developments might upset this radiobiological dogma. Stereotactic ablative radiotherapy allows high dose for fraction delivery, with high dose rate. More DNA lethal damages, less sublethal damage reparation, endothelial cell apoptosis and clonogenic cell dysfunction are produced. The alpha/beta ratio in vivo ranged from 1.0 +/- 0.2Gy to 3.3 +/- 6.7Gy. These values are similar or superior to those of normal tissues that respond acutely. However, radiotherapy latest developments might upset. Indications of radiotherapy are currently reduced, since melanoma has low sensivity to conventional fractionation radiations (1.8-3Gy): it was demonstrated in vitro in melanoma cells. However, this radiobiological impasse might be upset by radiation therapy allowing high dose for fraction with high dose rate delivery. The aim of the present study is to clarify the potential place and role of adjuvant brachytherapy in selected patients with factors including narrow margins, deep desmoplastic, extensive neurotropism or locally recurrent melanoma local control.

Methods and Materials: In February 2015 in our Institute, a 82 years old man consulted his surgeon for intermittent rectal bleeding. Clinical findings showed a well-defined, low mobile, ulcerated anorectal tumor of 1.5 x 1.8 cm on anterior wall. A biopsy of the tumor was performed and the immune-histopathological finding conformed malignant nodular melanoma. Pelvic RMI, inguinal ultrasound and chest X-ray were necessary to underwent patient to surgery and in March 2015 endo-anal resection of the tumor was performed with the clear scope of sphincter preservation. The resection margins were carefully examined and assessed as positive right and left lateral and deep margins. After an extensive discussion with the patient and the Oncologist, an adjuvant brachytherapy was carried out, leaving the option of rectal amputation open as a salvage therapy after irradiation. Adjuvant chemotherapy did not be proposed for comorbidity. In August patient underwent to intracavitary brachytherapy once a dwith 25mm cylinder, irradiating only the anterior half of the circumference from 270 to 90 degrees with 5 cm active length. 3 fractions of 7 Gy using Nucletron HDR afterloading system with I-192 active source were delivered at 5 mm from the cylinder applicator surface and plan delivered used with Oncentra brachy.

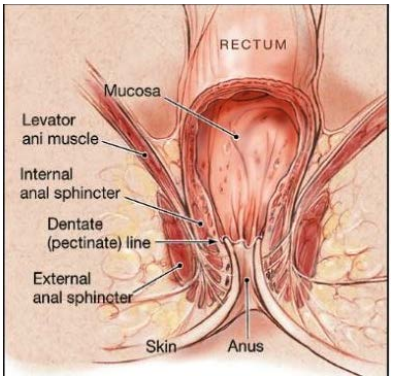

Figure 1.

Results: At the end of the treatment, the patient presented no acute toxicity: no bleeding and anal mucosa in order. At 45 days since brachytherapy proctoscopy was negative for local relapse, patient presented in fair general conditions and did not complain of pain or blood loss. After 6 months, new proctoscopy described anal mucosa was regular, smooth and pink, but RMI showed right inguinal metastasis, underwent to excision and adjuvant radiotherapy with conventionally fractionation (total dose 50Gy). In November 2016 TC total

body with mdc was performed and this exam was negative for systemic disease relapse. In March 2017 patient died for abdominal metastasis.

Conclusions: Rectal bleeding in patients is a remote condition of possible malignant melanoma and in such cases a representative biopsy in mandatory. Wide local excision is the best option for removal lesion and should be executed at first. The pathology report informs the clinician whether an adjuvant treatment. The presence of high risk factors for local failure is a strong argument for adjuvant radiation therapy with a hypofractionated scheme or brachytherapy delivering a high dose to the initial tumor bed, with a large dose/fraction in concordance with radiobiological features of this type of malignancy. The optimal HDR BT scheme remains to be defined; however endocavitary technique in this type of treatment plan should probably be avoided.

P173

OCCULT PRIMARY CANCERS OF THE HEAD AND NECK: THE DIAGNOSTIC ROLE OF HPV/EBV TESTING AND MRI TARGETED BIOPSIES

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Aims: Occult Primary Cancers (OPCs) of the Head and Neck (HN) are a rare condition and the proper management is still controversial. The aim of this study is to retrospectively investigate the diagnostic approach to patients with these tumors.

Methods: We treated 61 patients with OPCs of the HN from 2005 to 2017. Every patient underwent a nasopharyngolaryngoscopy (NPL), a contrast-enhanced MRI and/or a PET/CT. Biopsies were performed on neck nodes for every patient, HPV DNA/p16 and Epstein-Barr Virus (EBV) DNA were tested on biopsy specimens.

Results: Eighty-eight percent (88%) of patients were males with a median age of 61 (range: 25 - 84) and a PS of ECOG 1 (range: 0 - 1). Most of them (64%) were smokers with a median of 30 pack/years. The most frequent cN categories were cN2b and cN3 (56%), 23% were M+. Ninety-three percent (93%) of patients were stage IV (TNM AJCC VII ed). In 17 cases tumoral HPV/p16 and EBV DNA assessment was not performed. Twenty-six patients (59%) were HPV+ and/or p16+, 3 (7%) were EBV+. As for staging, MRI was performed in 83% of cases, PET/CT in 26%. Only 13 primary tumors (21%) were identified. Biopsies were performed in 33% of cases, and 28% of OPCs of the HN were diagnoses only by imaging. Therefore, biopsies guided by imaging suspicion were the most frequent procedure.

Conclusions: The majority of OPCs of the HN are HPV-related. For every case, HPV and EBV assessment should be provided. MRI followed by targeted biopsies is strongly recommended for occult primary site detection.

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THE ROLE OF ADJUVANT RADIATION THERAPY IN THE MANAGEMENT OF VULVAR CANCER. THE VUL.CAN MDT EXPERIENCE

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Aims: Vulvar cancer could be considered a rare disease, in the USA it determines 0.6% of women malignancies. Multidisciplinary treatment strategy should be evaluated in order to offer best clinical approach and an adjuvant External Beam Radiotherapy (EBRT)+/- Chemotherapy (CT) can be administered according to the presence of high risk factors. VULvar CANcer Multi-Disciplinary Team (Vul.Can MDT) was created in Policlinico Universitario A.Gemelli IRCCS, in order to discuss treatment approach and solutions for patients with vulvar cancer diagnosis. The aim of this abstract is to report the Vul.Can experience in the management of adjuvant radiotherapy.

Methods: A retrospective analysis regarding patients affected by vulvar cancer treated in adjuvant setting in our hospital from April 2013 to September 2017 and a follow-up of at least 4 months was conducted. The treatments were administered according to the internal protocol proposed by Vul.Can MDT. Indication for adjuvant EBRT+/-CT was mainly defined according to margin status, tumor invasion, nodal involvement. Patient received a radiotherapy doses from 50 Gy to 60 Gy to perineum and 45 Gy to lymph nodes; patients with nodal involvement received a radiotherapy doses

from 45 Gy to 60 Gy to the area of pathological positivity of lymph nodes. EBRT was performed with bolus. The CT schemes were the association of Cisplatin and 5-Fluorouracil (PlaFuR) or weekly Cisplatin. Patients after 2015 were treated using IMRT (Simultaneous Integrated Boost). Toxicity was revealed using CTCAEv4.0.

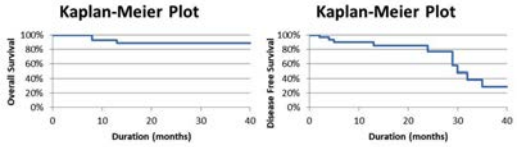

Figure 1.

Results: Data about 30 patients were analyzed, with a median follow-up time of 16 months. 18 patients underwent a concomitant CT, 12 patients underwent EBRT without CT. In our experience, the overall survival (OS) was at 12 and 24 months 93% and 88%, while the Disease-Free Survival (DFS) was respectively 90% and 77%. For the patients with nodal involvement, the OS at 12 and 24 months was respectively 94% and 88% and DFS at 12 and 24 months was respectively 90% and 75%. For patients without nodal involvement, the OS and DFS at 12 and 24 months were 90%. No grade 4 toxicity was reported, 4 patients (13%) experienced G3 acute cutaneous toxicity, in 1 patient (3%) occurred G3 late cutaneous toxicity; no other G3-G4 toxicity occurred.

Conclusions: Our work confirms that the adjuvant EBRT+/-CT in high risk Vulvar Cancer is safety and effective to prevent a local relapse and multidisciplinary approach can help the management of these patients.

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ENDOCRINOLOGICAL DAMAGES IN 82 PEDIATRIC PATIENTS WITH CENTRAL NERVOUS SYSTEM TUMORS TREATED WITH RADIOTHERAPY

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Aims: To investigate hormonal toxicity in pediatric patients affected by central nervous system (CNS) tumors who had been treated with intensity-modulated radiotherapy schedule (IMRT) or three-dimensional conformal radiotherapy (3D-CRT).

Methods: From January 1999 to September 2015 we retrospectively analyzed 82 patients: 30 treated with IMRT and 52 with 3D-CRT. Follow-up lasted from 1999 to 2018. Patients treatments schedule were the following: 47 patients RT+surgery+chemotherapy (CT), 29 RT+CT, 3 RT+surgery, 3 RT only. We analyzed different types of tumors: 16 astrocytomas, 1 atypical teratoid rabdoid tumor, 3 ependymomas, 2 Ewing sarcomas, 1 ganglioglioma, 19 germinoma, 5 gliomas, 33 medulloblastoma, 1 pinealoblastoma, 1 primitive neuroectodermic tumor. We treated 39 patients with craniospinal irradiation (CSRT) ± boost. All other patients were treated with involved field radiation therapy (IFRT) ± boost. We investigated thyroid and pituitary gland average dose: thyroid received a documented dose only in patients who underwent CSRT; in 16 patients on 39 thyroid dose evaluation was impossible. All 82 patients received a documented dose on pituitary gland except one (we excluded this patient from our study).

Results: Median patients age was 10 years old (range: 2 to 17). We analyzed three different types of central endocrinological disorders (GH, TSH, ACTH) and peripheral fT3 and fT4 one; we found these hormonal deficiencies: 48/81 GH, 30/81 ACTH, 22/81 TSH , 4/81 both TSH and fT3 + fT4, 12/39 fT3 + fT4 only. Thirty-one patients on 48 with GH deficiency were irradiated with CSRT (dose range: 23,4 to 39,0 Gy) ± boost, while 17 of 48 with IFRT (dose range: 24,0 to 54,0 Gy) ± boost. Nineteen patients on 30 with ACTH deficiency underwent CSRT (dose range: 23,4 to 39,0 Gy) ± boost, 11/30 faced IFRT (dose range: 24,0 to 59,4 Gy) ± boost. Twelve patients on 22 with TSH deficiency were treated with CSRT (dose range: 23,4 to 39,0 Gy) ± boost, while 10/30 with IFRT (dose range: 24,0 to 54,0 Gy) ± boost. All patients with central and peripheral hypothyroidism underwent CSRT (dose range: 23,40 to 39,00 Gy) ± boost. Eight patients on 12 with fT4-fT3 deficiency were treated with CSRT (dose range: 23,40 to 39,00 Gy) ± boost, 4/12 with IFRT (dose range: 23,40 to 60,00 Gy) ± boost.

Conclusions: Our data confirm the high frequency of hormonal disorders post RT in pediatric patients; relationship between dose delivered – damage to pituitary gland and thyroid is ongoing.

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LOCAL TREATMENT FOR RELAPSING GLIOBLASTOMA: A DECISION-MAKING TREE FOR CHOOSING BETWEEN REIRRADIATION AND SECOND SURGERY

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Aims: To give an algorithm to use in the clinical practice for choosing between reirradiation (Re-RT) and second surgery (Re-S) for relapsing glioblastoma (rec-GBM).

Methods: Literature data from 1995 to 2018 were identified by searching the PUBMED database with the

following as keywords: recurrent glioblastoma, radiotherapy, radiosurgery, stereotactic radiotherapy, second radiotherapy, repeat radiotherapy, reirradiation, second surgery, repeat surgery, re-surgery.

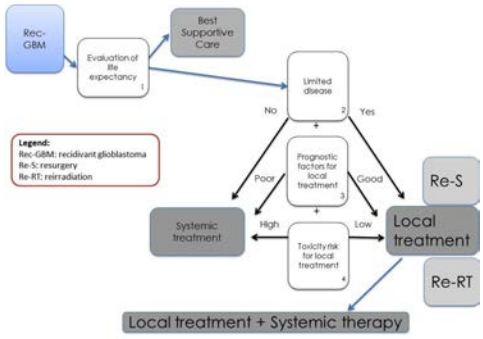

Figure 1.

Results: The first step in our decision tree is to consider the life expectancy of each patient to understand whether the patient should be excluded from active treatment, based on a poor life expectancy (<3 months). Gorlia et al (2010) provided a calculator that can be used to compute the life expectancy of patients with rec-GBM (www.eortc.be/ tools/recgbmcalculator/ calculator.aspx). The next point to take into account is whether the disease is limited. In case of circumscribed disease, the following step is the assessment of prognostic factors specific for local treatment. Based on the existing prognostic score systems [Park JK et al 2010, Park CK et al, 2013, Combs *et al.* 2013, Niyazi *et al.*, 2018] patients who should be excluded from local treatments may be identified; based on the same prognostic indices, one or the other local treatment should be preferred. In addition, the preoperative estimate of possibility of performing a gross total resection is another crucial point in the decision process. The last point to evaluate in order to define the factors impacting on expected toxicity: they are patient-related factors (age, comorbidity), tumor-related factors (size and site of the tumor), and treatment-related factors (time from previous treatment). Regarding the attempt of reducing the toxicity of radiotherapy, patients should be stratified according their tumor volume and treated with different fractionation schedules [Scoccianti *et al.*, 2018]. Since the addition of systemic therapy has been reported as a strong significant factor, patients with very good prognostic factors may be treated with both treatments.

Conclusions: In conclusion, patients with a relatively good life expectancy and with circumscribed disease should be evaluated for local treatment. The choice between second surgery and repeat reirradiation should be based on a careful pretreatment assessment of prognostic factors and expected toxicity.

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SEQUENTIAL VS SIMULTANEOUS INTEGRATED BOOST ADJUVANT RADIOTHERAPY OF EXTREMITIES/TRUNK SOFT TISSUE SARCOMAS: PRELIMINARY RESULTS

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Aims: Adjuvant radiotherapy (RT) is indicated in resected intermediate-high grade primitive or recurrent soft tissue sarcoma (STS) of the extremities and trunk to improve local control (LC). We report our preliminary experience in patients with localized STS treated with adjuvant Intensity Modulated Radiotherapy (IMRT) and Volumetric-modulated Arc Therapy (VMAT) in sequential or Simultaneous Integrated Boost (SIB) modality.

Methods: All consecutive patients treated since February 2014 were retrospectively identified. The inclusion criteria were primary or recurrent localized soft tissue sarcoma of the extremities/trunk without evidence of distant disease. Considering α/β ratio 10 in high grade sarcomas, we have calculated SIB schedule having BED similar to the sequential treatment in conventional fractionation. Side effects were scored according to the Common Terminology Criteria for Adverse Events v4.0 (CTCAE). Overall survival (OS) and disease-free survival (DFS) were estimated using the Kaplan-Meier method. Median follow-up is 22 months (range 1-48 months).

Results: Sixty-two patients were analysed. Median age was 65 years (range 28-84). Seven patients had recurrent tumours and 55 primitive sarcomas, of which 17 at stage IIA, 10 at stage IIB and 35 at stage III. All patients underwent a limb-sparing surgical excision and postoperative EBRT. Chemotherapy was administered neoadjuvantly and adjuvantly in 8 and 19 patients, respectively. 25 patients were treated in sequential modality (60-66 Gy in 30-33 fractions), 37 patients in SIB modality: 62.5 Gy/25 fractions (fr) in 21 patients; 63 Gy/28 fr in 3 patients; 60.2 Gy/28 fr in 13 patients.

Local control (LC) was obtained in 61 patients (98%). Acute radiation dermatitis Grade 2 (G2) was observed in 31 patients (50%): 15 (48%) and 16 patients (52%) treated in SIB and sequential modality, respectively. Acute wound complication G2 was observed in 2 patients (3%) treated in sequential modality. Late complications were: fracture in 1 (2%) patient treated with SIB modality, joint stiffness in 1 patient (2%) in sequential modality, edema G2 in 1 patients (2%)treated with sequential modality and fibrosis G2 in 12 patients (19%), equally distributed in the two groups. No grade 3-4 toxicities were observed. At 2 years, OS is 90% and DFS is 82%.

Conclusions: Radiotherapy is a well-tolerated (both acute and late) adjuvant treatment, regardless its the fractionation.

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MULTIMODALITY TREATMENT IN THYMIC EPITHELIAL TUMORS: A RETROSPECTIVE ANALYSIS AND EVALUATION OF ACCORDANCE WITH NEW ESMO GUIDELINES

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Aims: Surgery represents the mainstay treatment for Thymic Epitelial Tumors. Due to the lack of prospective randomized studies, the role of postoperative radiotherapy (PORT) is not supported by high levels of evidence. We retrospectively assessed whether the decision regarding the postoperative radiotherapy at Campus Bio-Medico University has been taken according to the new ESMO guidelines.

Methods: All consecutive patients with Thymic Tumors from 2005 to 2018 were analyzed and a complete review of medical records was performed.

Results: 51 patients underwent surgery up-front. Median age at diagnosis was 64 years (range 33-82). Tumors histology was thymoma (A-AB-B3) in 47 (92%) patients or thymic carcinoma in 4 (8%) patients. Complete resection (R0) was achieved in 35 (67%) patients. Other patients had R1 resection. Applying 8° TNM system edition, 1 patients with Masaoka stage III was reclassified to stage II and I stage and one IV A. Decision of delivering PORT was in accordance with ESMO guidelines in 94% of the 51 patients. Two patients with R1 resection, with B1 and B2 thymoma and negative postoperative CT scan, did not receive radiotherapy for excessive delay after surgery. Median total dose was 46 Gy and was variable depending of radical resection: median total dose was 45 Gy after R0 resection and 54 Gy after R1 resection. Only G1-2 acute esophageal and G1 acute lung toxicities were reported. No in-field local recurrences were reported; four patients had pleural and distance metastases. With a median follow up of 47 months (range 7.2-155 months), median overall survival was 9.7 years.

Conclusions. Our data suggest that PORT is a safe and effective treatment for Thymic Epitelial Tumors in patients with stage II (B2-B3), Stage III Masaoka-Koga, R1 resection and Thymic carcinoma, in accordance with ESMO guidelines.

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IMPACT OF EVOLVING RADIOTHERAPY TECHNOLOGY IN THE TREATMENT OF NASOPHARYNGEAL CANCER: SINGLE CENTER EXPERIENCE

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Aims: To report the clinical outcome and toxicity of patients affected by nasopharyngeal cancer (NC) treated with different radiotherapy (RT) techniques, namely 3-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT).

Methods: Between January 2000 and December 2017, 83 patients underwent concomitant chemo-radiation with curative intent. By January 2007. Progression-free survival (PFS) was defined as the time from first day of treatment to progressive disease (PD) or death from any cause; overall survival (OS) was defined as the time from first day of treatment to death from any cause. Acute and late toxicities were retrospectively evaluated according to NCI Common Terminology Criteria for Adverse Events (CTCAE version 4.0) and LENT SOMA scale, respectively.

Results: Fifty-two patients (62,1%) were treated with 3DCRT while 31 with IMRT (37.9%). The majority of patients (58; 70,7%) were diagnosed with locoregional advanced disease and they were treated with a conventionally-fractionated, 7 weeks RT regimen delivered in a sequential approach (50Gy at low risk site of microscopic infiltration, 60 Gy to macroscopic uninvolved sites but deemed at high risk of disease presence or relapse, 70 Gy to tumor and involved nodal clinical target volumes (CTV's). In 25 patients (30%) the IMRT technique allowed the simultaneous delivery of different doses per fraction, namely 1.8 Gy, 2 Gy and 2.12 Gy aimed at the same volumes described above within a shorter overall treatment time (33 fractions delivered in 6 weeks). A total of 48 of patients received cisplatin-based concomitant chemotherapy. Twenty-eight patients of the whole cohort needed to recieve induction chemotherapy before concomitant chemo-radiation. In terms of clinical outcome, the 30-month PFS was 54,8%; PD was diagnosed in 24 patients (29,2%), among them 17 treated with 3DCRT and 7 with IMRT. In terms of OS, at a median follow-up of 51 months, 50 patients (60%) were alive. Regarding acute toxicity, the most frequent adverse event was severe (G3-G4) mucositis which was diagnosed in 18 patients in the 3DCRT group (32,7%) and in 8 in the IMRT group (32%). The 12-month xerostomia of moderate-severe intensity (G2-G3) was also more frequently found in the 3DCRT cohort (29% and vs the 15% in IMRT).

Conclusions: Our experience supports the positive impact of IMRT in the treatment of NC, in terms of reduced acute and late toxicity without any detrimental effect on disease control.

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CASE REPORT: THE ROLE OF ADJUVANT RADIATION THERAPY IN THE LOCAL CONTROL OF CASTLE TUMOR

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Aims: CASTLE tumor (carcinoma showing thymus-like differentiation) is a rare malignant neoplasm (accounting for less than 0.15% of thyroid neoplasms) that histologically resembles thymic carcinoma and arises in the thyroid gland or adjacent neck soft tissue.

Methods: In April 2016, a 55-year-old man was referred to general practitioner for dysphonia and neck mass. Past medical history was not significant. Physical exam and ultrasound of the neckshowed a thyroid cancer with a right deviation of trachea. A computed tomography (CT) scan confirmed the presence of this mass with latero-cervical adenopathy. In May 2016 the patient was submitted to debulking surgery and histopathological result revealed a CASTLE tumor. A contrast CT scan performed one month after the surgery showed a locoregional persistence of disease with a solid paratracheal tumefaction in the tumor bed and bilateral pathological laterocervical nodes. The case was discussed in the multidisciplinary team and the patient was than referred for CTRT; The RT treatment was performed with DHX LINAC VARIAN System with IMRT technique, using 6MV photons. We utilized a head-shoulder thermoplastic mask as immobilization system. The prescribed doses was 61.60 Gy (delivered in 28 fractions) on tumor mass and pathological limphnodes and 50.40Gy (delivered in 28 fractions) on tumor bed and locoregional nodes. Concomitant chemotherapy with weekly cisplatin 40mg/mq was delivered for 6 cycles. In July 2016 the patient completed the treatment and began a follow-up with CT scan performed every 3months.

Results: The therapy was well-tolerated (disgeusya G1 and erythema G1). The CT scan showed a locoregional partial response. In April 2017 a CT scan documented two epathic metastases (mts) treated with trans arterial chemoembolization (September2017) but the subsequent CT showed a progression of treaded lesions and the appearance of new mts. In absence of progression of primitive tumor, the patient was submitted to surgical excision of hepatic mts with confirmation of CASTLE tumor. After a follow-up of 2 years the patient is still alive without evidence of disease.

Conclusions: In CASTLE tumor, complete resection is important to improve the long-term survival rate and the locoregional recurrence rate. After a debulking surgery, RT dose of 61-62 Gy plus chemotherapy has proved to be sufficient to control macroscopic residual of disease with acceptable toxicity.

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A CASE OF RARE ADVANCED SCC OF SCALP RESPONSIVE TO RADIOTHERAPY

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Aims: Cutaneous squamous cell carcinoma (SCC) is the second most frequency of all skin tumours. Incidence of SCC has risen significantly due to an increased sun exposure and the number of immunodeficient patients. Generally, locoregional surgery is curative and systemic therapy is not indicated. The aim of our report is to show the good results obtained with radiotherapy in terms of local control, complete response, and aesthetic outcome in a large SCC cranial tumour.

Methods: At our department, on July 2017 we treated a 74 years-old patient affected by advanced unresectable relapse of SCC of the frontal region. In march 2017 he was submitted to excisional biopsy with diagnosis of G1 SCC, uninvolved margins. After 3 months, the patient come to our first observation, with an advanced lesion in fronto-parietal region. The lesion was about 25 cm, exophytic, mammellonata, with necrotic and granulation tissue areas. At massive facial and neck CT scan there was also a nodular formation of 24mm in correspondence of the right parotid as intraglandular colloquated lymphadenopathy. Patient's quality of life of was poor due to pain and to non-aesthetic injury of scalp. After a CT scan, a 3D treatment plan was developed to CTV1 (Ib-II-III right laterocervical nodal level) at dose of 50 Gy and CTV2 (right parotid+frontal lesion) at total dose of 70 Gy with conventional fractionation (2Gy/fz) using multiple 6 MV fields. Based on evaluation of the dose-volume histogram, a bolus was not considered necessary.

Figure 1.

Results: From 24/07/2017 to15/09/2017 the patient was treated without serious toxicity. The treatment was good tolerated without interruption. The esophytic keratotic lesion gradually dropped out after 50 Gy remaining a large ulcerated area. After 2 months the lesion was already healed by secondary intention. The treatment obtained a complete pathological response as demonstrated in instrumental examinations. At the last follow up, after 8 months from end of radiotherapy, the quality of life resulted significantly improved without pain and with a good aesthetic response.

Conclusions: The radiotherapy on SCC was effective and feasible. A longer follow-up is necessary to confirm these excellent results.

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CASE REPORT: THE ROLE OF RADIOTHERAPY IN NON-HODGKIN'S LYMPHOMA OF THE NASOPHARYNX

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Aims: Lymphomas are malignant neoplasms of the lymphocyte cell lines. They are mainly classified as either Hodgkin's or non-Hodgkin's lymphoma (NHL), and, on the bases of cell of origin, as B-lymphocyte or T-lymphocyte origin. Despite primary NHLs of the nasopharynx are rare, lymphomas represent about 2,5% of head and neck tumours. The present abstract aims to describe the CT and MR imaging features and the response and safety to radiotherapy in a rare nasopharynx NHL referred to the Radiotherapy Unit of Pisa University Hospital.

Methods: In November 2016, a 71-year-old woman was referred to otolaryngologist with unilateral hearing loss. Past medical history was not significant, and the patient was non-smoker. Physical examination and nasal endoscopy demonstrated a swelling of the left tubal ostium. A computed tomography (CT) scan confirmed the presence of a nasopharingeal mass with lateral cervical adenopathy. The biopsy revealed NHL: extranodal marginal zone B-cell lymphoma CD20+, CD5+, CD10-, bcl-6-, Ki67:35%. From October 2016 to February 2017, six cycles of chemotherapy with R-Bendamustine were administered, then a disease restaging with PET/CT, CT and MRI scan demonstrated a partial response with a significant size reduction in nasopharyngeal mass and cervical lymphadenopathy. After CT, the patient was referred for Radiation Therapy Department. The RT treatment was performed with DHX LINAC VARIAN System with IMRT technique, using coplanar beams of 6 MV photons. We utilized a head-shoulder thermoplastic mask as immobilization system. The prescribed doses was 42 Gy (delivered in 20 fractions; 2.1 Gy/ fraction) on tumor mass and pathological limphnodes and 36 Gy (delivered in 20 fractions; 1.8Gy/fraction) on primary disease and the retropharyngeal and laterocarvical nodes.

Results: The therapy was not well-tolerated for appearance of xerostomia, nausea and weight loss. These symptoms disappeared one month after the end of radiotherapy. The patient has repeated radiological examinations (CT scan and PET) every three months after the end of radiotherapy. No signs of recurrence are currently present.

Conclusions: Considering the low incidence, the optimal management of primary nasopharyngeal NHL is still unclear. Since NHLs exhibit both high chemosensitivity and radiosensitivity, combined modality treatment, comprising of CT and RT (with an RT dose of ≥40 Gy), results in satisfactory outcome in patients with this rare neoplasm.

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EFFECT OF RADIOTHERAPY OR SYSTEMIC THERAPY ON SURVIVAL IN PATIENTS WITH RECURRENT GLIOBLASTOMA MULTIFORME: RESULTS FROM A SINGLE INSTITUTION

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Aims: There is no standard treatment available for recurrent high-grade gliomas. Despite some evidence of improvement in progression-free survival, no significant increase in overall survivor (OS) has been demonstrated with any particular approach. This retrospective analysis evaluates the impact on OS with different salvage therapies, including no treatment, systemic therapy, or radiation and systemic therapy in patients with Glioblastoma (GBM).

Methods and Materials: Patients (pts) treated for GBM between January 2009 and May 2016 with Stupp's Schedula and who developed recurrence disease, were included in this retrospective study. Those who died less a month after progression or with a poor performance status were excluded. Survival from diagnosis was compared between patients receiving no therapy, systemic therapy alone , or in combination with radiotherapy.

Results: The analysis included 153 pts who developed relapse, excluding those who died less a month after progression or with a poor performance status. At a median follow-up time of 48 months, the median survival (MS) from diagnosis was 18 months. A total of 69 patients (45%) received neither reirradiation nor systemic treatment at progression, 63 (41%) received systemic treatment only, and 21 (14%) received both radiation and systemic therapy. Patients who received no treatment had a median survival of 14 months, lower than systemic therapy alone (28 months), and both radiation and systemic therapy (30 months).There was statistically significant survival difference between

three groups (p=0.0001).

Conclusions: Patients who received no salvage treatment had poorer survival than those who received chemotherapy alone or in combination with radiotherapy. Latter have had a significantly better survival then chemiotherapy group. Further investigations are needed to define the optimal choice of therapy, and in particular the role of reirradiation and systemic treatment in patients with recurrent GBM.

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INITIAL OUTCOMES OF SINONASAL MALIGNANCIES TREATMENT AT TRENTO PROTONTHERAPY CENTRE

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Aims: We reviewed our experience for the treatment sinonasal cancers (SNC) of different histology treated with protontherapy (PT) alone or in combination with photons in terms of disease control and early toxicity

Methods: From August 2015 to May 2018, 20 patients (pts) with SNC, of which 13 males and 7 females. Median age 63 years (range: 15-88). Site of origin maxillary sinus in 10 cases, nasal fossa in 6, ethmoid sinus in 4. Pathology was: adenoid cystic carcinoma 4, adenocarcinoma 4, sarcomas, tumours with neuroendocrine differentiation 3 (2 esthesioneuroblastoma and 1 sinonasal undifferentiated carcinoma), 2 squamous cell carcinoma, 1 carcinoma with myoepiteliod sarcomatoid differentiation and 1 ameloblastoma. There were 2 stage IV C pts; for one a solitary metastasis had been deemed resectable, pending control of primary disease, for the other a complete response was achieved after induction chemotherapy. Two pts were stage IVB, 8 stage IVA, 3 stage III, 2 stage II; 2 estesioneuroblastomas Kadish C stage. 12 pts were referred at initial diagnosis 8 for recurrence. In 8 cases radical surgery was attempted before PT, in 12 a definitive treatment was given. Surgical margins were negative in 3 cases, microscopically positive in 3 and macroscopically in 1. Chemotherapy was administered pre-PT in 1 pt, concomitant in 1, pre-and concomitant in 3 and pre-and post-PT in 1. PT was reirradiation for 4 pts at a median time of 3 years (range: 1-16); A combined photon(Ph)-PT treatment was done twice. Planning technique was Simultaneous Integrated Boost in 9 pts. Multi field optimization (MFO) was employed 5 times, a combined technique SFO-MFO in one. Elective neck irradiation was performed 6 times, (2 with ph). Median dose was 69.3 Gy(RBE) (range: 50-70) high risk, 60 Gy(RBE) (range: 60.0-66.0) intermediate risk and 54 Gy(RBE) (range: 54.0-59.4) low risk PTV .

Results: All pts complete PT without side effects stopping it. One patient discontinued PT for his own choice. At a median follow up of 13 months (range: 1-29) 4 local progressions have developed with 2 pts succumbing to them; 1 pt is alive with local disease, 1 has a distant metastasis. Acute toxicity was mild with G3 mucositis, dermatitis and dysgeusia developing in 4, 4 and 2 pts respectively. A dehiscence of the surgical scra was the only G3 late side effect.

Conclusions: PT for sinonasal malignancies seems a feasible and tolerable treatment for SNC. Longer follow up is needed to gather more consistent evidence

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EXPERIENCE OF THE U. O. RADIOTHERAPHY OF THE AZIENDA OSPEDALIERO- UNIVERSITARIA PISANA IN THE IRRADIATION OF PARAGANGLIOMAS

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Aims: Athough paragangliomas are generally slow-growing benign tumors, they can significantly compromise the patient's quality of life in relation to their onset site and to the symptoms they cause such as tinnitus, dysphonia, facial paralysis, difficulty in speech, sense of pharyngeal repletion and hearing loss. The surgery approach is not always feasible so radiotherapy can be a good alternative: the aim of our study is to demostrate how radiotherapy can be a good strategy able to guarantee reduction or stability of the tumor mass giving to the patients a satisfying quality of life.

Methods: From June 2011 to October 2017 we treated 8 patients between 31 and 73 years old with paraganglioma. The left carotid bulb, the right jugular sinus, the left upper laterocervical area, the right jugular tympanic area, the right thyroid-jugular area, the left paracardiac level and bilateral laterocervical areas were the anatomical sites involved. Five patients were treated with radiosurgery whit a total dose of 16 Gy, 1 patient was subjected to stereotactic radiotherapy with a total dose of 21 Gy in 3 fractions, 1 patients performed stereotactic radiotherapy with a total dose of 25 Gy in 5 fractions and 1 patient, who had a jugular exeresis in 2012 and recurrence in 2015, was treated with conventional radiotherapy with a total dose of 50 Gy in 25 fractions.

Results: Four of the 8 patients showed reduction in tumor mass; in 3 cases the size of the paraganglioma remain stabilized and in 1 case there was a progression with a consequent worsening of the symptoms. One patient who showed stability, have developed 3 years after radiotherapy new lesions in other sites. All 8 patients had excellent treatment tolerance without any noteworthy acute and late side effects. We also observed that radiosurgery dose offer a better outcome than stereotactic radiotherapy: in 5 patients treated with radiosurgery, 3 of them showed disease reduction and 2 presented stability; instead the others patients, 2 of them had showed stability and 1 had increase of the tumor mass.

Conclusions: Our results show that radiotherapy is safe and efficacious and offers a good tumor control with minimal side effects and better quality of life.

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IMPACT OF MULTIDISCIPLINARY TUMOR BOARD IN BRAIN TUMOR MANAGEMENT ON A PERSOLIZED MEDICINE CHALLENGE: THE OMNYBUS PROJECT

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Aims: Multidisciplinary clinics have become the standard practice for cancer care worldwide. As technology and research in rare cancer care are advancing, more specialties are involved in the diagnosis, treatment and follow-up of patients with brain tumors. The aim of the OMNYBuS project is to investigate the role of tumor board in an attempt to established, maintaining and improving the multidisciplinary discussion in order to obtain the best personalized treatment plan.

Methods: The project provides a retrospective and a prospective phase. In this retrospective phase we collected data obtained from the first year experience of multidisciplinary tumor board. It involves neurosurgeons, radiation oncologist, radiologist, anatomo pathologists and residents. The analysis is a descriptive evaluation in order to arrange the management of prospective phase. The primary endpoint was the management change rate in terms of exchange, addition, or subtraction of treatment modality. The secondary endpoints were the delay considering treatment starting time, extra diagnostic work-up and time needed for academic discussion.

Results: Diagnostic imaging results and interpretation, medical, surgical, and/or radiation treatment planning, and pathology results and interpretation were the most commonly identified aspects of patient care discussed. Our retrospective study included 148 consecutive cases, presented at brain tumor board between March 2017 and March 2018: 33,3% high grade gliomas, 10,8% anaplastic astrocytomas, 6,5% oligodendrogliomas, 2,2% low grade gliomas, 14% meningiomas, 14% single metastases, 8,6% multiple metastases, 5,4% other type of lesion. No delay was observed in treatment starting time, reduction of diagnostic work-up accounted for 65,7% and time for case discussion was about 10 minutes per patient with a median presence of 22 clinicians. The implementation rate of treatment changes after tumor board was 9.2% and diagnosis, diagnostic work-up, and radiological findings were influenced after multidisciplinary meeting.

Conclusions: This data emphasizes the fact that in a relevant number of cases the initial treatment strategy could be modified after a multidisciplinary discussion, especially in rare disease as brain tumors. This retrospective phase allows us to elaborate a data collection strategy to prospective analyze the adherence to guidelines, the reduction of diagnostic work-up and the patients related outcomes.

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PROTONTHERAPY OF PARAGANGLIOMAS: PRELIMINARY RESULTS OF THE PROTONTHERAPY CENTRE OF TRENTO

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Aims: Paragangliomas (PGL) are rare usually benign, but locally aggressive tumors, Overall and specific Survival analyses reveal that most patients do not die of PGLs thus local control and QoL are a meaningful endpoint for comparative decision making. Proton therapy (PT) can spare more healthy tissue than conventional and/or intensity-modulated X-ray therapy (IMRT) and it can result in fewer side effects. The aim of this study is to evaluate PT safety, feasibility and dosimetric aspects in the definitive treatment of PGL.

Methods: From December 2015 to May 2018, 10 pts, 6 females and 4 male, median age 53.0 years (range, 42-88 years) were treated for histological or radiological confirmed H&N PGL. 4 patients (pts) had positive familiar history (3 SDHD, 1 SDHB mutation). 6 pts had > 1 PGL, for a total of 20 PGLs treated. Locations were: jugulotimpanic (6); timpanic (1); jugular (1); vagal (3); carotid body (6), paravertebral (3). Maximum diameter ranged between 20 and 45 mm. All pts but two were irradiated with definitive intent, 1 was treated postoperatively because of residual disease and 1 for relapse. Acute and late toxicities were evaluated according to the CTCAE v 4.0. Quality of Life (QoL) was evaluated using the EORTC QLQ-C30 and H&N35 questionnaires.

Results: All pts were treated with active beam scanning PT, 2-3 fields with single field optimization (SFO) for a median total dose of 50.0 GyRBE (range 50-60 GyRBE). Median PTV was 89.0 cc. Posterior beam arrangement was preferred in order to spare as much as possible critical structures. All patients completed PT

without interruptions. No acute toxicity > G2 was observed. Only one late toxicity G1 (soft tissue fibrosis) was observed. Two pts had improvement of symptoms related to the disease: 1 pt 1 dysphonia improvement 1 month after PT; 1 pt improvement of VII cranial nerve paresis and reduction of tinnitus 1. All pts reported stability or improvement in the evaluation of their health status and QoL. At a median FU of 17.1 months (range 10.3-28.9 months) all patients are locally controlled.

Conclusions: Proton therapy for PGLs is a safe, feasible, and well tolerated treatment. The superiority in dose distribution compared to X-ray therapy could translate in better results in terms of long-term toxicity and QoL .

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DOSIMETRIC EVALUTATION OF VOLUMETRIC MODULATED ARC THERAPY (VMAT) IN SINONASAL CANCER RADIOTHERAPY

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Aims: To assess dosimetric parameters of volumetric modulated arc therapy (VMAT) for nasosinusal malignancies with regard to the coverage of planning target volume (PTV) and the sparing of organs at risk (OAR).

Methods: Nine patients with naso sinusal malignancies were treated with postoperative radiotherapy (VMAT, 2-3 non coplanar arcs) between 2015 and 2016. Seven patients were treated on primary target volume only (tumor bed), two patients required also nodal irradiation. Planning goals were the following: PTV: > 98% volume covered by >95% of prescribed dose; >107% of prescribed dose to < 2% PTV volume; for organs at risk (OARs): maximum doses (D(max)) < 60 Gy to the brainstem, < 54 to the optic chiasm, < 50 to the optic nerves, <40 Gy to the eyes and < 5 Gy to the lenses. Dose was prescribed to the median dose according to ICRU 83. Dose-volume histogram, the maximum, minimum, and mean doses to the target volumes and organs at risk, and monitor units (MUs) were evaluated.

Results: VMAT offered a good tumor volume coverage and provided a good sparing of OARs (mean Dmax ipsilateral optic nerve:45,8 Gy, mean Dmax contralateral optic nerve: 43,3; mean Dmax optic chiasm: 46,4 Gy; mean Dmax brainstem: 37,9 Gy; mean Dmax ipsilateral eye: 47,6 Gy; mean Dmax contralateral eye: 33,3 Gy). VMAT showed low MUs (mean MUtot: 583,7) and low treatment delivery.

Conclusions: VMAT's plans further reduce doses to critical structures that are in close proximity to the target volume, and reducing treatment delivery time, decrease the effects of intrafractional uncertainties that can occur because of patient movement during treatment delivery.

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DOSE VARIABILITY IN DIFFERENT LYMPH NODE LEVELS DURING LOCO-REGIONAL BREAST CANCER IRRADIATION: THE IMPACT OF DEEP INSPIRATION BREATH HOLD (DIBH)

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Purpose: Aim of the present analysis was to evaluate the movement and dose variability of the different lymph node levels of node-positive breast cancer patients during adjuvant radiotherapy with regional nodal irradiation (RNI) in deep-inspiration breath hold (DIBH).

Methods: Thirty-five consecutive node-positive breast cancer patients treated from October 2016 to February 2018 receiving postoperative RT of the breast or chest wall including RNI of the supra-/infraclavicular lymph node levels (corresponding to level IV, III, Rotter LN (interpectoral) and some parts of level II) were analyzed. To evaluate the lymph node level movement, a center of volume (COV) was obtained for each lymph node level for free breathing (FB) and DIBH plans. Geometric shifts and dose-differences between FB and DIBH were analyzed.

Results: A significant movement of the COV in anterior (y) and cranial (z) dimensions was observed for lymph node levels I-II and Rotter lymph nodes ($p<.001$) due to DIBH. Only minor changes in the lateral dimension (x axis) were observed, without reaching significance for levels III, IV and internal mammary. There was a significant difference in the mean dose of level I (DIBH vs FB: 38.2Gy/41.3Gy, $p<0.001$) and level II (DIBH vs FB: 45.9Gy/47.2Gy, $p<0.001$), while there was no significant difference in level III ($p=0.298$), level IV ($p=0.476$) or internal mammary nodes ($p=0.471$).

Conclusions: A significant movement of the axillary lymph node levels was observed during DIBH in anterior and cranial directions for node-positive breast cancer patients in comparison to FB. The movement leads to a significant dose reduction in level I and level II. Considering the potential relevance of unintended regional nodal irradiation of lymph node in the era of deescalated axillary dissection or following neoadjuvant chemotherapy regimens, it remains difficult to estimate the real impact on local control rates. Further clinical trials are needed to establish the most effective treatment strategy in this patient population.

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CARBON IONS RADIOTHERAPY IN THE TREATMENT OF PANCREATIC ADENOCARCINOMA

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Background: Pancreatic cancer is one of the most lethal cancer. Complete surgical resection is the only curative treatment, but unfortunately a small percentage of patients are candidable at time of diagnosis. Also after radical surgery, local control (LC) and survival rates are very low. Chemotherapy and radiochemotherapy are the standard of care in unresectable tumor, but due to its inherent chemoradio-resistance, the LC remains poor Carbon ions radiotherapy (CIRT) has a higher relative biological effectiveness compared to photons or protons which may result in increased efficacy as shown in other radioresistant diseases.

Aims: to report the early preliminary experience with CIRT in the treatment of pancreatic adenocarcinoma (PA).

Methods: We retrospectively analyzed 13 patients with PA who have been treated with CIRT at National Center of Oncological Hadrontherapy (CNAO) between September 2014 and March 2017 . Six (46%) patients presented already in recurrent situation and 7 (54%) had a locally advanced disease. Syngo RT Planning TPS, version C13, was used for plan optimization and calculation of RBE-weighted dose distributions according to the Local Effect Model (LEM). Intensity modulated particle therapy (IMPT) was employed. Median total dose was 57.6 GyE (range: 43.2-57.6 GyE) delivered in median number of 12 fractions (range: 8-12 fractions). Median dose for fraction was 4.8 GyE (range: 4.6-4.8 GyE). Toxicity was recorded according to CTCAE 4.0.

Results: All patients completed the scheduled treatment and CIRT was well tolerated. Acute toxicity was mild, no grade 3 side effects were observed. No severe late toxicity (grade 3) was scored. Overall, 1- and 2-years Overall Survival (OS) were 68% and 20%, respectively. We observed LC in 6 (46%) patients translating into estimated 1- and 2-year LC rates of 38%. Progression Free Survival (PFS) and Metastasis Free Survival (MFS) were reached in 4 of 13 (31%) patients, therefore the estimated 1- and 2-years PFS rates were 23%. and 1- and 2-years MFS rates were 51% and 34% respectively.

Conclusions: CIRT seems to be feasible, safe and well tolerated treatment for PA that for its radio-resistance, could be an ideal disease to test the efficacy of CIRT. Hadrontherapy for PA should be further investigated in a prospective trial.

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PHASE 2 CLINICAL STUDY FOR THE PREOPERATIVE TREATMENT OF OPERABLE OR BORDERLINE OPERABLE ADENOCARCINOMA WITH CHEMOTHERAPY AND CARBON ION HADRONTHERAPY

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Background: At the National Centre for Oncological Hadrontherapy (CNAO), we started a phase II clinical trial for neoadjuvant chemotherapy (NACT) followed by preoperative carbon ion radiotherapy (CIRT) for patients with resectable or borderline resectable pancreatic cancer

Aims: Primary endpoint of PIOPPO trial is local progression free survival and secondary endpoints are overall survival, R0 resectability rate and treatment toxicity (including intra and perioperative toxicity).

Methods: PIOPPO is a prospective, phase II, multicentre and single-arm study. Thirty patients will be enrolled in the study, the sample size being defined with an expected probability of success proportion of success at 24 months of 60% vs 35% (H0: $p <= 0.35$-H1: $p> 0.35$). Enrolled patients with a resectable or borderline resectable pancreatic cancer underwent to 3 cycles of FOLFIRINOX followed by CIRT at the dose of 38.4 Gy [RBE] carried out in 8 fractions, 4 fractions per week. 4D and breath gated planning is performed and rescanning is carried out. GTV is established using CT, MRI and PET images. CTV is defined as GTV with 5 mm margin, locoregional elective lymph node and neuroplexus region. From 4 to 6 weeks after completion of CIRT patients will undergo conventional pancreatic surgery. Subjects who meet the enrolment criteria but eventually decline to participate in the study will serve as controls. In the post-operative period, adjuvant chemotherapy is given according to clinical practice.

Results: Since January 2018 four patients have been so far enrolled and two have completed the surgical phase. No significant acute toxicities, including surgery-related were observed. Our preliminary results suggest that CIRT does not affect negatively the surgical approach.

Conclusions: Our results provide initial evidence of the feasibility of the combined chemotherapy and CIRT in the neoadjuvant setting for resectable or borderline resectable pancreatic cancer.

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CARBON ION RADIOTHERAPY IN THE MANAGEMENT OF LIPOSARCOMA OF THE SPERMATIC CORD: A CASE REPORT

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Introduction: Spermatic cord (SC) is an unusual site for presentation of liposarcoma (LPS).To our knowledge, there are about 200 cases reported in literature of LPS of the SC but there are no reports concerning carbon ion radiotherapy (CIRT) for LPSs

Aims: To describe a rare pathology and discuss its treatment with CIRT

Material and Methods: We report a case of dedifferentiated LPS in a 82-year-old man who noticed a progressive painless swelling in the left inguinoscrotal. He was referred for surgery with diagnosis of hydrocele. Intraoperatively, urologist found a mass within the cord and a left orchiectomy was decided and performed.

Results: Pathology revealed a dedifferentiated LPS of the cord with rabdomiosarcomatous differentiation and positive microscopically margins (R1). Patient underwent to second surgery to clear surgical margins and no further treatment was recommended. After an asymptomatic follow-up of 11 month, MRI showed a scrotal tumor recurrence (21 x 15 mm) treated with resection and intra-operative radiotherapy (total dose 10 Gy). Final pathology was consistent with a dedifferentiated LPS extending into the subcutaneous tissue with R1 margins. Patient developed an early locoregional recurrence (32x27 mm) 2 weeks later and he was admitted for CIRT in our Center. Treatment planning: he was immobilized in the supine position with a custom thermoplastic mask; CT images (2 mm thickness) and a contrast-enhanced MRI were performed and rigidly registered; CE-marked Syngo RT TPS(Version C13) was used for plan optimization and calculation of RBE-weighted dose distributions according to the Local Effect Model (version I). Intensity modulated particle therapy was employed. The dose prescribed was 76.8 Gy (RBE) in 16 fractions, 4.8 Gy (RBE) per fraction (4 fractions per week). Treatment was well tolerated and no interruption was needed. At the end of CIRT, patient experienced grade 1 erythema (CTCAE 4.0 grading scale). No high late toxicity was reported (only grade 1 fibrosis). Patient relapsed after a progression free survival of 28 months.

Conclusions: We observed a similar therapeutic effectiveness to that of surgery in the treatment of relapse of LPS, with an acceptable rate of morbidity of normal tissues. We believe that CIRT should be considered for patients at high risk for local relapse or in case of multiple local recurrences.

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CARBON ION RADIOTHERAPY IN A DEDIFFERENTIATED ORBITAL LIPOSARCOMA: A CASE REPORT

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Introduction: About 40 cases of primary orbital LPSs had been previously reported in the literature.

Aims: To report a case of dedifferentiated LPS treated with carbon ion radiotherapy (CIRT) as conservative and radical treatment at CNAO.

Material and Methods: A 41-year-old Caucasian woman complained pain in her left eye. She had 10/10 visual acuity bilaterally with no limitation in motility. Magnetic resonance imaging (MRI) of the orbit showed an oval-shaped mass (maximum diameter: 1.3 cm) arising between the medial rectus muscle (MRM) and the globe, shaping and displacing the optic nerve laterally. It was characterized by an inhomogeneus high signal in T2–weighted. Tumor was removed and pathology revealed a dedifferentiated LPS, grade 2 according to French Federation of Comprehensive Cancer Centers Post-surgery MRI showed an inhomogeneus signal in the retrobulbar fat and a thickening of MRM, 18-FDG PET was negative but 11-C-Metionine PET showed a soft medial orbital uptake. Patient refused orbital exenteration followed by adjuvant radiotherapy and she was admitted for CIRT at CNAO. Treatment planning: she was immobilized with a custom thermoplastic mask; CT images (2 mm thickness) and contrast-enhanced MRI were performed and rigidly registered. Syngo RT Planning TPS(version C13) was used for plan optimization and calculation of RBE-weighted dose distributions according to the Local Effect Model (LEM). The dose prescribed was 73.6 Gy (RBE) in 16 fractions, 4.6 Gy (RBE) per fraction (4 fractions per week). A Single Beam Optimization (SBO)/ Intensity modulated particle therapy (IMPT) was employed for optimization. Treatment was well tolerated and no interruption was needed. At the end of CIRT, she experienced grade 1 erythema, grade 1 conjunctivitis (according to CTCAE 4.0) and a weak retro-bulbar pain. She was followed up with MRI and ocular examination every 3 months and toxicities was recorded. After a follow up of 28 months, there was no evidence of recurrence, she experienced only a sporadic deficiency of the ipsilateral rectus muscles and a grade 1 xerophthalmia .

Conclusions: In our experience CIRT seems to be feasible, safe and well tolerated and should be considered especially for patients refusing surgery.

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HELICAL TOMOTHERAPY IN THE TREATMENT OF LUNG CANCER PATIENTS: A MONO-INSTITUTIONAL STUDY (2014-2017)

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Aims: To evaluate the use of Helical Tomotherapy (HT) in the treatment of lung cancer. The HT system employs a compact 6 MV Linac-based on CT ring gantry to rotationally deliver intensity modulated fan beams. Patients are translated through-out the gantry on a treatment couch, resulting in helical irradiation geometry. The HT unit also contains a mega-voltage CT detector array located opposite the radiation source for pre-treatment verification, allowing accurate re-positioning. This technique permits to precisely target tumors while minimizing impact on surrounding healthy tissue.

Methods: 36 patients with early stage lung cancer (cT1-T2, cN0) were treated in our institution from 2014 to 2017 with HT. No patients had positive lymphnodes in previous CT or PET/CT scan. No patients were fit for surgical indication due to concomitant medical conditions. The patients was placed with arms above the head, while the hands held a support such as a handlebar. All the CT images were acquired from the skull base to 3 cm below the diaphragm. CT axial scanning was performed at 3-mm intervals: for this purpose a CT Multislice GE Healthcare Discovery 590HT was used. The radiation oncologists contoured the volumes of interest (CTV) according to the RTOG guidelines. The planning target volume (PTV) was generated from the CTV volume by adding a 3 mm margin in all directions. Accurate delineation of organ at risk was performed. In these patients, we used several radiotherapy schedules, according to volume and site of the lesions. Treatment plans were evaluated on a dedicated TPS.

Results: Grade 1 Radiation Pneumonitis was seen in 8/36 patients (22%) and Grade 2 was observed in 4/36 patients (11%). No patients need hospitalization. Radiation-induced rib fracture was not seen in our group of patients. Grade 1 dyspnea was observed in 4 patients (11%) and grade 2 in 2 patients (5%). Other major complications (cutaneous or hematologic) were not observed. At 9 months, we observed complete response in 9 patients (25%), partial response in 12 (33%), stable disease in 4 (11%), progressive disease in 10 (28%) and 1 patient was not evaluable. At 2 years, the LC rate for all patients was 69,5%.

Discussion: HT is a safe and feasible technique to treat patients with early stage lung cancer. Acute toxicity was acceptable. This study had several limitations: a small number of patients, an heterogeneous clinical and radiological presentation of treated lung cancer and a short follow up.

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CARBON ION RADIOTHERAPY FOR MALIGNANT MUCOSAL MELANOMA OF THE HEAD AND NECK: CNAO EXPERIENCE

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Aims: To evaluate efficacy (local control, LC) and safety of active scanning carbon ion radiotherapy (CIRT) for malignant mucosal melanoma (MMM) of the head and neck treated at the National Center of Oncologic Hadrontherapy (CNAO).

Methods: Data from 23 consecutive patients with pathologically confirmed MMM treated with CIRT between June 2013 and December 2017 were analyzed. Prescription dose was 65.6-68.8 Gy(RBE) in 16 fractions delivered over 4 weeks. Follow-up was performed every 3 months with a clinical examination and contrast MRI. Toxicity was scored according to the CTCAE 4.0 scale. Time to event data was calculated according to the Kaplan-Meier Method.

Results: Patients median age was 70 years (range 39- 87). Primary tumors were located in the paranasal sinus/nasal cavity (75%), orbit (9%), oral cavity (4%), oropharynx (4%), lacrimal duct (4%) and nasopharinx (4%). After a median follow-up of 12 months, 7 patients are alive and 14 patients dead with distant progression. Six patients experienced local progression. The actuarial 1 year LC was 72.9%, 1 year overall survival (OS) 69.8%, and 1 year distant progression free survival (dPFS) 54%. No G4 acute reactions were reported. Three patients experienced mucositis G3 that regressed at first follow-up. Maximum late toxicity observed were: 2 cases of mucositis < G2, 3 cases of G2 trigeminal neuralgia, 1 case of G2 trismus and 1 of G3 hypoacusia (expected toxicity).

Conclusions: Although the short follow-up CIRT for MMM is safe and, LC data are promising. The management of this rare malignancy requires a multidisciplinary approach to in order to improve prognosis.

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SIMULATION BY GEANT4 OF THE INTERACTION OF A X-RAY BEAM INSIDE A RADIOTHERAPY BUNKER: PHYSICAL ASPECTS AND DOSIMETRY

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Aims: Simulate through Geant4 the interactions of a x-ray beam, generated by a modern clinic Linac, within a radiotherapy bunker.

Methods: The Geant4 program, a toolkit developed at CERN in 1974 and continuously updated, allows to simulate the interaction of any kind of known particle within any geometry and material. The rapid evolution of this software has enabled its use in Medical Physics and especially in radiotherapy over the last few years for its ability to simulate interaction between particles and matter.

Results: The developed simulation software has been able to describe the propagation of the x-ray beam, emitted by the Linac gantry, and to follow its interactions through the complex geometric structure of the linac-Bunker system. The kinetic energy distributions of photons and secondary neutrons produced within the bunker have been studied. In addition, the energy deposited by the secondary particles on the walls and on the door was simulated, essential for dose quantification. Two different simulations were performed, in the presence and absence of air within the treatment room, to highlight the effect of air on the interaction of the particles. The simulation showed that the presence of a labyrinth within the bunker is necessary in order to reduce the flow of particles that will interact with the door.

Conclusions: The simulation environment created through the Geant4 toolkit has allowed us to assess the flow of neutron particles affecting the shielding walls of the bunker and in particular the emerging flow from the walls of the bunker as its thickness changes. In this first simulation phase, the walls of the bunker were considered as homogeneous concrete.

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BRACHYTHERAPY IN UTERINE CERVIX CANCER: POSSIBLE OPTIMIZATIONS USING RM IMAGES

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Aims: Use of morphologic Magnetic Resonance Imaging (MRI) in cervical cancer (CC) improved tumor targeting for women with CC in treatments with external beams radiation therapy (ERT) and HDR brachytherapy boost (BRT).

Methods: The improved efficacy of radiotherapy treatment results in part from huge imaging innovations. Advanced radiation techniques may significantly benefit CC patients, in terms of decreasing late toxicity and in terms of dose escalation. MRI is a very important imaging method for CC radiotherapy, its multiple planes allowing for a accurate definition of the target volume. The image-fusion TC-RMI allows careful contouring for both target and OARs. Indeed, concerning mobility of pelvic organs MRI is particularly useful to measure motion variability due to its excellent soft tissue visualization. A practical solution is to incorporate the observed variations for better target definition both for ERT treatment and even more for BRT local treatment.

Results: Patients initially performed BRT and subsequently ERT treatment. RMI helpful to reduce uncertainties in the definition of a shrinking target volume with a greater and more reproducible dose adaptation. Dose optimization is obtained adjusting the source loading and the dwell times. The analysis of DVH parameters has become standard: dose to CTV is evaluated in terms of dose covering 90% of the High Risk CTV (D90) and the dose volume constraints for OARs are 75 Gy (EQD2) in 2 cc of rectum and 90 Gy (EQD2) in 2 cc of Bladder.

Conclusions: MRI plays an important role in the development of modern radiotherapy as it provides information about organ motion and tumor volume shrinkage. MRI during treatment will allow for excellent soft tissue delineation, improved tumor targeting and dose optimization. MRI offers a superior dose optimization compared with a conventional CT-planning based approach, evaluated through the cumulative dose delivered by BRT+ERT treatment.

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A DOSIMETRIC COMPARISON BETWEEN DIFFERENT EXTERNAL PHOTON BEAM TECHNIQUES FOR ACCELERATED PARTIAL BREAST IRRADIATION

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Aims: To evaluate the advantages and limits of CyberKnife (CK) compared to the two external beam radiotherapy (RT) techniques (3D-CRT and VMAT), a dosimetric study was conducted with special focus on dose to organs at risk (OAR), and on target coverage and technical features.

Methods: Ten consecutive early-stage breast cancer patients were selected and for each one of them, three treatment plans were generated for 3DCRT, VMAT and CK. Dosimetric parameters, extracted from the dose volume histograms, were used to evaluate the differences in terms of PTV coverage and OAR sparing among the irradiation techniques. Conformity Index (CI) and

Homogeneity Index (HI) were also compared.

Results: VMAT and CK provided equivalent dose conformity, with CIs significantly higher compared to 3D-CRT technique. Besides, VMAT achieved the best results in terms of HI and target coverage ($p<0.05$). Significant differences were observed in the OAR dosimetric data, except for heart. 3DCRT achieved the best results in terms of the dose to the whole contra-lateral breast. The treatment session time is usually longer for CK (on average 60 minute) than for VMAT and 3DCRT techniques (15 to 20 minute).

Conclusions: In this dosimetric comparison, all RT techniques are feasible to delivery APBI.CK and VMAT provide higher conformity than 3D-CRT, although with 3D-CRT we observed a reduction of the dose to the OARs. In CK treatment organ motion is controlled and, despite the longer treatment times, the delivery accuracy is expected to be better than 3D-CRT and VMAT, especially if motion management systems are not used.

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IN VITRO STUDY OF CIEDS MALFUNCTIONS BY DIRECT EXPOSURE AT DOSES≥2GY

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Aims: Exposure to radiotherapy in patients with cardiac implantable electronic devices (CIEDs), both pacemakers (PMKs) or implantable cardioverter defibrillators (ICDs) seems to be still troubleshooting, since high dose photon radiation at even less than 6 MV power may lead to transient or permanent soft or hard damage of CIEDs. The aim of this study was to evaluate potential CIED malfunctions by direct exposure at doses≥2Gy in Radiotherapy.

Methods: 54 PMKs and 18 ICDs with at least 4 months to Elective Replacement Indicator (E.R.I.) were referred for study. To minimize external noise CIEDs were plugged with IS-1, DF-1 or DF-4 plugs, depending on type and model. All CIEDs underwent baseline interrogation. Single chamber devices were programmed in VVI/40 mode and dual or triple chamber ones were programmed in DDD/40 mode. Rate adaptive function was disabled. In ICDs, antitachycardia therapies were disabled with the ventricular tachycardia/fibrillation monitor still active. To build the corresponding treatment plan (Oncentra External Beam, Elekta Ltd, Crawley, UK) a centering CT was performed and CIEDs were randomly irradiated by a linear accelerator (Synergy Agility, Crawley, UK) in a homemade phantom, with three radio-opaque markers placed on its surface to mark the treatment isocenter. 6 MV photon beams at increasing doses of 2, 5 and 10 Gy (600 Um/min) were delivered. *In vivo* EPID dosimetry was performed to assess the effectiveness of the dose. During exposure, 8 wi-fi telemetry enabled devices were observed in a real-time session and real-time function was recorded. After exposure and after one month, all CIEDs were interrogated.

Results: During exposure, one wi-fi enabled ICD recorded ventricular oversensing with pacing inhibition and ventricular fibrillation detection at 2 Gy. The other devices recorded minor ventricular noise at 2, 5 or 10 Gy. No major failures were observed in most CIEDs after exposure. In less recent CIEDs 1 reset to emergency mode was observed in a PMK at 2 Gy, while 2 PMKs reached the E.R.I at 2 and one at 10 Gy, respectively. A part from the ICD that recorded real-time malfunction, none of the ICDs reported function impairment at 2, 5 or 10 Gy exposure.

Conclusions: Our data suggest recent CIEDs being safe during exposure at doses up to 10 Gy. However, larger series and longer follow-up are required to confirm these data.

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DOSIMETRIC EVALUATION AND ACUTE TOLERANCE OF HYPO-FRACTIONATED IMRT TO WHOLE BREAST / CHEST WALL PLUS REGIONAL NODES

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Aims: The optimal fractionation scheme for radiotherapy on breast/chest wall and regional nodes is actually debated. We reported the dosimetric data and preliminary clinical results of a three weeks hypofractionated schedule delivered with intensity modulated radiation therapy (IMRT).

Methods: We evaluated the clinical charts and radiotherapy treatment plans of locally advanced breast cancer patients treated with radiotherapy after conservative surgery or mastectomy and axillary nodes dissection. All patients were treated with pre- or post-surgery chemotherapy, while radiation was postponed after the end of chemotherapy. Radiotherapy was delivered with static IMRT on chest wall / whole breast plus regional nodes. Internal mammary nodes were included only in case of radiological or histological positivity. The prescribed dose was 40,05 Gy in 15 fractions, according to the UK guidelines. In case of conservative surgery, the tumor bed boost received an additional boost of 10Gy in 4 fractions. Dosimetric data of PTV, heart, omolateral lung, thyroid and contralateral breast were analyzed. Daily positioning was controlled with orthogonal x-ray. Acute toxicity was scored with Common Terminology Criteria version 4.0 scale. Homogeneity index was correlated with acute tolerance.

Results: Forty patients were treated between August 2017 and May 2018. All patients were at high risk of

acute and late toxicity, due to the large PTV volumes and the previous chemotherapy. Radiotherapy was delivered on chest wall and regional nodes in 21 patients, while 19 patients received to whole breast and regional node irradiation (with an additional boost on lumpectomy in 14 cases). Dosimetric and toxicity data were summarized in Table 1. The IMRT technique allowed a high homogeneity dose distribution inside the PTV. The organs at risk constraints were always respected. Only 7 patients (18%) developed grade 2 skin toxicity. No cases of Grade 3 or 4 toxicity were registered. Boost to tumor bed did not increase toxicity.

Conclusions: Hypofractionated IMRT for whole breast/chest wall and regional nodes irradiation permits a good dose homogeneity inside the PTV and limits the dose to lung, hearth, controlateral breast and thyroid. The treatment was well tolerated and no cases of severe acute toxicity were registered.

Table 1. Dosimetric and toxicity data.

		Chest wall + nodes RT				Whole breast + nodes RT			
PTV	HI	1.05 (1.03-1.08)				1.04 (1.03-1.08)			
	D2%	42.05 Gy (41.09 Gy – 43.29 Gy) 105% (102.6%-108.1%)				41.81 Gy (41.05Gy-43.21Gy) 104.4% (102.5%-107.9%)			
	Dmean	40.05 Gy (39.4 Gy – 40.97 Gy) 100% (98.4 %– 102.3%)				40.01 Gy (39.57Gy-40.89Gy) 99.9% (98.8%-102.1%)			
Lung	V20Gy	8.3% (5.4%-20.7%)				7.2% (3.9%-9.7%)			
	V10Gy	18.3% (8.8%-34.5%)				17% (9.4%-28.6%)			
Heart (only left side)	Dmax	21.23Gy (12.98Gy-25.75Gy)				15.7 Gy (2.6-23.2)			
	Dmean	1.84 Gy (1.00Gy-3.96Gy)				1.44 Gy (0.76Gy-2.5Gy)			
	V5Gy	3.35% (0.03Gy – 8Gy)				3% (0.5%-9.1%)			
Thyroid	Dmean	6.5Gy (2.2Gy-24.7Gy)				6.9Gy (3Gy-26Gy)			
Contr. breast	Dmean	0.8Gy (0.2Gy-0.8Gy)				0.55Gy (0.2Gy-2.6Gy)			
SKIN TOXICITY		G0: 10	G1: 8	G2: 3	G3:0	G0: 8	G1: 7	G2: 4	G3:0
SUBCUTANEOUS TOXICITY		G0: 20	G1: 1	G2: 0	G3:0	G0: 17	G1: 1	G2: 1	G3:0
PAIN		G0: 20	G1:1	G2: 0	G3:0	G0: 17	G1: 2	G2: 0	G3:0

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CHRONIC SIDE EFFECTS OF A HYPOFRACTIONATED SCHEME WITH SIMULTANEOUS INTEGRATED BOOST USING TOMODIRECT AS ADJUVANT RADIOTHERAPY IN EARLY BREAST CANCER

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Aims: To evaluate the dosimetric feasibility of implant sparing technique using intensity-modulated (IM) radiotherapy (RT) in patients with intermediate-risk breast cancer (BC). This approach, called HALFMOON, targets the actual clinical target volume (CTV), sparing the chest wall and the organs at risk (OARs) underlying the implant from receiving the full prescription dose.

Methods: HALFMOON technique was applied to BC patients with immediate breast reconstruction, with either expander or prosthesis. All patients underwent a hypofractionated treatment of 40.05 Gy in 15 fractions over 3 weeks, using Tomotherapy® Hi-Art System (Tomotherapy Inc., Madison, WI) in helical modality. The CTV consisted of skin, subcutaneous tissues and pectoralis major muscle overlying the reconstruction, excluding the deepest part of the implant, chest wall and bony thorax.

Results: From April 2016 to January 2018, 18 patients were treated with the HALFMOON approach, 13 left-side and 5 right-side. These plans were compared with dosimetric data of standard treatment plans undergoing the same hypofractionated scheme, in which the whole implant and the rib plane were included in the CTV. All the data concerning the treatment plans entered a dedicated databank (RTPR039-000-Tomotherapy-Breast) as part of a research project on IMRT and/or hypofractionated schedules, notified to the IEO Ethical Committee. The aim was to assess the differences in dose distribution throughout the planning target volume (PTV) and the OARs. No statistically significant difference was found in the PTV coverage for any of the analysed metric (V95%, V90%, Dmean and D0.03cc). Conversely, regarding OARs, a statistically relevant dose reduction was observed for the heart (D15%, $p=0.048$), for the stomach (Dmean, $p=0.015$) and for the ipsilateral lung (D15%, $p<0.0001$; D20%, $p<0.0001$; D35%, $p=0.003$). Moreover, when considering implant irradiation, V90% and D50% decreased by 50% and 8%, respectively, in the HALFMOON plans compared to the standard plans ($p<0.0001$).

Conclusions: The dose-painting approach of HALFMOON technique is technically feasible and resulted in high dose conformity of the target with a significant reduction of radiation dose delivered to the implant and adjacent OARs. A clinical study is needed to assess the impact on reconstruction cosmetic outcome and local control.

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INFLUENCE OF DIFFERENT BLADDER FILLING LEVELS IN DEFORMABLE IMAGE REGISTRATION (DIR) ALGORITHM PERFORMANCES (ANCILLARY STUDY OF AIRC PROJECT IG-14300)

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Aims: To evaluate the performances of RayStation Hybrid Deformable Image Registration (H-DIR) algorithm to different bladder filling levels in male pelvis anatomic site: this is a first step for further DIR performances evaluation on patient CT acquired with different treatment setup.

Methods: Different image datasets were computationally generated exploiting the ImSimQA package (Oncology System Limited, Shrewsbury, UK) to evaluate the performances of Raystation H-DIR algorithm (RaySearch Laboratories, Stockholm, Sweden). Six specific Deformation Vector Fields (DVF) were applied to an original synthetic man pelvis dataset (reference CT) resulting in deformed CTs (target CTs) with various bladder filling levels. Target CTs simulated three bladder shrinking and three bladder enlargement with respect to the reference CT. In all the cases, the bladder was deformed preserving femoral heads stiffness. Simulated bladder volumes were 206 ml for the reference CT and 72, 105, 141, 252, 293 and 327 ml for the target CTs. Two H-DIR were created between each target CTs and the reference CT: in the first case (DIR1), no controlling or focusing regions of interest (ROIs) were chosen, while the bladder was selected as a control ROI in the second case (DIR2). The obtained deformed ROIs were mapped to the target CT and then compared to ImSimQA generated ROIs. The evaluation was performed by computing the Dice Similarity Coefficient (DSC) and the Mean Distance to Conformity (MDC).

Results: In DIR1 case, the bladder ROIs DSC decreases when the variation between the reference and the target bladder volume increases, in both shrinking and enlargement directions. An opposite behaviour (increasing values with respect to bladder volume increasing variation) was observed for the MDC value. No specific trend was observed in DIR2 case. Bladder ROIs means and standard deviations were 0.84±0.08 and 1.00±0.00 for the DSC and 5.06±0.70 mm and 1.84±0.01 mm for the MDC in DIR1 and DIR2 case respectively. No significant difference was observed in the femoral heads ROIs coefficients when the two different DIR were applied, whereas the DSC and MDC of the prostate and rectum ROIs presented better results when DIR2 was performed.

Conclusions: Raystation H-DIR performances can be influenced by bladder filling fluctuation. Soft tissue ROIs values of DSC and MDC improve when DIR are performed exploiting controlling ROIs, while for bone structures no significant change is shown.

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PATIENT SELECTION FOR DEEP INSPIRATION BREATH HOLD FOR LEFT-SIDED BREAST CANCER RADIOTHERAPY: IMPACT OF ANATOMICAL FEATURES ON HEART DOSE SPARING

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Aims: To identify anatomical features correlating to heart dose sparing by deep inspiration breathhold (DIBH) IMRT technique compared to free-breathing (FB) IMRT for left-sided whole breast radiation therapy (RT) to guide the selection of patients who will effectively benefit from DIBH.

Methods: 35 consecutive patients who underwent (DIBH) left-sided breast RT had both FB and DIBH CT simulation. All patients were planned with two tangential fields 6MV-flattening-filter-free FFF (DIHB-IMRT), with prescription of 50Gy/25fr to whole breast and 60Gy to simultaneous integrated boost (SIB). A comparison plan was generated with two/four (FB-IMRT) 6MV IMRT tangential fields. Mean dose and dosevolume metrics (V5,V10,V20) were analyzed and compared for heart with both techniques. For each dose metric, differences between the two techniques were detected by using the Student's t test or Wilcoxon signed rank test for paired sample with significance level of $p \leq 0.05$. Correlation analyses were performed between such dose difference (D) metrics and patient (FB) anatomic features: maximal heart distance and length (MHD, MHL), breast separation (BS) and his sagittal component (Y). To test the impact of the anatomic features on heart dose metrics, linear regression analyses were performed between these anatomic features and heart dose difference metrics.

Results: All dose metrics for the heart were significantly reduced ($p<0.01$) with DIBH. A positive correlation were observed between BS and dose difference (D)_mean correlated with mean (Pearson's coefficient r=0,60, p=0,02), D_D2% (r=0,5, p=0,0037) and D_V5 (r=0,66, p=0,0019) by DIBH. Also Y and MHL showed a positive correlation with D_mean, (r=0.5 p=0037) and (r=0.5 p=0.006) respectively. For every 1-cm increase in MHD(FB) D_D2% increase 0f 4,4 Gy and D_V5 increase of 1.4%

Conclusions: In this patient cohort, DIBH technique has been shown to reduce dose to the heart. MHD(FB), MHL(FB), BS(FB) and Y(FB) served as significant predictors for heart dose sparing by DIBH. These parameters can be easily measured at the time of CT simulation and thus may be used as simple and quick tool to determine which patient may benefit from a DIBH technique.

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MODERATE HYPOFRACTIONATED SIMULTANEOUS INTEGRATED BOOST RADIOTHERAPY IN PROSTATE CANCER: RESULTS OF A STUDY COMPARING CONVENTIONAL AND HYPOFRACTIONATED TREATMENT

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Purpose: To report 5 year outcome and toxicity in organ confined prostate cancer (PCa) in low and intermediate risk patients treated with a moderate hypofractionated simultaneous integrated boost radiotherapy (RT) compared to a conventional schedule treatment.

Patients and Methods: Data of 384 patients with PCa treated between August 2006 and June 2017 were retrospectively reviewed. Treatment schedule consisted in hypofractionated RT (Group 1) with simultaneous irradiation of 70 Gy to prostate and 63 Gy to prostatic vesicles in 28 fractions or in conventional fractionated RT (Group 2) with a total dose of 80 Gy in 40 fractions. The intermediate-risk patients underwent androgen deprivation for a median duration of 6 months. The 5 year biochemical reapse-free survival (bRFS), cancer-specific survival (CSS) and overall survival (OS) were assessed. Furthermore, we evaluated gastrointestinal (GI) and genitourinary (GU) toxicities. Uni - and multivariate Cox regression analyses were used to test the impact of several clinical variables on both outcome and toxicity.

Results: A total of 185 patients were treated with hypofractionated RT and 199 with conventional schedule. At a mean follow-up of 5 years, no significant differences were observed in toxicity and outcome between the two groups. In Group 1, a biochemical relapse occurred in 7 patients (3.7%), whereas 5 patients (2.7%) reported a clinical relapse (1 local, 2 locoregional and 2 systemic recurrence, specifically). In Group 2, 6 patients (3.0%) experienced a biochemical relapse and 5 patients (2.5%) showed a clinical relapse (2 local, 2 locoregional and one systemic recurrence, more in detail). Early grade 1-2 GU and GI toxicities were observed in 41 (22.2%) and 26 (14.2%) patients respectively in hypofractionated group and in 77 (38.6%) and 38 (16.1%) patients respectively in conventional fractionated RT. Late GU and GI toxicities occurred in 4 (1.5%) and 6 (2.1%) patients respectively in Group 1. In Group 2, 6 (3%) and 12 (6%) patients experienced late GU and GI toxicities, respectively. The 5 year bRFS, CSS and OS were 96.3%, 97.3% and 88.1% respectively in Group 1, and 97.2%, 97.5% and 85% respectively in Group 2. At uni- and multivariate analysis, only early GU and GI toxicities reported a moderate correlation with the respective late toxicities endpoints in both groups.

Conclusions: Results obtained in this study showed that the moderate hypofractionated schedule used in our Centre could be an effective approach leading to very good outcome with an acceptable toxicity profile.

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HALFMOON (HELICAL ALTERED FRACTIONATION FOR IMPLANT PARTIAL OMISSION) FEASIBILITY STUDY: IMPLANT SPARING POST-MASTECTOMY HELICAL TOMOTHERAPY

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Aims: To evaluate the dosimetric feasibility of implant sparing technique using intensity-modulated (IM) radiotherapy (RT) in patients (pts) with intermediate-risk breast cancer (BC). This approach, called HALFMOON, targets the actual clinical target volume (CTV), sparing the chest wall and the organs at risk (OARs) underlying the implant from receiving the full prescription dose.

Methods: HALFMOON technique was applied to BC pts with immediate breast reconstruction with either expander or prosthesis. All pts underwent a hypofractionated treatment of 40.05 Gy in 15 fractions over 3 weeks using Tomotherapy® Hi-Art System (Tomotherapy Inc., Madison, WI) in helical modality. The CTV consisted of skin, subcutaneous tissues and pectoralis major muscle overlying the reconstruction, excluding the deepest part of the implant, chest wall and bony thorax (Figure 1A).

Results: From April 2016 to January 2018, 18 pts were treated with the HALFMOON approach, 13 left-side and 5 right-side. These plans were compared with dosimetric data of standard treatment plans undergoing the same hypofractionated scheme, in which the whole implant and the rib plane were included in the CTV (Figure 1B). The control group was selected in order to keep the same left/right-side ratio of HALFMOON plans. All the data concerning the treatment plans entered a dedicated databank (RTPR039-000-Tomotherapy-Breast) as part of a research project on IMRT and/or hypofractionated schedules, notified to the IEO Ethical Committee. The aim was to assess the differences in dose distribution throughout the planning target volume (PTV) and the OARs. No statistically significant difference was found in the PTV coverage for any of the analysed metric (V95%, V90%, Dmean and D0.03cc). Conversely, regarding OARs, a statistically relevant dose reduction was observed for the heart (D15%, $p=0.048$), for the stomach (Dmean, $p=0.015$) and for the ipsilateral lung (D15%, $p<0.0001$; D20%, $p<0.0001$; D35%, $p=0.003$). Moreover, when considering implant irradiation, V90% and D50% decreased by 50% and 8% respectively in the HALFMOON plans

compared to the standard plans (p<0.0001).

Conclusions: The dose-painting approach of HALFMOON technique is technically feasible and resulted in high dose conformity of the target with a significant reduction of radiation dose delivered to the implant and adjacent OARs. A clinical study is needed to assess the impact on reconstruction cosmetic outcome and local control.

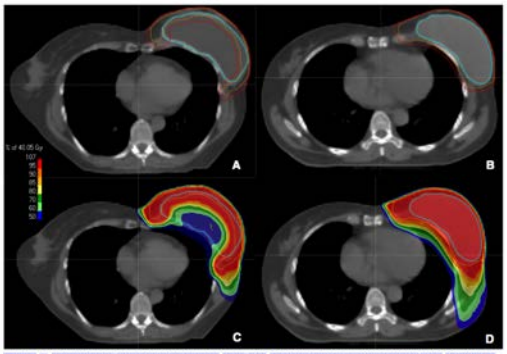

Figure 1: Transversal computed tomography views. A) Contouring of the CTV (orange), the PTV (red) and the implant (light blue) in HALFMOON plan. B) Contouring of the CTV (orange), the PTV (red) and the implant (light blue) in non-sparing implant plan. C) HALFMOON plan dose distribution. D) Non-sparing implant plan dose distribution.
Percentage isodoses of the prescription dose: red-orange dose cloud = 95-90%; green dose cloud = 70-60%; blue dose cloud = 50%.

Figure 1.

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COMPARATIVE ANALYSIS OF TREATMENT PLANS FOR BREAST RADIOTHERAPY

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Aims: The aim of this study was to compare two technique of treatment planning for breast cancer: two tangent fields to dynamic wedges and treatment planning with tangent fields to “field in field” technique (FiF).

Method: Five treatment planning for breast cancer radiotherapy were imported from the “oncentra” TPS system to the “monaco” TPS system recently installed at our radiotherapy center. The treatment plans planned on the “oncentra” TPS were developed using 3D techniques in tangent fields with wedge filters and were performed on the Linac Varian DHX. The re-elaboration of the same treatment plans, on the “monaco” system, was planned using the “FiF” 3D technique using beam segments in addition to the two main tangent beams, without using filters and assuming the treatment on the Linac Versa Hd also recently installed at our radiation therapy center. The total planned dose to the entire breast was 50 Gy, 2 Gy per fraction, for all treatments compared.

Results: The parameters compared for the CTV were: the 98% dose, the maximum dose and the average dose. In the “FiF” technique, the dose distribution to the target was significantly more homogeneous in all treatment plans (8.3% less average deviation of the maximum dose from the average dose), slight decrease in the average dose delivered (about 2% in less) to the target. The body dose was significantly lower in “FiF” care plans with hot spots that never exceeded 105%.

Conclusions: The “FiF” technique improves the dose homogeneity to the target, significantly decreases the body dose accumulations with probable reduction of acute side effects in the skin. The comparison between the two techniques could be considered an intermediate step for the planning of modulated treatments to be performed on the linac Versa Hd.

P207

TARGET DEFINITION IN SALVAGE RADIOTHERAPY FOR RECURRENT PROSTATE CANCER AFTER PROSTATECTOMY: FROM THE INVISIBLE TO THE VISIBLE CONCEPT

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Aims: The aim is to report feasibility, prostate specific antigen (PSA) response and toxicity of hypofractionated salvage radiotherapy (RT) for macroscopic local recurrence in the prostatic bed from prostate cancer (PCa) after prostatectomyin highly selected RT-naïve patients (pts).

Methods: Inclusion criteria were RT-naïve pts (no previous adjuvant pelvic RT); biochemical recurrence according to the European Association of Urology (EAU) guidelines followed by clinically evident local recurrence; N0, M0; written informed consent. Salvage RT was delivered only on the macroscopic/radiological relapse assessed by multiparametric magnetic resonance imaging or/and 11C-choline positron emission tomography/computed tomography. A PSA test was performed every 3 months after treatment: biochemical response (BCR) was defined as a reduction of PSA value >10% with respect to pre-RT PSA value, biochemical progression (BCP) as a PSA increase >10%, and biochemical stability (BCS) as a PSA stabilization between 10% and -10%. Clinical follow-up was performed at 6 and 12 months, and every 12 months afterward to assess genito-urinary (GU) and gastrointestinal (GI) toxicity (according to RTOG-EORTC guidelines).

Results: We retrospectively analyzed 38 pts treated between 6/2013 and 10/2017 for clinically visible PCa recurrence in the prostatic bed with hypofractionated intensity modulated (IMRT) schedules; median dose was 32.5 Gy (range 25-35) in 5 fractions. Initial PSA (iPSA) and Gleason score (GS) were 8.0 ng/ml (range 2.7-30) and 7 (range 5-9), respectively. Median interval between diagnosis of PCa and salvage RT was 84 months (range 3-248) and median PSA at clinical progression was 1.30 ng/ml (range 0.14-16). Biopsy confirmation was performed in 22 pts (57.9%). Five pts received concomitant hormonal therapy (HT). No GI or GU acute toxicity>G2 was reported. The analysis of clinical outcome is still ongoing. At 3 months, BCR was observed in 28 pts (73.7%), BCS in 1 patient (2.6%) and BCP in 2 pts (5.3%). 3-month PSA evaluation is not available for 7 pts. At median follow-up of 12 months, BCR was confirmed in 27 pts (71%); BCP occurred in 11 pts (28.9%). Clinical progression followed BCP in 9 cases (23.7%) after a median time of 18 months (range 8-30). No late GI or GU toxicity was reported at all.

Conclusions: Based on the available data, hypofractionated conformal IMRT is a feasible and safe approach for isolated macroscopic recurrence in the prostatic bed, with a low acute toxicity profile.

P208

RADIOMICS WITH TEXTURE ANALYSIS TO IDENTIFY ACTIVE BONE MARROW WITHIN THE PELVIS FOR BONE MARROW SPARING IMRT APPROACHES

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Aims: Concurrent chemo-radiation (CT-RT) is the standard of care for anal cancer patients. IMRT is frequently used. Even when this approach is employed, acute hematologic toxicity remains an issue. Bone marrow (BM) sparing IMRT decreases this type of toxicity. This strategy requires the correct identification of active BM within the pelvis. Functional imaging with 18FDG-PET has been explored for this purpose. We compared a radiomic approach based on texture analysis to a 18FDG-PET-based strategy to identify pelvic BM in anal cancer patients treated with concurrent CT-RT.

Methods: A total of 10 patients submitted to IMRT was analyzed. Several bony structures were defined: pelvic and lumbar-sacral (LSBM), lower pelvis (LPBM) and iliac (IBM) bone marrow. Active BM characterized employing 18FDG-PET was defined as all subregions within pelvic bone marrow having Standard Uptake Values (SUVs) higher than SUVmean. For the radiomic approach, an octagonal element made of 5-by-5 pixels moving by 1 pixel at time in both directions was considered. A set of 36 features was computed for each octagonal element: 4 statistics (mean, standard deviation, skewness and kurtosis) and 32 texture features were analyzed. Five texture features were extracted with the Gray Level Difference Method. We extracted: contrast, angular second moment, entropy, mean, and inverse difference moment. The training set and the classifier were constructed. The discrete training set was used for constructing a Decision Tree for each patient. We employed the CART algorithm for the tree construction and the Gini Index for the identification of the best splitting rule for each node. We then compared the active bone marrow masks obtained from PET with those returned by radiomics. The comparison was carried out using three indices:

Dice index (overall overlap between the two segmentations):
$Dice=(2\cdot(RS\cap CT))/(RS+CT)$
Precision (over-segmentation):
$Precision=(RS\cap CT)/CT$
Recall (under-segmentation):
$Recall=(RS\cap CT)/RS$

Results: Median Dice index was 0.91 (range 0.75-0.99) for LSBM, 0.88 (range 0.65-0.97) for IBM and 0.57 (range 0.22-0-75) for LPBM (Figure 1). Median Precision was 92% for LSBM, 88% for IBM and 43% for LPBM. Median Recall was 89% for LSBM, 82% for IBM and 45% for LPBM.

Conclusions: A radiomic approach based on texture analysis has a good performance in identifying active BM within the pelvis compared to 18FDG-PET for LSBM and IBM. The poor performance for LPBM needs further evaluation.

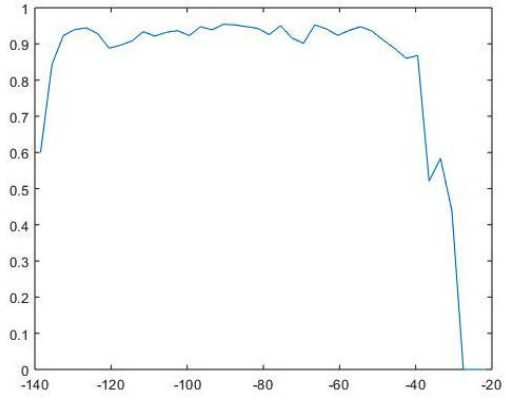

Figure 1.

P209

CARBON ION RADIOTHERAPY FOR LOCALLY RECURRENT RECTAL CANCER IN PATIENTS WITH PRIOR PELVIC IRRADIATION

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Aims: To evaluate effectiveness and tolerance of carbon ion radiotherapy (CIRT) in patients with locally recurrent rectal cancer.

Patients and Methods: Between August 2014 and February 2017, a total of 10 patients (M:F= 8:2) with a median age of 58.5 years (range: 46-78) were treated with CIRT as re-irradiation for locally recurrent rectal cancer at CNAO. All patients had a history of, at least, a surgery for rectal adenocarcinoma. Except a case in which external beam radiotherapy (EBRT) was delivered for a prostatic cancer (total dose: 76 Gy), the previous pelvic EBRT ranged from 45 Gy to 50.4 Gy. Moreover, 1 patient received brachytherapy boost (total dose: 20 Gy) after pelvic EBRT and 1 patient, at time of the first recurrence, underwent to reirradiation with stereotactic radiotherapy (30 Gy in 6 fractions). Seven (70%) relapses originated in the presacral, 1 in perineal, 1 in perianal and 1 in pre-coccigeal region. In three patients, the target tumor was located close to the bowel and before CIRT they underwent to surgery to place a spacer between the tumor and the digestive tract. Toxicity was scored according CTCAE 4.0 scale.

Results: Median time from the previous pelvic EBRT to CIRT was 89.3 months (range: 13.8 - 138.2). Median total dose of 60 GyRBE (range: 35-76.8) was administered in a median number of 16 fractions (range: 15-20) over 4 weeks (from 3 to 4.8 Gy RBE/fraction). The median gross tumor volume (GTV) was 28.42 cc (range: 7.21-300.8 cc) and the planning target volume (PTV) ranged from 53.55 to 742.64 cc. All patients completed the scheduled treatment course. Acute toxicity was mild and mainly neuropathic: grade 2 (G2) neuropathic pain in 1 (10%) and G1 in 2 (20%) patients. The major late toxicities were peripheral neuropathy (20%, G2). No G≥3 acute/late reaction were observed. After a median follow-up of 13 months, local progression was seen in 4 patients after a median local disease free survival (L-DFS) of 11.4 months (range: 2.4- 39.7). The estimated 1-year-local control rate was 80%.

Conclusions: Our first experiences using CIRT as re-irradiation in the management of reccurent rectal cancer are encouraging. CIRT offers an advantage in terms of local control and toxicity rates are low. More data and longer follow-up are required to investigate the long-term disease control and to determine late effects.

P210

A SYSTEMATIC REVIEW ABOUT IMRT WITH SIB IN MALIGNANT GLIOMAS

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Aims. Malignant gliomas represent the most common primary brain tumors in adults, with poor outcome and survival. The pattern of failure after definitive or post-operative radiation therapy (RT) is primarily local recurrence, and this could be due in part to inadequate therapeutic doses limited by the tolerance of normal tissues to irradiation. The use of intensity modulated RT (IMRT) with its possibility of minimizing adjacent tissue dose and of focal increasing primary tumor dose might lead to better outcome and survival. The aim is to present a systematic review of clinical results on overall survival (OS) and disease free survival (DFS) after IMRT with simultaneous integrated boost (SIB) in gliomas.

Methods. A systematic review of published literature was performed on PubMed and the Cochrane Library. Retrospective and prospective clinical trials reporting outcome in patients treated with IMRT-SIB have been analyzed. RT doses were converted in biologically 2Gy-equivalent doses (EQD2) to better compare the results.

Results. A total of 220 patients from 9 studies were included. These studies are characterized by small sample size and different RT doses and fractionations, but with similar planning analysis. In all studies, the gross tumor volume was defined as the contrast-enhancing residual tumor on the T1-weighted pre-RT brain magnetic resonance imaging scan plus the entire surgical cavity. This volume was the target of focal dose increase. Mean EQD2 dose of 72.5 Gy (range 60-101.3) was delivered. Acceptable toxicities were reported, with 8/220 (6,3%) patients experiencing severe acute (≥ G3) toxicity and 5/220 (2,27%) patients experiencing severe late (≥ G3) toxicity. Mean OS and PFS were respectively 18.2 (range 14.8-22.4) and 10.7 (range 7.8-12) months. However local failure is still the most common site of recurrence.

Conclusions. IMRT-SIB contribute to the control of the disease, resulting in satisfactory OS and PFS, with acceptable toxicities.

P211

STEREOBODY RADIOTHERAPY FOR NODAL RECURRENCES IN OLIGOMETASTATIC PATIENTS: AN INTERIM ANALYSIS FROM TWO PHASE I CLINICAL TRIALS

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Aims: Stereotactic body radiotherapy (SBRT) has been shown to achieve high local control rates in limited metastatic burden of disease. Few papers reported on the efficacy of SBRT in limited nodal metastases. The primary aim was to review institutional outcomes of patients with solitary or oligometastatic lymph nodes treated with SBRT.

Methods: Data from DESTROY-1 phase I and SRS-DESTROY-2 phase I clinical trials were reviewed and analyzed. These trials were a 5 fractions SBRT trial and a single fraction radiosurgery study, respectively. Endpoints were the detection of toxicities, overall response rate (ORR), and local control (LC). Tumor response was assessed according to the RECIST and EORTC PET criteria. Patients with all metastatic sites, primary tumor types and histologies were included between December 2003 and January 2018.

Results: 180 patients (M/F: 94/86); median age: 67, range 37-88) treated with SBRT for a total of 253 nodal recurrences were analyzed. Patients with different cancer types were included in the analysis, in particular the primary were: gynaecological (N°=49; 27.2%), prostatic (N°=38; 21.1%), gastrointestinal (N°=25; 13.9%), lung (N°=22;12.2%), breast (N°=16; 8.9%), genito-urinary (N°=12; 6.7%), head and neck (N°=11; 6.1%) and skin tumours (N°=7; 3.9%). The most common metastatic sites were the thorax (N°=92; 36.4%) and the pelvis (N°=88; 34.8%), followed by abdominal (N°=61; 24.1%) and neck regions (N°=12; 4.7%). The majority of lesions (79.8%) were treated with VMAT technique, while the former by 3DCRT or IMRT techniques. Dose prescription to the Planning Target Volume varied from 12 Gy/single fraction to 50 Gy/5 fractions. With a median follow-up of 21 months (2-124) no grade 3 acute or late toxicity was recorded. ORR based on CT/MRI/PET was 79.8% (CI 95%: 73.3-85) with a complete response rate of 57.7% (CI 95%: 50.3-64.5). 24-and 48-months actuarial local control (freedom from progression in the irradiated site) was 81.3% and 69.6%, respectively.

Conclusions: These data on a large series of lymph node recurrences in oligometastatic patients demonstrate low risk of morbidity after SBRT and favourable long term local control.

P212

ADAPTIVE INDIVIDUALIZED HIGH-DOSE RADIOTHERAPY IN HIGH RISK RECTAL CANCER: FINAL RESULTS OF A PHASE II STUDY

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Aims: Aim of this study was to evaluate the pathological response (pR) of locally advanced rectal cancer (LARC) after adaptive high-dose neoadjuvant radiation therapy (RT) with concomitant and sequential boost based on [18F]FDG-PET/CT performed two weeks after RT start.

Methods: Patients (pts) with high risk biopsy proven LARC were included. Pts with potentially resectable metastases were not excluded. Primary end-point was pR rate. Secondary objectives include acute and late toxicity. The sample size was calculated based on the two-stage design by Simon. All pts performed [18F]FDG-PET/CT at baseline (PET0) and after 2 weeks during RT (PET1). Intensity modulated RT (IMRT) technique was performed concurrently with capecitabine-based chemotherapy in all pts. Tumor volume (TV) was delineated using a gradient-based delineation method; the maximal standardized uptake values (SUVmax) were calculated. The dose to rectum, mesorectum and pelvic lymph nodes was 45 Gy (1.8 Gy/fr). A simultaneously integrated boost (SIB) was delivered to GTV+2 cm margin with a total dose (td) of 50 Gy (2 Gy/fr). A sequential boost was delivered to GTV+5 mm margin with a td of 5 Gy in 2 fractions (2.5 Gy/fr) for a td of 55 Gy. PR was expressed by Dworak tumor regression grading (TRG); toxicities were scored

according to the CTCAE v4.03 scale; quality of life (QoL) was evaluated using the EORTC QLQ-C30 questionnaire at the beginning and at the end of the RT.

Results: Nineteen pts (14 M, 5 F), median age 58.4 years, cT2-4, N0-2 M0 were enrolled. 1 patient (pt) was M1 (liver): he was treated with concurrent chemo-RT after 2 cycles of chemotherapy. The median SUV max of the rectal lesions was 14.5 (range: 4.5-45) at PET0 and 9.7 (range: 5.6-20.4) at PET1 ($p<0.001$). TV measured by PET was 20.87 mL (range: 1.1-90.9) at PET0 and 9.79 mL (range: 0.4-62.3) at PET1 (p:0.001). All pts underwent surgery 7-12 weeks after RT while 1 pt refused surgery after evidence of cCR. According to Dworak system, 6 pts (31.6%) had TRG=4 (complete regression) and 1 pt had TRG=3 (near complete regression). 1 pt had acute G≥3 toxicity (haematological and GI G4 toxicities) due to enzymatic deficit of DPD. Based on EORTC QLQ-C30 questionnaire, no pt had relevant (>20) changes of QoL.

Conclusions: Using an adaptive boost strategy with [18F]FDG-PET/CT in LARC, able to deliver a sequential high-dose boost on a significantly reduced volume, we recorded 36.8% rate of pathological complete or near-complete regression.

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ULTRA-HYPOFRACTIONATED PROSTATE CANCER RADIOTHERAPY: DOSE-VOLUME ANALYSIS FOR TOXICITY EVALUATION

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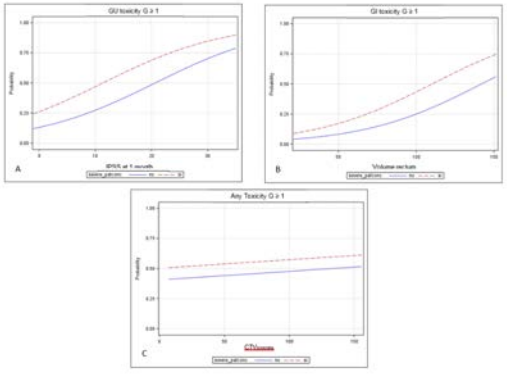
Aims: This is an ancillary study of a prospective phase II trial (AIRC-IG 13218). The purpose is to evaluate dosimetric and clinical parameters that might predict genitourinary (GU) and gastrointestinal (GI) toxicities, after ultra-hypofractionated simultaneous integrated boost (IMRT-SIB) with two dose levels (5 fractions, 7.25 Gy/fraction for the whole prostate gland and 7.5 Gy/fraction for dominant intraprostatic lesion), using volumetric modulated arc therapy.

Methods: Patients were enrolled in this study as part of an ongoing prospective clinical trial, between October 2014 and April 2017. Toxicity was assessed and scored according to Radiation Therapy Oncology Group and European Organization for Research and Treatment of Cancer scoring criteria and International Prostatic Symptoms Score (IPSS). A set of standard dose-volume specific endpoints (DVSEs) were recorded from each patient: rectum volume receiving 18 Gy (V18), 29 Gy (V29), 33 Gy (V33) and 36 Gy (V36); bladder volume receiving 18 Gy and 36 Gy. We calculated the area under the dose-volume histogram between 18 and 36 Gy both for the rectum and the urinary bladder. Logistic regression models were carried out to investigate independent variables associated with toxicities.

Results: In the univariate analysis of the entire population, we found no relationship between acute GU toxicity and any bladder-related parameter (bladder V18, V36, bladder volume). Similar results were observed for rectum, except for the association between rectum volume and GI acute toxicity, which was borderline significant ($p=0.051$ at univariate analysis and $p=0.06$ at multivariate analysis, adjusting for age and severe concomitant diseases). IPSS changed significantly ($p=0.004$) from baseline to 1 month and changes during time were significantly different by symptomatic score at first month (mild, moderate and severe, $p<0.0001$). IPSS at 1 month was significantly associated with the risk of acute GU toxicity ($p=0.04$ at univariate analysis and $p=0.03$ at multivariate analysis, adjusting for age and severe concomitant diseases). Prostate clinical target volume (CTV) is not significantly associated with any toxicity. Predicted GU toxicity probability increased with increasing IPSS at 1 month and with increasing rectal volume, whereas "any toxicity" probability did not change at varying prostate CTV (Figure 1).

Conclusions: Ultra-hypofractionated IMRT-SIB showed a good toxicity profile. Accurate patient selection is essential for the avoidance of acute toxicity.



Grade≥1 predicted toxicity probability with or without severe concomitant pathologies.

Figure 1.

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EXTREME VS MODERATE HYPOFRACTIONATION FOR LOCALIZED PROSTATE CANCER: A PROPENSITY SCORE COMPARISON OF OUTCOME AND TOXICITY

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Aims: The aim of this study is to compare clinical outcomes and toxicity of two cohorts of clinically localized prostate cancer (PCa) patients treated with two different radiotherapy (RT) regimens: Extreme hypofractionation (35Gy or 32.5Gy in 5 fractions) vs moderate hypofractionation (Fox-Chase regimen, 70Gy/26 fractions), both using intensity modulated RT (IMRT).

Patients and Methods: The analysis included two cohorts of patients with clinically localized PCa treated in our institution: 227 PCa patients treated in the period 2007-2015, receiving 70.2 Gy in 26 fractions at 2.7 Gy/fraction using IMRT and 194 patients treated primarily with extreme-hypofractionated RT using image-guided IMRT (IG-IMRT) from 2012 to 2015. Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer criteria (RTOG/EORTC) and Houston definition (nadir +2) were used for toxicity and biochemical failure evaluation, respectively. Multivariate proportional Hazard Cox models, stratified for propensity score strata, were used to compare the two populations in term of overall survival (OS), clinical progression free survival (cPFS), biochemical PFS (bPFS) and gastro-intestinal (GI) toxicity and genito-urinary (GU) toxicity.

Results: Median age of the 421 overall sample was 75 years (range: 50-89). Median follow-up was 43 months. Compared with extreme hypo-fractionation, in moderate- group we found significantly less patients at intermediate or high risk (14% vs 30%, P<0.001), less patients with indication to RT due to volume (52% vs 74% prostate + seminal vesicles, P<0.001). As concerning GI toxicity, compared with extreme hypo-fractionation, in moderate group acute G>1 events were significantly more (3% vs 9%, P=0.007). As concerning GU toxicity, compared with extreme hypo-fractionation, in moderate group acute G>1 events were registered in 11% vs 26% (P<0.001). Multivariate Cox regression models showed no significant differences between the two cohorts in term of late GI and GU toxicity, OS (P=0.91), cPFS (P=0.32) and bPFS (P=0.44).

Conclusions: Utilizing the Propensity Score Comparison there was no difference in terms of oncological outcomes at a median follow-up of 43 months comparing the two RT modalities. Moreover, the two RT regimens were associated with similar toxicity profiles.

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RADIOMICS AND SOFT TISSUE SARCOMAS: A SYSTEMATIC REVIEW

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Aims. Soft tissue sarcomas (STS) often require a multidisciplinary approach treatment including surgery, radiotherapy and chemotherapy. Radiomics attempts to quantify complex aspects of cancer images below the assumption that this information is related to tumor biology and can be very useful for tumor characterization, tumor staging, prediction of metastases and evaluation of treatment response.

Methods. A systematic review of the literature was performed. The endpoint was to identify the rationale of radiomics on MRI and PET in STS in finding new diagnostic models that could personalize therapies and predict outcomes We included studies published in English regarding radiomics and STS. Four studies analyze role of radiomics in Magnetic Resonance Imaging (MRI) for a better characterization of tumor and two studies are about radiomics models in PET for the prediction of lung metastases.

Results. A total of 256 patients from 6 eligible studies were included. Different radiomic features were calculated for each image according to the hypothesis that image features can quantify information regarding intra-tumor heterogeneity, highlighting tumor phenotype and this heterogeneity could have profound implica-

tions on tumor prognosis. The studies show that a radiomic signature extracted from MRI improve prediction of PFS and OS over clinical features alone and can also characterize grade of pathologies. The variations of MRI and PET image acquisition parameters on individual texture could enhance the response and the predictive properties of a texture-based model because FDG-PET and MRI texture features could act as strong prognostic factors of STSs and could provide insights about their underlying biology. Use of PET radiomics features toward imaging biomarker discovery hold great promise for prediction of metastases to lung in STS patients.

Conclusions. Radiomics seeks to quantify complex aspects of tumor images related to tumor biology and this could lead to improvements in treatment personalization and patient outcomes. Prospective studies are needed.

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ACUTE GASTROINTESTINAL AND GENITOURINARY TOXICITY IN HYPOFRACTIONATED RADIOTHERAPY OF PROSTATE CANCER: A COMPARISON BETWEEN VMAT AND 3DCRT WITH DAILY IGRT

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Aims: Randomized Trials suggest that in men with pre-RT Genitourinary (GU) and Gastrointestinal (GI) morbidity some hypofractionated regimens may be associated with increased toxicity. At the same time, IMRT with or without image-guided RT (IGRT) seems to decrease post-RT GI toxicity. A limited number of clinical data are available about the incidence of GU and GI toxicity in men undergoing hypofractionated RT (HyRT) and treated by Volumetric-Modulated Arc Therapy (VMAT) and IGRT. This study aims to compare the acute GI and GU toxicity of men undergoing HyRT and treated by three-dimensional conformal radiation therapy (3DCRT) or VMAT with daily IGRT.

Methods: A retrospective cohort 83 men with low/intermediate risk prostate cancer (Pca) according to NCCN criteria were selected. Patients underwent a moderate HyRT (60 Gy in 20 fractions) with daily IGRT. A regular weekly clinical assessment during treatment was arranged for the detection of early toxicity. Men were treated with VMAT (13 subjects) or with 3DCRT (70 subjects). The post treatment follow-up visits were performed at 1, 4 and 12 weeks after the end of radiotherapy. The acute GI and GU toxicities was rated according to the Radiation Therapy Oncology Group (RTOG) scale for early side effects. Differences in the incidence of toxicities between the two groups were evaluated by the Fisher's exact test. A p-Value lower than 0.05 was considered statistically significant.

Results: One week after RT, Grade 2 or more GI and GU toxicity were 41.4% vs 0% (p=0.003) and 40% vs 7.7% (p=0.027) in men treated by 3DCRT and VMAT, respectively. At four weeks after RT, although a trend toward a decreased Grade 2 or more GI (27.2%) and GU (20%) toxicity was found in the group treated by 3DCRT, a significant difference persisted only for GI toxicity with respect to VMAT (GI toxicity: 0%; p=0.033; GU toxicity: 0%; p=0.11). At 12 weeks after RT, similar G≥2 GU and GI toxicity were found in men treated with 3DCRT (GI: 4.3% and GU: 7.2%) or VMAT (GI: 0% and GU: 0%) with no significant differences between the two techniques.

Conclusions: Men undergoing HyRT with image guided VMAT experienced a significant lower GI toxicity one and 4 weeks after RT with respect to men treated by 3DCRT. A similar trend was found for GU toxicity only one week after RT. This advantage was not maintained 12 weeks after RT. Our results must be considered preliminary and more powered studies will be necessary to investigate this understudied topic.

	RTOG GI Acute Toxicity				
	3DCRT		VMAT		p value*
	No.	%	No.	%	
1 week post RT					
Grade ≤ 1	41/70	58.6	13/13	100	0.003
Grade ≥ 2	29/70	41.4	0/13	0	
4 weeks post RT					
Grade ≤ 1	51/70	72.8	13/13	100	0.033
Grade ≥ 2	19/70	27.2	0/13	0	
12 weeks post RT					
Grade ≤ 1	67/70	95.7	13/13	100	1.0
Grade ≥ 2	3/70	4.3	0/13	0	

	RTOG GU Acute Toxicity				
	3DCRT		VMAT		p value*
	No.	%	No.	%	
1 week post RT					
Grade ≤ 1	42/70	60	12/13	92.3	0.027
Grade ≥ 2	28/70	40	1/13	7.7	
4 weeks post RT					
Grade ≤ 1	56/70	80	13/13	100	0.11
Grade ≥ 2	14/70	20	0/13	0	
12 weeks post RT					
Grade ≤ 1	65/70	92.8	13/13	100	1.0
Grade ≥ 2	5/70	7.2	0/13	0	

Table 1.

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THE TREATMENT OF INTRAOCULAR MELANOMA WITH SCANNING PROTON BEAM AT ITALIAN NATIONAL CENTER FOR ONCOLOGICAL HADRONTHERAPY (CNAO)

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Introduction: At most of protontherapy center, traditionally, uveal melanoma is treated using a dedicated passive line with a passive dose delivery system. At CNAO, it is not available dedicated passive line. We used for ocular melanoma treatment the active delivery system. The aim of our treatment technique was to make available our beam for ocular melanoma treatments. These are the preliminary results of feasibility and safety of this technique.

Methods and Materials: Between August 2016 and April 2018, 76 patients with uveal melanoma were treated at CNAO using active scanning proton beams. All patients underwent tantalum clips placement to localize the tumor. They performed simulation both in the supine (computed tomography) and seated position previously immobilized in customized support and thermoplastic mask. The patient's gaze was fixed by custom Eye Tracking System, rigidly connected to the treatment chair, including a fixation light. The tumor volume contour was based on the tumor size, position and number of tantalum clips and ocular fundus image. Each plan was approved by radiation oncologist, medical physicist and ophthalmologist and verified in the treatment room with the patient sitting on the treatment chair. All patients were treated in the seated position using one horizontal beam line.

Results: The prescribed dose was 52 Gy (RBE) in 4 fractions, in 4 consecutive days for the first 47 patients. All procedures were well tolerated and carried out without any complication. Excellent intra- and interfraction patient set-up reproducibility was achieved. Based on the good tolerance and absence of acute toxicity, after one year we increased the dose prescription to 60 Gy (RBE) in 4 fractions as usual dose used in the in most proton therapy centers. From October 2017, 29 patients were treated with this higher dose.

Conclusions: The ocular treatment process with scanning proton beams at CNAO was carefully checked step by step. The successful commissioning of the ocular proton beam line, as well as the clinical validation of all the involved sub-systems led us to start the clinical activity for intraocular melanoma treatment in August 2016.

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POSTOPERATIVE RADIOTHERAPY IN BREAST CANCER PATIENTS WITH DEEP INSPIRATION BREATH HOLD (DIBH): EVALUATION OF REPRODUCIBILITY AND STABILITY OF TREATMENT

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Aims: To quantify set-up uncertainties during DIBH radiotherapy for left sided beast cancer patients (pts).

Methods: In our center from a total of 218 pts treated with DIBH radiotherapy using Real Time Position Monitoring (RPM) system and daily Image Guided Radiotherapy (IGRT), we selected randomly 50 patients (pts) with median age of 59 years (34-78). We performed off line review for a total of 1600 daily orthogonal kilovoltage (kV) 2D images sets (anteroposterior [AP] and lateral [LAT]), 300 Kv tangential portal film images (twice weekly) and 1600 breath hold curve (one for each IMRT field). According to the literature, we used a range of 5 mm in respiratory breath hold curve. The interfraction reproducibility of the DIBH system was evaluated defining the Breath Hold Level (BHL), which is the distance between the chest wall and the vertebral body on AP and LAT set-up images at isocenter level, and the Central Lung Distance (CLD), which represents the error in the AP/LAT direction for the chest wall at isocenter level in portal images. Eventually, the inter or intrafraction stability of RPM signal was estimated defining the discrepancy between the respiratory curves on both IMRT fields. For all measures we calculated the mean value, the standard deviation (SD), the systematic error (Σ) and the random error (σ) using statistics program SPSS version 17.0.

Results: The mean of BHL on LAT set-up images was 0.24 mm ± 2.43 SD, the σ of BHL was 2.5 mm, the Σ of BHL was 2.6 mm, the mean of CLD on portal images was -0.06 mm ± 2.49 SD; there were no differences in the mean value of BHL on AP set-up images depending on the limited motion in this direction. The mean shift between the range of minimum and maximum value of the treatment breath hold curve was 0.82 mm (± 1.42 SD) and 1.04 mm (± 1.30 SD) for the first and second field, respectively. No correlation was showed in reproducibility, between BHL and CLD, and stability in RPM signal.

Conclusions: Despite of no correlations between reproducibility and stability, in our preliminary experience, DIBH resulted feasible and accurate; we suggest to use daily on line IGRT based on AP set up images and medial kV tangential portal film images. In the future, we will try to study the intrafraction reproducibility of the gating DIBH technique and the verification of heart position.

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CAROTID AND BULB SPARING RADIOTHERAPY: DOSIMETRIC ADVANTAGES OF VMAT VS 3D-CONFORMAL RT IN EARLY GLOTTIC CANCER ACCORDING TO THE NEW INTERNATIONAL CONSENSUS CONTOURING GUIDELINES

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Aims: Volumetric modulated arc therapy (VMAT) is the best suitable approach for carotid sparing. Recently, new contouring guidelines for head and neck cancer have been proposed by Gregoire et al. Our aim is to investigate if VMAT maintains its superiority on 3D conformal therapy (3DRT) for carotid sparing in early glottic cancer (EGC) in the light of reduced target volumes.

Methods: CTV was contoured in 10 pts with cT1aN0 EGC according to Gregoire *et al*. indications. Carotid arteries were separately delineated in their extracranial course. Since carotid bulb is the most critical structure involved in atherosclerosis, it was also outlined including two cm superior and inferior to carotid bifurcation according to Framingham Heart study. A 1 mm isotropic margin was applied to account for anatomical changes during cardiac cycle. 3DRT and VMAT plans specifically optimized for carotid sparing were generated. The prescribed dose was 63 Gy in 28 fractions. In all plans at least 95% of the PTV was requested to receive ≥95% of the prescription dose and a spinal cord maximum dose of 25 Gy was allowed. Ipsilateral and contralateral bulbs and carotids Dmax, Dmean, V35, V50 were determined and compared between the two plans. T test for paired data with logarithmic transformation for continuous variables was used to compare dosimetric parameters. Mean and confidence interval of 95% were used to summarize continuous variables. A Two-sided α error of 5% was used as significance threshold.

Results: Mean ipsilateral bulb and carotid Dmax significantly decreased from 51,9 Gy to 36,2 Gy (p<0.0001) and from 54 Gy to 44,5 Gy (p=0,0005) for 3DRT and VMAT, respectively. VMAT also significantly lowered ipsilateral bulb (3DRT:25,3Gy; VMAT:16,5Gy; p=0.0002) and carotid Dmean (3DRT:13Gy; VMAT:10Gy;p=0,02) as well as ipsilateral bulb (3DRT:35%; VMAT:3,2%; p=0,0038) and carotid V35 (3DRT:19,9%; VMAT:4,6%; p=0,0002). VMAT dramatically lowered mean contralateral bulb (3DRT: 42,1Gy; VMAT: 16,4Gy; p<0,0001) and carotid Dmax (3DRT: 45Gy; VMAT: 19Gy; p<0,0001). Moreover, contralateral bulb (3DRT: 21,8Gy; VMAT: 8Gy; p<0,0001) and carotid Dmean (3DRT: 13Gy; VMAT: 4,8Gy; p<0,0001) and contralateral bulb (3DRT:25,5%; VMAT:0%; p=0.02) and carotid V35 (3DRT: 15,2%; VMAT:0%; p=0,005) were higher with 3DRT. No differences were observed for the other dosimetric parameters (Table 1).

Conclusions: Even with the new target delineation method, VMAT could be a new standard for the carotid sparing in EGC.

Table 1. Dosimetric comparison of 3DRT vs VMAT for carotid sparing early glottic cancer treatment.

Dosimetric Parameters	3DRT MEAN (CI 95%)	VMAT MEAN (CI 95%)	P value
Ipsilateral bulb			
Dmax (Gy)	51,9 (48,5 to 55,3)	36,2 (30,5 to 42)	<0,0001
Dmean (Gy)	25,3 (17 to 33,5)	16,5 (11,3 to 21)	0,0002
V35%	35 (13,6 to 56,4)	3,2 (1 to 9)	0,0038
V50%	7,6 (2,2 to 18)	0,1 (0,08 to 0,3)	0,13
Contralateral bulb			
Dmax (Gy)	42,1 (39,8 to 44,5)	16,4 (12,5 to 20,3)	<0,0001
Dmean (Gy)	21,8 (13,8 to 29,7)	7,9 (4,8 to 10,9)	<0,0001
V35%	25,5 (4,6 to 46,3)	0	0,02
V50%	0	0	NA
Ipsilateral carotid			
Dmax (Gy)	54 (51,2 to 56,9)	44,5 (39,6 to 49,4)	0,0005
Dmean (Gy)	13,5 (10,1-17,1)	10,1 (8,4-11,9)	0,022
V35%	19,9 (12,5 to 27,3)	4,6 (1,5 to 7,7)	0,0002
V50%	3,8 (0,15 to 7,8)	0,1 (0,1 to -0,3)	0,053
Contralateral carotid			
Dmax (Gy)	45,4 (43,2 to 47,6)	19,1 (15,5 to 22,7)	<0,0001
Dmean (Gy)	13,1 (9,1 to 17)	4,8 (4,1 to 5,5)	<0,0001
V35%	15,2 (5,8 to 24,5)	0	0,0052
V50%	0,023 (0,01 to 0,07)	0	0,34

VMAT: volumetric Modulated Arc Therapy; 3DRT: 3-D conformal Radiotherapy; V35: volume percentage receiving ≥ 35 Gy; V50: volume percentage receiving ≥ 50 Gy; NA: not assessable.

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RETROPROSPECTIVE STUDY TO PREDICT THE PHARYNGEAL CONSTRICTOR MUSCLE DOSE-RESPONSE CORRELATION IN HEAD AND NECK CANCER PATIENTS TREATED WITH IMRT-SIB-IGRT

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Aims: Radiotherapy, alone or combined with chemotherapy, is the treatment modality most used in advanced head and neck cancer. Delineation of organs at risk in the head and neck is very important for at risk radiation-induced swallowing dysfunction (RISD). Irradiation of the Pharyngeal Constrictor Muscle (PSCM) seems to play a crucial role in swallowing dysfunctions and in particular in the voice and speech quality changes. The aim of this retrospective study was

to identify which dose volume histogram (DVH) parameters are most significant to predict patient radiation-induced swallowing dysfunction, voice and speech quality.

Methods: Twelve patients with head and neck cancer who previously underwent IMRT-IGRT treatment by Tomotherapy are selected. The prescribed radiotherapy is based on SIB technique for all PTVs irradiated simultaneously over 30 daily fractions. Doses of 67.5 Gy , 60 Gy and 54-57 Gy were prescribed to primary tumour, high-risk nodal regions and low-risk nodal regions, respectively. Upper PSCM, middle PSCM and lower PSCM were outlined separately and DVHs are stored for each patient using basal planning CT. Statistical analysis (p-value ≤ 0.05 was considered significant) is performed to identify dosimetric predictors of toxicity using appropriate questionnaires taking into consideration the actual delivered dose.

Results: The study started in July 2017 and up to May 2018 12 patients have been included in the study. Mean follow-up is 5.3 months. Mean dose [range] is 60.1 [47.5-71.0] Gy, 57.4 [42-70.1] Gy and 61.8 [54.3-69.8] Gy for lower, upper and middle PSCM respectively. Preliminary results show that acute dysphagia and xerostomia are observed (62.5%). The most predictive dosimetric indices for the PSCMs were found to be the mean dose ($p \leq 0.05$); No correlation seems evident between DVH parameters and toxicity in lower PSCM; V20Gy,V30Gy,V40Gy,V50Gy and V55Gy are not correlated with toxicity for lower, upper and middle PSCM; V60Gy,V65Gy and V70Gy are correlated with toxicity for upper and middle PSCM .

Conclusions: From these preliminary results, the most predictive dosimetric indices for the PCMs seems be the mean dose.V60Gy,V65Gy and V70Gy seems correlate with toxicity for upper and middle PSCM. It is mandatory to include more patients in the study to fully confirm these preliminary results.

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CARBON IONS RADIOTHERAPY ALONE FOR THE TREATMENT OF SACRAL CHORDOMA. PRELIMINARY RESULTS AT NATIONAL CENTER OF ONCOLOGICAL HADRONTHERAPY (CNAO)

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Introduction: Chordoma is a rare bone malignant tumor originating from remnants of the embryonic notochord. The common site of origin is the sacrum (50%). En-bloc resection surgery with negative margins is often associated to significant morbidity including bowel, bladder and motor impairment. Radiotherapy, besides its role as postoperative treatment in R1- R2 resections, has been used for the radical treatment of sacral chordoma for patients not suitable for surgery. In the last decade carbon ion radiotherapy (CIRT) has been used as exclusive therapy reaching similar local control as surgical resection. The purpose of this study is to present preliminary results concerning response to CIRT for unresectable primary sacral chordoma treated at CNAO (National Center for Oncological Hadrontherapy) in Pavia.

Methods: Between March 2013 and December 2017, 59 patients with histologically proven sacral chordoma, previously judged not resectable, were treated with CIRT using active scanning beam delivery system at CNAO. All patients received a total dose of 70.4 - 73.6 Gy equivalents (GyE) in 16 fractions. We evaluated tumor volume response by high field magnetic resonance (MRI) performed every three months. For each examination, T2w FS axial images were used both to measure lesion maximum diameter and to get a manual segmentation of the tumor . RECIST 1.1 were used to evaluate chordoma response to CIRT. Similarly, the same response criteria were applied to volume modifications for treatment response. The median follow-up period was 24 months (range 12- 60 months).

Results: The preliminary results showed radiological partial response in 38 patients (64%), stable disease in 15 patients (25%) and progression disease in 6 patients (10%).

Conclusions: Our preliminary data confirm encouraging results of carbon ion treatment for primary sacral chordoma in terms of local control and acceptable toxicity. Longer follow-ups are needed to confirm the effectiveness of CIRT as an alternative to surgery in the absence of late severe side effects.

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SALVAGE RADIOTHERAPY WITH IMRT-SIB TECHNIQUE AND IGRT IN NON SMALL-CELL LUNG CANCER PATIENTS WITH POSTSURGICAL MEDIASTINAL RELAPSE AFTER SURGERY: A PILOT STUDY

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Aims: The aim of our study is to evaluate the feasibility, toxicity profile and local effectiveness of salvage intensity modulated radiotherapy (IMRT) delivered with simultaneous integrated boost (SIB) associated or not to concomitant weekly cisplatin in patients affected by NSCLC with mediastinal nodal recurrence after surgery. Patterns of recurrence, outcomes and prognostic factors were assessed.

Methods: 14 consecutive patients with stage IB-IIIA initially treated with surgery and/or adjuvant chemotherapy, received 25 fraction of 50Gy/2Gy to the elective nodal stations and boost up to 62.5Gy/2.5Gy to the macroscopic mediastinal lymph node metastases.

Concomitant weekly cisplatin (40 mg/m2) was administered to 8 (57.1%) patients.

Results: Five (35.7%) patients experienced grade 2 pneumonitis and 5 (35.7%) patients had grade 2 esophagitis. One case of grade 3 pneumonitis occurred and was successfully treated with antibiotics and steroids with no sequelae. No patient recurred locally in the boost volume (local control 100%). Loco-regional control was 79% with 3 patients that developed nodal recurrence principally marginal to the elective volume. Seven patients developed distant metastases. Median OS and PFS were 24 months and 7 months, respectively. The nodal involvement of station 7 was associated to a significantly lower median OS (4 months vs. 24 months, p=0.0001) and lower median metastasis-free survival (4 months vs. not reached, p=0.036).

Conclusions: Salvage radiotherapy with IMRT is a feasible and a well-tolerated treatment option for mediastinal recurrent NSCLC after surgery. The role of more intensified regimens of systemic therapy remain to be evaluated in further studies.

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PEDIATRIC CRANIOSPINAL IRRADIATION: EARLIES EXPERIENCES WITH VMAT AND COMPARE WITH 3D-CRT

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Purpose: To compare pediatric cranio-spinal irradiation (CSI) Volumetric Modulated Arc Therapy (VMAT) with conventional radiotherapy (3D-CRT).

Methods and materials: We evaluated the clinical use of VMAT in craniospinal irradiation in children with MB and compared the release of radiation dose to target organs and organs at-risk (OAR) in 3D CRT treatments. We have studied the feasibility of VMAT in CSI in six pediatric patients ; isocentric treatments plans of 3D-CRT and VMAT plans were created (with two or three isocenter) and the resulted dose distribution to target and to organs at risk (OAR) were compared. CSI is a complex technique that requires the use of different isocenters and field edge matching; this matching is critical for dose inhomogeneities (risk of over or under dosage in junction areas), VMAT plan expected an overlapping regions between arcs of different isocenters: cranial and spinal fields were optimized in a single plan without field matching; in this way the delivery dose is more homogeneous and the patient misalignment between different isocenters are minimised. To perform RT plans we used Monaco Planing Station (Monte Carlo Gold Standard XVMC photon Algorithm for VMAT plans and Collapsed Cone Algorithm for 3D-CRT). Four patients were treated with ELEKTA VERSA HD Linac and two with ELEKTA PRECISE Linac. Patients age varied between 4 and 15 years; the lenghts of PTV ranged from 51 cm. to 71,5 cm. and the dose prescription from 23,6 Gy to 31,2 Gy (b.i.d.). Dose to PTV, OAR and non target tissue are reported for each six patients and for both treatments. Regarding the set-up verification we used CBCT and 2D Kv in VMAT daily and portal images in 3D-CRT. Pre-treatment dosimetric verification of VMAT was performed by Octavius system.

Results: Rating of VMAT compared with 3D-CRT in CSI shows an improve dose coverage and homogenity in target volume and in vertebral bodies; VMAT technique was better in terms of OAR sparing the for all organs, in particular for hearth, liver, thiroid and esophagus compared 3D-CRT.

Conclusions: VMAT with IGRT implies better compliance and excellent dose homogeneity to the target, with dose sparing to adjacent healthy tissues improving treatment accuracy and reducing the risks of dosimetric uncertainty in the region of the field junctions and beam matching between the typical fields and the complexity of 3D-CRT treatment against a potential increase in diffuse irradiation at low doses.

P224

CARBON ION RADIOTHERAPY FOR RECURRENT PLEOMORPHIC ADENOMA AT CNAO: PRELIMINARY RESULTS

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Aims: To evaluate response and toxicity of carbon ion radiotherapy (CIRT) for recurrent pleomorphic adenoma patients (pts).

Methods: Inclusion criteria based on the CNAO phase II clinical protocol CNAOS10/2012/C were: (1)prior histological diagnosis of pleomorphic adenoma;(2)relapse after at least one previous surgical approach;(3)further surgery excluded (due to high risk of facial nerve damage/medical contraindications/refusal of the patient);(4)no previous radiotherapy. CIRT prescription dose was 65.6 Gy[RBE] in 16 fractions (4.1 Gy[RBE]/fraction). Local response and toxicity (tox) were respectively evaluated using RECIST and CTCAE v.4.0 criteria. MRI was performed after treatment every 3-4 months (mo.) in the first 2 years, every 6 mo. in the third year, then once a year.

Results: Between November 2012 and May 2017, 24 pts were treated. Median age was 47 years (range 20-68). Median time from first diagnosis to CIRT was 17.4 years (range 1–33.5). Median number of previous surgeries was 3 (range 1-6). Median time from last surgery to CIRT was 16.8 mo. (range 9.8–274.4). Two and 22

pts were treated for uninodular and plurinodular recurrence, respectively. Mean GTV was 19.8 cc (range 1.1–91.1). Mean CTV was 83.5 cc (range 25.6–148.6). Median follow-up (FU) time was 23.3 mo.(range 7.8–64.4). Radiological response at first FU was partial response and stabilization in 2 and 22 pts, respectively. At last FU, all pts were alive with local control maintained. Only 1 patient treated for plurinodular tumor had out-field recurrence at 4.5 years after CIRT. Tox during/at the end of treatment was G0, G1, G2 for 3 (12.5%), 9 (37.5%), and 12 (50%) pts, respectively. Acute tox within 3 months was G0, G1, G2 for 10 (41.7%), 11 (45.8%), and 3 (12.5%) pts, respectively. Maximum late tox was G0, G1, G2 for 3 (12.5%), 13 (54.2%), and 8 (33.3%) pts, respectively. No G3-G4 late tox was observed. Among pts with late tox, 11 (45.8%) had peripheral neuropathy (G1 and G2 in 8 (33.3%) and 3 (12.5%) pts, respectively). No patient experienced facial nerve damage as treatment-related tox.

Conclusions: In our experience, CIRT in recurrent pleomorphic adenoma pts has shown excellent local control and good toxicity profile. It might be a good alternative to invasive surgery especially when the latter is judged to be at high risk of facial nerve damage. However, a larger series of patients and a longer follow-up are needed to better investigate outcomes, especially in terms of late toxicity.

P225

LOCAL CONTROL RATE IN PATIENTS WITH SKULL-BASE CHONDROSARCOMA AFTER PARTICLE THERAPY AT CNAO

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Aims: Chondrosarcoma is a rare bone tumor that arise from the cartilage. Skull-base location is reported in about 6% of cases. The therapeutic approach to chondrosarcoma of the skull-base is still controversial and clinical experience is limited because of the relative rarity of this tumor. The aim of the study was to assess the local failure rate and overall survival (OS) of patients treated with particle therapy (Proton therapy – PT and Carbon Ion radiotherapy -CIRT) after maximal surgery or in the exclusive setting.

Methods: Between September 2011 to May 2017 35 patients (pts) (17 male, 18 female) with a median age of 45 years (range, 13-78) with histologically proven skull-base chondrosarcoma were treated with PT or CIRT at National Center of Oncological Hadrontherapy (CNAO). 17 pts (49%) underwent previous surgery. A total of 13 pts had grade I (well differentiated), 20 pts had grade II (moderately differentiated) and 2 pts had grade III (poorly differentiated) chondrosarcoma. 6 pts had brainstem involvement, 1 pts optic pathway involvement. 17 pts were treated with CIRT, 18 pts with PT. Median gross tumor volume (GTV) was 16,4 cm3 (range, 1,64 – 28,28). Median prescribed total dose was 70,4 Gy RBE (range 66-70,4 Gy RBE) in 15-16 fractions (median 16 fractions) of 4,4 Gy RBE for CIRT, and 74 Gy RBE (range 70-74 Gy RBE) in 35-37 fractions (median 35 fractions) of 2 Gy RBE for PT. Clinical outcome (local control -LC- and overall survival -OS-) and toxicity profile (according to Common Terminology Criteria Adverse Events -CTCAE V4.03-scale) were evaluated.

Results: The median follow-up was 34 months (range, 5-70 months). Only 1 patient had local progression 24 months after the end of the treatment. The LC rate was 97%. The 1-year, 3-year and 5-year LC rates were 100%, 96% and 96% respectively; the corresponding OS rates were 97%, 93% and 93% respectively (Figure 1). The toxicity profile was favorable. No pts developed late G4 treatment-related toxicity. G3 late toxicity occurred in 2 (5.7%) of pts: 1 case of hearing impairment and 1 case of ocular toxicity (sight reduction).

Conclusions: Particle therapy is a safe and effective treatment in pts with chondrosarcoma of the skull-base.

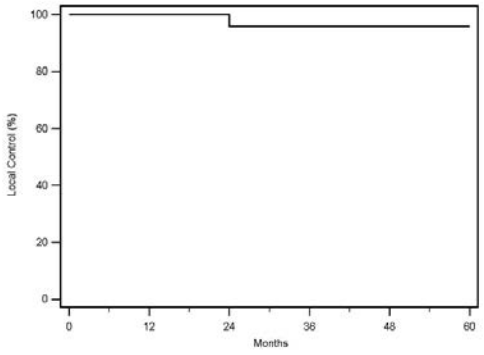

Figure 1. Local control and overall survival in patients with skull-base chondrosarcoma treated with particle therapy.

P226

PROTON THERAPY BOOST IN LOCALLY ADVANCED HEAD AND NECK CANCER: TOXICITY AND CLINICAL OUTCOME

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Aims: Evaluation of feasibility, acute toxicity and early clinical outcome in patients (pts) with locally advanced head and neck cancer (LAHNC) treated with exclusive sequential mixed beam (MB) approach: intensity modulated radiation therapy (IMRT) followed by proton therapy (PT) boost on high risk areas.

Methods: Between July 2012 to January 2018, 41 pts (29 male,12 female), median age 51 years (range, 18-74), with histologically proven LAHNC (stage III and IV) were treated using a MB approach: IMRT of the neck and macroscopic disease, followed by PT boost on the pre-treatment macroscopic disease. Tumor sites were: nasopharynx 28 pts (69%), oropharynx 5 pts (12%), larynx 1 patient (2%), sinonasal 4 pts (10%) and oral cavity 3 pts (7%). The histology was: squamous cell carcinoma for 11 pts (28%), neuroendocrine tumor for 2 pts (5%); nasopharynx tumor were classified according to World Health Organization (WHO) classification (2005): I type 4 pts (10%), II type 19 pts (47%) and III type 4 pts (10%). IMRT prescription dose was 54-60 Gy (elective irradiation of the neck and macroscopic disease), PT prescription dose was 10-20 Gy Relative Biological Effectiveness (RBE), for a total dose up to 70-74 Gy RBE. Local control (LC) and toxicity profile (according to Common Terminology Criteria Adverse Events -CTCAE V4.03- scale) were evaluated

Results: Twenty-three pts (56%) received platinum based induction chemotherapy, 39 pts (95%) received concurrent chemoradiation therapy. The median follow-up was 12 months, (range, 4-57). Treatment was well tolerated, 11 (27%) pts developed grade 3 acute radiation-related toxicity: 2 pts (5%) mucositis, 1 patient (2%) skin reaction and 5 pts (12%) dysphagia. No pts had high grade (grade 3-4) late toxicity. Grade 2 late toxicity was xerostomia found in 12 (29%) pts. Two pts (5%) developed G1 brain radionecrosis at 14 and 16 months after the end of the treatment respectively, in both cases it was resolved at least follow-up. LC was 83%. Four pts had local recurrence at 12, 11, 8 and 8 months after treatment respectively. Three pts developed distant metastases at 6, 18 and 25 months after the end of the treatment. Three pts died for tumor specific-causes.

Conclusions: For pts with LANHC a MB approach was feasible and our results showed good short-term outcome and limited radiation-related side effects. Preliminary results are encouraging but a longer follow-up and large patient accrual are required

P227

APEX WITH FFF IN RADIATION CLINICAL PRACTICE

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Aims: Apex is a micro multifeaf collimator mounted on the Elekta Versa HD. It has 56 leaf pairs with leaf thickness of 2.46 mm at isocenter and maximum field size of 12x14 cm2. Apex has been commissioned on treatment planning system (TPS) Pinnacle 9.10 for high dose rate stereotactic treatment using volumetric modulated arc therapy (VMAT) technique in conventional (6/10 MV) and flattening-filter free energies (6FFF/10FFF).

Methods:All measurements were done according the request of the TPS: Percentage Dose Depth, Profiles, Output factor, Absolute dose with PTW MP3-M water tank phantom using a synthetic diamond detector (PTW microdiamond 60019) and ionization chamber (PTW Farmer 30013, PTW Semiflex 31010) for field dimension showed in Figure 1; the validation of TPS model, was carried out by comparing calculated and measured doses acquired in water phantom for different source surface distance (SSD), detector depth and field configuration. Leaf leakage and transmission test was evaluated with PTW Octavius SRS 100.A comparison with multileaf Agility has been done.

Results: Comparison between Agility and Apex showed an average reduction of 25%. Discrepancies between calculated and measured dose were in tolerance, 2% or 3%, according the complexity of the geometry. Mean intra leaf transmission were 0.31% and 0.40% (6/10 MV FFF). Mean inter leaf leakage were 0.32% for 6 MV FFF and 0.39% for 10 MV FFF.

Conclusions: The high resolution of multileaf gives dosimetric advantages in penumbra of profiles and less dose outside the filed, thanks to smaller leaves double focused. Unfortunately, there is few literatures on this specific topic so our experience could be useful to other center starting a similar commissioning. The time needed to mount the micromultileaf and manual fine tuning takes several minutes. Must be taking account several electronic troubles of this technologies with high dose FFF delivered during a commissioning. Our aim is to apply this technology to stereotactic radiosurgery in order to obtain a dosimetry comparable with Gamma

Knife. We are evaluating if stereotactic body application are possible.

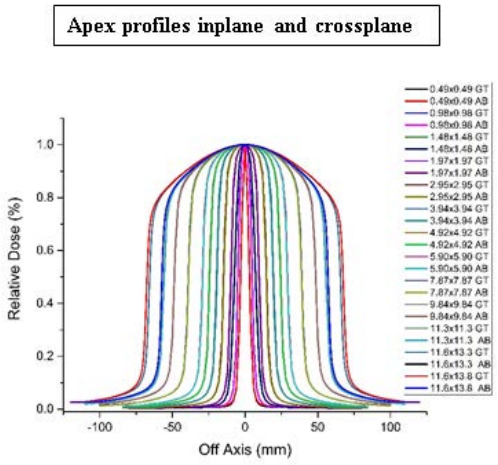

Figure 1.

P228

COMBINED PHOTON-PROTON RADIOTHERAPY TREATMENT FOR ADVANCED HEAD NECK CANCER: EXPERIENCE OF TRENTO HOSPITAL

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Aims: To report the first results of a combined photon-proton radiotherapy internal protocol for advanced head neck cancer

Methods: Patients were considered eligible for combined proton-photon treatment in case of advanced sinonasal or nasopharynx cancer deserving bilateral neck coverage as part of their treatment. The combination of proton and photon treatment aimed to exploit photon and proton intrinsic features such as robustness to anatomical changes (photons) and better dosimetric distribution (protons) in order to optimize outcome and resource allocation. A single CT set with a single immobilization system (Posifix, CIVCO®) was used for both proton and photon planning to avoid registration's uncertainties. Radiation modality' specific planning treatment volumes were adopted. Proton and photon's dose distributions were registered, summed and analyzed together before plan approval. Proton therapy was initially set as a boost treatment for high risk regions; proton doses could vary between 14 and 24 Gy Rbe with standard fractionation. A total (proton-photon) dose of 74 Gy was prescribed for nasopharynx cancer. In order to prevent the risk of proton replanning due to anatomical changes between planning CT treatment and proton treatment delivery, proton boost was administered at the beginning of radiotherapy treatment Results Between June 2016 and February, 2018 five patients underwent combined photon-proton radiochemotherapy with radical intent. Prescription doses for low, intermediate and high risk volumes were 50-54, 60-66 and 70-74 Gy Rbe, respectively. Single field optimization technique was used for proton treatments. All patients completed the combined radiation therapy treatment without interruptions. Acute toxicities were mild-moderate; one nasopharynx patient experienced G3 mucositis requiring enteral feeding. All patients experienced complete-near complete response to treatment; with a median Follow-up of six months (range 3-18), overall survival, local and distant control were 100%. No ≥G3 late toxicity were experienced so far

Conclusions: Our experience demonstrates that proton-photon combined radiotherapy treatment resulted as a feasible and very effective treatment for advanced sinonasal-nasopharynx cancer patients. Further implementation of the internal protocol are ongoing (enlarging clinical indications, implementation of multifield optimization technique for proton plans, shifting of photon-proton treatment combination).

P229

PROGNOSTIC IMPACT OF HAEMATOLOGICAL PROFILE IN LOCALLY ADVANCED OROPHARYNGEAL CANCER TREATED WITH CURATIVE RADIOTHERAPY: RETROSPECTIVE ANALYSIS OF TWO ITALIAN CENTERS

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Aims: To evaluate the role of baseline neutrophil-to-lymphocyte ratio (NLR), neutrophil, platelet and

monocyte count as a prognostic marker in locally advanced squamous cell carcinoma of the oropharynx (LAOPC) treated with definitive radiotherapy (RT) or chemo-radiotherapy (CT-RT).

Methods: A retrospective analysis of 129 patients (pts), affected with LAOPC and treated between 2010 and 2015 at two tertiary cancer centers in Northen Italy (European Institute of Oncology, Milan and Centro di Riferimento Oncologico, Aviano) was performed. Inclusion criteria were: age>18 years, stage III or IV, definitive RT or CT-RT. Progression-free survival (PFS) and overall survival (OS) curves as well as subgroups analysis between patients with Human Papilloma Virus (HPV) related and unrelated LAOPC were evaluated using the Kaplan-Meier method. Multivariate Cox proportional hazard models were applied to obtain hazard ratios adjusted for other prognostic factors and confounders.

Results: Median age was 61 (42-82) years and 74% patients were male. HPV status was available in 81% patients and among them 74% pts had HPV/p16+ related LAOPC. Definitive RT and CT-RT was administered in 3% and 97% pts, respectively. Of the 125 pts treated with CT-RT, sequential, concurrent and induction followed by concurrent CT-RT schedule was delivered to 43, 71 and 11 pts, respectively. Median follow up was 50 months (range 5 - 95 months). A value of NLR≥3 was associated with poorer OS (fig. 1) with almost a triple increased risk of death: HR=2.7 (95%CI:1.2, 6.2; p=0.02, adjusted for age, gender, chemotherapy, HPV status and ECOG performance status). Two-years OS was 91% and 81% in pts with NLR<3 and ≥3, respectively. NLR showed a significant prognostic role also in pts with HPV related and unrelated LAOPC. Both in the former and in the latter group, NLR≥3 was associated with poorer OS (p=0.05 and 0.05, respectively). No correlation was found between other hematological parameters and patients' prognosis.

Conclusions: In our cohort, a baseline NLR≥3 at treatment initiation represented a negative prognostic marker for LAOPC treated with definitive RT and CT-RT. This prognostic role was also maintained in the subgroup analysis according to HPV status. Our results are in line with literature data. Therefore, this inexpensive and readily available marker could be considered for risk stratification of pts with LAOPC.

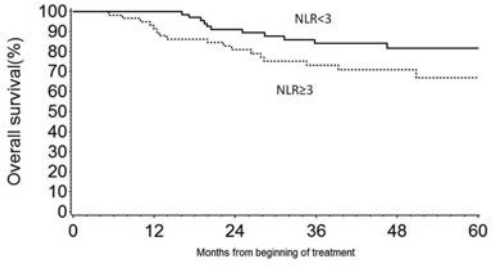

Figure 1.

P230

A SYSTEMATIC REVIEW ABOUT ROLE OF STEREOTACTIC BODY RADIATION THERAPY IN CHOLANGIOCARCINOMA

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Aims. Cholangiocarcinoma (CC) are uncommon neoplasms with poor prognosis and 5-year overall survival (OS) less than 20%. Radical surgery is the only potential curative treatment but most of patients at diagnosis present with unresectable disease. Radiochemotherapy or radiotherapy (RT) are a treatment option in unresectable disease. Different series demonstrated a clear relationship between dose and OS. SBRT is a technique able to deliver a high and very conformed RT dose in few fractions, resulting, therefore, promising. The aim of this systematic review is to define the clinical role of SBRT in CC.

Methods. A systematic literature searches was conducted on PubMed, Scopus and Cochrane library, using the PRISMA methodology. Studies with at least 10 patients with histopathologic or radiological diagnosis of inoperable CC independently of anatomic location, with/without chemotherapy were included. The primary endpoint was OS and secondary endpoints were local control (LC) and toxicity. Cochrane tools were used to assess the bias risk.

Results. Eight articles fulfilled the inclusion criteria and were included in this review. Seven studies were reported with moderate to serious risk of bias. One year OS and median OS ranged from 45% to 83% (median: 58.5%) and from 10 months to 35.5 months (median: 15.3 months), respectively. One year LC ranged from 78% to 100% (median: 86.5%). The toxicity was acceptable with a 4.5% median G ≥ 3 late toxicity rate .

Conclusions. The role of SBRT in cholangiocarcinoma is not supported by robust evidence in literature. Due to low evidence of the published studies it is not possible to draw any meaningful conclusions about pro-

gnostic factors correlated with tumor control and toxicity. Prospective controlled trials are needed to clarify the role of SBRT in CC.

P231

RAPIDARC VERSUS IMRT IN A CASE OF POSTOPERATIVE IRRADIATION OF A RECURRENT LEFT BREAST CANCER WITH INTERNAL MAMMARY LYMPH NODE INVOLVEMENT

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Aims: Dosimetric comparison between RapidArc(RA) and IMRT (Intensity Modulated Radiotherapy) for a recurrent left breast cancer with internal mammary chain (IMC) involvement.

Table 1.

PTV boost		
Dose prescrizione		
2,37 Gyx25 fr =	59,25	Gy
	RapidArc	IMRT
Vol Isodose 95% (cc)	3,96	2,69
D98 (%)	96,72	94,78
D95 (%)	97,3	95,8
D50 (%)	100	100,3
D5 (%)	102,66	103,35
D2 (%)	103,3	103,62
C.I.	3,96	2,69
H.I.	1,055087	1,07881

Somma PTV (parete+cmi)		
Dose prescrizione		
2 Gyx25 fr =	50	Gy
	RapidArc	IMRT
Vol Isodose 95% (cc)	283,02	243,41
D98 (Gy)	50	47,58
D95 (Gy)	50,5	48,35
D50 (Gy)	52	50,92
D5 (Gy)	54	54,3
D2 (Gy)	54,8	55,4
C.I.	2,026783	1,743125
H.I.	1,069307	1,123061

	RapidArc	IMRT
U.M.	633	728

OAR			
		RapidArc	IMRT
Polmone Sx			
	Dmedia (Gy)	8,14	15,4
	V10 (%)	22,1	60,7
	V20 (%)	8,24	28,1
Polmone Dx			
	V5 (%)	24,8	22
Cuore			
	Dmedia (Gy)	6,43	6,98
	V10 (%)	10,9	22,2
	V30 (%)	0	0
Mammella C.L.			
	Dmedia (Gy)	6,4	1,6
Midollo			
	Dmax (Gy)	5,1	10,8
	D2% (Gy)	4,27	8,2

Methods: A 46 years old woman with peri-prosthetic recurrent breast cancer was evaluated in September 2017 for postoperative left chest wall, homolateral periclavicular and IMC irradiation, with the inclusion of PET positive internal mammary node (PET + IMN). Prescription dose(PD) to left chest wall and homolateral IMC was 50Gy(2Gy/die) with the addition of a 1 cm tissue equivalent bolus;PD to left periclavicular region was 46,8Gy(1,87Gy/die); the PET + IMN received a simultaneous integrated boost up to 59,25Gy (2,37Gy/die; EQD2 64Gy with estimated alfa/beta=3). We compared RapidArc with 5 beams step and shoot IMRT according to target coverage, conformity index (CI) and homogeneity index (HI), dose to the Organs at Risk (OARs) lungs, heart and spinal cord. Controlateral breast dose was not evaluated because of the presence of a prosthesis; number of monitor units (MU) and treatment delivery time were also considered. Plans were calculated with Aria TPS (Varian MS).

Results: RA allows a better dose coverage and dose homogeneity compared to 5-beam step-and-shot IMRT. RA also enables a better normal tissue sparing, with fewer monitor units and shorter delivery time. Except for a radiodermatitis G2 (CTCAE v4 scale), no acute toxicities were observed. Contrast chest-abdomen CT performed in Avril 2018 showed a complete regression of IMN for this patient.

Conclusions: RA allows to obtain optimal target-coverage and adequate dose-sparing for OARs, in agreement with literature data. It would be possible to control the respiration-induced target motion using breath hold techniques.

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ANALYSIS OF PATIENT POSITIONING ERRORS AND INTERFRACTION TARGET MOTION IN IMAGE-GUIDED RAPIDARC RADIOTHERAPY FOR PROSTATE CANCER

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Aims: Daily image-guided radiotherapy (IGRT) according to intraprostatic fiducial markers (FM) reflects both positioning uncertainties and interfraction (IF) prostate motion; IF patient position variability is usually evaluated by daily matching according to bone anatomy. This study evaluates both IF patient position variability and target motion with the aim to support existing data in literature on the improvement of treatment reproducibility and accuracy by using an IGRT method based on FM displayable on cone-beam CT (CBCT).

Methods: Between 2013 and 2015 we selected 10 patients with prostate cancer for radical RT with VMAT technique using intraprostatic FM. During the radiation course, daily CBCT (320) were acquired and a matching according to FM was performed. We measured lateral-lateral (LL), anterior-posterior (AP) and cranial-caudal (CC) coach shifts required for isocentre correction. To evaluate IF setup error related to positioning uncertainties, bone anatomy displacements were retrospectively taken into account for 235 CBCT. To obtain IF prostate motion, differences between FM and bone

displacements were considered. To evaluate the impact of each component on systematic and random error, we compared, for each direction, the following statistical measurements related to population FM displacements, bone displacements and IF prostate motion: standard deviation to estimate total systematic error, root mean square for random error.

Results: The highest Standard Deviation values occurred for FM displacements, especially in the AP (3,2 mm) and SI (2,63 mm) directions. The highest value of root mean square was related to IF prostate motion. Our data were comparable to measurements reported in the literature.

Conclusions: IGRT based on FM displayed on CBCT allows to analyze IF variability related to patient positioning and target motion. Our results confirm that the proposed FM based-IGRT reduces both systematic and random errors compared to bone anatomy-based IGRT.

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HELICAL TOMOTHERAPY WITH DAILY IMAGE GUIDED RADIOTHERAPY FOR NEOADJUVANT TREATMENT OF RECTAL CANCER: A BI-CENTRIC SWISS EXPERIENCE

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Aims: We report the clinical outcomes of a large population of locally-advanced rectal cancer (LARC) patients treated with neoadjuvant HT and chemotherapy (CT) with daily image guidance (IGRT) followed by surgery.

Methods: Data from 117 LARC patients treated in two Swiss Radiotherapy departments were collected and analyzed. All the patients receive RT to the rectum + the mesorectum + the presacral nodes + the obturatory nodes + the internal iliac nodes (Clinical target volume 1, CTV1). In one of the 2 institutions, a CTV2 was also defined, encompassing rectal GTV with a 2-cm margin in the cranio-caudal direction + the corresponding mesorectum, + the nodal GTV (in N+ pts) (n = 70). Planning target volumes (PTVs) were obtained by adding 5-mm margin to the CTVs (PTV1 and PTV2, respectively). PTV1 received 44-45 Gy (1.8-2 Gy/fraction), while PTV2 received a simultaneous integrated boost up to a total dose of 50 Gy (2 Gy/fr). Chemotherapy consisted of capecitabine 825 mg/m2, twice daily, during the RT days. After a median interval of 53 days (95% confidence interval, 95% CI: 53–65 days), all patients underwent surgery. The resection status was classified as R0 in 107 patients, and R1 in 3 patients (not reported in 7 patients).

Results: Median follow-up was 45 months (range: 4 – 90 months). The overall rate of G2 or more toxicity was 19% (n = 22). Four patients (3%) presented a grade 3 toxicity, as dermatitis (n = 1) or diarrhea (n = 3), and one patient (1%) a grade 4 rectal toxicity. None of the patients presented a grade ≥3 hematologic toxicity. Six patients (5%) presented a grade 3 late gastrointestinal toxicity. Data on TRG were available for 101/117 patients (86%). Tumor regression (TRG 1-4) was noted in 74% of the patients. Fourteen patients (14%) presented a pathological complete response (pCR). The 4-year local control rate was 88% (95% CI: 87.5 - 88.5%). Patients who received a SIB (n = 57 patients) presented more frequently a TRG = 1 (12/57 patients vs 2/41 patients if no SIB, $p = 0.017$) or a TRG = 1-2 (33/57 patients vs 10/41 patients if no SIB, $p < 0.001$). The interval between the end of radiotherapy and surgery, evaluated at different timepoints, did not influence the possibility of obtaining a TRG = 1 or a TRG 1-2.

Conclusions: CRT delivered with HT and daily IGRT shows excellent toxicity and 4-year local control rates. Higher doses obtained better rates of pathological complete response, thus supporting dose escalation in rectal cancer

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RECONSTRUCTION FAILURE RATE AFTER POST-MASTECTOMY LOCOREGIONAL HYPOFRACTIONATED RADIOTHERAPY TO TEMPORARY TISSUE-EXPANDER OR PERMANENT BREAST IMPLANTS: 3-YEARS RESULTS

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Aims: To assess the rate of reconstruction failure (RF) in postmastectomy radiotherapy (PMRT) with hypofractionated intensity-modulated radiotherapy (IMRT), after immediate breast reconstruction (IBR) with temporary tissue-expander (TE) or permanent implant (PI).

Methods: This retrospective analysis included data of patients affected by stage II–III breast cancer, treated with PMRT using helical IMRT (Tomotherapy®) from May 2012 to May 2015. Patients were divided in two

groups according to the type of IBR: one stage (PI group) and two-stage (TE replaced with the PI group). The clinical target volumes comprised the chest wall and the infra/supraclavicular nodal region. Dose of prescription was 40.05 Gy in 15 fractions, five days per week. Primary endpoint was the rate of RF defined as major revisional surgery (removal of PI or conversion to autologous). Secondary endpoints included minor revisional surgery (substitution of the PI with another PI), capsular contracture (CC) rates according the four-grade Baker scale and cosmesis (poor, fair, good, excellent). Follow-up started from the date of the mastectomy. Neoadjuvant and adjuvant systemic therapy were allowed.

Results: The study included data of 114 patients: 69 pts belonged to the TE-group and 45 to the PI-group. Clinical characteristics were well-balanced between the 2 groups. Median age was 46 years (25-73 years). Median follow-up of was 36.1 months (10.8-60.1 months). RF was evaluated in 62 TE-pts because 7 pts did not completed the planned two-stage reconstruction (3 pts died before replacement and 4 pts kept the TE in place for personal reasons). RF occurred in 13% (8/62) of TE-pts (3 TE removal and 5 conversion to autologous breast reconstruction). RF occurred in 7% (3/45) PI-pts (1 PI removal and 2 conversion to autologous breast reconstruction). Minor revisional surgery were performed in 7/62 (11%) and 11/45 (24%) TE and PI patients, respectively. Statistical analysis and comparison with a control group (ongoing) will be available for the congress.

Conclusions: Rate of RF after postmastectomy hypofractionated locoregional IMRT was about two times higher in the PI-group compared to TE-group. Risk of minor and major revisional surgery seems acceptable, especially for the TE-group. Further statistical analysis (ongoing) will describe the cosmesis and CC.

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FEASIBILITY OF A SCHEME OF HYPOFRACTIONATED CARBON ION RADIOTHERAPY FOR HIGH-RISK PROSTATE CANCER PATIENTS

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Aims: The purpose of this study was to evaluate feasibility of 4-weeks treatment schedule of carbon ion radiotherapy (CIRT) for high-risk prostate cancer at National Center of Oncological Hadrotherapy (CNAO). This series will serve as a benchmark for the AIRC study Nr N-14300 regarding carbon ions boost followed by pelvic photon intensity modulated radiotherapy for high-risk prostate cancer.

Methods: Between July 2013 and May 2017, 21 patients with high-risk prostate adenocarcinoma were treated according to the phase II study of CIRT (protocol CNAO S16/2012/C) with 66.4 Gy (RBE) in 16 fractions over 4 weeks. The primary endpoint of the study was clinical tolerance during treatment. Secondary end points were rates of acute and late side effects evaluated during follow up based on the Common Terminology Criteria for Adverse Events version 4.0 and RTOG/EORTC (Radiotherapy Oncology Group/ European Organization for Research and Treatment of Cancer) toxicity scales, biochemical recurrence-free survival, disease-free survival and local control rate.

Results: Median age was 66 years (range 56-89). Median follow-up time was 16.7 months (range 1.6-53.0). One patient died because of pancreatic cancer without recurrence at 38.2 months, and the remaining 20 patients were alive at the time of this analysis. Only one patient that discontinued hormonal treatment had biochemical failure 14.4 months later. The most frequent acute toxicity of 21 patients, grade 1 (G1) urinary frequency and/or cystitis was observed in 11 (52%) patients. Grade 2 (G2) urinary frequency was observed in 4 (19%) patents. Acute G1 gastrointestial toxicity (mild rectal hemorrhage) appeared in only 1 (5%) patient. In the analysis of late toxicities, 6 (29%) patients showed G1 urinary frequency (urgency and/or cystitis) and 1 (5%) patient showed G2 urinary infection. No late gastrointestinal toxicity was observed during the follow-up period.

Conclusions: The preliminary findings of our phase II study are considered as feasible for high-risk prostate cancer. Further studies with more patients and long-term outcome are required. Toxicity and outcome data of this study can be employed for the comparison with our prospective AIRC study.

Acknowledgment: This study was partially supported by Associazione Italiana per la Ricerca sul Cancro (AIRC), project IG-14300 "Carbon ions boost followed by pelvic photon intensity modulated radiotherapy for high-risk prostate cancer", registered at ClinicalTrials.gov (NCT02672449).

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SAFETY AND USEFULNESS OF FRACTIONATED STEREOTACTIC RADIATION IN THE TREATMENT OF RECURRENT HIGH GRADE GLIOMA PATIENTS

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Aims: Available approaches for high grade glioma (HGG) include surgery and adjuvant chemoradiation in operable cases. In patients with recurrence of disease,

few experiences exists to improve survival. We report our experience with stereotactic radiotherapy (SRT) in patients with recurrent disease after standard chemoradiation or radiation therapy alone.

Methods: From January 2007 to November 2017 we retrospectively analysed all the patients affected by recurrent HGG submitted to stereotactic re-irradiation using a robotic linear accelerator. For all cases retrieved, the clinical target volume (CTV), radiation delivered dose, number of fractions, and overall survival (OS) have been calculated.

Results: 49 patients (25 M and 24F; men age 56.3 ±11.9 years) with recurrent HGG after surgery and chemoradiation or radiation therapy alone (mainly 60Gy in 30 fractions through external beam radiation therapy) were retrospectively evaluated. 9 were high grade astrocytoma, the remaining 40 had GBM. Mean clinical target volume (CTV) was 15.35 ml (range 2.2-115). The median delivered dose was 12Gy (range 10-30Gy), and the median number of fractions was 3 (range 1-5). 33 patients were treated also with temozolomide (TMZ), one received TMZ and fotemustine and one received TMZ and bevacizumab. Meadian overall survival (OS) from the end of FSRT was 12 months; OS at 6 and 12 months was 48.9% and 40.8%, respectively. Interestingly, 11/49 (or 22.4%) patients reached a survival ≥ 18 months: among them, one died 84 months after FSRT delivery and another is alive after 96 months from treatment. In 4/49 (8.1%) pts radionecrosis occurred.

Conclusions: Our study has demonstrated that re-irradiation in patients affected by recurrent GBM is a feasible option and that FSRT delivered with linear accelerator equipped with robotic arm is safe and effective after chemoradiation or radiation therapy alone: this modality allows to obtain a higher OS than standard treatments, also superior to 30 months, with limited toxicity.

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ACTIVE SPOT-SCANNING PROTON THERAPY FOR INTRACRANIAL MENINGIOMAS: NATIONAL CENTER OF ONCOLOGICAL HADRONTHERAPY - CNAO- EXPERIENCE

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Aims: Meningiomas are the most common primary intracranial tumors. If therapy is necessary, the standard treatment is gross total surgical resection. Proton therapy (PT) is an alternative therapeutic option for unresectable meningiomas, mostly located in the skull-base that are difficult to access, and a complementary treatment for complex and irregular tumors and lesions located in close proximity of critical organs at risk (OAR) as optic-pathways and brainstem where only subtotal or partial resection is possible. Aim of the study was to evaluate treatment results and toxicity in patients (pts) with meningiomas treated with active spot-scanning PT

Table 1. Patients, tumor and treatment characteristics.

Characteristics	N. of patients (%)
Total	79 (100)
Sex	
Male	29 (37)
Female	50 (63)
Age (years): median (range)	57 years (range, 14-86)
Histologic classification	
WHO Grade I	33 (42)
WHO Grade II	13 (16)
WHO Grade III	4 (5)
No histology	29 (37)
Clinical timing	
Newly diagnosed tumors	44 (56)
Post surgery recurrence	35 (44)
Tumor site	
Skull-base meningioma*	59 (75)
Non-skull-base meningioma	20 (25)
GTV (cm^3): median (range)	22.8 (2.3-205.71)
Total (and fraction) doses (Gy RBE)	
50.4 (1.8)	3 (4)
54 (1.8)	11 (14)
55.8 (1.8)	31 (39)
56 (2)	2 (3)
57.6 (1.8)	4 (5)
59.4 (1.8)	9 (11)
60 (2)	7 (9)
64 (2)	1 (1)
66 (2)	11 (14)

Methods: 79 pts (29 men and 50 women) with a median age of 54 years (range 15-85) with intracranial meningioma (histologically proven 50/79) were treated with PT between October 2012 to December 2017 at CNAO. Pts, tumor and treatment characteristics were summarized in Tab 1. 59 pts had skull-base lesions. 44 pts were treated as primary treatment (exclusively PT= 32 pts, postoperative PT = 12 pts), 35 pts were treated for recurrence after surgery. For pts with histological diagnosis, 33 pts had a diagnosis of World Health Organization (WHO) Grade I, 13 of WHO Grade II and 4 of WHO Grade III respectively, while 29 pts had radiological diagnosis (28/29 skull-base lesions) and in all these cases 68Ga-DOTATOC-PET was performed before treatment. All pts were treated using pencil-beam active scanning PT. The median administered dose was 55.8 Gy (relative biological effectiveness - RBE) (range, 50.4- 66) at 1.8-2.0 Gy RBE per fraction. Gross tumor volume (GTV) ranged from 2.3-205.71 cm3 (median 22.8, mean 36.5). Late toxicity was assessed according to Common Terminology Criteria for Adverse Events –CTCAE- V4.03 scale.

Results: median follow-up was 17 months (range, 4.8-62.3). Very low rates of side-effects developed, including headaches, nausea and dizziness during treatment. No high-grade (grade 3-4) treatment-related toxicity was observed. Local control was 99%. Only one

patient, affected by atypical meningioma, had local recurrence 22 months after the end of the treatment. Two pts with atypical and anaplastic meningioma respectively had "out-of-field" recurrence 20 and 8 months after the end of the treatment.

Conclusions: PT is a safe and effective treatment for pts with intracranial meningiomas, and it allows to deliver high local doses even in complex anatomy (as skull-base lesions) while sparing critical OARs.

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COMPLETE CLINICAL RESPONSE PREDICTION IN HYBRID MAGNETIC RESONANCE RADIOTHERAPY OF LOCALLY ADVANCED RECTAL CANCER: THE CONTRIBUTION OF RADIOMICS

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Aims: Aim of this study was to evaluate the variation of radiomics features, defined "delta radiomics", in patients (pts) affected by locally advanced rectal cancer (LARC) undergoing hybrid MR guided radiotherapy (MRgRT) and correlate it with complete clinical response (cCR) prediction.

Methods: T2*/T1 MR images acquired with a hybrid 0.35 T MRgRT unit from pts undergoing neoadjuvant CRT were considered for this analysis. Prescribed dose was 55 Gy to primary tumor and corresponding mesorectum (PTV1) and 45 Gy to pelvic nodes and mesorectum (PTV2) delivered through a simultaneous integrated boost approach. An imaging acquisition protocol of 6 MR scans per pt was performed: the first MR was acquired at first simulation (t0) and the remaining ones at fractions 5,10,15,20 and 25 A true fast imaging with steady state precession (TRUFI) sequence was used for image acquisition with a resolution of 1.5x1.5x1.5 mm^3 and acquisition time of 175 sec. The gross tumor volume (GTV) contours were agreed by two radiation oncologists and radiomics features were extracted using a dedicated software and then correlated with the corresponding delivered dose The variations of each feature during treatment were then quantified and the ratio between the values calculated at different dose levels and the one extracted at t0 was calculated too. The Wilcoxon Mann Whitney test was performed to identify the features whose variation can be predictive of cCR, assessed with a MR acquired 6 weeks after CRT and digital examination (DE).

Results: 16 pts (13 male and 3 female) were enrolled, out of which 5 pts (31%) showed cCR at restaging MRI and DE. 53 radiomics features (morphological, statistical, textural and fractal) were firstly analyzed, while a total of 260 ratios of features was then calculated, defining the "delta radiomics approach" during treatment. 57 of these features resulted to be significant in discriminating cCR pts from not responding ones and 4 of them showed significance for all considered ratios, demonstrating a continuous predictive power for the considered outcome. The most significant feature appeared to be the ratio between the "L least", that is the axis along which the object is least extended, calculated during the second week (t10) of treatment and the corresponding value obtained during simulation ($p<0,0005$).

Conclusions: These results suggest that Delta radiomics approach can successfully predict cCR MRgRT, allowing innovative treatment personalization in LARC pts.

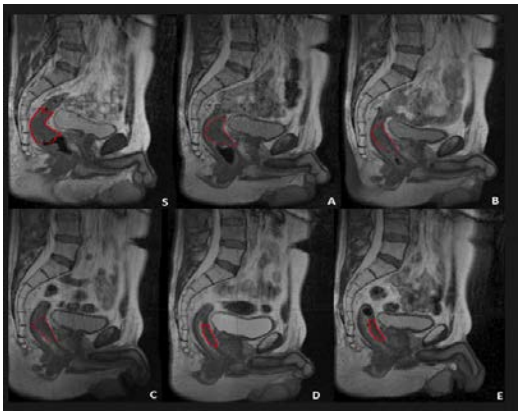

Figure 1.

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POST MASTECTOMY LEFT CHEST WALL PLUS SUPRA- AND INFRA-CLAVICULAR NODES IRRADIATION: A COMPARISON BETWEEN TWO TECHNIQUES

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Aims: The aim of the present study is to compare two different planning techniques for the irradiation of left mastectomy breast chest wall plus supra- and infra-clavicular lymphnodes. 3D CRT with half beam block technique and a single arc VMAT technique were compared in terms of target coverage and doses to OAR.

Methods: All patients had post mastectomy breast implant or tissue expander and were treated with VMAT. For each of 10 patients two plans, a 3DCRT with half beam block (Philips Pinnacle3 TPS) and single arc VMAT (Elekta Monaco TPS) were generated in order to obtain the best compromise between target coverage and OAR sparing. For each plan were registe-

red: target coverage of the two PTVs in term of V95, V98, mean dose, Conformity Index (CI) and Homogeneity Index (HI); lung doses for ipsilateral, controlateral and total lung in terms of V20, V5 and mean dose; heart doses in term of V30, V5 and mean dose; spine maximal dose; right breast V5 and mean dose. A two tailed paired sample t-test was used to evaluate the difference in each dosimetric parameter.

Results: Mean ± SD of each dosimetric parameter in each group of 10 plans (3D and VMAT) are reported in Table, together with the statistical analysis. VMAT plans show highly significant better coverage both for breast chest wall and lymphnodes and result in highly significant better CI and HI. Moreover, due to better conformity of the technique, V20 of ipsilateral and total lung in VMAT are slightly significant lower ($p \approx 0.1$) than the 3D ones and heart V30 are significantly lower ($p<0.05$). OAR low doses are generally higher for VMAT. In particular V5 for ispilateral, controlateral and total lung are significantly higher in VMAT ($p<0.01$), similarly heart V5 and mean dose like as right breast V5 and mean dose in VMAT are significantly higher ($p<0,05$ for heart and $p<0,01$ for right breast). Finally spine maximal dose is lower but not significant in VMAT ($p=0.14$). No relevant toxicity was observed in the entire group.

Conclusions: Our results show that VMAT technique for the irradiation of left breast chest wall plus supra- and infra-clavicular nodes offers better target coverage and superior CI and HI than 3D CRT. Moreover VMAT shows better V20 in lung and V30 in heart and higher low dose parameters for all the observed OAR. In our department VMAT technique is becoming the favourite even if needs to be further investigated in terms of late side effects due to low dose bath.

Table 1. Statistical analysis in terms of two tailed paired sample t-test (=0,05); * where p<0,05.

	VMAT	3D	Probability
	MEAN± SD	MEAN± SD	
POSTMASTECTOMY CHEST WALL COVERAGE	$V_{95\%}$=93,1±2,7	$V_{95\%}$=84,1±6.5	p=1,7E-3*
	$V_{98\%}$=74,2±8,6	$V_{98\%}$=70,8±9,7	p= 5,2E-1
	D_{mean}=(49,5±0,3)Gy	D_{mean}=(49,0±0,8)Gy	p= 9,5E-2
	HI=0,11±0,03	HI=0,25±0,15	p=2,5E-2*
	CI=0,93±0,03	CI=0,84±0,06	p=3,2E-3*
SUPRA- AND INFRA-CLAVICULAR COVERAGE	$V_{95\%}$=93,0±4,0	$V_{95\%}$=83,9±6,2	p=5,1E-2*
	$V_{98\%}$=71,4±13,8	$V_{98\%}$=69,9±9,2	p= 7,6E-1
	D_{mean}=(49,4±0,5)Gy	D_{mean}=(48,9±0,7)Gy	p= 9,9E-2
	HI=0,12±0,04	HI=0,43±0,2	p=1,9E-3*
	CI=0,93±0,04	CI=0,84±0,06	p=3,1E-3*
IPSILATERAL LUNG	V_{20Gy}=17,2±3,8	V_{20Gy}=19,7±7,1	p= 9,4E-2
	V_{5Gy}=53,3±5,1	V_{5Gy}=35,9±10,4	p=2.0E-4*
	D_{mean}=(10,4±1,2)Gy	D_{mean}=(10,1±3,0)Gy	p= 6,5E-1
CONTROLATERAL LUNG	V_{20Gy}=0,09±0,13	V_{20Gy}=0,004±0,01	p= 7,5E-2
	V_{5Gy}=20,4±10,2	V_{5Gy}=0,11±0,16	p=1,0E-4*
	D_{mean}=(3,5±0,7)Gy	D_{mean}=(0,43±0,10)Gy	p=1,3E-7*
TOTAL LUNG	V_{20Gy}=8,1±1,9	V_{20Gy}=9,2±3,5	p= 1,1E-1
	V_{5Gy}=35,4±7,4	V_{5Gy}=16,7±5,1	p=4,6E-7*
	D_{mean}=(6,7±1,0)Gy	D_{mean}=(4,9±1,5)Gy	p=9,9E-5*
HEART	V_{30Gy}=0,2±0,4	V_{30Gy}=0,9±0,9	p=4,8E-2*
	V_{5Gy}=15,6±8,6	V_{5Gy}=8,3±5,9	p=3,6E-2*
	D_{mean}=(3,6±0,9)Gy	D_{mean}=(2,5±1,1)Gy	p=1,9E-2*
SPINE	D_{max}=(23,1±3,8)Gy	D_{max}=(25,2±6,0)Gy	p= 1,4E-1
CONTROLATERAL BREAST	V_{5Gy}=10,0±3,5	V_{5Gy}=1,1±2,9	p=5,4E-5*
	D_{mean}=(2,8±0,3)Gy	D_{mean}=(0,6±0,4)Gy	p=1,3E-7*

P240

TOXICITY IN PROSTATE CANCER PATIENTS SUBMITTED TO RE-TREATMENT FOR LOCALLY RECURRENT DISEASE

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Aims: To evaluate toxicity in prostate cancer patients, submitted to re-irradiation.

Patients and Methods: From December 2013 to April 2018 we retrospectively analysed all the patients with locally recurrent prostate cancer submitted to retreatment. For all cases retrieved, the radiation delivered dose, number of fractions, D-Max bladder, D-Max rectum, toxicities and progression free survival (PFS) have been calculated.

Results: A total of 6 patients previously irradiated have been observed. 4/6 had intermediate risk (GS 7) and 2 high risk (one GS 8, one GS 9) at diagnosis. The previous median total dose delivered was 66.95 Gy (range 54 – 78 Gy). At the time of retreatment, the median age was 70 years (range 48-77). 4/6 patients have been submitted to re-irradiation with stereotactic radiotherapy after fiducial marker placement while two patients was treated by VMAT. In stereotactic re-treatment the median total dose delivered was 32.5 Gy prescribed at a median isodose of 73.5% (range 69-80) in 5 fractions. One of the two patients submitted to VMAT technique received a total dose of 21 Gy/5fractions and the other one 19.5 Gy/3 fractions. We calculated a median bladder D-Max of 24.7 Gy and a median rectum D-Max of 22.55 Gy. One patient had diarrhea and nausea G1 and one patient had dysuria G1; the others did not have toxicity (G0). Up-to-date no patient showed progression of disease, with a median PFS of 9.97 months (range 5-58). Late toxicities have not been observed.

Conclusions: Re-irradiation in locally recurrent prostatic cancer seems to be both feasible and safe with low toxicities profiles. More data should be collected.

P241

ACTIVE BEAM SCANNING PROTON THERAPY RADIOSURGERY: TECHNICAL IMPLEMENTATION AND EARLY OUTCOMES

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Aims: Stereotactic radiosurgery (SRS) is an important treatment option for intracranial lesions and several photon-SRS techniques have been developed. Proton

therapy (PT) has special characteristics that allow normal tissues to be spared better than with the use of photons but limited data are available for proton-SRS. Nowadays, PT-SRS is delivered only with passive scattering technique while active pencil beam scanning (PBS) that is considered the most advanced proton technique has not been applied to SRS treatments yet. Here we describe the technical implementation of PBS PT SRS and the early clinical outcomes.

Methods: The technical implementation aimed to verify the beam spot features (beam model) and spot delivery accuracy, the gantry and treatment table geometrical accuracy, the immobilization systems devices accuracy, the applicability of the quality assurance procedure (QA) to this specific scenario, the verification of treatment planning dose calculation with Monte Carlo code, verification of the whole procedure with so-called end-to-end test in anthropomorphic phantom. Moreover, between June 2017 and April 2018 nine patients (pts) with ten lesions underwent PT SRS. Median age was 67 years (range, 28-88). Four were female. Tumors included 7 meningiomas (MG) and 3 vestibular schwannoma (VS). Pts were immobilized using a frameless system: Type-S Proton Overlay and Type-S Proton Mask (CIVCO Medical Solutions,Kalona, IA, USA) together with Moldcare headrest (Q-Fix Systems,Avondale, PA, USA). All pts were treated with active beam scanning PT using 2-4 fields with single field optimization technique. Median GTV was 1,8 cc (range, 0.2-3.68). Dose prescription was 12 GyRBE in one fraction for VS and 14-15 GyRBE for MG. Mean follow-up (FU) was 3 months (range, 1-9).

Results: The tests accomplished for technical implementation fulfilled all the requested goals. The treatments had excellent patient compliance and no side effects were registered during the procedure. Registered acute and late side effects include grade 1 (11%) fatigue, and grade 2 (22%) alopecia. There were no grade 3 or higher acute and late toxicities. Currently, absolute tumor control is 100% regardless the type of tumor. Despite the short follow-up radiological reduction was registered in two pts (20%).

Conclusions: Technical implementation of PBS PT SRS has been accomplished. Patient treatments were feasible and safe. Longer follow-up is necessary to assess definitive safety and efficacy.

P242

IMPACT OF SENTINEL LYMPH-NODE BIOPSY AND FDG-PET IN STAGING AND RADIATION TREATMENT OF ANAL CANCER

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Aims: To assess the role of sentinel lymph-node biopsy (SLNB) and FDG-PET in staging and radiation treatment (RT) of anal cancer patients (pts).

Methods: 80 pts (m:32, f:48), median age 61 years (38-87) with anal squamous cell carcinoma were treated from 3/2008 to 3/2018. Twenty-seven/80 pts (34%) were HIV+. Pts without evident clinical inguinal LN metastases (mts) and with discordance between clinical and imaging were considered for SLNB. FDG-PET was performed in 69/80 pts. Pts with negative imaging in inguinal LNs and negative SLNB could avoid RT on groin. CTV included GTV (primary tumour and positive LNs) and pelvic ± inguinal LNs. PTV1 and PTV2 corresponded to GTV and CTV, respectively, adding 0.5 cm. RT dose was 50.4 Gy/28 fractions (fr) to PTV2 and 64.8 Gy/36 fr to PTV1, delivered with 3DCRT, VMAT (RA) or Tomotherapy, concomitant to NIGRO scheme chemotherapy.

Results: FDG showed inguinal uptake in 20/69 pts (29%) and in 11/20 pts lymphoscintigraphy was performed: SLNB confirmed inguinal mts in 4/11 (36%) pts, 6/11 (54.5%) pts were false positive and SLN not found in 1 pt. FDG-PET was negative in 49/69 pts (71%) and in 30/49 (61%) lymphoscintigraphy was performed: 6/30 (20%) showed mts, 23/30 (77%) were true negative and SLN not found in 1 pt. PET was false positive in 50% HIV- pts versus no HIV+ pts. Fifty-four/80 pts (67.5%) received RT on groin (RA: 26 pts, 3DCRT: 14 pts and Tomotherapy: 14 pts); 19/54 pts were HIV+. Pts treated vs no treated on groin showed more inguinal dermatitis toxicity (G1-G2: 27 (50%) vs 3 pts (11.5%) and G3-G4: 9 pts (17%) vs 0%. HIV+ pts treated on groin had more G3-G4 perineal dermatitis toxicity (9 (33.5%) vs 5 pts (18.5%)). All pts treated on groin showed higher G3-G4 hematological toxicity versus not treated pts independently of HIV status. RA better avoid inguinal region than 3DCRT. Tomotherapy was better than 3DCRT and RA in perineal toxicity (28.5% vs 43% and 42.5%, respectively), and is superior to 3DCRT in inguinal toxicity (14% vs 36%). Seventy-six/80 pts with a median follow-up of 27.5 months (5-91) were evaluated: 65 pts (85.5%) showed a complete response, 10 pts (13%) a partial response, 1 pt (1.5%) a stable disease, while 11 pts (14.5%) a local relapse (3 with distant mts). No pts showed inguinal relapse.

Conclusions: SLNB improve FDG-PET inguinal LNs staging which has a large false positive and negative rate, independently of HIV status and guides decision in inguinal RT. Advanced RT techniques should better avoid toxicity especially in HIV+ pts.

P243

REIRRADIATION OF RECURRENT GLIOMAS WITH RADIOSURGERY/STEREOTACTIC RADIOTHERAPY USING CYBERKNIFE SYSTEM: A MONOISTITUTIONAL EXPERIENCE

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Aims: The aim of our study was to retrospectively evaluate the efficacy and toxicity of reirradiation with Cyberknife (CK) stereotactic radiosurgery (SRS)/ stereotactic radiotherapy (SRT) in patients with recurrent gliomas preirradiated.

Methods: Between May 2013 and April 2018, 29 patients (51 lesions) with reccurent gliomas (RGs), previously treated with standard Radiotherapy (RT) (50-60 Gy;1.8-2Gy/fx) with or without concomitant and adjuvant temozolomide (TMZ), were reirradiated with CyberKnife® SRS/SRT. The median time interval between primary RT and reirradiation was 22 months (range 5-229). Seventeen patients had a grade IV (GBM), 9 grade III, 2 grade II and 1 grade I gliomas. Median Karnofsky performance status was 80 (range 30-100). The total prescription dose of CyberKnife® SRS/SRT retreatment was 20-30 Gy in 5 fractions (fs), 20-26Gy in 4 fs, 15-24 Gy in 3 fs, and 12-24 Gy in single fraction (fx) at isodose line of 80% (range 75-80%). We calculate median overall survival (OS) from the diagnosis date and median OS from reirradiation. Acute and late toxicities were graded according to Radiation Therapy Oncology Group scale.

Results: Median follow-up (FU) was 13 months (range 2-43). 24 patients were evaluables for the FU, 5 patients were not evaluable as they died before the first FU. Median OS after SRS/SRT was 13.31 months (range 0.72-43.2) for all patients, 7 months (range 0.72-40.5) for GBM and 18.34 months (range 1.71-43.2) for Gliomas grade I-III. Median OS from the diagnosis was 40.7 months (range 12.6-274) for all patients, 30.5 months (range 12.6-80) for GBM and 111 months (range 17-274) for Gliomas grade I-III. All patients completed the CK treatment. Only one patient had acute toxicity grade 1 (headache). No patient developed severe toxicity. Radiation necrosis was observed in 6 patients (21%).

Conclusions: Our retrospective experience demostrates that CK SRS/SRT retreatment is a feasible and well tolerated treatment option for recurrent Gliomas previous irradiated. In these patients the better treatment choice remain individual and based on a multidisciplinary evaluation. However, a longer follow-up and enrollment of more patients are needed to confirm our results and guide us in choosing the most appropriate treatment.

P244

2 GY-TOTAL BODY IRRADIATION USING TOMOTHERAPY: A SINGLE-INSTITUTION EXPERIENCE

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Aims: Hematologic malignancies may require allogeneic bone narrow transplantation. Total body irradiation (TBI) induces immunosuppression to prevent the rejection of donor narrow. To evaluate the feasibility and the safety of TBI with Tomotherapy.

Methods: From February 2016 to May 2018, 17 adults patients (11 males and 6 females) were treated at Our Department (European Institute of Oncology, Milan), with a TBI of 2 Gy in single dose, the day before the narrow transplantation. All the patients were treated with Tomotherapy. The planning target volume (PTV) was obtained cropping 2 mm from the body surface; we used a TomoHelical-technique, through photon energy of 6 MV, with slice-thickness of 5 mm and pitch of 0.285. The treatment was performed in supine position, with a cast immobilizing the whole body, and 2 termoplastic masks, one for the head and one for the feet. The irradiation was split in 2 segments: head-first (from the apex to the knees) and feet-first (from the feet to the knees). The junction-dose was evaluated through a plan sum performed on Eclipse system. To control the position of different body segments, we acquired 2 MegaVoltageComputedTomography (MVCT) for each patient orientation (head-shoulders and abdomen-pelvis for head-first orientation, knees and ankles-feet for feet-first one). For each phase, we collected the shifts in the 3 couch directions, calculated by the system in the 2 MVCT, and we applied the median values, before the treatment delivery.

Results: The median Monitor Units for head-first supine treatment were 21.500 with a median delivery time of 36 minutes; the median. Monitor Units for feet-first supine treatment were 10.200 with a median delivery time of 25 minutes. TBI was well-tolerated in all patients, without acute complications. Despite the difficulty in maintaining the same position for a long time, only in one case, we premedicated the patient with anxiolytic drug.

Conclusions: In our experience, TBI with Helical Tomotherapy is a feasible treatment and seems to allow a high homogeneity in dose distribution and a high set-up accuracy. Further investigation is warranted to fully evaluate this approach.

P245

HYPOFRACTIONATED, ADAPTIVE RADIOTHERAPY CONCOMITANT WITH CHEMOTHERAPY AS PREOPERATIVE TREATMENT FOR RECTAL ADENOCARCINOMA

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Aims: To report our clinical experience with hypofractionated, adaptive radiotherapy (RT) concomitant with chemotherapy (ChT) as preoperative treatment for rectal cancer.

Methods: patients (pts) with T3/T4N0 or any TN+ rectal adenocarcinoma were studied. Chemotherapy consisted of Oxaliplatin 100 mg/m^2 on days -14, 0, +14 and c.i. 5FU 200 mg/m^2/day or oral capecitabine 825mg/m2x2/day (from 2015 on). RT started on day 0, was delivered with Tomotherapy, and was divided into two phases of 12 and 6 fractions (Frs). Pts were positioned on Comby-Fix® and underwent a simulation CT and MR, subsequently matched. In the first RT phase CTV included mesorectum, perineum in case of tumor < 6cm from anal canal, and regional lymph-nodes. PTV was defined as CTV with a margin of 0.5 cm and received 27.6 Gy in 12 fractions (2.3 Gy/Fr). A simulation CT and MR were repeated after two cycles of ChT and 9 Frs of RT. Two new volumes were considered: GTVadaptive, defined as the residual tumour (T and N) visible on the intermediate MR images, and PTVadaptive, created from GTVadaptive with a margin of 0.5 cm. In the second RT phase, the adaptive phase, PTV again received 2.3 Gy/fr x 6 Frs (total dose 41.4 Gy in 18 Frs), while PTVadaptive received a simultaneous integrated boost of 3.1 Gy/Fr x 6 Frs (total dose 46.2 Gy in 18 Frs).

Results: From 9/2009 to 5/ 2017, 82 pts were prospectively enrolled, T2=5, T3=72, T4=5, N+=67. Median distance from anal canal was 6.5 cm (0 cm in 18 pts), median cranium-caudal tumor length was 5 cm. Toxicity. No G4 toxicity occurred. G3 toxicity: diarrhoea in 10/82 pts (12%), proctitis in 4 pts (5%). Diarrhoea always occurred before the adaptive phase. Treatment feasibility. Eighty pts (97%) completed RT; median duration of RT was 25 days. Fifty-seven (70%) and 74 (84%) received > 75% of oxaliplatin and fluoropyrimidines dose, respectively. Responses. Two pts achieved complete clinical response and refused surgery, 1 pt was lost, 1 pt had early distant progression. Seventy-eight pts were resected (73 R0, 5 R1), six pts had abdominal-perineal amputation. Twenty-two pts (28%) had pathological complete response, 23 pts (31%) had TRG3 with 1-5% of residual vital cells. At a median follow up of 41.4 months 3 pts had local and 20 pts distant relapse. Median survival was 30.2 months.

Conclusions: Hypofractionated, adaptive RT concomitant with oxaliplatin and fluoropyrimidines results in very encouraging major responses and acceptable G3 toxicity rate.

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STEREOTACTIC BODY RADIATION THERAPY (SBRT) IN PANCREATIC CANCER (PCA): THE VERONA UNIVERSITY HOSPITAL EXPERIENCE

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Aims: SBRT is an emerging treatment option able to provide high rates of local control (LC) and margin-negative (R0) resection for locally advanced pancreatic cancer (LAPC) and borderline resectable pancreatic cancer (BRPC), delivering high radiation doses within a few fractions to the tumor while sparing the surrounding organs at risk (OARs). The aim of this study was to evaluate local control rate (LCR), overall survival (OS), progression-free survival (PFS) and toxicity of SBRT in PCA patients (pts) treated in a high volume Centre

Methods: We retrospectively reviewed 30 pts with PCA (13 BRPC, 17 LAPC) treated from October 2016 to February 2018 at our Institution. All pts received induction chemotherapy prior to SBRT (12 Folfirinox, 18 Gemcitabine-Paclitaxel). SBRT was delivered over 5 consecutive fractions using a dose painting technique including 10 Gy/fraction to the region of vessel abutment/encasement and 6 Gy/fraction to the remaining Planning Target Volume (PTV) tumor. We reduced the dose to 5 Gy/fraction on the overlap area between the PTV and OARs. The SBRT was delivered with Volumetric Modulated Arc Therapy (VMAT) using a Varian DHX LinAc (20 pts) or with TomoTherapy (10 pts). Daily on-line volumetric image-guided RT was performed. Restaging CT were performed at 4 weeks, and subsequently pts were considered for resection

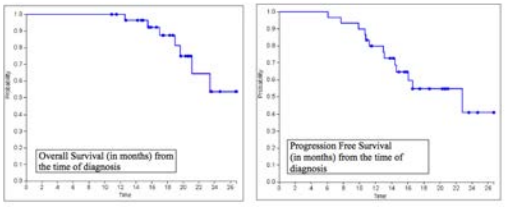

Figure 1.

Results: Median follow up time was 8.1 months (range 3.0-16.5 months). 29 pts (97%) completed the planned treatment. At the first restaging CT, 21 pts (67%) had a radiographic stable disease, 8 pts (26%) had partial response while only 1 pt had local progression. 16 pts (53%) underwent exploratory laparotomy and 12 pts (75%, 11 BRPC and 1 LAPC) surgical tumor resection (8 pts achieved R0 resection, 67%). At the last follow-up 23 pts (77%) were alive, with a median OS of 18.5 months from the time of diagnosis and a median

PFS of 15.3 months. Tumor relapse occurred in 13 pts (43%), distant failure alone in 11 pts and distant plus local failure in 2 pts. Overall, a LCR of 86% was obtained in nonsurgical patients. 1 patient (3%) developed acute G4 gastro-intestinal toxicity that required interruption of SBRT after 3 fractions. No other acute or late G ≥3 toxicities were observed

Conclusions: In our experience, SBRT for PCA is effective and feasible, able to achieve a high local control rate with a favorable toxicity profile, even if a larger case series with a longer follow-up period is necessary to draw definitive conclusions.

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FROM CLINICAL RESEARCH TOWARDS A PERSONALIZED MEDICINE: DEVELOPMENT OF PREDICTION MODELS IN STEREOTACTIC EXTERNAL RADIOTHERAPY (PRE.M.I.S.E. PROJECT) IN ORDER TO BUILD A DECISION SUPPORT SYSTEM (DSS)

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Aims: Recent advances in modern radiation therapy techniques, including stereotactic radiotherapy (SRT) has created new challenges leading the clinical practice towards a personalized medicine thus conferring an essential role to DSS. Softwares, apps, nomograms are all based on the creation of predictive models (PM) requiring standardization of data collection. Ontology represents a fundamental tool to establish a common language. The aim of this study is the implementation of systems that analyse large heterogeneous datasets, without knowing beforehand, which data could be the most relevant for a specific hypothesis. This is, to our knowledge, the first example of a multicentric study with the aim of collecting data in order to build up a PM which is specific for SRT technique. In phase I we focused on brain SRT.

Methods: A multidisciplinary team has been created from the first two centers involved including physicians, physicist, nurses and therapists. The team used a GANTT chart to schedule project's workload and deadlines and met every two weeks drafting a detailed report every time. First the team identified variables to be inserted in the ontology and validated them. Second, in order to collect data according to the predefined ontology the team needed a system which is able to define variables' characteristics and their relationships. The semantic web technology was implemented and the team is now using a dedicated software called BOA (Beyond Ontology Awareness) with its own WEB platform to collect data.

Results: We selected more than 130 variables related with brain SRT (isodose line prescription, distance among treated lesions, resolution grid, etc.), organized into three levels (registry, procedural and research level). We created BOA Web platform and the first two centers involved are now collecting data using Case Report Form (CRF).

Conclusions: We created a brain SRT ontology that shares features with other cancer sites and keeps SRT specific characteristics. Furthermore, we constructed a platform for multiple dataset sharing which facilitates the creation of large communal databases. Our project innovation resides mainly in having created the ontology for a particular radiation therapy technique. To our knowledge no predictive model focusing on a treatment technique is available in literature. Our future perspectives are both to include other centers in collecting data and to validate ontology for stereotactic body radiation therapy.

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DOES VOLUNTARY DEEP INSPIRATION BREATH HOLD TECHNIQUE AFFECT QUALITY OF LIFE IN BREAST CANCER PATIENTS UNDERGOING RADIOTHERAPY? PRELIMINARY RESULT OF THE INHALE (INSPIRATION BREATH HOLD AND HEALTH RELATED QUALITY OF LIFE ASSESSMENT) STUDY

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Aims: Breath holding (BH) techniques enable clinicians to reduce radiation dose to the heart and the left descending artery (LAD) in left breast cancer patients. Despite such advantages, BH radiotherapy (RT) compared to free breathing RT (FB RT) has been shown to require more efforts during simulation and treatment delivery for both clinicians and patients. The aim of this study is to evaluate whether BH RT affects QoL and physical (fatigue) as well as psychological distress in breast cancer patients. Herewith we report the preliminary results.

Methods: All breast cancer patients aged less than 60 years old who were referred to our department of radiation oncology were asked to participate in this study. Patient-reported outcomes (PROMs) including EORTC QLQ CD30-BRC23 questionnaire (22 items), FACIT – Fatigue Scale vers. 4 (13 items), Hospital Anxiety and Depression Scale - HADS (14 items) were prospectively collected before the start of adjuvant radiotherapy (baseline) and at the end of treatment. All scores were square-root transformed (scale 0-10).

Analysis of covariance (ANCOVA) was used with pre and post radiotherapy change in questionnaires scores as dependent variable, the treatment group (BH vs FB) as independent variable and the baseline measure as covariate.

Results: Thirty-one consecutive breast cancer patients (12 of them had left breast cancer, 19 right breast cancer) deemed to start radiotherapy treatment were asked to participate. All accepted to fulfill the questionnaires. Pre and post radiotherapy questionnaires were available for 26 patients (83.9%). Mean age was 48 years (range 33-59 years). Thirteen patients (41.9%) completed chemotherapy before radiotherapy, five patients (16.1%) had trastuzumab and twenty-five patients (80.6%) had hormone therapy during radiotherapy course. Depression scores, health related quality of life and fatigue did not change significantly during radiotherapy treatment for both groups (see table1). Patients reporting severe fatigue (FACIT – Fatigue Scale score >7) were 1/26 (3.8%) before and 3/26 (11.5%) after radiotherapy. Interestingly only one of these patients received BH radiotherapy. Anxiety and depression level was higher than mean score in all patients (see table1).

Conclusions: The study is still ongoing. Preliminary results suggest that BH RT seems to not affect quality of life, psychological distress and fatigue in breast cancer patients undergoing radiotherapy.

Table 1.

Outcome	Treatment type	Mean (SD) T0	Mean (SD) T1	Adjusted mean change (95% CI)	Adjusted between group mean change (95% CI)	p
Overall QOL	FB	4.2 (0.9)	4.3 (1.1)	0.1 (-0.3 to 0.5)	-0.6 (-1.4 to 0.1)	0.097
	BH	4.2 (1.0)	4.9 (0.3)			
Fatigue	FB	4.0 (1.7)	4.5 (1.4)	0.4 (-0.1 to 1.0)	0.0 (-1.0 to 1.0)	0.992
	BH	4.7 (1.2)	4.9 (1.7)			
Anxiety/depression	FB	6.1 (0.6)	5.9 (0.7)	-0.2 (-0.5 to 0.1)	0.1 (-0.5 to 0.7)	0.631
	BH	6.5 (0.5)	6.2 (1.2)			

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CARBON ION RADIOTHERAPY FOR GYNECOLOGICAL MELANOMA

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Introduction: Malignant melanoma (MM) of the lower genital tract is a rare disease known to have a poorer prognosis than cutaneous MM. In the clinical trial of CIRT for gynecological melanoma at NIRS, local control (LC) was promising (3-years-LC: 49.9%) with an acceptable profile of toxicity.

Aims: To report our preliminary experience with CIRT in the treatment of gynecological MMs at the National Center of Oncological Hadrontherapy (CNAO). Patients and methods: Between January 2016 and February 2017, 4 patients with VM (3) and CM (1) were admitted for CIRT at CNAO. No concomitant chemotherapy was administered. CM patient was treated with palliative aim because of the large macroscopic disease (GTV: 380.96 cc) The total dose was 24 GyRBE in 3 fractions and the clinical target volume (CTV) was defined as the macroscopic disease (GTV), uterine cervix and corpus. VM patients were irradiated with a total dose of 68.8 GyRBE in 16 fractions delivered over 4 weeks. CTV1 (total dose: 38.7 GyRBE) was the small pelvic space including GTV and CTV2 (total dose: 30.1 GyRBE) was confined to GTV with a margin of 5 mm. GTV ranged from 1.2 cc to 28.01 cc with a median of 25.29 cc. Toxicity was scored according CTCAE 4.0 scale. Time to event data was calculated from the end of CIRT.

Results: The age of the women ranged between 49 and 72 (median 60.5 years). All patients were BRAF/NRAS wild type and c-KIT mutation was identified in one VM. Treatment was well tolerated in all patients and all women completed the scheduled treatment course. During CIRT, toxicity was mild: G3 erythema (1 patient) and G1 vaginitis (2 patient). Three months after the end of the treatment, we observed only a case of G2 vaginitis. At time of analysis, the median LC of VM was 10.23 months, the woman with CM relapsed locally after 7.26 months. All patients experienced systemic progression.

Conclusions: In the management of gynecological MM, a more conservative treatment approach, instead of extensive surgery, may be warranted because of the high rate of distant metastases and unsatisfactory survival benefit. In our first experiences, CIRT appears to be a safe non-invasive option but more data and longer follow-up are necessary to evaluate the effectiveness and late effects. A strong collaboration between Gynecologic Oncologists and Radiation Oncologists treating MMs is of upmost importance to make a step forward in the treatment of female genital tract MM.

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STEREOTACTIC ABLATIVE RADIATION THERAPY PRIOR TO LIVER TRANSPLANTATION IN HEPATOCELLULAR CARCINOMA

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Aims: Stereotactic ablative radiotherapy (SABR) is a safe treatment approach for hepatocellular carcinoma (HCC) with comparable effectiveness to other local therapies. Only scant information is available concerning the role of SABR prior to liver transplantation (LT) for

HCC. We present a consecutive case series investigating the role of SABR as a bridge or downstaging option in HCC patients subsequently submitted to LT.

Methods: Between September 2012 and May 2018, 22 patients for a total of 32 lesions underwent SABR prior to LT. Inclusion criteria were a pathological or radiological diagnosis of HCC, lesion size ≤ 6cm or lesion number ≤ 3 with a total diameter ≤ 6 cm, no extrahepatic metastases, Child-Pugh class A-B, ECOG performance status ≤ 1. Patients were prescribed 36-48 Gy in 3-5 fractions, in 3-5 consecutive days according to clinical and dosimetric decision making. Radiological response was evaluated according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Pathological response was assessed through the rate of tumor necrosis relative to the total tumor volume. Acute and late toxicities were scored using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4 (CTCAE v 4.0).

Results: Among the 32 pathologically evaluated lesions, 13 (40,6%) lesions had a complete response, 11 (34,4%) had a partial response and 8 (25%) showed stable disease. Three patient developed a non-classic RILD with a shift in Child-Pugh category > 2 points due to bilirubin increase. Only one modification in the surgical strategy was needed during LT.

Conclusions: SABR proved to be a safe and effective local therapy prior to LT in HCC patients. Prospective controlled clinical trials are needed to evaluate its efficacy compared to other local therapies in this setting.

Table 1. Patient characteristics.

Age (yrs)	
Mean (range)	56 (41-68)
Gender	
Female	3
Male	19
ECOG Peformance Status	
0	21
1	1
Underlying liver disease	
HBV	5
HCV	11
HBV+HDV	1
Esotoxic	4
Autoimmune	1
Prior treatments	
Exclusive	21
Post RFA	4
Post TACE	4
Post RFA + TACE	2
Post TACE + Sorafenib	1
Child-Pugh class	
A5-A6	15
B7	5
B9	2

P251

AUTOMATIC TREATMENT PLANNING AS A DOSE ESCALATION STRATEGY FOR STEREOTACTIC RADIATION THERAPY IN PANCREATIC CANCER

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Aims: Stereotactic body radiation therapy (SBRT) has been suggested as a new treatment strategy for locally advanced pancreatic cancer. However, the close proximity of highly radiosensitive organs prevent the administration of high doses to the vascular infiltration areas, aiming for a radical resection. Aim of this study was to perform a planning feasibility analysis of an automated planning system (Pinnacle3 Autoplanning) using a VMAT-SIB technique as a dose escalation strategy.

Methods: Twelve patients with unresectable pancreatic head adenocarcinoma due to vascular infiltration, were included in this study. CTVv was defined as involved vessels plus 5 mm or contact between the gross tumor volume (GTV) and vessels. The vascular PTV (PTVv) was obtained adding an anisotropic margin (5 mm craniocaudal direction, 3 mm in other directions). The tumor PTV (PTVt) was defined as the GTV plus an anisotropic margin (5 mm craniocaudal direction, 3 mm in other directions) and including the PTVv. A duodenum-PRV was defined by adding an isotropic 5 mm margin. SBRT was delivered in 5 fractions with a SIB strategy. For each patient 3 plans were optimized. Plan 1: 30 Gy (6 Gy/fraction) to PTVs; plan 2 and plan 3 escalated PTVv dose to 40Gy (8 Gy/fraction) and 50Gy (10 Gy/fraction), respectively. Corresponding EQD2 were 40Gy, 60Gy and 83.3Gy (a/b equal to 10). The dose-volume constraints for OARs were based on the AAPM TG101 recommendations. Automated plans were generated by Pinnacle Autoplanning module by means of VMAT dual-arc. A progressive optimization algorithm is used to continually adjust initial targets/OARs objectives while tuning structures are automatically added to increase the dose fall-off outside targets. The primary endpoint was to achieve PTVt and PTVv coverage in terms of D95%>95%, respecting all OARs constraints.

Results: OARs constraints were achieved in all

patients. PTVv D95% was 30.8±0.1Gy, 36.1±5.4Gy and 39.2±12.0Gy at level 1, 2 and 3, respectively. In particular, the primary endpoint D95%> 95% was achieved in 12 patients (100%), 8 patients (67%) and 7 patients (58%) for level 1, 2 and 3, respectively. The mean dose to PTVv was 40.6±1.1 Gy and 49.7±2.3 Gy at level 2 and 3, respectively. PTVv mean dose was >90% in all patients.

Conclusions: Autoplanning reported a great potential for a tailored SBRT in advanced pancreatic cancer, allowing dose escalation and showing the feasibility to administer in all patients strongly differentiated doses.

P252

AUTOMATED VMAT PLANNING IN PINNACLE3: A DOSIMETRIC STUDY IN HEAD-NECK CANCER

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Aims: Treatment plans for head-neck cancer are highly complex due to large irregular shaped target volumes, multiple dose prescription levels and to several OARs close to the target. We assessed the performance of the Auto-Planning module present in the Pinnacle TPS (version 16.0), comparing automatically generated VMAT plans (AP) with the historically clinically accepted manually-generated ones (MP) for head-neck cancer patients.

Methods: Twelve consecutive patients treated with VMAT-SIB for bilateral head-neck cancer were re-planned with the Auto-Planning engine. The PTV1 included the primary tumor, PTV2 and PTV3 included the high-risk and low-risk lymphnodal areas, respectively. PTV1, PTV2 and PTV3 were simultaneously irradiated over 30 daily fractions at 67.5Gy, 60.0Gy and 55.5 Gy, respectively. All manually (MP) and automatically (AP) generated plans were created by means of the 'dual arc" feature. For the MP plans, additional non-anatomical structures needed to be delineated in order to interactively guide the optimization process. For AP plans, a progressive optimization algorithm is used to continually adjust initial targets/OARs objectives; tuning structures are automatically added during optimization to increase the dose fall-off outside targets and improve the dose conformity. Various dose and dose-volume metrics (D98%, D95%, D50%, D2%, Dmean, V95% for target volumes; Dmean, Dmax and various Vx% for OARs), as well as conformity (CI) indexes and healthy-tissue integral dose (ID) were evaluated. A Wilcoxon paired test was performed for plan comparison with statistical significance set at $p<0.05$.

Results: Differences in all dose coverage metrics (in terms of V95%, D98%, D50%, D2% and Dmean) for all PTVs were not statistically significant ($p<0.05$). AP plans reported a better CI for PTV3 (MP:1.43 vs. AP:1.35, $p=0.01$). No significant differences in maximum doses were found for eyes, lens and optic chiasm. AP plans reduced maximum doses to PRV spinal cord and brainstem by 1.3Gy ($p=0.04$) and 4.3Gy ($p=0.02$), respectively, and mean dose for parotids by 3.4Gy ($p=0.02$). In addition, AP plans provided a significant decrease in Integral Dose of 6.6%. The mean number of MUs was higher for AP (586 vs. 451, $p=0.01$), suggesting an increased degree of fluence modulation.

Conclusions: The Pinnacle Auto-Planning module was able to produce highly consistent treatment plans for this complex anatomical sites. The working time was substantially reduced with Auto-Planning.

P253

AUTOMATED VMAT PLANNING IN PINNACLE3: A DOSIMETRIC STUDY IN HIGH-RISK PROSTATE CANCER

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Aims: Treatment plans for high-risk prostate cancer are highly complex due to large irregular shaped target volumes, multiple dose prescription levels and several OARs close to the target. The quality of these plans is highly inter-planner dependent. We aimed to assess the performance of the Auto-Planning module present in the Pinnacle TPS (version 16.0), comparing automatically generated VMAT plans (AP) with the historically clinically accepted manually-generated ones (MP).

Methods: Twelve consecutive patients treated with VMAT-SIB for high-risk prostate cancer were re-planned with the Auto-Planning engine. The PTV1 included the prostate and the seminal vesicles; the PTV2 inclu-

ded the pelvic lymph nodes. Both PTVs were simultaneously irradiated over 25 daily fractions at 65Gy (2.6 Gy/fraction) and 45Gy (1.8 Gy/fraction). All manually (MP) and automatically (AP) generated plans were created by means of the 'dual arc" feature. For the MP plans, additional non-anatomical structures needed to be delineated in order to interactively guide the optimization process. For AP plans, a progressive optimization algorithm is used to continually adjust initial targets/OARs objectives; tuning structures are automatically added during optimization to increase the dose fall-off outside targets. Various dose and dose-volume metrics (D98%, D95%, D50%, D2%, Dmean, V95% for target volumes; Dmean, Dmax and various Vx% for OARs), as well as conformity (CI) indexes and healthy-tissue integral dose (ID) were evaluated. A Wilcoxon paired test was performed for plan comparison with statistical significance set at $p<0.05$.

Results: Differences in all dose coverage metrics (in terms of V95%, D98%, D50%, D2% and Dmean) for both PTVs were not statistically significant ($p<0.05$). Differences in CI reached significance only for PTV2 (MP:1.59 vs. AP:1.48). Differences in DVHs were no significant in overall dose range for rectum, bladder and small bowel (rectum: V50Gy: 31.7 vs. 32.2Gy, V60Gy: 21.1 vs. 22.5Gy, Dmean: 40.6 vs. 40.5Gy; bladder: V65Gy: 19.6 vs. 20.6, Dmean: 44.3 vs. 43.8Gy). For small bowel: V15Gy: 105.0 vs 119.1cc, Dmean: 13.3 vs. 12.8cc. AP plans provided a decrease in Integral Dose of 5.1%. The mean number of MUs was very similar between MP (537) and AP (546).

Conclusions: The Pinnacle Auto-Planning module achieved highly consistent treatment plans in the cases of complex anatomical sites. The working time was substantially reduced with Auto-Planning.

P254

STATISTICAL PROCESS CONTROL FOR VMAT QUALITY ASSURANCE: AN EIGHT-YEAR RETROSPECTIVE STUDY

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Aims: Statistical Process Control (SPC) is a tool widely used in industrial engineering for monitoring and improving a process through statistical analysis. We applied this strategy for patient-specific VMAT pre-treatment verification.

Methods: In the last eight years, more than 1700 patients were treated with Elekta VMAT at our institution. Plans were re-grouped according to treatment technique and disease sites Group 1: 736 high-modulated complex treatments using SIB (H-N, pelvic and brain tumors); (2) 441 low-risk prostate treatments and (3) 558 metastasis treated with SBRT. A total of 4942 planar dose measurements were performed with the PTW 729 array/Octavius phantom. Doses comparison were evaluated using 3%/3mm γ-analysis: (a) γ%: points-percentage with γ-value less than one, (b) γmean: mean gamma value and (c) γ1%: the near-maximum gamma defined as the 99th percentile of the γ-distribution. Clinical specifications were: γ%>90%, γmean<0.67 and γ1%<2. Shewhart charts were used to calculate the central (CL), upper control (UCL) and lower control limits (LCL). The capability of the processes was evaluated by means of Cpk indexes. A Gage R&R study was also perfomed to assess the capability of our ion-camber device.

Results: γ pass-rate values significantly depend on plan complexity. For γ%, CL and LCL were 93.8%, 99.1%, 99.5% and 87.9%, 96.6%, 97.9%, for group 1,2 and 3 respectively. For γmean, CL and UCL were 0.42, 0.36, 0.29 and 0.54, 0.49, 0.40, for groups 1, 2 and 3 respectively. For γ1%, CL and UCL were 1.87, 0.98, 0.94 and 2.69, 1.34, 1.31, for groups 1, 2 and 3 respectively. For the groups 2 and 3, all processes are in control and within clinical specifications (State I). For group 1 only the γmean process is in a state I; the γ% process is in a state IV (out of control and out of clinical specifications) while the γ1% process is in a state II (within the control limits but out of clinical specifications). The capability index of the 729 array was 6.5, implying that this device is statistically capable. The Cpl/Cpu capability indices for γ%, γmean and γ1%

resulted equal to 0.33, 1.07 and 0.10 in group 1; 2.85, 1.64 and 2.11 in group 2; 4.20, 2.60 and 2.01 in group 3, respectively. With 5%-3mm specifications, also γ% and γ1% processes in group 1 moved in a state I (Cpl and Cpu were 1.87 and 1.57, respectively).

Conclusions: SPC is a powerful tool to quantifiably evaluate the QA process performance in advanced radiotherapy.

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POTENTIAL RELATIONSHIP BETWEEN BODY MASS INDEX AND SET-UP CORRECTIONS IN IMAGE GUIDED RADIOTHERAPY FOR PROSTATE CANCER PATIENTS

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Aims: To investigate the relationship between body

mass index (BMI) and intrafraction displacements in patients undergoing prostate cancer image-guided radiotherapy (IGRT).

Methods: A retrospective analysis was performed using data for ninety-five prostate cancer (Pca) patients who received volumetric arc therapy/image guided (VMAT/IGRT) between January 2017 and April 2018. Body mass index was calculated using the World Health Organisation (WHO) definition of the weight (kilograms) divided by the square of the height (metres). Patients were divided in two category: normal or underweight patients, named category 1, had BMI < 25 kg/m^2; overweight patients, named category 2, had BMI ≥ 25 kg/m^2. Setup corrections were determined and corrected using 3D online registrations of CBCT images with the planning CT. The range of displacements in the three space directions was calculated for each patient in centimeters (cm). Mean range of displacements was assessed for each category.

Results: Of the 95 patients, 43% were included to category 1, 57% to category 2. Mean ranges of displacements for category 1 were 1.71 cm, 1.23 cm, 1.17 cm for vertical, longitudinal and lateral directions, respectively. Mean ranges of displacements for category 2 were 1.68 cm, 1.29 cm, 1.55 cm for vertical, longitudinal and lateral directions, respectively. Mean ranges differences in lateral direction between the two categories resulted statistically significantly with a p-value <0.05 (p=0.0036).

Conclusions: Our data indicate that Pca patients with higher BMI had a greater interfraction displacements in the lateral direction compared to patients with a lower BMI. Daily IGRT, especially for these patients, may lead to improve treatment quality.

P256

THE USE OF VMAT-IGRT FOR RE- IRRADIATION OF LUNG LESIONS THAT HAVE RELAPSED IN FIELD AFTER SBRT

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Aims: Nevertheless, Stereotactic body radiotherapy shows good results in the treatment of primary and metastatic lung lesions, relapses in field are not unusual. Retreatment of recurrences is a challenge for the risk of severe toxicity. The aim of this study is to investigate the possibility offered by volumetric intensity modulated arc therapy (VMAT) technique to deliver more accurate and optimized dose distribution in terms of toxicity, Local Control .

Methods: Between 2011 and 2017, 56 pts recurred in the lung, after previous EBRT or SBRT delivered to the same site. Median age was 69.5 yr ,with KPS >70. The histology was Squamous cell carcinoma , Adenocarcinoma , other and unknown in 12,29,9 and 6 pts respectively. 29 pts had primary tumor and 27 pts had metastatic lesions (14 CRC, 8 NSCLC, 5 other). 16 pts had synchronous mets at the time of diagnosis and metachronous mets was present in 24 pts at the time of re-irradiation. 20 pts received chemotherapy after first course of RT and 12 pts after retreatment. Recurrences were detected by CT in 100% pts and in 53% pts also Pet scan was performed. Seven percent of tumors received prior EBRT and 93% received prior SBRT. All pts were re-irradiated with SBRT. Previous median volume GTV was 21.25 cc (1.25-186 cc), median retreated volume GTV was 22.6 cc (1.9-192 cc). First treatment median dose was 30 Gy in median number of 3 fraction, the median re-irradiation dose was 33.5 delivered for a median of 3 fractions prescribed to the 70% isodose in 35 lesions. (Median BED10 > 100 Gy in 64% lesions). SBRT was delivered by 6MV Linac using beam modulator (ELEKTA SynergyS)equipped with 4 mm MLC, through two co-planar and no coplanar arcs with VMAT optimization. Breath-hold and free breathing technique was employed in 24 pts and 32 pts respectively during re-irradiation. Set-up and isocenter position was controlled before each fx using CBCT .The response was evaluated 60 days after SBRT by CT and PET scan and every 4 months successively. Toxicity was assessed by CTCAE score.

Results: All pts were evaluated for response. Median FU was 17 (range 7-57) months. Median time to re-irradiation was 14 (range6-105) months. The crude local control (LC) was 80.4% (100% at 6 and 12 months, and 71% at 2 year. Analysis did not demonstrate any factors statistically significant for LC .The median overall survival (OS) was 56.18 months. OS was 100% and 88% , at 1 and 2 year respectively. At Univariate and Multivariate analysis time to re-irradiation >12 months and synchronous mets were found to be statistically significant for OS (p<0.02) . No patients experienced grade 3-4 toxicity. Only one pts showed atelectasis after re-SBRT.

Conclusions: In our experience re-irradiation by VMAT for in field lung recurrences after SBRT is safe and effective, providing excellent crude LC (80.4%,) and it could be considered as valid option for pts that recurred after previous SBRT. The toxicity was mild and not influenced by the time between first and second treatment .

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EVALUATION OF INTER – FRACTION MOTION IN STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR PELVIC OLIGOMETASTASES

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Aims: SBRT represent a widely treatment option in oli-

gometastatic prostate cancer. This analysis describes our preliminary experience with treating mHSPC patients with SBRT alone.

Methods: Between January 2016 and March 2018 eleven mHSPC patients were treated with exclusive SBRT, delivered using LINAC with daily cone beam CT. All patients underwent [(11)C] choline or [(64)Cu] positron emission tomography(PET) for biochemical relapse after local primary treatment (RT or surgery): eight patients had isolated abdominal or pelvic nodal disease and three patients had single bone metastases. Prescribed dose was 30 or 35 Gy in 5 fractions. We did not prescribe concomitant androgen deprivation therapy (ADT) in all these patients who had PSA doubling time > 6 months Response to treatment was assessed with periodical PSA evaluation and a further PET in patients with biochemical increase.Toxicity was evaluated according to CTCAE vers.4.02.

Results: The median age was 71 years; the median follow-up was of 10 months (range 3-26) and the median PSA pre-SBRT was 1.1 ng/ml (0.43-2.8). A significant and persistent reduction of PSA was observed in 7/11 (63%) patients; 2 patients started with ADT for multimetastatic disease progression after SBRT; other 2 patients required a second salvage SBRT for metachronous nodal relapse after 8 and 12 months of biochemical control but one of them started palliative ADT for further disease progression. All patients with biochemical and clinical control disease had a pre-SBRT doubling time > 10 months. Acute and late toxicities greater than G1 were not recorded.

Conclusions: Despite the small number of patients and the short follow-up, our experience shows that salvage PET-guided SBRT is safe and effective in deferring the start of palliative ADT in selected low-volume and low biochemical kinetics mHSPC patients.

P258

A NEW MODALITY OF AUTOMATIC VMAT PLANNING FOR BREAST CANCER RADIOTHERAPY

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Aims: Adjuvant radiotherapy after conserving surgery of breast cancer represents a large number of patient planning. The Auto-Planning makes the process faster and more reproducible, but requires the 'ad hoc' license purchase. The objective of this study was to evaluate a workflow for the automation and standardization of breast treatment plan, using a commercial TPS without buying expensive licenses. The procedure requires only two user interactions. The Automated tangential volumetric modulated arc therapy (AVMAT) technique was compared to standard tangential field in field method (FinF).

Materials and Methods: 28 women with left-sided breast cancer were enrolled. The prescription dose was 50 Gy in 25 fx. Treatment plans were created for a Linac equipped of 40 leaf pairs of 4 mm width. The treatment energy was 6 MV. Two treatment plans were generated for each patient: 1) standard tangential field-in-field (FinF), 2) Automated tangential VMAT (AVMAT) with two dual arcs of 60°. The AVMAT plans were created with TPS based on XVMC algorithm. The Template plan was standardized with constrained radiobiological cost functions in two steps: multi criterial optimization to improve OAR sparing and Pareto optimization to increase PTV coverage. A standard deviation of 0.5% was used in Monte Carlo dose calculation with a dose grid of 3.0 mm. The 3D-CRT FinF plans were generated in TPS with Superposition dose calculation algorithm with the same dose grid. Quantitative and dosimetric evaluation of the plans was performed using the DVH. The number of Monitor Units (MUs) was also recorded.

Results: In ipsilateral lung AVMAT plans decreased the high dose areas (V20VMAT=1,57%±0,6 vs V20FinF=5,3%±1,2), however increased the low dose ones (V5VMAT=12,2%±1,8 vs V5FinF=8,7±2,1).

Significant cardiac dose sparing (V25 and the mean dose) was achieved with AVMAT technique, and non-significant reduction of V2 of the heart was achieved with FinF. There were no differences in the mean dose of contralateral breast, but AVMAT plan increased the Maximum dose (DmaxVMAT=3,8±0,9Gy vs DmaxFinF=2,1±0,5Gy). The dose coverage was better with AVMAT plan (97,8%vs 92,2%) The average number of MUs in one fraction were 659±93MU and 255±5 MU for AutoVMAT and FinF respectively.

Conclusions: The AVMAT technique is an effective method for achieving a homogeneous dose coverage reducing doses to heart and lung. Furthermore it is a fast planning process that doesn't require the manual interaction.

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LEFT ANTERIOR DESCENDING CORONARY ARTERY (LAD) SPARING ACCORDING TO VOLUNTARY DEEP INSPIRATION LUNG VOLUME

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Aims: Voluntary deep inspiration breath hold technique (vDIBH) it's real help to cardiac sparing in whole breast irradiation. This study compared two plan with two different technique: one with free breathing (FB), and the other one with vDIBH to evaluate if left anterior descending coronary artery (LAD) maximum dose reduction depends on individual patient vDIBH volume

Methods: Patients with left-sided breast cancer underwent whole breast Radiotherapy, with vDIBH using Varian Real-time Position Management (RPM). It was provided a training session to achieve the personal deep inspiration level and two different CT: one in FB and one in vDIBH. For each woman it were optimized two 2-field tangential plan, respectively for FB/CT and

vDIBH/CT with the Irregular Surface Compensator (ISC) in Eclipse (Varian Medical System), calculating with Anisotropic Analytical Algorithm (version 10.0.28).

Results: Fifteen patients underwent Radiotherapy with 50Gy in 25 fractions and Dose-Volume Histogram (DVH) is used to compare the dose to the Target and to the Organs at Risk between FB plan and vDIBH plan. In Beam of view (BEV), the minimum distance (DLAD) between LAD and target was measured. The most significant results are the LAD Dmax (p=0.000), with a mean dose reduction from 10,5Gy in FB plan to 6,5 Gy vDIBH plan and DLAD increase from 1,35cm in FB plan to 0.05cm in vDIBH plan. For all patients LAD dose reduction is inside 40-60%, also in patients with a big breath inspiration (Vol vDIBH/Vol FB=2,22) and a big DLAD. (DLAD vDIBH- DLADFB = 3 cm). There is not significant variation for Lung V20 and Vmean.

Conclusions: vDIBH improves cardiac dosimetry in all patients without worsen DVH constraints for lung. However, we did not detect any difference in LAD maximum dose according to patient specific DIBH volume. Therefore, a big deep inspiration breath hold seems not necessary to achieve better results.

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CYBERKNIFE ROBOTIC STEREOTACTIC BODY RADIOTHERAPY AS TREATMENT FOR PRIMARY AND SECONDARY LUNG LESIONS: A MONO-INSTITUTIONAL EXPERIENCE

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Aims. The purpose of this study was to evaluate treatment patterns and outcomes of robotic Stereotactic Body Radiotherapy (rSBRT) for primary and metastatic lung lesions. Two target tracking methods are currently available with the CyberKnife® System: the first one, fiducial tracking, requires the use of radio-opaque markers implanted near or inside the tumor, and theXsight® Lung Tracking System, (XLTS). With XLTS targeting is synchronized directly with target motion, which occurs due to respiration.

Methods. We selected 76 eligible patients who were treated at our Institutions with rSBRT to primary and metastatic lesions from March 2012 to November 2017. We evaluated Overall survival (OS), disease free survival (DFS), local control (LC)and treatment-related toxicity. OS and DFS were determined using Kaplan-Meier method. Toxicity was reported using Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

Results: 76 patients with 97 lesions were treated with rSBRT, including primary lung cancers (39%), and pulmonary metastases (61%). Two lesions were treated with fiducials tracking, 95 lesions with XLTS. The median age was 70 years (range 40-91), 52 male and 24 female. Median follow-up time was 16 months. The ECOG performance status (PS) was 0 for 30 patients, 1 for 42 patients and 2 for 4 patients. Median number of fractions was 3 (range 1-8) and median total dose was 35,14 Gy (range 18-60 Gy), median isodose line prescription was 74.35% (range 68-85%). Average BED was 85,68 Gy (range 37,5-180 Gy). Patients were followed with physical examination and CT imaging. The 1-year LC rate was 61%, DFS at 1 and 2 years was 51% and 21%, OS at 1 and 2 years was 80% and 72%, respectively. Toxicity rates were low, with no Grade 3 or higher acute or late toxicity reported.

Conclusions: Stereotactic ablative radiotherapy using the CybeKnife system as the treatment of primary and metastatic lung lesions seems to be a safe and effective treatment option with low toxicity rates.

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IMPACT OF TARGET VOLUME DELINEATION ON WEEKLY SIMULATION CT DURING CONFORMAL RADIOTHERAPY IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Aims: Anatomical changes during radiotherapy in lung cancer might contribute to target missing and discrepancies between planned and delivered doses. Modern radiotherapy techniques manage the geometrical uncertainties of treatment planning and treatment delivery and thereby improve target coverage with a much steeper dose gradient and less irradiated normal tissue. The aim is to evaluate the shrinkage of target volume in patients with locally advanced NSCLC treated with concurrent radiochemoterapy (RCT) with an adaptive approach

Methods: Patients with locally advanced NSCLC treated with RCT were investigated. All patients had stage IIIA/IIIB or intrathoracic relapse after surgery. Treatment was performed with a linear accelerator (Varian Medical System) in a photon regimen, with a 6/15-MV nominal energy and three-dimensional conformal technique with multiple planar and nonplanar beams. Concurrent chemotherapy regimens were platinum-based doublets or monotherapy. All patients received a weekly CT simulation. On each weekly CT the CTV was delineated and in case of tumor's shrinkage, a new CTV was created and a new treatment plan outlined ("replanning")

Results: From 2012 to 2014 replanning was outlined in 50 patients of 217 patients with locally advanced NSCLC treated with RCT and subjected to weekly simulation CT. Patients' characteristics were: mean age 69.6 years (range 38-92), squamous histology 56%,

32% adenocarcinoma, other 12%, stage IIIA 58% and IIIB 42%. The median total dose delivered was 66.6Gy (range 45-75.6) with standard fractionation. Median CTV at CT simulation was 125.2 cc. Contouring CTV on the weekly CT, we observed a progressive shrinkage of the target volume, in particular at the median dose of 19.8, 27, 36 Gy and 45 Gy we registered a reduction of 13%, 20%, 16%, and 43% respectively. The replanning has been performed at a median dose of 45Gy. Median CTV at replanning volume was 74.7 cc.

Conclusions: Tumor shrinkage is common during RCT in NSCLC. There are points in time during the treatment course when it may be appropriate to adapt the plan to improve sparing of normal tissues. In our patients population in which an adaptive replanning was performed we early observed a tumor reduction (13% after 2 weeks of treatment). We are trying to understand if there are volume reduction patterns that can influence prognosis and therefore help to classify lung neoplasms in different groups.

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CLINICAL EXPERIENCE IN PATIENTS WITH ESOPHAGEAL OR ESOPHAGEAL GASTRIC JUNCTION CANCER TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY AND IG-IMRT PET BASED

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Aims: To report our experience in patients (pts) with esophageal (EC) or esophageal gastric junction (EGJ) cancer treated with IG-IMRT PET based.

Methods: From April 2014 to April 2018, 56 pts (m:43, f:13), with histologically proven EC or EGJ were treated according to CROSS study. Median age at diagnosis: 56 years (28-80), median KPS: 90 (80-100). Twenty-eight pts had adenocarcinoma (50%), 27 pts had squamous cell carcinoma (48.2%), 1 pt had adenosquamous carcinoma (1.7%). All pts underwent c-e CT and PET simulation, repeated for restaging. Radiotherapy (RT) consisted in 41.4 Gy in 23 fractions combined to chemotherapy (ChT) with carboplatin and paclitaxel.

Results: Clinical stage was: T1: 1pt, T2: 14 pts, T3. 38 pts, T4: 3 pts, N0: 11 pts, N+: 45 pts. The site of tumor was proximal/middle third in 5 pts, middle/middle-distal third in 34 pts, distal third/distal-EGJ/ EGJ in 17 pts. Median tumor length was 4 cm (0.8-15). RT was delivered by Tomotherapy in 36 pts and by VMAT in 20 pts. All pts completed RT. Median cycles of ChT was 5 (2-6 cycles), 70% pts received a full dose of ChT. G3 acute haemathological toxicity was: neutropenia in 3.5% (2pts), lymphopenia in 67.8% (38 pts), anemia in 1.7% (1pt). G3 gastrointestinal toxicity occurred in 14.2% (8 pts). Three pts (5.3%) had bacterial pneumonia (1 pt G5). Responses: 55/56 pts were available (1 pt early lost). Median time to restaging was 42 days (14-87). CT/PET showed local RP in 27 pts, SD 9 pts, RC 18 pts, PD in 1pt. Median time from CT/RT to surgery was 61 days (15-148). Forty-two pts (75%) underwent surgery, 13 excluded (7 for PD, 3 for worsening clinical condition, 1died, 1 lost, 1 pt had cCR), 1 pt early restaged. One pt underwent urgent surgery 15 days after CT/RT because of aorto-esophageal fistula. Post-surgery stage was T0: 7pts, T1: 9 pts, T2: 11 pts, T3: 14 pts, T4: 1 pt; N0: 25 pts, N+: 18 pts. Forty/ 42 pts (95%) had R0. Mandard TRG was: TRG1: 7 pts (16.6%), TRG2: 7 pts (16.6%), TRG3: 22 pts (52.3%), TRG4: 4 pts (9.5%). Median OS was 15 months (2.8-45.5). Eighteen/42 pts (42.8%) are disease free at a median follow up of 15 months (7.6-45.5). Twenty-one/42 pts (50%) had a progression disease at a median time to progression of 8.5 months (1.5-27).

Conclusions: our data seems to be comparable to CROSS data in term of R0 and toxicity profile. Combination of IG-IMRT and ChT, lymphopenia was the major cause of not optimal tolerability of treatment and could explain the onset of pneumonia and the difference between TRG responses.

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EFFICACY AND TOLERABILITY OF CYBERKNIFE STEREOTACTIC ROBOTIC RADIOSURGERY FOR PRIMARY OR SECONDARY ORBITAL LESIONS: A SINGLE-CENTRE RETROSPECTIVE EXPERIENCE

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Aims: Orbital lesions are rare, but are likely to become symptomatic and can impact on patients' quality of life. Local control is often difficult to obtain, because of proximity to critical structures. CyberKnife stereotactic robotic radiotherapy could represent a viable treatment option.

Methods: Data of patients treated for intraorbital lesions from solid malignancies were retrospectively collected. All patients underwent treatment with CyberKnife system (Accuracy Inc., USA). We analyzed local control (LC), response rate, symptoms control, PFS and OS, acute and late toxicity.

Results: From January 2012 to May 2017, 20 treatments on 19 patients were performed, with dose ranging from 24 to 35 Gy in 1-5 fractions, prescribed at an average isodose line of 79,5% (range 78-81). After a mean follow up of 14,26 months (range 0-58), overall response rate was 75%, with 2 and 4 patients presenting a partial and complete response, respectively. Mean time to best measured response was 15,16 months (range 2-58). Thirteen patients were alive, with a local control rate of 79%. Mean time to local progression was 5 months (range 3-7). Three patients reported improvement of symptoms after treatment. Mean PTV dose

coverage was 97,2% (range 93,5-99,7). Mean maximum dose (Dmax) to eye globe, optic nerve, optic chiasm and lens was 2380,8 cGy (range 290-3921), 1982,82 cGy (range 777,3-2897.8), 713,14 cGy (range 219,5-2273) and 867,9 cGy (range 38-3118,5). Four patients presented acute toxicity.

Conclusions: This current retrospective series demonstrated that CyberKnife robotic stereotactic radiotherapy is a feasible and tolerable approach for intraorbital lesions.

Table 1. Baseline features of study population.

Characteristic	
Sex	M: 9(47%) F: 10(53%)
Age (mean)	58,4 years (34-85)
Performance status	0: 11 (58%) 1: 6 (31%) 2: 2 (11%)
Lesion	Primary: 6 (32%) Metastatic: 13 (68%)
Histology	- Breast: 4 (21%) - Sarcoma: 3 (16%) - Lung cancer: 2 (11%) - Basalioma: 2 (11%) - Plasmocitoma: 2 (11%) - Lymphoma: 1 (5%) - Colon cancer: 1 (5%) - Apocrine carcinoma: 1 (5%) - HCC: 1 (5%) - Adenoid cystic carcinoma: 1 (5%) - Lacrimal gland adenocarcinoma: 1 (5%)
Side	Right: 4 (21%) Left: 13 (68%) Bilateral: 2 (11%)
Intraorbital structures involvement	Roof: 11 (58%) Medial wall: 10 (53%) Floor: 7 (37%) Lateral wall: 8 (42%)
Previous surgery	Yes: 5 (26%) No: 14 (74%)
Symptomatic lesion	Yes: 14 (74%) No: 5 (26%)
Total	19 (100%)

HCC: Hepatocellular carcinoma

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FEASIBILITY OF A MR-GUIDED RADIOTHERAPY FOR NEOADJUVANT LOCALLY ADVANCED RECTAL CANCER (LARC) TREATMENT

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Aims: Evaluation of efficacy and feasibility of a radiation therapy delivered with MRIdian in patients affected by Locally Advanced Rectal Cancer (LARC) based on toxicity profile and pathological outcomes.

Methods: MRIdian system is composed of 0.35 T MR scanner integrated with a robotic 3-headed 60Co delivery system, providing a dose rate of 550 cGy/min. Patients (pts) with LARC were considered for this analysis. 5-FU based chemoradiation was delivered: 45 Gy on the pelvis and 55 Gy on the tumor in 25 fractions. In each session a real-time MR was acquired during treatment delivery and a gating protocol was applied on PTV. Acute toxicity was recorded according to v.4.0 CTCAE scale. Surgery was planned after 8 weeks.

Table 1. Acute toxicities according CTCAE v.4.0 scale (events).

	Grade according to CTCAE v4.0	1	2	3	4	5	TOT
Hematological	10029366 (neutrophil count decreased)	4	1				5
	10035528 (platelets count decreased)	7					7
	10002272 (anemia)	1					1
Gastrointestinal	10063190 (rectal mucositis)	1					1
	10000060 (Abdominal distension)	2					2
	10009887 (colitis)	1		1			2
	10012727 (diarrhea)	2	1	3			6
	10047700 (vomiting)		1				1
	10036774 (proctitis)	4	4				8
	10038064 (rectal hemorrhage)	1	1				2
Genitourinary	10062225 (urinary tract pain)	1					1
	10063057 (cystitis noninfective)	1					1
Skin	10061103 (dermatitis radiation)		1				1

Results: From February 2017 to January 2018 12 patients were treated. Median age was 67 years [range 41-86]; Male/Female was 10:2. At diagnosis 9 pts (75%) were MRF+. All pts had advanced disease, cT3 (7 pts, 58%); cT4 (5 pts, 41%); cN+ (10 pts, 83%). In 7 cases (58%) tumor was low-located. No grade 4 or 5 toxicities of all categories were recorded. GI toxicity was recorded in all pts, G3+ in only in 3 patients (25%). (Table 1). Compliance was good, and the radiation dose was delivered entirely in all pts. Mean days of interruptions were 2.7. Surgery was performed on average 13 weeks after last RT session [range 9-22]. Four pts (33%) presented a complete (ycCR) and major clinical response (ycMR) at restaging. Surgery was proposed to all pts: Abdominal-Perineal Resection (APR) 1 pt (8%); Low Anterior Resection (LAR) 8 pts (67%), Transanal Endorectal Microsurgery (TEM) 1 pt (8%); 2 pts (16%), with cCR, who were proposed an APR procedure, refused surgery and were referred to watch and wait strategy. Pathological response was: ypT0ypN0 1 pt (8%); ypT1ypN0 1 pt (8%). Tumor Regression Grade (TRG, Mandard scale) was recorded as follows: TRG1: 1 pt (8%) TRG2: 2 pts (16%), TRG3: 5 pts (41%), TRG4: 2 pts (16%) TRG5: 0 pt. 9/10 pts showed a pathological node response, ypN0 in 5 pts (50%).

Conclusions: To the best of our knowledge, this is one of the first clinical reports of the MR guided radiotherapy in LARC. The clinical outcomes and tolerance were good. Although the number of patients is too low to draw any firm conclusions, these results open room for investigating real-time IGRT to promote dose-escalation and PTV-margin reduction protocols.

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WHICH IMRT IN BREAST RADIOTHERAPY?

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Aims: 3DCRT (+/- breath hold in case of left breast) is the best technique to spare OAR and it might be the first choice in the majority of patients when the dose to PTV results adequate, reserving IMRT treatments to particular situations. IMRT, in fact, allows each dose of radiation to be custom-tailored according to the geometrical shape of the breast or chest wall, also after surgical complex reconstructions, helping to spare healthy surrounding tissue. Unfortunately, the low dose bath of organ at risk is the main concern for radiation oncologists considering the use of IMRT for breast radiation. The availability of both Tomotherapy (TOMO) and VMAT (Varian RapidArc - RA) pushed us to carry out a dosimetric comparison aimed to optimize their clinical use.

Methods: Treatment planning of 38 breast cancer patients treated with IMRT, 19 RA and 19 TOMO were evaluated. The CTV was breast or chest wall (CTV B), plus skin if necessary, +/- lymph nodes (CTV B+N). VMAT plans were generated using 3 arcs (180-220°) in order to reduce the interplay effect due to dynamic delivery and briefing motion; a virtual 10 mm bolus helped extending the dose fluency outside the body to compensate for small changes in shape and volume due to respiration or oedema; a physics bolus was also placed only on 2 of the 3 arcs to give the correct dose to the skin (if included in the CTV)avoiding skin toxicity. V5,V10, Dmean at contralateral lung (C lung); V5, V10, V25, Dmean at heart; V5, V10, D mean at contralateral breast (C breast) and V95%, V107%, Dmax at skin-3mm were recorded both in case of RA or TOMO plans.

Table 1.

OAR median dose values, with TOMO or RA, in case of CTV B or CTV B+N

	contralateral lung				ipsilateral lung				heart(L breast)				contralateral breast				skin -3mm		
	V5 Gy	V10 Gy	Dmax (Gy)	Dmean (Gy)	V10 Gy	V20 Gy	V30 Gy	Dmean (Gy)	V5Gy	V10Gy	V25Gy	Dmean (Gy)	V5Gy	V100Gy	Dmean (Gy)	V95%	V-107%	Dmax (Gy)
RA CTV B+N	17%	1%	14,6	3,7	57%	28%	14%	15,7	95%	50%	7%	12,70	15%	1%	3,2	96,5%	0,0%	54,7
TOMO CTV B+N	86%	27%	26,2	8,4	98%	43%	25%	23,6	100%	57%	8%	13,65	41%	2%	5,1	96,5%		54,7
RA CTV B	6%	0%	11,4	3,1	50%	16%	7%	12,2	82%	29%	3%	9,10	9%	0%	2,7	96,9%	0,1%	54,5
TOMO CTV B	77%	28%	26,4	6,5	74%	28%	15%	18,7	100%	84%	8%	16,10	71%	4%	5,9	95,5%		54,2

Results: Results were mainly better with RA (Table 1). Tomotherapy allowed a better skin coverage but a worse sparing of heart, C lung and C breast. The mean dose to C breast was almost double with TOMO compared to RA (5.9 Gy vs 2.7 Gy and 5.1 Gy vs 3.2 Gy in case of CTVB and CTVB+N respectively); heart V5 was 100% vs 95% and 100% vs. 82% with TOMO vs RA; Dmean of heart was 16 Gy vs 9 Gy and 13.6 Gy vs 12.7 Gy with TOMO vs RA, in case of left CTVB and left CTVB+N respectively. V5Gy of the C lung was dramatically better in RA, 6% vs TOMO, 77% in case of CTVB and 17% vs 86% in case of CTVB +N.

Conclusions: Our results suggest an adequate selection of the patients for IMRT. TOMO (without Tomo Direct) is not indicated to treat breast. Its use might be confined to cases where a suitable skin dose is required. RA results a good technique to treat breast for a significant reduction in low doses at OAR.

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WEIGHT LOSS AS AN INDICATOR OF REPLANNING IN H&N RADIOTHERAPY

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Aims: The weight loss during H&N radiotherapy is an event that must be carefully monitored, as could lead to significant set up and dosimetric changes, resulting in increased side effects. The aim of this work was to identify a cut off as percentage of weight loss during radiotherapy that can alert us to consider re-planning.

Materials and Methods: 48 patients (11 women and 37 men) affected by head-neck cancer were treated with Tomotherapy between January 2016 and March 2018, 33 adjuvant and 15 curative; 34 out of 48 received concomitant chemotherapy. The prescribed dose was 70/ 66 Gy, 59Gy, 56Gy 33fractions SIB. Weight (weight 0) and height was recorded for each patient at the beginning of the radiation treatment; weight was also recorded weekly during radiotherapy. Body mass index (BMI) has been calculated. All patients carried out a re-evaluation planning TC at the end of the 3rd week of radiation treatment Thickness at parotid (Θ par) and laryngeal (Θ lar) level was recorded, weekly on MVCT, for each patient. Agreement between patient thicknesses and dose variations has been verified and correlated by the analysis of the sinograms of the daily treatment.

Results: Almost all patients lost weight during radiotherapy. The recorded weight loss, compared to weight 0, was <6% in 24 patients; between 6% - 8% in 5 patients, >8% - 10 % in 8 ; 9/48 patients lost more than 10% of the initial body weight, entering the area at risk of malnutrition and 2/48 reached slimming levels that exceeded 15%. It was found that none of these

patients had lost more than 4-5% of the body weight in the first 3 weeks (fraction 15) of radiotherapy, except 4 patients whose weight loss was between 5-10%. Weight loss significantly increased mainly after fraction 20. A correlation was found between weight loss and Θ par and Θ lar; larger set up uncertainties were also recorded when Θ par and/or Θ lar were >= 10 mm.

Conclusions: In our experience weight loss >= 10% resulted related to thickness reduction >= 10mm at parotid and/or larynx level, with a significant increased rate of set up errors. Therefore weight loss > 10% might be the cut off to consider replanning. Fraction 20 is the convenient time to perform planning CT in order to replanning.

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PALLIATIVE RADIOTHERAPY CONCOMITANT WITH NIVOLUMAB BEYOND PROGRESSION IN STAGE IV NSCLC: WHEN LOCAL APPROACH HELPS DRUGS TO IMPROVE SISTEMIC DISEASE CONTROL

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Aims: Immune checkpoint inhibition (CPI) as a therapeutic principle to boost the immune response to tumors has renewed interest in a phenomenon that is known as the "abscopal effect" (eliciting a systemic antitumor response using a local triggering treatment). We present a patient case where systemic progression during CPI treatment was followed by a systemic response after a local radiotherapy treatment (RT).

Methods: In August 2016 a seventy-three year old male patient, former smoker, was referred to our Institute for a treatment of bone metastasis from Non Small Cell Lung Cancer. His oncological history was characterized by previous prostate cancer (submitted to prostatectomy in 2012), urothelial cancer (treated with radical RT in 2015) and a stage IV (nodal, controlateral lung and bone mts) squamous cell carcinoma of the left lung (diagnosed in 2016 using EndoBronchial UltraSound). He underwent first line chemotherapy with initial partial response rapidly evolving in disease progression with bilateral lung nodules, a paracardiac lesion, mediastinal nodal and bone metastasis. In April 2016 he started immunotherapy with Nivolumab every two weeks as second line therapy. In July 2017 a shoulder CT scan showed a bone lesion of the left scapula causing severe pain not well controlled by opioid drugs. Due to progression and pain we decided to submit the patient to cytoreductive/pain relieving RT.

Results: The patient underwent a planning CT scan, in supine position, with arms along the body. The target was represented (GTV-CTV-PTV) by almost all of the left scapula. We planned a 3D-Conformal RT treatment delivering 30 Gy in ten fractions (3gy/die). At the end of the therapy shoulder pain was significantly reduced and the patient was continued on two-weekly Nivolumab. During follow up CT scans (February and June 2017) showed a persistent partial response of the lesion treated (scapula) concomitantly with a remarkable reduction of parenchymal lung nodules and mediastinal nodes suggesting a systemic response in line with a possible "abscopal effect"

Conclusions: Often RT may be safely delivered concomitantly with immunotherapy. Our case report suggests the synergistic effects of RT with new drugs being able to enhance the response to systemic therapy probably trough immunological pathways (abscopal effect), as also recently suggested by several trials. Further studies are needed to confirm these preliminary observations.

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SAFETY IN CONCOMITANT IMMUNO-RADIOTHERAPY WITH ATEZOLIZUMAB

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Aims: Evaluate acute toxicity profile and tolerance of concurrent Radio-Immunotherapy (Atezolizumab)

Methods: We report the case of a 69-year-old male with diagnosis of stage IV NSCLC (histology, adenocarcinoma) in October 2017. At initial diagnosis, patient presented malignant pleural effusion and bone metastasis. One month after the end of first line chemotherapy (Platinum and Pemetrexed), was observed a progression at bone and nodes sites. After the appearance of symptoms like right sciatic pain and deambulation difficulty, he started immunotherapy with Atezolizumab (1200 mg g1,q21) and palliative radiation therapy. Atezolizumab is a check-point inhibitor, act on PDL-1 protein that is expressed in high concentration in same cancer cells. Normally, the binding of PD-L1 to PD-1 alters the immune activity by modulating it to inhibit autoimmune disease. However, some cancers use this route to block the immune response of the patient and continue growing. The new agent immunotherapy against lung cancer aims to block the ability of tumor cells to resist patient' immune response by acting on the check-point of immune cells. Moreover patient came to our department of Radiation Therapy (A. O. Pugliese-Ciaccio Catanzaro, Italy) to underwent right hemipelvis bone irradiation. Radiation treatment was applied with 6 MV photons beams once daily; four fractions to a total dose of 20 Gy. The potentially toxicities were evaluated with CTCAE-4 Criteria (Common Terminology Criteria for Adverse Events), while the pain was assessed with NRS (Numerical Rating Scale).

Results: Treatment was well tolerated without any acute side effects. The patient noted an almost complete

regression of the above-mentioned pain and neurological symptoms.

Conclusions: This Case report showed the efficacy and good acute toxicity profile of concomitant radioimmunotherapy. The integrated treatment was feasible with achievement of pain palliation of symptoms and good radiological bone response. The clinical evidence regarding this association with new target-therapies drugs is limited. It would be desirable to create clinical trials that confirm this result and to provide a good chronical outcome.

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CONCOMITANT RADIOTHERAPY AND TARGET-THERAPY WITH OSIMERTINIB: A CASE REPORT

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Aims: Evaluate tolerability and toxicity profile in radiotherapy and Osimertinib combined treatment

Methods: A 70-year-old woman with metastatic NSCLC (histology, adenocarcinoma), EGFR-mutated, was treated initially with surgical brain metastasis resections and subsequently biological first line treatment with EGFR tyrosine kinase inhibitors (Gefitinib 250 mg/die). However, after 3 months, was observed a bone progression disease and she started a second line treatment with Osimertinib 80 mg/die. She went to the UOC of Oncology Radiotherapy, Pugliese-Ciaccio (Catanzaro, Italy) for pain palliative radiation therapy on the hemipelvis bone metastasis. The patient underwent a 3D-conformational treatment delivered 5 Gy x 4 fx (total dose 20 Gy) with photons 18 MV using a Linac (Sinergy Elekta Medical System). All acute toxicities were assessed according to CTCAE-4 Criteria (Common Terminology Criteria for Adverse Events), while pain intensity was evalueted with NRS (Numerical Rating Scale).

Results: The combined treatment was effective and well tolerated. No side effects or acute toxicity was reported during and after treatment. Pain was improved from 8 pre-treatment to 4 post-treatment (NRS).

Conclusions: The aim of our experience is to show the tolerability and toxicity profile of concomitant radiation treatment with Osimertinib. Osimertinib is a third generation irreversible EGFR TKI, indicated for the treatment of patients with metastatic EGFR T790M mutation positive NSCLC, whose disease has progressed on after EGFR Tyrosine Kinase inhibitor (TKI) therapy. One of the most common adverse event is skin toxicity (rash, dry skin, nail toxicity), that are also common radiotherapy toxicity. However, although the concomitant treatment, the patient didn't show side effects with very low toxicity profile.

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ABSCOPAL EFFECT AND SAFETY IN CONCURRENT AFATINIB AND WHOLE BRAIN IRRADIATION: A CASE REPORT

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Aims: Show the clinical efficacy and tolerability of concomitant brain radiotherapy and second-generation EGFR-TKI (Afatinib)

Methods: In January 2016, for worsening dyspnea, a 59-year-old woman went to the emergency room and started the diagnostic procedure. CT showed an heteroplastic lesion in the right lung. Subsequently thanks to EBUS-TNA has been diagnosed an Exon 21 (L858R) mutation, ALK and Pan RAS negative lung adenocarcinoma, stage IV for bone, lung and brain metastasis. Due to Exon 21 mutation, she starded first-line Target Therapy with Afatinib 40 mg/day. Afatinib is a second-generation irreversible covalent inhibitor of the EGFR-TKI. In March, known 4 brain metastasis caused neurological symptoms and she underwent WBI for a total dose of 20 Gy in 5 fx with 6 MV. The response rate was evaluated by RECIST criteria and clinical improvement; acute and chronic toxicities were assessed according to CTCAE-4.

Results: Whole-brain RT with concurrent Afatinib resulted in a complete regression of neurological symptoms as well as good radiological response. Infact, in according with RECIST criteria, 3 of the 4 brain metastasis showed complete response and 1 of them an almost complete response, as well as the other systemic metastasis sites. This response is ascribable to Abscopal Effect that could explain systemic effect of local irradiation. Radiological response and clinical benefit manteined in terms of PFS for 12 month.

Conclusions: We could affirm that two approaches synergize in disease response, because the WBI may breaks the blood-brain barrier with a consequent increase of its permeability and an higher Afatinib uptake. Furthermore we hypothesize that Radiotherapy treatment can stimulate both pro-immunogenic and immunosuppressive pathways with a potential net beneficial effect on anti-tumor immune activity, recognized as abscopal effect that may explain the systemic response observed. Infact, we know that the abscopal effect is a phenomenon in the treatment of metastatic cancer where localized treatment not only provides a shrinking of the treated tumor but also a shrinking of tumors outside the scope of the localized treatment.

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CONSENSUS IN HEAD AND NECK CANCER PATIENTS' MANAGEMENT: AN EXPERT OPINION MEETING OUTCOME

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Background: Squamous cell carcinoma of the head and neck (SCCHN) accounts for 6% of all malignancies. The majority of SCCHN patients are diagnosed with loco-regional disease, while 10% of patients present with metastatic disease at diagnosis. About 40% of the locally advanced patients experience a recurrence of disease. There are still several unmet medical needs in head and neck (H&N) cancer patient's management and a lack of clinical criteria and consensus in defining: patient populations suitable or unsuitable for concurrent chemoradiotherapy; platinum refractory patients' population; the best management of recurrent H&N cancer according to patients' clinical history and status.

Material and Methods: 10 Italian experts in SCCHN treatment, with previous experience from consensus initiatives using risk assessment models, promoted the whole initiative and proposed the set of scenarios, besides having participated in the meeting as chairpersons. An Expert Panel of 40 specialists with extensive experience in SCCHN patient management participated in the Expert Opinion meeting. Finally, a total of 50 medical specialists with special experience in the treatment of SCCHN were involved, in order to evaluate the appropriateness of clinical scenarios. A comprehensive evaluation of the results obtained from the Expert Opinion meeting was performed.

Results: A group of 50 experts in the field of H&N cancer (oncologists, radio-oncologists, surgeons) from 24 Italian medical centers convened in 10 April 2018 in Rome to discuss a set of clinical criteria by 71 scenarios analyzed with the RAND Appropriateness Method [1], to fill the knowledge gap and with the aim of improving clinical decision making.

Conclusions: Of 71 proposed scenarios, 52 met a common consensus and 19 did not. The further work and focus on these unmet needs will better define the best approach to head and neck cancer patients in the Italian clinical practice.

Acknowledgement: The Expert Panel Meeting was funded by Merck Serono.

Reference

1. Fitch K et al. The RAND/UCLA Appropriateness Method User's Manual. Santa Monica, CA: RAND Corporation, 2001.

P272

FRACTIONATED BRAIN STEREOTACTIC RADIOSURGERY WITH CONCURRENT IMMUNOTHERAPY OR TARGET THERAPY: PRELIMINARY RESULTS

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Aims: To evaluate cerebral toxicity and early outcomes in patients with brain metastases undergoing concomitant fractionated stereotactic radiosurgery (FSRS) and immunotherapy or target therapy.

Methods: Between January and March 2018, 13 patients were treated at our center with FSRS for 18 brain metastases. All patients received immunotherapy or target therapy concomitantly to FSRS as follows: 9 (50%) lesions were treated during immunotherapy (Nivolumab or Pembrolizumab), 5 (27.8%) with anti-HER drugs (Pertuzumab, Trastuzumab) and 1 (5.5%) with antiangiogenetics agents (Bevacizumab) and 3 (16.7%) with TKI (lapatinib, Ipilimumab). We considered concomitant treatment all cases where time between radiation and medical therapy was inferior than 14 days. FSRS with volumetric modulated arc therapy (Rapid Arc) was adopted. The treatment occurred after the packaging of a repositionable stereotactic mask and the treatment plan was performed merging CT / RM images. The mean measure of lesion size was 11mm (range 5-32 mm). Gross Tumor Volume (GTV) was expanded of 2 mm to create the Planning Target Volume (PTV). The mean volume of PTV was 7.44 cc (range 0.75-13.41 cc). The total dose to PTV ranged from 24 to 27 Gy in 3 consecutive fractions of 8-9 Gy each one. All patients underwent a Magnetic Resonance Imaging (MRI) with a contrast enhanced within 4-6 weeks after the end of the treatment to evaluate the treatment response, intended as a reduction in size of the treated lesion, and acute toxicity, represented by the percentage of perilesional oedema.

Results: 5/18 lesions showed a complete response , 8 / 18 a partial response to treatment and 2/18 had stable disease. MRI toxicity's evaluation showed reduction of perilesional oedema in all lesions treated. Three patients died before the first follow up due to systemic disease progression.

Conclusions: Our preliminar data confirm efficacy of FSRS and (immunotherapy/target) new therapy without relevant acute toxicity. Longer follow up and larger series are needed in order to eventually confirm these data.

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INTERSTITIAL PNEUMONITIS IN PREVIOUSLY IRRADIATED AREA IN PATIENT TREATED WITH NIVOLUMAB AND STEREO ABLATIVE RADIOTHERAPY (SABR) FOR NSCLC: A CASE REPORT

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Background: Recently Nivolumab had demonstrated to improves significantly outcomes also in patients previously chemiotreated. Radiotherapy is demonstrated to have an active role to increase immunogenic responses guided by anti-PD1. However new toxicities have emerged principally immune-related.We present a patient with a serious and potentially life-threatening interstitial lung disease (ILD) .

Case Report: From december 2013 to October 2015, a 64-years old man with a lung adenocarcinoma KRAS+, EGFR wt, staged cT4N3M1 was treated with two chemotherapy-lines (a first-line with CDDP plus pemetrexed for 6 cycles plus adiuvant RT-total dose 42 Gy into 14 fractions at apical segment LSD- and a second-line with carboplatin plus paclitaxel for 7 cycles). The restaging CT scan performed in October 2015 revealed a pulmonary disease progression. Immunotherapy with nivolumab (3 mg/kg intravenous every 14 days) was administered as the third-line regimen, obtaining a partial response for 13 months, without relevant toxicities. In November 2016, a CT scan showed an increasing of the lesion at lung posterior LID so that patient underwent SABR (36 Gy in 3 fractions) during nivolumab somministration. A partial response of radiotreated nodule was obtained and an important reduction in another nodule sede was observed. In the next CT scan November 2017, a stable disease was detected. However an interstizial pneumonitis was observed principally in the area previously radiotreated the first time (LSD). Currently the patient is in poor clinical conditions because of dyspnea and cought and treated with steroid .

Consideration: Our experience suggests that nivolumab and radiotherapy is an effective combination , however a very careful workup is needed to reduce the risk of side effects by this combination. It is necessary further evidences to rethink a role of RT in NSCLC .

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COULD NIVOLUMAB INCREASE PNEUMONITIS OCCURRENCE IN IRRADIATED LUNGS? A GENERATING HYPOTHESES STUDY: YTHACA 1.1 LUNG

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Aims: In the last decade, the prognosis of advanced non-small-cell lung cancer (NSCLC) has been improved by development of immune checkpoint inhibitors (ICIs) such as nivolumab for second-line treatment. Immune-related pneumonitis is a potentially fatal toxicity of anti-PD-1/PD-L1. This study investigates the role of chest radiotherapy (RT) and the development of immune-related pneumonitis in NSCLC treated with nivolumab.

Methods: Consecutive patients with locally-advanced or metastatic NSCLC treated with nivolumab as second or third-line therapy for recurrent or progressive disease, between May 2017 and March 2018 were included. Patient demographics, treatment, adverse event and RT data including type of RT, volume of RT and number of courses were collected. Toxicity was evaluated according to the common terminology criteria for adverse events (CTCAE) version 4.0.

Results: Seventeen patients were treated, mostly male (65%), current or former smokers (76.5%) with Eastern Cooperative Oncology Group (ECOG) PS score <2 (88%). Median age was 67 years (range: 49-79). Previously 15/17 (88.2%) patients had undergone radiotherapy on the thoracic disease or for metastatic sites. Mean number of nivolumab cycles was 12 (range: 1-26). 11/17 (64.7%) patients had only locally-advanced disease. Of 15 patients who received any RT, we observed 3/15 (20%) G2/G3 pneumonitis and 1/15 (6.6%) G4. Only 1/4 (25%) pneumonitis occurred in RT field.

Conclusions: Even if pneumonitis incidence is maybe higher in irradiated lung patients treated with nivolumab, the finding of clear factors that could cause this event needs to be identified. Moreover, research of preliminary predictive factors (functional tests, RT technique, patients intrinsic factors) could be useful to improve treatment option choices and also toxicity occurrence prevention.

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MONO INSTITUTIONAL RETROSPECTIVE ANALYSIS OF LOCAL RELAPSE AFTER BRACHYTHERAPY LDR WITH SEEDS IMPLANTATION IN PROSTATE CANCER

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Purpose: We retrospectively analyzed the clinical records of 510 consecutive patients with diagnosis of low-intermediate risk of PCa, according to NCCN risk group and ASTRO-EAU- EORTC guidelines treated from Sept 1999 to Dec 2016 with I 125 BT LDR as monotherapy, using a real time approach. As the nadir PSA value is a time-dependent variable, a landmark analysis method was used, and this demonstrated that lower nadir values at 3 years (fixed time point) after BT translated into improved long-term biochemical outcomes.

Materials and Methods: The seeds implantation was performed using Mick applicator in the first 190 pts and Quick-link system in the last 320 cases and intra-opera-

tive planning with Variseed 8.1. Biochemical failure was defined according to the Phoenix criteria (nadir +2 µg/mL), and distant metastasis as imaging evidence of recurrence correlated with a rising PS and symptoms.

Results: 491 pts were disease free and biochemical failure was assessed in 19 pts (3.7%) to an average of 48 months (range 6-144). With a median follow-up of 90 months (range 22-168) from BT, OS at 3 and 6 years were 97.4% and 94.5%, respectively and DFS at 3 and 6 years were 98.5% and 97.5%. Out of these pts, 14 underwent biopsy, and other 2 showed a systematic disease. Biopsy showed a PCa in 10 pts who underwent RP(6pts) and EBRT(4 pts) respectively. 4 pts with negative biopsy were treated with ADT as remaining other 3 pts. In all patients who failed, abdominal CT and/or Pet TC with choline and bone scan was performed, that were positive in 2 patients. A patient undergoing RP died 122 months after BT and developed distant relapse 36 months after RP. We analyzed whether there's a relationship between relapse and PSA rapid increase or D90<145Gy and evently Gleason recidived patients (seen graphic attachments). Out of 19 patients, only one exhibited a rapid increase of PSA, and D90>145 in 18/19 and in particular D90>160 Gy (our actually target) in 8/19. More than half of the relapse had Gl 6.

Conclusions: In our experience we don't point to a correlation between early rise of the PSA and relapse. It's certainly essential to D90> 145 Gy or better D90> 160Gy to guarantee good local control and also a seed-volume ratio. It should be emphasized the importance of a long and light follow up because the few recurrences we have verified for a long time. The small number of pts in recurrence after BT, underline the validity of this method, and we can only supposed underlie biopsies or bad selection of these few cases.

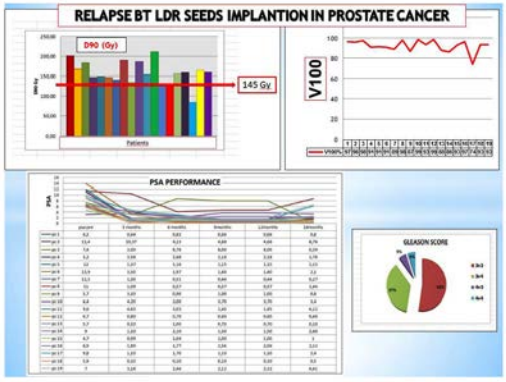

Figure 1.

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PSYCHONIC (PSYCHOSOMATIC MEDICINE IN ONCOLOGIC AND CARDIAC DISEASE)

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Aims: In our Department of Cardiovascular Diseases from 20014 to 2011 a randomized research of psychotherapeutic intervention was carried out in patients (pts) with acute myocardial infarction, treated with emergency angioplasty. Compared to the control group treated with standard and rehabilitative therapy the study group received the same treatment with a short psychotherapy cycle using a psychodynamic approach, which used the interpretation of body language and oniric analysis. In the psychotherapy group there was a statistically significant improvement in the medical prognosis in the 1° year, a reduction in the level of depression and an improvement in the quality of life. Researches with this psychological methodology had never been conducted in cancer patients.The goal of PSYCHONIC (PSYchosomatic medicine in Oncologic and Cardiac disease)STUDY is to investigate this specific psychological aspects in breast cancer and cardiac disease and to demonstrate the effectiveness of Ontopsychological psychotherapy at 1 and 5 years follow-up.

Methods: In the observational research Psychonic will be enrolled 50 cardiac pts, 50 women operated on breast cancer (BC) and 90 healthy pts (control group).The 2 groups of pts will be given the chance to follow a psychological training. The body perception , recent and past dreams, with use of psychometric tests will be assessed in each groups.

Results: Psychological and clinical data will be evaluated at 1 and 5 years follow-up.

Conclusions: Finally, we will want to explore this psychological area and to demonstrate the effectiveness of Ontopsychological psychotherapy , having noted the importance of using this approach as part of care.

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INTEGRATIVE ONCOLOGY IN RADIOTHERAPY: SCIENTIFIC EVIDENCE AND CLINICAL MANAGEMENT OF SIDE EFFECTS

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Aims: The total given dose is one of the most important factor that determinates the success of radiotherapy in eradicating a tumour, but it can be limited by normal

tissues tolerance. The clinical manifestations of either acute (occurring during or within few weeks after the treatment) or late (occurring from 6 months to many years later) radiation toxicity are well documented. One of the aims of oncological treatment is to enhance the radiosensitivity of the tumor, while decreasing that of normal tissues. Due to the inadequacy of most of the radio-protectors in controlling the side effects of conventional cancer therapy, complementary and alternative medicines have attracted the attention of researchers and medical practitioners.

Methods: In recent years several Associations have presented guidelines or recommendations for use of CIM in the management of cancer side effects, validated by clinical evidence or based on published randomized clinical trials. The side effects addressed in these recommendations include anxiety/stress, depression/mood disorders, cancer related fatigue, quality of life, nausea and vomiting, lymphedema, hot flashes, pain and sleep disturbance.

Results: There are some evidence about the use of herbal medicine for cancer-related fatigue, nausea and vomiting, pain, radiodermitis, mucositis, diarrea, anxiety and depression. Acupuncture is one of the best-studied complementary therapies. There is also a proven efficacy of sport/physical activity and nutrition in oncology, and that why a regular diet of fruit and sport/physical activity are recommended. Physical activity is recommended even during chemo/radiotherapy for the reduction of treatment side effects. Dietary modification such as caloric restriction has been shown to decrease tumor initiation and progression and could be used during radiotherapy course as a novel therapeutic intervention to enhance cytotoxic therapies and reduce the cytotoxic effects on normal tissue.

Conclusions: In summary, the field of integrative oncology represents a high priority for research as the overarching goal is to identify safe and efficacious integrative therapies to address unmet patient needs. Future research will have to be oriented to identify specific endpoints in large high-quality trials on CIM, with longer follow up, using standardized assessment scales and also focusing on possible side effects and interactions with conventional oncological therapies.

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INTEGRATED MEDICINE IN ONCOLOGY: THE PATH OF INTEGRATION OF RADIOTHERAPY DEPT OF ICS MAUGERI – IRCCS, PAVIA

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Aims: The use of complementary and integrative medicine (CIM) among cancer patients is high; prevalence is about 1out of 5 of them. Patients diagnosed with cancer have many needs and deficiencies in the practice of conventional medicine lead to adoption of CIM. Quality-of-life research has indicated that the diagnosis and subsequent treatment of cancer impair patients' work and social activities, housekeeping, family and other relationships, sleep patterns, and sexual activity. In addition, studies exploring the psychologic sequelae of cancer have suggested that cancer patients experience clinically significant levels of anxiety and depression. It's also known that exercise improves fitness, strength, energy balance, sexuality, coordination and muscles tone. Exercise therapy and a balanced/healthy diet have effects on cancer fatigue and pharmacological side effects. Recent studies have demonstrated that an adequate level of exercise and also a modify of diet is suggests to reduce the risk of some cancer recurrence.

Methods: Since 2012, The Breast Unit of ICS Maugeri introduced the use of CIM, such as Homeopathy/Phytotherapy, Exercise Therapy and Nutritional Therapy for cancer patients support as recommended by EUSOMA (European Society of MAstology). We carried out more than 450 visits of Homeopathy and Phytotherapy (mean age 57), 90 pts required exercise therapy (average age 54) and 180 pts had a consultation with the dietitian (mean age 55). In May 2017 an Ambulatory dedicated to Integrative Oncology (Ambulatorio delle Medicine Integrate in Oncologia) began its activity, in order to respond to the many request of the patients.

Results: CIM is usually required for the treatment of vasomotor syndrome, skin toxicity from radiation therapy, cancer realted fatigue (CRF), anxiety, insomnia, gastrointestinal disorders and to improve QoL. Pts who followed the training program had an improvement of maximum oxygen consumption (VO2 max), ventilation (VE), respiratory parameters (FVC, FEV1, Tiffenau Index) but not adecrease in BMI. Pts who followed the nutritional program had a reduction of BMI.

Conclusions: Our 6 years experience with CIM, nutritional consultation and exercise program demostrated to be safe, well accepted and able to meet the unmet needs of cancer patients

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A REPORT FROM TIKUR ANBESSA HOSPITAL RADIOTHERAPY CENTER: PREVALENCE AND MANAGEMENT OF PAIN

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Aims: Prevalence of cancer is on a rise globally, in particular in developing countries. Pain is one of the most feared and burdensome symptoms in cancer patients

and it remain a public health problem in cancer care in Ethiopia. Aim of this study was to identify the baseline prevalence of pain among in-patients at the general medical and oncology wards at a tertiary teaching hospital Tikur Anbassa Hospital in Addis Ababa, the pattern of pain management by the health care providers; and to assess the knowledge, attitude and practice of pain management of health care providers

Methods: This was a cross sectional, quantitative, observational study design conducted in Tikur Anbassa Hospital, in relation to knowledge and attitude of health care professionals in addressing pain in Tikur Anbassa Hospital. The characteristics of the pain and its management were assessed using the "Short Brief Pain inventory" (Cleeland C.S. 1991)

Results: 648 patients admitted to the oncology wards were interviewed out of which 265(40.9%) were males, and 383(59.1%) females. Of the total, 390 (60.2%) had experienced pain in the previous 24 hours. Out of the 390 patients with pain 161(41.28%) had severe pain. Out of the 390 patients with pain, 255(65.4%) were prescribed analgesics, and 135(34.6%) patients with pain were not given any analgesics. Out of the 161 patients with severe pain only 50(31.0%) were given morphine for their pain. The remaining 111 patients (69.0%) were given other analgesics. Considering recommendations of analgesic regimen for the hypothetical patient with severe cancer pain, 50% recommended morphine, the rest recommended NSAIDs Tramadol, and paracetamol. 50% of prescriptions were for oral medication and 50% for parental medication.

Conclusions: Pain is highly prevalent and undertreated in cancer patients at the oncology center at TASH. Health care professionals lack the basic knowledge and harbor misconceptions about the clinical use of morphine for cancer pain treatment. Creating training opportunities for medical staff is necessary to increase their awareness and knowledge of effective cancer pain management.

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WHOLE LUNG IRRADIATION (WLI) IN PATIENTS WITH OSTEOSARCOMA AND EWING SARCOMA: A SYSTEMATIC REVIEW

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Aims: Whole Lung Irradiation (WLI) represents a standard therapy for patients with pulmonary metastases from Ewing Sarcoma although the impact on clinical outcomes and toxicity is still unclear. Aim of our study was to evaluate toxicity after WLI in patients with Ewing Sarcoma and osteosarcoma as well as overall survival and event-free survival.

Methods: A systematic review of studies on bilateral pulmonary irradiation treatments for prophylactic or curative therapy was performed based on PRISMA methodology. Electronic data base searches on PubMed and Cochrane Library from the earliest time possible through 31st March 2018 were carried out. Combination with other treatments as chemotherapy and surgery were allowed. Only articles published in English were considered.

Results: Toxicity was evaluated in 640 patients enrolled in 13 of the 14 analyzed studies. Grade 3 acute pneumonitis toxicities were reported in 12 patients (1.8%). Grade 2 late toxicity was mainly recorded in patients who received boost irradiation, previous thoracic surgery, chemotherapy or who were smokers. Lack of WLI significant impact on OS was reported in comparative studies, although patients undergoing WLI showed higher survival in most studies.

Conclusions: Although, the rate of severe toxicity was very low, the real impact of WLI on patients' outcomes remains unproven probably due to the narrow dose limits that can be delivered to the whole lung parenchyma. New strategies to prevent or treat lung metastases in these patients should be tested. Ultra-fractionated RT concurrent with modern chemotherapy protocols could be tested in this setting due to chemo-sensitizing effect and the negligible radio-induced toxicity of fraction doses < 0.5 Gy.

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A FAQS TOOL TO IMPROVE QOL OF PATIENTS UNDERGOING METABOLIC RADIOTHERAPY IN THYROID CANCER. A PILOT PROJECT OF THE AIRO METABOLIC RADIOTHERAPY RESEARCH WORKING GROUP (AIRO MRT)

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Aims: Differentiated thyroid carcinoma is a common malignancy with an increasing incidence. It carries a favorable prognosis and patients have a long life expectance, but usually they appear very worried about radioactive treatment (RAI). The recommendation of a low iodine diet before treatment and the remaining radioactivity after discharge from the protected hospitalization appear to be the most critical issues. An accurate information during medical examination can reassure patients. Nevertheless, patients often perform on-line search with the risk to fall in disinformation. Consequently, apprehension gets worse and induces the patient to increase diet and social restrictions to unnecessary levels. The final results are poor patients' QoL and anxiety. The aim of the project is to provide a consensus document that physicians can provide to patients as a paper booklet and also downloadable on-line.

Methods: Three residents in radiation therapy of 3 different centers collected questions made by 100 patients. Preliminary answers have been carried out, then the document was shared among 3 experts for first validation. A psycho-oncologist and onco-geriatric physicians have been involved to modulate the language in confidential way. Moreover, images have been prepared and chosen with the psyco-oncologist on the basis of the quiet they give to patients. Finally, an external validation of the document was achieved involving members of the AIRO MRT.

Figure 1.

Results: The document presents the results as FAQs with confidentially language. First section "To know more" collects general informations about RAI. Second section "Before the hospitalization" gives informations about diet, drugs, preparation for treatment, and the third one "After the hospitalization" about symptoms, elimination radioiodine way, side effects, radioprotection of family, social life after discharge. A fourth section has been provided to let each center to insert further informations. A psyco-oncological test have been prepared in order to investigate benefit on patients anxiety after reading.

Conclusions: A practical FAQs book has been prepared to be provided to patients and also downloadable on line with the aim to reassure patients with a complete consensus guide and to avoid a "do-it-yourself" behavior before and after treatment. Pictures have been realized to make the book more reassuring. A research using a psycho-oncological test is planned to evaluate the psychological patients result of this project.

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EVALUATION OF QUALITY OF LIFE (QOL) IN WOMEN TREATED FOR GYNECOLOGIC MALIGNANCIES WITH RADIATION THERAPY AND CORRELATION WITH DOSE–VOLUME PARAMETERS

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Aims: The purpose of this study is to assess self-reported overall QoL and QoL related to urinary, bowel symptoms and sexual functioning and correlate them with dose–volume parameters of organ at risks (OARs) in patients affected by cervical and endometrial cancer after radiation therapy and in regular follow-up.

Methods: The anonymous EORTC QLQ-C30 questionnaire is planned to be administered to 53 patients, 41 with endometrial cancer and 12 with cervical cancer, selected among the patients treated with pelvic radiotherapy and vaginal brachytherapy from 2011 to 2017 and in regular follow-up in our center. This questionnaire is combined with EORT QLQ-EN24, in case of endometrial cancer, or with EORT QLQ-CX 24, in case of cervical cancer. There are no limitations with regard to age or performance status. We plan to analyze overall health and overall quality of life, bladder symptoms, dysuria, bladder incontinence and fecal incontinence and correlate with dose–volume parameters of OAR (whole bladder, bladder trigone, rectum and lumbosacral plexus (LSP)).

Results: We have collected until now questionnaires from 15 patients. Nobody refused to compile the questionnaire. The patients found that the questions were clear and easy to understand. All the items exhibited good compliance with no missing values, except for values about sexuality (3/15, 20%). Twelve out of 15 (80%) women judged their overall health and QoL good and only three patients (20%) judged their QoL poor. No patient had fecal incontinence but 5/15 (33.3%) had bladder incontinence or dysuria.

Conclusions: Patients exhibit good compliance to questionnaires. From preliminary analysis, it emerges that treated women have quite good QoL with less limitations of daily activities. We expect to have enough data to trace conclusions and to identify patient- disease-related factors and dose-volume parameters associated with QoL.

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SPHINCTER SAVING SURGERY IN LOW RECTAL CANCER PATIENTS, TREATED WITH NEOADJUVANT CHEMORADIOTHERAPY: SPHINCTER FUNCTION EVALUATION AND OUTCOMES

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Aims: To evaluate long-term effects on anorectal function and bowel disorders in patients affected by low rectal cancer treated with neoadjuvant chemoradiotherapy (CRT) and sphincter sparing surgery.

Methods: Between 2000 and 2018, 53 (M:35; W:18) patients with low (0-30 mm from the anorectal ring) rectal adenocarcinoma were treated in our Radiotherapy Department, and retrospectively analysed. A sphincter preserving surgery was performed in all patients. The pathologic response was evaluated according to Mandard tumor regression grade (TRG) score. The Memorial Sloan-Kettering Cancer Center score was used for the evaluation of anal sphincter function. Acute and late toxicities were assessed using the Radiation Therapy Oncology Group (RTOG) scale and the RTOG/European Organization for Research and Treatment of Cancer (EORTC) late radiation scoring system. The Memorial Sloan–Kettering Cancer Center score was used for the evaluation of anal sphincter function. Patients were evaluated to assess the impact of bowel function on QoL, using indexes by cancer linear analog scales (CLAS). Impact on well-being (CLAS1), fatigue (CLAS2), and ability to perform daily activities (CLAS3) were considered mild (1–4), moderate (5–7), or severe (8–10).

Results: The median follow-up time was 78 months (range: 1-188). The median age was 65 (range: 32-87) years. Three patients (5.7%) resulted not fit for conservative surgery and underwent abdominoperineal resection. The pathologic complete response rate was obtained in 16 patients (30.2%). Acute toxicities were reported in Table 1. Overall sphincter function resulted excellent in 17 (32.1%) patients, good in 3 (5.7%), fair in 1 (1.9%) and poor (incontinence) in 11 (20.8%) patients. Thirteen patients presented stoma, due to the impossibility to close the provisional colostomy. Thirty patients were evaluated for CLAS (Table 1). Six patients were lost at the follow-up. None patient reported late toxicities ≥ G3. Two (4%) patients showed local recurrence. The 5- and 10-year disease-free-survival (DFS) and overall survival (OS) rates were 83.0%±5.6%, 60.8%±8.5%, 85.0%±5.3% and 62.2%±8.6%, respectively.

Conclusions: Our study confirmed the effects of neoadjuvant CRT on tumor down-staging and the possibility to assess sphincter saving surgery. Furthermore, it resulted in good results in terms of sphincter function and quality of life. An evaluation with defecography and manometry is ongoing in order to quantify anal continence.

Table 1. Acute Toxicities and CLAS evaluation.

Acute Toxicities (53 pts)	G0	G1	G2	G3
Skin Toxicity	26 (49.0%)	11 (20.8%)	15 (28.2%)	1 (1.9%)
GI Toxicity	12 (22.6%)	14 (26.4%)	25 (47.2%)	2 (3.8%)
GU Toxicity	43 (81.1%)	8 (15.1%)	1 (1.9%)	1 (1.9%)
Hematologic Toxicity	39 (73.6%)	4 (7.5%)	10 (18.9%)	0 (0%)

CLAS (30 pts)	*CLAS1 well-being*	*CLAS2 fatigue*	*CLAS3 ability in daily activities*
Mild	27 (90.0%)	29 (96.7%)	28 (93.3%)
Moderate	1 (3.3%)	0 (0%)	0 (0%)
Severe	2 (6.7%)	1 (3.3%)	2 (6.7%)

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WHAT IS THE ROLE OF PSYCHOLOGICAL SUPPORT IN PATIENTS WITH PRIMARY BRAIN TUMOR DURING RADIOTHERAPY? FINAL REPORT OF A PROSPECTIVE STUDY

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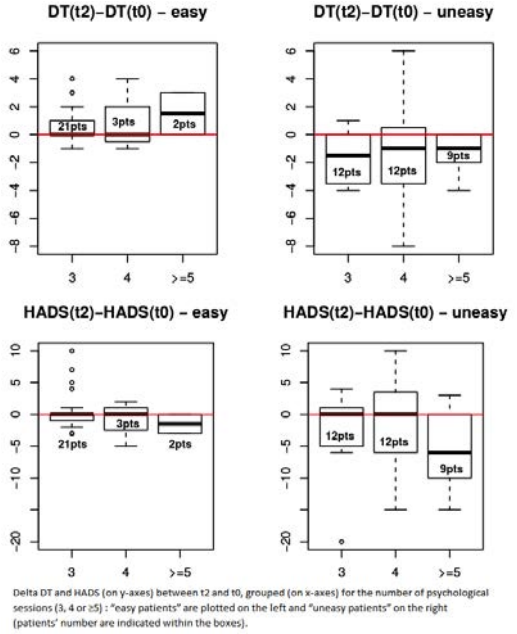
Aims: Patients with primary brain tumor (BT) often show significant distress and numerous physical and emotional changes, which can have consequences in everyday life. Radiotherapy sometimes induces side effects that often significantly influence patients' quality of life (QoL). In our Radiotherapy division a Psycho-Oncological Support Service (RT-POSS) is available for all patients. Aim of this study is to evaluate distress, mood (anxiety/ depression) and QoL during RT and after three months in patients with BT.

Methods: Consecutive BT patients who had access to RT-POSS during RT were included. A psycho-oncologist followed them for the whole RT course and psychological tests were administered at the beginning (t0), at the middle (t1) and at the end of RT (t2). Tests were: Distress Thermometer (DT), Hospital Anxiety and Depression Scale (HADS) and Functional Assessment of Cancer Therapy (FACT-Br). Psychological support was personalized for each patient depending on the psychological profile and patients' needs. A final interview was performed three months after the end of RT (t3).

Results: Sixty patients (34M 26F, median age 55) were included between January 2016 and April 2017.

All patients received post-operative RT with a median total dose of 60 Gy (range 54-60). Forty-seven out of sixty (78.3%) received concurrent CT with Temozolomide for high grade tumor. In patients with psychological wellbeing at T0 ("easy patients") (DT<4;HADS<14) there is no significant statistical evidence of any change over time. Patients distressed and anxious/depressed ("uneasy patients")(DT≥4 and/or HADS≥14)(N=33) showed a statistically significant improvement in DT and HADS when comparing T1 vs T2 (p<0.001). Emotional and functional wellbeing subscales of FACT-Br improved over time (T0 Vs T3) (p<0.001). As expected "easy patients" underwent a number of sessions lower that "uneasy patients". Evaluating the course of DT and HADS scores during RT in relationship with psychological sessions' number (3, 4 or ≥5) we observed that DT scores of "uneasy patients" had a slightly significant improvement in all three conditions (The most representative distribution are shown in Figure 1).

Conclusions: "Uneasy patients" with psychological support improved in distress, mood and QoL whereas the psychological support preserves the psychological well-being in "easy patients". These results encourage us to standardize a psychological support model for these patients.



Delta DT and HADS (on y-axes) between t2 and t0, grouped (on x-axes) for the number of psychological sessions (3, 4 or ≥5) : "easy patients" are plotted on the left and "uneasy patients" on the right (patients' number are indicated within the boxes).

Figure 1.

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FRAMELESS STEREOTACTIC RADIOSURGERY FOR THE TREATMENT OF TRIGEMINAL NEURALGIA

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Aims: Trigeminal neuralgia (TN) is a common craniofacial pain disorder difficult to manage either pharmacologically or surgically. On the other hand, during the last decade, isocentric stereotactic radiosurgery has proved to be a valuable approach for the treatment of both typical and atypical TN. Here in, we report on our experience on radiosurgical rhizotomy in patients with TN by using non-isocentric stereotactic radiation beams distribution technique.

Methods: We retrospectively evaluated all the patients with TN who underwent to stereotactic radiosurgery from January 2009 to December 2017 in our center. A non-isocentric beams distribution was chosen so that a 5- to 6-mm segment of the trigeminal nerve were included in the 80% isodose line. The Barrow Neurological Institute (BNI) pain scale was administered at the first examination date and at the 6-months follow-up after the radiosurgery in order to assess the effects on pain and sensory disturbance.

Results: Sixty-five patients (median age 67 years-old, age range 44-88 years-old) with TN were included in the analysis. Stereotactic treatments were performed in a single session. The prescribed dose was 56-60 Gy, the median maximal target dose was 72.5 Gy (range, 70-75 Gy), the median number of beams was 97 (range 64-161), and the maximal dose to the brainstem was <12 Gy. The mean nerve volume was 40 cc (range 10-70 cc). Significant pain relief was achieved in 30 out of 65 patients (46%), whereas 22 out of 65 (33%) patients did not benefit neither ameliorated pain control. The remaining thirteen patients, instead, worsened pain intensity.

Conclusions: TN patients treated with frameless stereotactic radiosurgery reported significant improvements in pain and numbness discomfort. However, further studies should be fostered to evaluate the long-term pain control and the possible sensory complications which could be related to the long-term side effects of radiotherapy.

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QUALITY OF LIFE AND PSYCHOPATHOLOGICAL ISSUES IN SURVIVORS AFTER UPFRONT RADIOTHERAPY FOR HEAD AND NECK CANCER: PRELIMINARY EXPERIENCE AT NIGUARDA CANCER CENTER

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Aims: To investigate quality of life (QoL) issues in a cohort of long-term survivors after treatment with upfront radiotherapy (RT) for head and neck (H&N)

cancer.

Methods: We selected two questionnaires (Qs) to evaluate QoL issues, the EORTC QLQ-C30 and the EORTC H&N cancer-specific module (H&N35), and the Hospital Anxiety and Depression Scale (HADS) to evaluate the presence or risk of concomitant anxiety/depressive conditions. All three Qs were submitted to patients surviving for >3 years seen in routine follow-up visits at the multidisciplinary H&N cancer clinics of Niguarda Hospital. We compared our results with reference standards validated in the literature: for QLQ-C30, EORTC publication (2008) on 2,929 H&N cancer pts pre-treatment; for H&N 35, Hammerlid *et al.* (2017) on 1,504 people representing the general Swedish population; for HADS, criteria proposed by Costantini *et al.* (1999).

Results: This analysis involves a preliminary series of 15 consecutive patients seen on May 2018. The series includes 12 males and 3 females aged 55-85 yrs (median 70 yrs). As far as QLQ-C30 is concerned, results in our series are more favourable compared to reference in all scales and items: for instance, scoring for scale "Social functioning" (worst = 0, best = 100) is 98 in our series vs 82.6 in EORTC reference, meaning that social recovery after treatment is nearly complete in our pts. Considering H&N35, scoring in our series is not surprisingly worse compared to reference (general "healthy" population). However, results are mixed as the decrease in QoL seems to be acceptable for some scales: for instance, scoring for "Dysphagia" (worst=100, best=0) is 9 in our series vs 1.6 in reference population, scoring for "Feeling ill" is 2 in our series vs 14 in reference population; on the contrary, scoring for "Xerostomia" and "Sticky saliva" are 44 and 38 in our series vs 12 and 6 in reference population, respectively. Scoring at HADS evaluation showed favourable results: average score was 2.9 for anxiety and 3.8 for depression (best=0, worst=21), but 2 pts are at risk (score 8-11) for developing depressive conditions and 1 is at risk for both conditions.

Conclusions: Evaluation of QoL issues proved feasible in clinical practice. Preliminary results confirm overall good results in terms of recovery of general functions, but still significant problems in terms of local late effects of RT; risk of anxiety/depression conditions exists in few patients.

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QUALITY OF LIFE (QOL) IN EARLY BREAST CANCER PATIENTS TREATED WITH RADIOTHERAPY. PROSPECTIVE OBSERVATIONAL STUDY

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Aims: Radiotherapy (RT) after conservative surgery is the standard of care in the most of breast cancer patients. The fear of acute and late side effects could influence quality of life (QoL) both during and after RT. Currently there is a growing interest in QoL as the number of long-surviving patients is increasing. The aims of our prospective observational study is to evaluate the impact of RT on the QoL and estimate patient's satisfaction of care.

Methods: Inclusion and exclusion criteria are reported in Table 1. The patients will sign the informed consent or the refusal to participate in the study. The FACT-B (Functional Assessment of Chronic Illness Therapy) version 4 questionnaire will be administered for QoL functional evaluation. The questionnaire is specific for breast cancer and it has been provided in its Italian original version. The Body Mass Index (BMI) will also be evaluate as an independent risk factor for QoL. The timing of questionnaire administration is the following: RT start and end, first and second follow up visit, follow-up visit after 18 months and 30 months after radiotherapy. In addition, to selected patients will also be offered to participate in relaxation sessions (Mindfulness) before the start of RT with dedicated Psychologists. To patients who intent to participate at Mindfulness, the questionnaire will also be administered at first relaxation session. The selected patients will be analyzed from the date of approval of the Ethics Committee up to the enrollment of at least 200 patients.

Results: On 9th May 2018 we obtained ethical approval. After the approval, we started to enroll patients. Currently a total of 20 patients were enrolled to the study.

Conclusions: In the literature the QoL of breast cancer patients is rarely investigated or briefly reported. We presented our institutional protocol to QOL evaluation using FACT-B questionnaire.v

Table 1.

INCLUSION CRITERIA	EXCLUSION CRITERIA
SEX: FEMALE	ADJUVANT/NEOADJUVANT CHEMOTHERAPY
AGE: > 18	NEOADJUVANT ORMONAL THERAPY
HISTOLOGY: DUCTAL,LOBULAR AND IN SITU BREAST CANCER	MAJOR PSYCHIATRIC DISORDERS OR ADDICTIONS
STAGE: I-II	UNCOMPENSATED COMORBIDITY
SURGERY: CONSERVATIVE	LOCO-REGIONAL RECURRENCE
ADJUVANT RADIOTHERPY	ACUTE COLLAGENOPATHIES
INFORMED CONSENUS	PREVIOUS TUMOR DIAGNOSIS
	DISTANT METASTASES

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RESULTS OF A MINDFULNESS-BASED STRESS-REDUCTION PROGRAM FOR BREAST CANCER PATIENTS TREATED WITH RADIOTHERAPY

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Aims: Cancer patients are subject to a high psycho-

pathological risk that could affect Quality of Life (QoL) and care compliance. Furthermore interest in QoL is increasing as the number of long-surviving patients. Aim of this study is to determine the effectiveness of a Mindfulness-based stress-reduction program on QoL in women with breast cancer treated in our Institute.

Methods: The project was financed by an international no-profit association. Mindfulness meetings were proposed to all breast cancer patients who are candidates for RT. Patients were enrolled solely on the basis of their willingness to attend sessions. The course included 4 meditation sessions with Psycho-Oncologists of our Breast Unit. The questionnaire was administered twice: at first and last meeting. The FACT-B (Functional Assessment of Chronic Illness Therapy - v. 4) questionnaire in its Italian version was administered for QoL functional evaluation. FACT-B is specific for breast cancer and consists of the following subscales: physical well-being (PWB), functional well-being (FWB), emotional well-being (EWB), social/family well-being (SWB) and breast cancer specific concerns (BCS). Three scores can be obtained by summing some of subscales: FACT-B G(PWB+SWB+ EWB+FWB), FACT-B TOI(BCS + PWB + FWB) and FACT-B TOT (sum of all subscales as general wellness on breast cancer). Response scales range from 0 (not at all) to 4 (very much) for a total of 37 items. The items without answers were scored, too.

Results: At the moment, the first eight patients enrolled concluded Mindfulness sessions. The patients had the following features: mean age 53 years (range 35-70), 87,5% had children, 62% had healthy weight and 38% had over weight, all of them had conservative surgery. Regarding systemic adjuvant therapies, 3 patients (35,5%) received chemotherapy and 7 patients (87,5%) hormonal therapy. A total of 16 FACT-B questionnaires were analyzed. The comparison between the initial and final questionnaire showed a statistically significant improvement of QoL for the following subscales: +1,87 for EWB, + 3,83 for BCS, +4,91 for FACT-B G, +8,75 for FACT-B TOT.

Conclusions: Despite the small sample, our data suggest a beneficial contribution and several potential benefits of Mindfulness and other relaxation techniques, as reported in literature, too.

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SALERNO PEDIATRIC RADIOTHERAPY: THE HUMANIZATION OF THE CARE

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In the Pediatric Radiotherapy of A.O.U. San Giovanni di Dio e Ruggi d'Aragona of Salerno we have structured a program for children cancer patients reception. Pediatric radiotherapy is undoubtedly one of the most difficult situations for health professionals to deal with because assistance to the little patient can not and must not be reduced to a simply technical aspect but it is necessary to establish a relationship of trust and collaboration from beginning. that which allows greater serenity and less trauma for the child. With the support of the "Association 30 ore per la Vita" and the "Open Onlus", we have created a completely child-friendly area within the Radiotherapy department. The aim is to create a climate of serenity in a reassuring environment through a greater humanization of the health context of a radiotherapy department to establish a good relationship of trust with children and their families by following well-established paths so as not to destabilize or confuse the children. The "Isola dei Tesori" was born, a welcoming and relaxing environment that has iconographically incorporated the most beautiful aspects of our territory: the sea, the beach and the sun, composed of a large rec center, a covered garden and two patient rooms used as clinic and as pre-anesthesiological and recovery room. In this magical place the children have the freedom to move and play by involving all the professionals who are part of the care path: doctors, nurses, TSRM, psychologists and volunteers. The "bunker" was then renovated, transforming it into an underwater village " Bunker Acquario" that helps the child to think positive inserting it into a fantastic world animated by funny underwater creatures that accompany him on the journey to healing helping him overcome his fears. Normalizing the hospital environment for young cancer patients is the main objective of our multidisciplinary team beyond treatment over the care.

Figure 1.

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PREDICTIVE GENETIC TESTS AND RADIOSENSITIVITY: A SURVEY OF WOMEN UNDERWENT RADIOTHERAPY

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Aims: To explore patients'(pts) views on a potential predictive genetic test that should provide an individual risk probability for toxicity after radiotherapy (RT). To establish, if any such test could help or influence decision-making process of physician or breast cancer pts with respect to the treatment choice (RT + lumpectomy vs mastectomy alone).

Methods: At the end of RT breast cancer pts underwent semi-structured interviews conducted by a radiotherapist and a radiotherapy technician. Transcripts were analyzed by reorganization based on common themes regarding pts perspective on RT. Particularly we focused on the comprehension and impression about benefits of the test, RT side effects, decision making, emotions.

Results: 11 pts had been interviewed. About benefits of the test all pts understand its aim and considered it a chance to become more confident with the treatment. None thought about it as a tool to choose between mastectomy or RT. Regarding side effects the majority of pts felt prepared to RT but not without fear. Many women considered important to have the largest and reliable information, also about negative experiences. Pts appreciated physical/psychological advices to protect them from strong morbidity: use of cream, positive attitude, beloved people, visualization techniques. All pts thought to mastectomy as a very invasive treatment when compared to RT, furthermore, RT toxicity was felt not so serious as a not suitably treated cancer. Prevailing emotions were anxiety and fear but not connected to genetic test's result. At last women underlined that trust and gratitude versus Hospital/Physician were often more relevant for the treatment choice than the response of a test.

Conclusions: These interviews underlined that the genetic test could help to deal with RT and its side-effect and it might help clinician to optimize RT. Nevertheless RT toxicity is commonly perceived as tolerable, and preferable to mastectomy or tumor control failure.

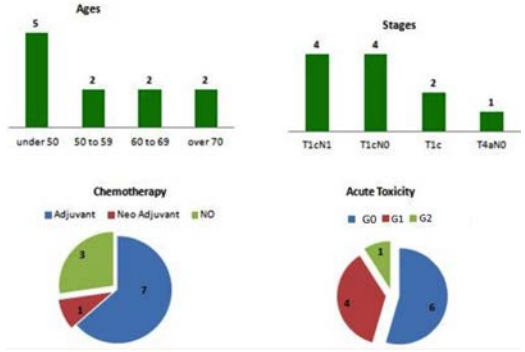

Figure 1.

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QUALITY OF LIFE IN PATIENTS WITH ACUTE LYMPHOBLASTIC LAEUKEMIA TREATED WITH TOTAL BODY IRRADIATION. EXPERIENCE OF A SINGLE CENTER

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Aims: The total body irradiation is an important component of bone marrow pre trasplant conditioning in paediatric patients suffering from Acute Lymphoblastic Laeukemia (LLA). Increased survival global rates draw attention to the evalutation of adverse effects and standard living. This study analyses acute and late toxicity (CTCAE 4.0) in patients receiving myeloablative TBI.

Methods: From 2005 up to 2017 Tbi have been performed on patients suffering from LLA aged 2 to 18 years old , in our centre. The delivered dose was of 12 Gy in twice daily dose of 2 Gy.

Results: In acute phase episodes of nausea and vomiting occurred in 58% of patients (G1) headache in 29% (G2), generalized itching in 13% (G2). To this day 15 out of 29 trasplanted patients are now in complete recovery, the other 14 are deceased. At 5 years median follow-up (range 1-12) surgical treated bilateral cataracts occurred in 66% of patients,endocrine disruption (decrese GH level, with subsequent delayed corporeal growth, hypothyroidism and delayed pubertal development) in 40% esophageal stenosis in 6%. With regard to the document causes of death, 33% of cases relate to transplant complications,58% to disease progression, 3% to veno-occlusive disease; 6% of patients deceased before transplant.

Conclusions: The examination of the sample subjected to TBI shows that delayed endocrinal and ophthalmological adverse effect are common and have a moderate impact on the standard of living.

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QUALITY OF LIFE IN DISEASE-FREE SURVIVORS OF NASOPHARYNGEAL CANCER TREATED WITH TOMOTHERAPY

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Aims: To evaluate the quality of life in disease-free survivors of nasopharyngeal cancer treated with Tomotherapy, using Washington University Quality of Life Questionnaire (UWQOL).

Methods: 21 patients with undifferentiated nasopharyngeal cancer underwent IMRT with Tomotherapy in our institution from 2013 to 2018. Median age was 52 years, median ECOG PS was 1.

Radiation treatment dose to GTV-T and N was 70 Gy, only two patients did not receive concomitant cisplatin. All patients completed treatment without any G3-4 toxicity according to CTCAE 4.0. Median weight loss was 5 Kg, median days of unplanned interruptions were 7 and 6 patients needed replanning.

Results: With a median follow-up of 20 months we interviewed all patients with WUQOL v4 that consists in 12 questions about pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood, anxiety and a subjective rate of quality of life. We reported for each category the first and the second more frequent answer: 52% of patients have no pain while 19% have severe pain controlled by medication; 38% have minor changes in their appearance while 29% remain active even if their appearance bothers them; 33% don't go out because don't have the strenght while 24% are often tired and have slowed down their activities; 34% of patients still get out and enjoy life while 19% mostly stay at home and watch tv; 67% of patients cannot swallow certain solid foods while 19% can only swallow liquid foods; 48% can eat soft solids but cannot chew some food while 28,5% cannot even chew soft solids; 71% of patients speech as always while 14% have difficulty saying some words but can be understood over the phone; 71% of patients have no problem with shoulder while 19% cannot work due to problems with shoulder; 38% can taste most foods normally while 38% can't taste some foods; 52% of patients have too little saliva while 24% have less saliva then normal but it is enough; regarding the mood 39% are neither in a good mood nor depressed about the cancer while 19% have a generally good mood and only occasionally a mood affected by cancer; 43% of patients is anxious about the cancer while 24% is not. The quality of life during the seven past days is "fair" for 34% of patients and "good" for 24%.

Conclusions: quality of life after IMRT with Tomotherapy for undifferentiated nasopharyngeal cancer is good or fair for the majority of survivors according to UWQOL.

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COSMETIC ASSESSMENT IN INTERVENTIONAL RADIOTHERAPY (BRACHYTHERAPY): A REVIEW OF LITERATURE

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Aims: The long-term success of Interventional Radiotherapy (brachytherapy) can be evaluated in terms of disease free survival and rate of toxicities. With the introduction of new technologies more attention is dedicated for preventing toxicity also in terms to achieve not only functional but also cosmetic wellbeing of the patients. Nevertheless, the cosmetic assessment remains a complex issue since non-standardized evaluation systems usually work with very different methods. Thus, the purpose of this study is to define the state of the art of the cosmetic evaluation methods in literature.

Methods: We conduct a literature review of the major experience from the bibliographic databases PubMed, Scopus and Google Scholar. In order to identify the relevant works two independent authors (TZ, RA) screened citations at the title and abstract level to identify potentially relevant studies without any duplication. Potentially eligible citations were retrieved for full-text review and any uncertainty was resolved by two other radiation oncologists experts in Interventional Radiotherapy (LT and VL) of different Institutions. Another team composed by 3 radiation oncologists (MAG, VV and GK) not involved in the review process, performed an independent check for definitive approval.

Results: Some systems use qualitative, others quantitative methods. Additionally, a cosmetic evaluation system could be subjective or objective. Some groups published their experiences using specific scoring systems for radiotherapy, others, considering the nature of this procedure, preferred a system used in the post-surgery assessment. The most frequently applied systems are: EORTC-RTOG, LENT-SOMA, CTCAE, Harvard NSABP, Breast Retraction Assessment (BRA), Facelift Outcomes Evaluation (FOE), the Rhinoplasty Outcomes Evaluation (ROE), the Blepharoplasty Outcomes Evaluation (BOE), and the Skin Rejuvenation Outcomes Evaluation (SROE). Recently, new technologies are involved for this issue, which can provide an objective estimation of the treatment effects through the use of high definition images, 3D scanners or photogrammetric methods. Moreover, methods using dedicated software solutions are spreading in the clinical practice.

Conclusions: The standardized objective cosmetic assessment could play a central role for analyzing the results of interventional radiation therapy especially for the comparison with those of other treatments such as external beam radiotherapy or surgery.

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RE-START INITIATIVE: ONE DAY EVENT TO PROMOTE HEALTH AND WELLBEING AMONG LUNG CANCER PATIENTS SURVIVORS

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Aims: Advances in therapies have led to an increased survival for patients with lung cancer, therefore there is a need for dedicated survivorship care for these patients. The aim of this study was to investigate multidimensional health status of lung cancer survivors and the impact of one day wellbeing event (RE-START initiative) on their health and quality of life.

Methods: Patients with primary lung cancer treated in our institution, after the completion of treatment and in clinical remission were asked to participate in the event. Caregivers were invited also. During this event, there were talks providing information on diet, keeping active and managing stress. During the event participants completed a survey package that included the Psycological General Well Being Index (22 items) for distress assessment, NCCN Survivorship Assessment for physical wellness evaluation (14 items), World Cancer Research Fund Cancer Risk derived questionnaire for Dietary and Lifestyle Habits (11 items). The same survey package was completed 3 months after the event by phone interviews.

Results: From 2015 to 2017, 100 lung cancer patients survivors were asked to participate in the event. Fifty-one patients (51%) agreed to participate but only 19 (19%) patients and 10 caregivers were present. Baseline mean anxiety level and depression severity were 15.8 (scale 0-25, where the highest score corresponds to the lowest level of anxiety) and 11.83 (scale 0-15, where the highest score corresponds to the lowest level of depression) respectively. Only 25% of patients reported high level of anxiety. Only one patient (8%) showed severe depression. No change was detected three months after the event. Almost half of patients presented pain at baseline (56%) while 38% of patients experienced fatigue. Pain and fatigue improvement after the event occurred in 4 patients (27%). Most of patients reported healthy diet (100% consumed vegetables, 67% drank less than 2 glasses of wine per day, 89% ate less than 500 gr of red meat). Improvement in diet after the event was also reported (5-10%).

Conclusions: Few patients participated in the event, probably because of the peripheral location or for the emotional distress of being in a place that was part of their cancer treatment. However, information provided during the event led patients to modify their habits. Through questionnaires, we identified a group of survivors with severe anxiety and depression to whom dedicate intervention strategies.

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INTEGRATED MANAGEMENT OF SECONDARY LYMPHEDEMA IN PATIENTS TREATED WITH RADIOTHERAPY FOR BREAST CANCER

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Aims: Lymphedema can be defined as the tissue fluid accumulation that can result from axillary surgery followed or not by radiotherapy. The changes in surgical technique and the use of more precise radiotherapy modalities have accounted for the reduced incidence of the upper limb lymphedema. Physical therapy (complex decongestive therapy, combined physiotherapy) is the approach to improve lymphatic drainage. The aim of this work is to show the usefulness of an integrated approach to this symptom to avoid complications.

Methods: From January 2016 to March 2018, we treated 56 women with adjuvant radiotherapy on the lymph node district after breast surgery. All patients were discussed into a multidisciplinary team (Breast Unit), to define the best therapeutic approach. A dedicated physiotherapist is constantly present in the group, to ensure specific expertise. Eighteen of the examined women presented lymphedema symptoms.

Results: The average number of surgically removed nodes in the 56 patients was 12 (r.7-21), the radiotherapy treatment was performed with 3D-CRT or IMRT technique on breast (38) or chest wall + expander/prosthesis (18) and III level lymph nodes (II level was treated only in 6 with inadequate axillary dissection). All patients were instructed on the possible increased risk of arm edema and on the preventive maneuvers to avoid it. The cases in which the edema was detected after surgery and before radiotherapy (7) were subjected to joint clinical evaluation with the physiatrist. No active rehabilitation treatments were performed during radiotherapy: at least 3 months after the end of it the patients were re-evaluated and sent to a specific treatment. The intervention included manual lymphatic drainage, exercises, non-elastic wrappings and compressive garments and meticulous skin hydration and care. All the patients undergoing this integrated approach had reduction of functional impotence, with a range varying between 20 and 85%.

Conclusions: This experience with integrated management of lymphedema after surgery and radiotherapy for breast cancer decreased our rate of upper limb edema and significantly reduced the negative impact of this symptom on Quality of Life. Long-term follow-up is necessary to better understand the preventive role of rehabilitation in this clinical setting.

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RADIOTHERAPY (RT) FOR SQUAMOUS CELL OF HEAD AND NECK CANCER (HNSCC) IN PATIENTS UNFIT FOR RADICAL TREATMENTS: INITIAL RESULTS WITH A HYPOFRACTIONATED SCHEDULE

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Aims: Uncontrolled HNSCC leads several symptoms that significantly influence quality of life. The aim of this retrospective analysis is to investigate the feasibility and the effects on local control and palliation of symptoms of subradical-dose RT in patients (pts) unfit for surgery or for radical RT.

Methods: In our Institution, from 2015 to 2018, 20 pts with HNSCC were treated with 45 Gy in 15 fractions (3 Gy/fx). Pts were considered unfit for radical treatments because of age, comorbidity or stage. Median age was 78 years (range 34-95). In 8 pts SCC occurred in the oral cavity, in 7 pts in the oropharynx, in 3 pts in the larynx and in 2 pts in the hypopharynx. Ninetyfive%(19/20) of pts were in stage IV (5 of them in stage IVc for metastasis), the remaining 5% (1/20) in stage III. In 38% (8/21) RT was performed for a loco-regional recurrence after previous surgery. Karnofsky performance status ranged between 60 and 90%. Distressing pain (40%), dysphagia (70%) and weight loss (45%) were common symptoms at presentation.

Results: All pts (20) received a total dose of 45 Gy to the high risk volume (PTV1) and in 6/20 pts also to the elective neck, while in 3/20 pts the elective neck was irradiated with a total dose of 30 Gy and in 1/20 pt of 39 Gy. Median PTV 1 volume was 422 cc (range 80-1015). In 5 pts 3D-conformal RT was used, in 8 pts Volumetric Modulated Arc Therapy, in 2 pts Static Intensity Modulated RT (IMRT) and in 5 pts IMRT with Tomotherapy. Only 2/20 pt developed dysphagia G3-G4 (both for local progression during RT) and 1 pt showed oral mucositis G4. No other toxicity G3-G4 was observed. Weight loss occurred in 75% of pts. Only 2 pts stopped RT definitively (1 pt at 30 Gy,1 pt at 21 Gy), both for locally progressive disease (PD). Three pts needed to temporarily stop RT for acute toxicity (from 1 to 4 days of interruption). In 80% of pts clinical benefit regarding local pain was observed. In 6 pts there was an improvement of dysphagia. Thirty% (6/20) of pts had complete response, 50%(10/20) partial response, 5% (1/20) of pts stable disease and 15% PD. The median freedom from loco-regional progression (FFLRP) time is 8 months, median progression free survival (PFS) is 6 months, median overall survival (OS) is 14 months, with 56% of pts living at 1 year.

Conclusions: This schedule seems to be effective on symptoms relief with good results on local control, it seems feasible for pts unsuitable for radical treatments and may open possibilities for combination therapies with low cumulative toxicity.

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POTENTIAL IMPACT OF IL-13 AS PROGNOSTIC BIOMARKER IN PATIENTS WITH EARLY STAGE LUNG CANCER TREATED WITH STEREOTACTIC ABLATIVE RADIOTHERAPY

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Aims: Early stage (IA-B) non-small cell lung cancer (NSCLC) patients not eligible for surgery are ideal candidate for stereotactic ablative radiotherapy (SABR). SABR have demonstrated excellent results in terms of local control, tolerability with a cancer specific survival (CSS) of about 70% at 3 years. A substantial proportion of patients still relapse and die due to systemic disease progression and adjuvant oncological treatment should be considered, but prognostic factors are lacking. IL-13 is a pleiotropic Th2 cytokine that plays an important role in biological systems regulation. IL-13 may be considered a promising prognostic marker and a potential therapeutic target in NSCLC. Aim of this experience is to estimate the prognostic role of plasmatic levels of IL-13 in patients with early stage NSCLC treated with SABR.

Methods: Fifteen patients were prospectively enrolled in this study from January 2010 to December 2012. Blood samples were collected at the following time: first day of SABR (TFd), last day of SABR (TLd) and 45 days (T45d) after the end of SABR. Firstly, we aimed to investigate whether IL-13 levels were associated with cancer specific survivals (CSS). Secondly, we tested if different IL-13 levels might identify specific subgroups of patients at higher risk of radiation-induced lung toxicity.

Results: All patients received a radiation dose prescription of 52 Gy in 8 fractions (prescribed to the 80–85% isodose-line) for stage IA-B NSCLC. IL-13 levels, measured at TFd (p=0.038) and T45d, resulted significantly associated with lower CSS (p=0.045). Additionally, a trend of correlation between IL-13 levels at T45d and late moderate-severe chronic radiological lung injury was also observed (p=0.06)

Conclusions: In this study, we showed the potential role of IL-13 as prognostic marker in early stage NSCLC patients treated with SABR. We are planning to expand this prospective training cohort and, if the finding will be confirmed, to further validate IL-13 as prognostic biomarker in two separate cohorts of surgical and SABR patients

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CAN BIOMARKERS PREDICT PATHOLOGIC COMPLETE RESPONSE AFTER PREOPERATIVE CHEMORADIOTHERAPY FOR RECTAL CANCER?

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Aims: Approximately 20% of all patients with locally advanced rectal cancer (LARC) experience pathologically complete responses (pCR) following neoadjuvant chemoradiotherapy (nCRT) and standard surgery. Molecular biomarkers could have the potential to select patients than can benefit from CRT. The aims of this preliminary study were to evaluate the expression of two biomarkers, p53 and SOX2 and to correlate this expression with the pathologic response. The p53 tumor suppressor gene is the most frequently mutated tumor-associated gene in malignant human tumors, including colorectal cancer. Sex determining region Y-box 2 (SOX2) is a major regulator of self-renewal and pluripotency of embryonic stem, and is involved in tumor proliferation and differentiation. Our study attempted to outline the prognostic role of expression of these two biomarkers in pathologic specimens from patients with LARC before they underwent nCRT and radical surgery.

Methods: We retrospectively analyzed patients with LARC treated with intensity-modulated radiotherapy (IMRT) and concurrent Capecitabine was administered. Treatment response was evaluated in terms of disease down-staging and TRG scored according American Joint Commission on Cancer (AJCC). P53 and SOX2 expression was assessed by immunohistochemistry on paraffin embedded (FFPE) tumor samples collected before nCRT. Sections were incubated with p53 (DO7, Roche Ventana) and SOX2 (SP76, Roche Ventana) antibodies and staining was carried out on BenchMark XT Automated IHC/ISH slide staining system (Roche Ventana).

Results: Between January 2017 and February 2018 45 patients with operable stage IIII rectal adenocarcinoma were treated. A dose of 50 Gy was prescribed with standard concomitant capecitabine. Surgery was scheduled 8-10 weeks after the completion of CRT. Histological score ranged from 0 (no staining), to + (<50%) and ++ (>50%). Of these, p53 and SOX2 were evaluated in 7 patients. P53 was overexpressed in TRG0 (28.6%), TRG2 (14.3%), TRG3 (14.3%). No association of SOX2 expressions with TRG was uncovered.

Conclusions: Our preliminary data indicate that SOX2 has no potential prognostic significance as observed, for example, in esophagogastric junction adenocarcinoma. p53 expression could be associated with clinical response to CRT but additional studies are needed. In future clinical trials of nCRT for rectal cancer, these biomarker should be prospectively evaluated to determine their utility as predictors of outcome.

Table 1.

	Sox2	P53	TRG
1	0	++	0
2	0	++	2
3	+	++	0
4	0	0	2
5	0	0	3
6	0	++	3
7	0	0	0

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DOES BASELINE [18F] FDG-PET/CT CORRELATE WITH TUMOR STAGING, RESPONSE AFTER NEOADJUVANT CHEMORADIOTHERAPY, AND PROGNOSIS IN PATIENTS WITH RECTAL CANCER?

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Aims: [18F] fluorodeoxyglucose positron emission tomography/computed tomography ([18F] FDG-PET/CT) can be used for tumor staging and prognosis in several tumors but its role in rectal cancer is still debated. The aim of the present study was to assess the correlation of baseline [18F] FDG-PET parameters with tumor staging, tumor response, and outcome in a series of patients affected by locally advanced rectal cancer (LARC) treated with neoadjuvant chemoradiotherapy (CRT).

Methods: One hundred patients treated with neoadjuvant CRT and radical surgery were enrolled in the present study. Maximum standardized uptake value (SUVmax), SUVmean, metabolic tumor volume (MTV), and total lesion glycolysis (TLG) at the baseline [18F] FDG-PET were calculated. Correlations of these PET parameters with tumor staging, tumor regression grade (TRG), disease-free and overall survival were analyzed.

Results: SUVmax (p=0.01) and SUVmean (p=0.01) of primary tumor were statistically associated with T4-stage (both ORs 8.4; 95% CI 1.8-39.7), however PET parameters of complete responders (16%) after CRT were not significantly different from those of non-responders. Moreover, none of PET parameters resulted statistically associated with TRG. Finally, no PET para-

meter was significantly associated with disease-free or overall survival.

Conclusions: Our results showed that baseline [18F] FDG-PET parameters correlated with tumor staging, however they failed to predict complete tumor regression after neoadjuvant CRT, as well as disease-free and overall survival after treatment completion.

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CAN IMAGING PREDICT PATIENT OUTCOME TO RADIOTHERAPY? A PROSPECTIVE STUDY USING MURINE AND HUMAN MODELS

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Aims: To compare murine and human imaging texture analysis (ITA) features of prostate cancer, exploring its potential diagnostic value in assessing tumoural inflammatory microenvironment.

Methods: We will subcutaneously inoculate prostate tumor cells in male mice that display low and high levels of inflammation. These animal models will be imaged twice during the experiment with YAP-PET. Tumour images will be studied with ITA in order to explore its diagnostic power for both CT and PET in discriminating the two groups. At the end of experiment, tumor mass will be analysed by immunohistochemistry (IHC) to evaluate peritumoral inflammatory infiltrate. We will build a prospective bio-medical database of human patients with histologically proven prostate cancer, imaged with both PET-CT and MRI, from which we will extract ITA features of the lesion, in order to pair the human model with the murine model.

Results: In the murine model, we expect to identify ITA tumoural features able to distinguish different levels of inflammation, confirmed by the histopathological evaluation. We will compare these results with those obtained in the human model, looking for ITA features that could be applied for therapy planning.

Conclusions: We speculate that RT induced flogosis could have a key role in selecting the best treatment approach for each patient. This translational study could provide useful data towards a tailored RT, in order to help radiation oncologists in selecting the best strategy and maximizing outcome.

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PREDICTIVE AND PROGNOSTIC VALUE OF PRE-TREATMENT [18F] FDG-PET PARAMETERS IN HEAD-AND-NECK CANCER

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Aims: To evaluate the predictive and prognostic value of [F18] FDG-PET parameters performed prior to radiotherapy in head-and-neck cancer patients (pts).

Methods: Thirty-eight pts with newly diagnosed head-and-neck cancer and candidate to concomitant chemoradiotherapy (CRT) underwent [F18] FDG-PET before the treatment course. Maximum and the mean standardized uptake value (SUVmax, SUVmean), metabolic tumour volume (MTV), and total lesion glycolysis (TLG) were analysed. Multiple threshold levels were tested in order to evaluate the most suitable for tumour metabolic activity: a fixed threshold of 41% and 50% of the SUVmax (SUV41%, SUV50%) and an adaptive threshold segmentation (ATS) algorithm were selected. We evaluated the relationship of mean values of SUVmax, SUVmean, MTV, and TLG with tumour characteristics, treatment response, local recurrence, distant metastasis and disease-related death. Receiver-operating characteristic (ROC) curve analysis was done to obtain the optimal predictive cut-off values for PET parameters. Disease-free (DFS) and overall survival (OS) were examined according to these cut-offs.

Results: The mean value and range of each parameters were calculated. A higher SUVmeanATS was associated to higher primary tumour staging (p=0.04). Thirty-two out of 38 pts (84.2%) achieved complete response, 4/38 (10.5%) partial response, and 2/38 (5.2%) no response 8 weeks after the completion of treatment. No PET parameters resulted predictive for tumour response. After median follow-up of 22 months, 6/38 (15.8%) pts developed local recurrence and 6/38 (15.8%) distant relapse. 8 pts (21.1%) died of tumour progression. The TLGATS was predictive of local recurrence (p=0.04). ROC curves analysis showed a cut-off value of 19.6 for SUVmax, and 13.7 for SUVmeanATS (AUC 0.72, p=0.03 and AUC 0.72 p=0.03, respectively). The 2-year DFS rate was significantly lower in patients with a SUVmax >19.6 (p=0.001) and with a SUVmeanATA >13.7 (p=0.02).

Looking at OS, ROC curves analysis revealed a cut-off value of 19.6 for SUVmax, 8.6 for SUVmeanATS and 49.1 for TLGATS (AUC 0.8, p=0.03; AUC 0.9 p=0.007, and AUC 0.8 p=0.01 respectively). The 2-year OS rate was significantly lower in pts with a SUVmax >19.6 (p=0.004), with a SUVmeanATS >8.6 (p=0.03) and TLGATS >49.1 (p=0.004).

Conclusions: Adaptive threshold-based SUVmean, MTV, and TLG and SUVmax could have a role in predicting DFS and OS in head and neck cancer patients treated with concomitant CRT.

P302

BEYOND HUMAN EYE: TEXTURE ANALYSIS IN PROSTATE CANCER RADIATION RETREATMENT

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Aims: To explore the diagnostic value of imaging texture analysis (ITA) in focal prostate recurrence after radical radiation program.

Methods: The PET-CT and MRI pre-radiation (prRT) and post-radiation (poRT) retreatment images of 7 patients with radiological and biochemical RT response of prostate cancer recurrence were retrospectively evaluated. All patients were re-treated using VERSA HD Linac in VMAT technique (6 MV FFF), delivering 36,25 Gy in 5 fractions, after a primary radiotherapy of 78 Gy in 39 fractions. A polygonal ROI was drawn on the pre-treatment DWI images (b=2000s/mm^2) and overimposed on the PET-CT and T2-weighted (T2W) prRT and poRT co-registered images (MIM Maestro V.6.5.5). A control additional mirror-ROI was drawn on the non-cancerous side using the gland's axis of symmetry. Lesional and non-cancerous first and second order ITA features were extracted using a commercially available software (LifeX V.4.0) and prRT and poRT metrics were compared.

Results: A significant difference (p<0.001) between prRT and poRT T2W ROIs was found for percentage change in skewness, kurtosis and contrast. A median change in skewness of +118% (IQR: +82%, +143%), a median change in kurtosis of +49% (IQR: +14%, +63%) and a median change in contrast of -27% (IQR: -37%, -12%) was found, whereas no significant change in ITA metrics was found between prRT and poRT contralateral mirror-ROIs. No significant difference (p>0.05) between prRT and poRT ITA metrics was found on the PET-CT images.

Conclusions: ITA of diagnostic pre- and post-retreatment images showed promising results in terms of response assessment, and could provide quantitative data for objective interpretation of images. These results should be further validated in prospective studies including wider cohorts.

P303

PSOAS VOLUME AND INTENSITY AS A PROGNOSTICATOR IN NSCLC PATIENTS UNDERGOING CHEMOTHERAPY AND/OR RADIATION THERAPY FOR LOCALLY ADVANCED OR METASTATIC DISEASE

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Aims: To evaluate the volume and median intensity of psoas muscle on CT imaging at the time of diagnosis as a prognosticator in patients with locally advanced or metastastic NSCLC undergoing chemotherapy or radio/chemotherapy.

Methods: We included eighty patients with NSCLC undergoing chemo or radio/chemotherapy at our Department betweeen january 2010 and december 2017. We contoured the volume of right and left psoas volume from the cranial border of L4 till the caudal border of L5. We calculated the median volume between the sides and we divided the median volume for the height of the muscle (Median Area, MA), and we also divided the MA for the median intensity in Hounsfield Units (MA/I). Cut-offs used for survival analysis were calculated with the software X-Tile. We analyzed overall survival (OS) with these parameters and the known prognosticators (age, ECOG, stage), with Kaplan Meier method (univariate) and Cox Regression Analysis (multivariate).

Results: We included 81 patients (57 males and 24 females), with a median age of 67 years (mean 64 years, range 30-84 years). We found a cut-off value for both the MA (8 cm^2) and MA/I (0,165 cm^2/HU). At univariate analysis of OS, the significant parameters were the ECOG (p<0,001), the MA (p:0,034) and the MA/I (p:0,021). At multivariate analysis, only ECOG (p:0,004) and MA/I (p:0,043) resulted significant.

Conclusions: MA and MA/I in NSCLC patients could represent an independent prognosticator of survival, and could help to stratify the patient's prognosis.

P304

ROLE OF PERILESIONAL EDEMA AS PROGNOSTIC FACTOR IN PATIENTS WITH GLIOBLASTOMA DIAGNOSIS UNDERGOING ADJUVANT CHEMO-RADIATION

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Aims: The present study was designed to evaluate the role of perilesional edema calculated on pre-surgery MRI as a prognostic factor in patients with glioblastoma undergoing adjuvant chemo-radiation.

Methods: We performed a retrospective analysis on 140 patients with glioblastoma undergone surgery and adjuvant chemo-radiotherapy (C-RT) between January 2010 and December 2015. Both perilesional edema (PE) and gross tumor volume (GTV) were contoured on MRI. We also calculated PE/GTV ratio, and PE + GTV (TV). Cut-offs were calculated with the software X-Tile. We correlated progression free survival (PFS) and overall survival (OS) with these parameters and the known prognosticators (surgery, KPS, age, MGMT status), with Kaplan Meier method (univariate) and Cox Regression Analysis (multivariate).

Results: A total of 140 patients were included in the analysis (mean age 61 years, median 64 years, range 35-84 years, 91 males and 49 females). Ninety-nine (70%) developed recurrence, whereas 90 patients (64%) died during the follow up. We weren't able to calculate a cut-off value for both PE and GTV, but the found a cut-off for the PE/GTV ratio (>4) for OS survival analysis. The significant parameters at univariate analysis were KPS (p<0,001), surgery (p<0,001) and MGMT status (p<0,001) for PFS analysis, KPS (p<0,001), surgery (p:0,005), MGMT (p:0,001) and PE/GTV ratio (p:0,005). At multivariate analysis of OS, the only significant parameters were MGMT (p:0,011), KPS (p:0,008) and PE/GTV (p:0,034).

Conclusions: Our results suggest that the PE/GTV ratio, together with the known clinical parameters, could play a role in the prognosis of glioblastoma patients.

P305

LEVELS OF INFLAMMATORY MARKERS IN PATIENTS TREATED WITH RADIOTHERAPY FOR PROSTATE CANCER

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Aims: Evaluation of inflammatory marker levels and correlation with urinary and gastrointestinal toxicity in patients(pts)treated with radical or post-operative radiotherapy(RT)

Methods: Pts were enrolled in a prospective observational trial and treated in 2017 with conventional(70 or 78Gy at 2 Gy/fr) or moderately hypofractionated(65 Gy at 2.6 Gy/fr)VMAT image-guided RT in 5 fr/week. Blood samples were collected before RT(T0), between 16-24 Gy (T1) and at the end of RT(T2). Plasma levels of three cytokines and two receptors were evaluated:CCL2,TNF-α,TNFR1,TGF-β1 and PDGF-BB. Urinary and gastrointestinal symptoms were evaluated through the Common Toxcity Criteria for Adverse Events before RT, weekly during RT, and at the end of RT. Primary endpoint for toxicity was grade >= 2 at the end of RT.Inflammatory cytokine kinetics and plasma levels of pts with or without toxicity were evaluated with Kruskall-Wallis test by ranks and Wilcoxon signed-rank test, respectively. Descriptive results are expressed as median values and interquartile ranges in pg/ml units.

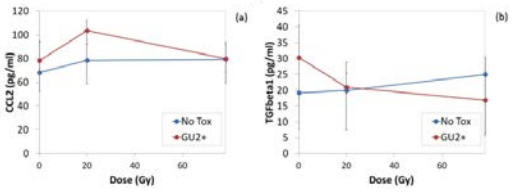

Figure 1.

Results: 50 pts were included: 14/50(28%) showed acute G2 urinary(GU2+) and 12/50(24%) intestinal(GI2+) toxicities. No G3 toxicities were registered. Considering the whole cohort, CCL2 levels had a peak at T1(p=0.006)and PDGF-BB linearly decreased during RT(p=0.003); the other markers did not show significant variations during RT. Pts with GU2 toxicity showed early CCL2 absolute concentrations(T1) significantly higher than those of pts without symptoms: 103(77-112)vs 78(61-92), respectively (p=0.048)(See Figure 1a). In addition, TGF-β1 values of pts with or without GU2 toxicity had an opposite behaviour during RT: 30 (17-41) vs 19 (8-30) at T0 (p=0.048); and 17 (8-25) vs 25(6-31) at T2, respectively (p=0.063) (Figure 1b). A similar trend was seen for TNF-α: 17(7-20)vs 15(5-24) at T0 (p=0.89), and 10(5-21)vs 19(10-28)at T2(p=0.08).Finally, pts with GI2 toxicity showed a trend for significantly lower TNFR1 at baseline (T0):100(79-105)vs134(90 – 215)(p=0.06).

Conclusions: Among the five inflammatory markers evaluated in this analysis, it is interesting to note that the CCL2 and TGF-B1values of patients with GU2+ were significantly higher after 16-24 Gy and at baseli-

ne, respectively and their TGF-B1 values decreased during RT. Patients with intestinal toxicities also showed a trend for lower TNFR1 values at baseline. These results, if confirmed in a larger cohort of patients, might allow timely identification of patients with increased risk of toxicity.

P306

CORRELATION BETWEEN NEUTROPHIL-LYMPHOCYTE RATIO, PLATELET-LYMPHOCYTE RATIO AND SURVIVAL IN PATIENTS WITH LOCALLY ADVANCED PANCREATIC CANCER: NEW PROGNOSTIC FACTOR IN PANCREATIC CANCER?

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Aims: The aim of the study was to investigate the role of inflammatory markers such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in predicting the prognosis of patients with locally advanced pancreatic cancer (LAPC) treated by radiochemotherapy (RCT).

Methods: Fifty-two patients (F:30; M:22; median age 64 years, range 40-75 yrs) with histologically proven pancreatic ductal adenocarcinoma enrolled in a prospective one-armed phase II study were evaluated. All patients were treated with gemcitabine-based RCT after an accurate pre-treatment staging. NLR and PLR were calculated from data collected within 14 days before the start of the concurrent RCT. We stratified population into groups according to the cut-off values: NLR<3 (n=30 pts), NLR ≥3 (n=22 pts), PLR<200 (n=38 pts), PLR ≥200 (n=14 pts). Survival data among subgroups classified by each factor were analyzed via the Kaplan–Meier curve and compared by the log-rank test.

Results: For NLR<3 and NLR≥3 groups, respectively, median OS were 17.7 months and 13 months (p=0.15), and median PFS were 12.4 months and 18.1 months (p=0.4). For PLR<200 and PLR≥200 groups, respectively, median OS were 21.5 months and 12.4 months (p<0.001), and median PFS were 20 months and 12.5 months (p=0.2).

Conclusions: These data suggest that high NLR and high PLR could predict worst OS and PFS. More studies with a large population may be useful in order to validate NLR and PLR as predicting markers for prognosis of patients with LAPC.

P307

A RADIOMIC FEATURES BASED PREDICTIVE MODEL OF RESPONSE FOR PATIENTS WITH NASOPHARYNGEAL CARCINOMA: A PILOT STUDY

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Aims: Radiomics is an emerging field that promises to predict treatment outcome and prognosis in cancer patients (pts). The aim of this study is to create a predictive model of response using radiomic features obtained from CT and FDG-PET in pts treated with radiotherapy (RT) for nasopharyngeal cancer.

Methods: Pts diagnosed with nasopharyngeal carcinoma treated with RT were included in this study. Clinical and instrumental follow-up (F-UP) was performed every 3 months. Pre-treatment PET/CT-scans were collected, and radiomic analysis was performed only on the imaging of the primary tumor (T). After image preprocessing, which included re-sampling and filtering (Gaussian, LoG, Median and no filter), a total of 651 shape, size, histogram-based and textural radiomic features were calculated on contoured GTV in the CT and PET images. A t-test was used to select features correlated ($p<<0.05$) with the outcome. Radiomic models were trained using the MATLAB Classification Learner Toolbox on the patient dataset for prediction of local control (no appearance of disease in the treated site during follow-up) with 5-fold cross validation, and evaluated for predictive power using various scores.

Results: Thirty-two pts were enrolled [M/F: 22/10, median age at diagnosis: 49 years (range: 19-77 years), stage: I-II 25%, III 25%, IV 50%]. RT alone and RT-CT were administered in 1 (3.1%) and 31 (96.9%) pts, respectively. All pts were treated with IMRT technique with the delivery of a total dose of 70.95 Gy in 33 fractions to the GTV. At last F-UP (median: 26.4 months, range 9.4-85.8 months) 25 pts (78.1%) showed complete local control, and 7 (21.9%) progression of local disease. At time of this analysis 29 pts (90.6%) were alive (24 pts with no evidence of local disease, 5 with local disease progression), and 3 (9.4%) were dead (2

for progression at primary site, 1 for distant progression). The best classification model was Linear SVM classifier whose results were in good agreement with the clinical and radiological ones obtained during F-UP. The model scored 87.5% Accuracy, 96% Specificity, 63% Sensitivity, 0.86 AUC and 0.59 Younden Index.

Conclusions: Our preliminary results showed that the creation of predictive model with radiomic features is useful in this setting. These results encourage further evaluation on larger cohort of patients to validate this model.

P308

ROLE OF 68-GA PSMA-11 PET/CT IN THE MANAGEMENT OF BIOCHEMICAL RECURRENCE AFTER RADICAL PROSTATECTOMY (RP) FOR PROSTATE CANCER (PCA): A RETROSPECTIVE ANALYSIS

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Aims: Recurrence after primary treatment of PCa is one of the major challenges in uro-oncology. Biochemical recurrence (BCR) occurs in up to one third of the pts undergoing RP. Our aim was to retrospectively evaluate how 68-Ga PSMA-11 PET/CT (GaPET) could change the management of patients (pts) affected by BCR after RP for PCa.

Methods: Between April 2017 and May 2018 30 consecutive pts who had undergone RP were submitted to GaPET for BCR.At the moment of restaging the median age was 70,5 years,the median PSA value was 0,925 ng/ml (range 0,23-9,57) and the median PSA doubling time was 0,48 years (range 0,05–12,43). For each pt we established the therapeutic approach that we would have proposed before being submitted to GaPET. When referred to our Unit 11 pts were initially considered candidates for continued regular FUP, 15 for undergoing pelvic RT and 4 pts for receiving only androgen deprivation therapy (ADT). We decided to analyze changes in treatment assignment to these pts after having received the results of GaPET.

Results: The results of GaPET showed one or more uptakes compatible with localization of PCa in 16pts. Six of them were treated with adjuvant RT,8 with salvage RT,3 with palliative or stereotactic body RT (SBRT) for extra-pelvic localization and 6 with adjuvant/salvage ADT. Eleven pts had previous negative restaging with 18F-Choline PET/CT. In 3 pts a positive uptake was found in the prostatic bed,in 7 in pelvic nodes,in 1 in extra-pelvic node; 3 pts had bone uptake and 2 had 2 simultaneous uptakes, both in pelvic-nodes and bone. For 13pts (43,3%) who underwent GaPET restaging the initially suggested therapeutic approach was changed. Six pts moved from no treatment to RT(5pts) or ADT. Between pts previously candidates for pelvic RT, 2 received a boost on positive nodes, 1 was submitted to exclusive SBRT and 2 switched to ADT; 1 pt changed from ADT to no treatment and 1 to SBRT.Comparing previous restaging 18F-Choline PET/CT and GaPET, 8 of 11pts with negative Choline staging had pathological uptake with GaPET.

Conclusions: Restaging with GaPET seems to have a significant impact on management and decision-making for pts with BCR from PCa after primary local treatment.PSMA PET seems to provide better systemic staging of disease even for lower PSA levels causing changes in the therapeutic approach in almost half of pts. Further larger and prospective clinical trials are needed to better understand the real impact of this new radiotracer in pts with BCR from PCa.

P309

INTRAVOXEL INCOHERENT MOTION MR IMAGING AS BIOMARKER FOR EARLY RADIATION-INDUCED TOXICITY IN MAJOR SALIVARY GLANDS AND PHARYNX CONSTRICTOR MUSCLES: A RADIOMIC ANALYSIS

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Purpose: Purpose of the study is to investigate and evaluate early changes in irradiated salivary glands and pharynx constrictor muscles using IntraVoxel Incoherent Motion (IVIM) MR as a biological marker.

Materials and Methods: 14 patients (pts) affected by oropharyngeal cancer treated with radical radiochemotherapy were included in the study. Pts were treated with Tomotherapy (Accuray) with SIB (69.3 Gy on pathological lesions and 56.1 Gy precautional regions in 33 fractions) and underwent MR exams including diffusion weighted imaging for IVIM (b values: 0 50 100 150 200 400 800 1000 s/mm^2) before RT (pre-MR) and after 35 Gy during RT (mid-MR). Pts were examined every week during RT and every 3 months after the end of treatment. A questionnaire (VHNSS-IT) about xerostomia and dysphagia was submitted at every appointment. Apparent Diffusion Coefficient (ADC), D (pure-diffusion), D* (pseudo-diffusion) and f (perfusion fraction) maps were computed using a in-house algorithm developed in Matlab for both MR scans, in order to study the above mentioned quantitative indexes distributions in salivary glands and pharynx constrictor muscles as contoured on structural MR.

Results: 6 months after RT 13 pts reported none or mild dysphagia and only 1 declared severe dysphagia; 6 pts had mild and 8 moderate-severe xerostomia. At 12

months 12 pts reported mild dysphagia and 2 severe; nothing changed concerning xerostomia. ADC and D values increased significantly for all organs at mid-MR ($p<0.03$). No significant differences were found for f radiomic features between pre-MR and mid-MR for constrictor muscles. No differences were found between pts that reported mild or severe dysphagia. No difference was found between pts with mild and severe xerostomia for parothid radiomic features while for submandibular glands pts with severe xerostomia presented higher values of ADC and f map at 90th and 95th percentile ($p<0.038$) and mean and median value for f map ($p<0.001$) as well.

Conclusions: IVIM-MR allows to non-invasively detect early changes of salivary glands and pharynx constrictor muscles due to microstructural changes and presence of edema or perfusion. These preliminary data have shown that radiomic approach could be a useful tool to assess radiation damage during RT and pts outcome especially regarding xerostomia. A further analysis, that will include previsional and delivered dose to organs, will allow to include the effect of dose on these outcomes.

P310

MULTIDISCIPLINARY URO-ONCOLOGIC BOARD DECISION PROCESS AND PSMA PET/CT IN RELAPSING PROSTATE CANCER

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Aims: Literature supports the superiority of 68 Gallium-prostate specific membrane antigen (68 Ga-PSMA) ligand positron emission tomography/computed tomography PET/CT in terms of accuracy to recognize macroscopic relapses at lower levels of prostate-specific antigen (PSA). The core team of the uro-oncologic multidisciplinary group (GOM) of Aulss 1 Dolomiti Veneto analyzed the weight of 68 Ga-PSMA-PET/CT in decision for the patients with relapsing prostate cancer (PC) presenting a biochemical relapse after prostatectomy (RP) alone or after salvage radiation therapy (RT).

Methods: For a biochemical relapse, from March 2017 to February 2018, 7 patients who had undergone prostatectomy alone or after a salvage RT were addressed to 68 Ga-PSMA-PET/CT (and one patient to 18F-PSMA-PET/CT), performed in one of the few centers working in this field in Italy. The PSA level ranged between 0.22 and 2.01 ng/ml (median=0.78 ng/ml). The impact of additional data obtained from PSMA-PET/CT on the decision-making process in a multidisciplinary group was evaluated.

Results. Six out of 8 patients showed positive findings at PSMA-PET/CT and 3/8 after a negative Acetate PET/CT. Among them, 2 were positive in the prostatic bed, 3 just in the pelvic nodes, 1 presented different sites of relapsing nodes (in and out of pelvis). In our experience, PSMA-PET/CT data changed the therapeutic approach in 4/6 patients also with an impact on one already indicated local treatment. Two patients were candidated to no radiation treatment before 68 Ga-PSMA-PET/CT: one of them was finally addressed to SBRT; another one patient received IMRT on the pelvic nodes. Furthermore, one patient received salvage androgen deprivation therapy (ADT) and another one SBRT on positive node instead of a re-irradiation of prostatic bed.

Conclusions. In restaging of patients with a biochemical relapse of PC, 68 Ga-PSMA-PET/CT can be a useful tool with a change into the decision-making process of a multidisciplinary tumor board. The small size of the population limitate results. Prospective data will define the relevance in prostate cancer of this biomarker imaging.

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P311

IS THERE A PROGNOSTIC ROLE OF TEXTURE ANALYSIS AT PET/CT IN EARLY STAGE NSCLC TREATED WITH SBRT? A RETROSPECTIVE MONOCENTRIC STUDY

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Aims: Aim of this retrospective study was to evaluate the predictive value of texture parameters of 18F-FDG PET/CT in SBRT-treated early stage NSCLC.

Methods: Eighteen patients with early stage NSCLC between 2010 and 2016 underwent a 18F-FDG PET/CT before SBRT treatment. For each tumour a volume of interest was defined around the tumour by a single observer. An automatic segmentation was performed inside this volume by using a fixed threshold of 40% of maximum SUV (standardized uptake value). For each volume 45 textural features were calculated using LIFEx software. For each patients clinical data about age, gender, Karnofsky Performance Status (KPS), initial stage, histology, location, prescribed biological effective dose, local recurrence, regional recurrence, distant recurrence and death were acquired. Study endpoint was recurrence free survival (RFS). Cutoff values were obtained using a quadratic support vector machine (SVM) based analysis and RFS were compared using log-rank test analysis.

Results: Median age of the population was 72.5 years (range 53-90) with 14 men and 4 women. The majority of patients (14) had KPS ≥ 80. Stage was T1N0M0 in 7 patients, T2N0M0 in 9, T3N0M0 in 2. Pathological diagnosis was achieved in only 10 patients (4 adenocarcinomas and 6 squamous cell carcinomas). Tumor was located in upper lung field in 9 patients, in middle in 1 and in lower in 8. Most of the patients (14) were treated with ≥100 Gy in biological equivalent dose, calculated by a linear quadratic model with an α/β ratio of 10 Gy. The median follow-up period was 19.5 months for the entire population and 22.5 months for the surviving patients. 1-year OS was 61% (CI 42-88). At final follow-up, 10 patients had recurrences: local (n=1), regional (n=2), distant (n=5), local and regional (n=1), local, regional and distant (n=1). Quadratic SVM model found that HISTO_Kurtosis and GLRLM_LRLGE can describe patients with disease recurrence (AUC=0.70). A cutoff of HISTO_Kurtosis=2.5 obtained with log-rank test was able to classify the population in high and low recurrence risk (p=0.03) (Figure 1).

Conclusions: Among baseline 18F-FDG PET/CT textural feature HISTO_Kurtosis and GLRLM_LRLGE were predictors of RFS in our analysis. Although this needs further validation on a larger series of patients, it may reveal helpful in identifying patients who will benefit from closer surveillance or adjuvant therapy.

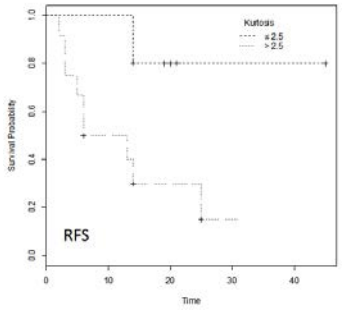

Figure 1.

P312

THE IMPACT OF FIRST MR IN CLINICAL DECISION MAKING ABOUT PATIENTS WITH HIGH GRADE GLIOMA TREATED WITH RADIO-CHEMOTHERAPY

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Aims: Standard up-front therapy of high grade glioma (HGG) is focused on the so called Stupp protocol, that includes surgical resection followed by radiotherapy (RT) combined with concomitant and adjuvant chemotherapy with temozolomide (TMZ). As supported by several international guidelines, disease assessment is performed using magnetic resonance (MR) one month since the end of RT and then every 3 months: in case of tumour progression the administration of temozolomide (the most active agent against glioma) is interrupted and salvage therapy or best supportive care are recommended. The aim of this study is to investigate in a retrospective manner the real value of first MR following RT and its relevance in clinical decision making about up-front therapy.

Methods: Between April 2005 and July 2017, data of 78 patients (pts) with a proven diagnosis of HGG and treated with Stupp protocol at the University Hospital of Pisa were collected. Tumor progression was defined according to Mac-Donald's Criteria. Considering the potential presence of pseudo-progression (PSP) and the evolutionary pattern of the suspected recurrences, lesions suggestive for tumor progression inside the radiotherapy field were investigate with a new MR after 6-8 weeks. Otherwise, the presence of new lesions outside the radiotherapy field was interpreted as disease progression (PD) and patient's therapy was changed. Presence or absence of symptoms, extent of surgery and MGMT methylation status were recorded.

Results: The first MR after RT-CT evidenced infield progression (interpreted as PSP) in 16 pts (20,5%) and outfield progression in 8 (10.2%).Three out of 8 patients with outfield progression were symptomatic for the tumor growth. The second MRI confirmed the presence of PSP in 10 pts out of 16 pts whereas in 6 patients a true progression (PD) was present since the first MR.

Conclusions: In absence of symptoms, the first MR after radio-chemotherapy influenced clinical decision making (sending the patients to further salvage therapy or BSC) only in 5 out of 78 patients (6.4%). In 72 patients, even in presence of radiological signs suggestive for disease progression inside the RT field, clinical decision making did not change. Further studies involving a higher number of patients are required in order to confirm our findings.

P313

PERILESIONAL EDEMA AND TUMOR VOLUME IMPACT SURVIVAL IN NON-SMALL CELL LUNG CANCER (NSCLC) UNDERGOING RADIOSURGERY (SRS) FOR BRAIN METASTASES

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Aims: To evaluate the volumetric perilesional edema in brain metastases undergoing radiosurgery (SRS) in relation to outcomes.

Methods: We included forty-six patients with 1-2 brain metastasis from NSCLC treated with radiosurgery (SRS). Both perilesional edema (PE) and gross tumor volume (GTV) were contoured on MRI. We also calculated PE/GTV ratio, and PE + GTV (TV). Cut-offs were calculated with the software X-Tile. We analyzed Brain Recurrence Free-Survival (bRFS), both in-field and out-of- field, and overall survival (OS) with these parameters and the known prognosticators (disease specific GPA, DS-GPA), with Kaplan Meier method (univariate) and Cox Regression Analysis (multivariate).

Results: On the overall population, only four patients (9%) showed in-field progression, with no correlation with perilesional edema, whereas 10 patients (22%) showed new brain metastases out of field, and this modality of progression was related to a lower PE/GTV ratio. Conversely, 38 patients died in the follow up (83%), and we found a worse prognosis in patients with higher GTV, PE and TV. On multivariate analysis of OS the only significant parameters were TV and DS-GPA.

Conclusions: PE, GTV and TV in brain metastasis from NSCLC could represent an independent prognosticator of survival, and could help together with DS-GPA to stratify the patient's prognosis.

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IN VIVO RADIOBIOLOGICAL ANALYSIS OF PROSTATE CARCINOMA TREATED WITH 12 GY SINGLE-SHOT IORT

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Purpose: To evaluate apoptotic pathways in prostate cancer treated with intraoperative radiotherapy (IORT), studying the effects on cells. We evaluated correlations between p53, Bcl2 and ki67, pathological staging and local control.

Materials and Methods: We selected 20 patients. Proteins involved in the apoptotic cascade were studied before and after 12 Gy in neoplastic tissues, high grade PIN areas and in healthy prostate cells. Immunofluorescent detection of antigens, were performed on bioptic sample and on surgical specimens 5-mm slices. Before and after IORT, Bcl2, p53, and ki67 were detected. Bax and caspases immunofluorescent positivity was compared in different areas and in neoplastic areas before and after IORT.

Results: Before IORT, mean Bcl2 in neoplastic cells is 2.23%, mean ki-67 in neoplastic area is 4.5% and mean p53 is 22.5%. After IORT mean Bcl-2 in neoplastic cells is 8.85%, mean ki-67 in neoplastic area is 7.8% and mean p53 is 24.9%. A significant increase in Bax expression was detected in tumour and PIN areas comparing treated and untreated samples ($p<0.05$). After 12 Gy - single dose, healthy areas expressed significantly lower level of Bax positive with respect to neoplastic cells ($p<0.0001$), while in PIN areas, Bax positive cells were significantly more present than in neoplastic areas ($p=0.0001$). Results about Caspases 3 and 9 were conflicting and we did not find significant differences in expression between neoplastic and healthy tissue cells after IORT. With multivariate analysis, we find that cancer cells with ki67 $\geq$8% show a trend toward greater expression of Bax ($p=0.0641$). We do not find correlations between ki67 and caspases activation. We also found an increasing in Bcl2 expression after IORT in neoplastic areas ($p=0.0041$); with multivariate analysis, we found that neoplastic cells with higher Bcl2 expression after IORT had a worsen local control with higher incidence in biochemical failure. Bioptic specimens with p53 higher than 18% and ki67 higher than 8% had worst post-operative staging with higher incidence in extracapsular invasion ($p<0.05$) and nodal positivity ($p<0.05$).

Conclusions: After 12 Gy, Bax is overexpressed in tumour and PIN cells. PIN areas seem to be more radiosensitive, showing an intrinsic radioresistance. Pre-operative ki67 and p53 definition could be use in clinical practice to predict patients with worsen pathological stage, while Bcl2 activation after IORT might be predictive factor for failure.

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DISRUPTION OF MEK/ERK/C-MYC SIGNALLING RADIOSENSITIZES PROSTATE CANCER CELLS *IN VITRO* AND *IN VIVO*

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Aims. Prostate cancer (PCa) cell radioresistance causes the failure of radiation therapy (RT) in localized or locally advanced disease. The aberrant accumulation of c-Myc oncoprotein, known to promote PCa onset and progression, may be due to the control of gene transcription and/or MEK/ERK-regulated protein stabilization. Here we investigated the role of MEK/ERK signalling in PCa.

Methods. LnCAP, 22Rv1, DU145 and PC3 PCa cell lines were used in in vitro and in vivo experiments. U0126, trametinib MEK/ERK inhibitors and c-Myc shRNAs were used. Radiation was delivered using an x-6 MV photon linear accelerator. U0126 in vivo activity alone or in combination with irradiation was determined in murine xenografts.

Results. Inhibition of MEK/ERK signalling downregulated c-Myc protein in PCa cell lines to varying extents by affecting expression of RNA and protein , which in turn determined radiosensitization in *in vitro* and *in vivo* xenograft models of PCa cells. The crucial role played by c-Myc in the MEK/ERK pathways was demonstrated in 22Rv1 cells by the silencing of c-Myc by means of short hairpin mRNA, which yielded effects resembling the targeting of MEK/ERK signalling. The clinically approved compound trametinib used in vitro yielded the same effects as U0126 on growth and C-Myc expression. Notably, U0126 and trametinib induced a drastic downregulation of BMX, which is known to prevent apoptosis in cancer cells.

Conclusions. The results of our study suggest that signal transduction-based therapy can, by disrupting the MEK/ERK/c-Myc axis, reduce human PCa radioresistance caused by increased c-Myc expression *in vivo* and *in vitro* and restores apoptosis signals.

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TARGETING OF THE EPHRIN RECEPTOR KINASE SIGNALLING BY GLPG1790 *IN VITRO* AND *IN VIVO* REVERTS ONCOPHENOTYPE, INDUCES MYOGENIC DIFFERENTIATION AND RADIOSENSITIZES EMBRYONAL RHABDOMYOSARCOMA CELLS

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Aims. EPH (erythropoietin-producing hepatocellular) receptors are clinically relevant targets in several malignancies. This report describes the effects of GLPG1790, a new potent pan-EPH inhibitor, in human embryonal rhabdomyosarcoma (ERMS) cell lines.

Methods. EPH-A2 and Ephrin-A1 mRNA expression was quantified by real-time PCR in 14 ERMS tumour samples and in normal skeletal muscle (NSM). GLPG1790 effects were tested in RD and TE671 cell lines, two in vitro models of ERMS, by performing flow cytometry analysis, Western blotting and immunofluorescence experiments. RNA interfering experiments were performed to assess the role of specific EPH receptors. Radiations were delivered using an x-6 MV photon linear accelerator. GLPG1790 (30 mg/kg) in vivo activity alone or in combination with irradiation (2 Gy) was determined in murine xenografts.

Results. Our study showed, for the first time, a significant upregulation of EPH-A2 receptor and Ephrin-A1 ligand in ERMS primary biopsies in comparison to NSM. GLPG1790 in vitro induced G1-growth arrest as demonstrated by Rb, Cyclin A and Cyclin B1 decrease, as well as by p21 and p27 increment. GLPG1790 reduced migratory capacity and clonogenic potential of ERMS cells, prevented rhabdosphere formation and downregulated CD133, CXCR4 and Nanog stem cell markers. Drug treatment committed ERMS cells towards skeletal muscle differentiation by inducing a myogenic-like phenotype and increasing MYOD1, Myogenin and MyHC levels. Furthermore, GLPG1790 significantly radiosensitized ERMS cells by impairing the DNA double-strand break repair pathway. Silencing of both EPH-A2 and EPH-B2, two receptors preferentially targeted by GLPG1790, closely matched the effects of the EPH pharmacological inhibition. GLPG1790 and radiation combined treatments reduced tumour mass by 83% in mouse TE671 xenografts.

Conclusions. Taken together, our data suggest that altered EPH signalling plays a key role in ERMS development and that its pharmacological inhibition might represent a potential therapeutic strategy to impair stemness and to rescue myogenic program in ERMS cells.

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PREDICTORS OF LATE TOXICITY AFTER POSTOPERATIVE RADIOTHERAPY OF CONSERVATIVELY TREATED BREAST CANCER: AN ANALYSIS ON 768 PATIENTS

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Aims: To retrospectively evaluate risk factors for skin and subcutaneous late toxicity in 768 patients (pts) conservatively treated for breast cancer.

Methods: We analysed 5-year G ≥ 2 skin and subcutaneous late toxicity-free survival (LTFS) stratifying pts based on potential risk factors: hypertension, diabetes, smoking habit, alcohol consumption, chemotherapy, hormonotherapy, stage, PTV volume, and EQD2.

Table 1. Univariate analysis of risk factors for 5-year late local toxicity.

			SKIN			SUBCUTANEOUS			
		patients	5-year late toxicity-free survival G2	p-value	5-year late toxicity-free survival G3	p-value	5-year late toxicity-free survival G2	p-value	5-year late toxicity-free survival G3	p-value
Hypertension	Not	499	94.6%	0.548	100%	0.043	87.6%	0.875	98.9%	0.475
	Yes	268	93.7%		98.5%		86.2%		99.4%	
Chemotherapy	Not	367	95.3%	0.224	100%	0.248	87.6%	0.639	100%	0.046
	Yes	401	93.4%		99.2%		86.6%		98.4%	
Type of chemotherapy	Not	367	95.3%	0.546	100%	0.182	87.6%	0.054	100%	0.125
	CMF	60	90.2%		97.3%		88.7%		98.1%	
	Anthracycline	214	93.7%		99.3%		89.9%		98.6%	
	Taxanes+Anthracycline	125	94.7%		100%		79.9%		98.1%	
Hormonotherapy	Not	136	96.9%	0.201	100%	0.693	90.5%	<0.0001	100%	0.787
	Tamoxifen (Tam)	410	92.3%		99%		89.1%		99%	
	Tam+LH-RH analogue	125	95.3%		100%		84.6%		98%	
	Aromatase Inhibitors	91	96.4%		100%		75.6%		98.9%	
EQD2 (PTV-BOOST)	44-50.7	317	92.9%	0.365	100%	0.07	89.6%	<0.0001	99.6%	0.735
	48.4-59.4	130	93.3%		98.2%		96.5%		99.2%	
	50-64.8	321	95.6%		100%		80%		98.6%	
N	0	522	95.5%	0.198	99.6%	0.809	88.9%	0.001	99.1%	0.42
	1	179	91.3%		99%		88.7%		99.2%	
	2	44	92.3%		100%		73%		97.7%	
	3	19	93.3%		100%		66.3%		100%	
PTV (cc)	102-380.9 cc	110	98.4%	<0.0001	100%	0.422	98%	0.121	100%	0.121
	381-541.1 cc	110	98.9%		100%		90.6%		97.8%	
	541.1-716.3 cc	109	89.2%		98.1%		91.8%		100%	
	716.3-1842 cc	110	80.1%		97.4%		87.3%		100%	

Results: Univariate analysis results are shown in Table 1. No correlation was found between G ≥ 2 LTFS and diabetes, smoking habit and alcohol consumption. Small but statistically significant correlations were found between hypertension and G3 cutaneous 5-y-LTFS (98.5 vs 100%) and between chemotherapy and G3 subcutaneous 5-y-LTFS (98.4 vs 100%). A trend suggesting an impact of taxan-based chemotherapy schedules on G2 subcutaneous late toxicity was observed. Hormonotherapy with Aromatase Inhibitors (AI) was significantly (p>0.0001) associated with worse G2 subcutaneous 5-y-LTFS (75.6% vs 84.6% and 89.1% for Tamoxifen plus LH-RH analogue and Tamoxifen alone respectively). EQD2 was also related to G2 subcutaneous toxicity: in particular, better outcomes were observed in the group of pts treated with 50.4 Gy in 28 fractions (fr) with sequential electron boost of 10 Gy in 4 fr (EQD2 PTV 48.4 Gy, EQD2 BOOST 59.4 Gy). This was probably related to the used technique for boost delivery (electrons vs concomitant boost with tangential fields in the other two groups). In the two groups treated with IMRT and concomitant boost, G2 subcutaneous toxicity was higher in the one with higher EQD2, as expected. An interesting correlation (p=0.001) was also found between nodal status and G2 subcutaneous toxicity: pts with N2-3 disease, who underwent regional lymphadenectomy (with consequent alteration of lymphatic drainage) had a worse outcome compared to pts with N1 disease, where lymphadenectomy rate was lower. This could also be explained by the different technique (hemi-fields) used for pts who needed lymph nodes irradiation (typically pN2-3). Finally, PTV volume was correlated with G2 skin LTFS (p<0.0001), with a significant difference between values below and above the median (5y-LTFS: 98.4% vs 80.1%).

Conclusions: our preliminary data confirm that some factors could be related to higher rates of late toxicity in pts treated for breast cancer. This analysis may represent the basis to develop predictive models of late toxicity.

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TOLERANCE OF SPINAL CORD TO RE-IRRADIATION OF SPINE METASTASES: A SYSTEMATIC REVIEW

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Aims: Spinal metastases that recur after radiotherapy have historically been difficult to manage due to concerns of spinal cord toxicity in the retreatment setting.

We performed a systematic review of the literature to determine the clinical efficacy and safety of spine re-irradiation in patients previously irradiated spinal metastases.

Methods: A systematic literature review was conducted using MEDLINE and EMBASE database, from 1995 to 2017. The search strategy included terms related to re-irradiation and spine. Election criteria for inclusion were: retrospective and prospective studies analyzing ≥10 patients, full text articles, toxicity and/or safety reported as outcome humans and English language.

Results: Forty-four publications were identified, of which 14 were appropriate for inclusion with a total of 985 patients suitable for analysis. Studies were largely retrospective (11/14; 78.5%). Different prior irradiation sites have been treated with photon external beam as 3D conformal, stereotactic (SBRT), or intensity modulated (IMRT) radiotherapy. Previous total dose ranged between 8 and 70 Gy with several dose/fraction (conventional in 3 studies). Time relapsed since previous irradiation and follow-up after re-irradiation were in median 12 months (6.8-21.3) and 12.5 months (6-36.6), respectively. Re-irradiation was delivered by 3D conformal or IMRT (9 studies) and SBRT/ Cyberknife (8 studies) techniques. Total dose and fractionation schedules of re-irradiation are variable among studies (8- 66 Gy). Late toxicities ≥G3 were described, mostly in terms of neuropathy, pain and/ or vertebral fractures. Globally, re-treatment was well-tolerated, only 30 (3%) patients experienced an acute or late episode ≥ grade 3 toxicity. The rate of acute and late toxicity has been paired to cumulative dose.

Conclusions: This systematic literature review suggests that Re-Irradiation to previously irradiated spinal metastases is safe and effective both in local control and pain relief.

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TOLERANCE OF THORACIC ORGANS AT RISK TO LUNG RE-IRRADIATION: A SYSTEMATIC REVIEW

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Aims: Re-irradiation (re-RT) is a treatment modality that has been actively investigated in recurrent lung cancer or in lung metastases appeared in previously irradiated areas. Side effects of thoracic organs at risk are often the major concern that constrains the choice of total dose and fractionation. The present systematic review of the literature aims to identify possible factors related to the toxicity incidence and severity of radiation pneumonitis/pulmonary fibrosis (RP/PF), esophagitis, chest wall pain/rib fracture, radiation dermatitis and any severe/fatal adverse event G4-G5 (AE).

Methods: Literature search of "Re irradiation/exp OR reirradiation OR re-irradiation AND lung" was performed on February 20th 2018, via PubMed. Inclusion criteria were: year of publication between 1995 and 2018, English-language, full-text article, available toxicity data. Studies with less than 10 patients (pts) were excluded. References listed in the screened articles were also evaluated for inclusion criteria.

Results: Of the 182 articles screened, 16 met the inclusion criteria. 12 more articles were obtained from

the references research, with a total number of studies of 28 (1 prospective, 27 retrospective). Total number of pts was 918 (range per single study: 10-102), total number of treatments was 935. Median follow- up ranged between 6.5 and 42 months; median time elapsed since previous irradiation ranged between 7.9 and 51 months. Re-RT technique was conventional RT, Stereotactic RT or proton/carbon ion in 10, 11 and 2 studies respectively. In 5 studies pts were treated with various techniques. RP/PF, esophagitis, skin toxicity, chest wall pain/rib fracture and cough/dyspnea (any grade) were reported in 149, 74, 34, 58 and 71 pts, respectively. Twenty-six (2.8%) pts experienced a severe/fatal AE (Table 1); the incidence of AEs per single study varied between 0% and 17.5%. The risk of esophagitis was higher in pts treated with conventional-fractionation ($p = 0.043$), while the risk of chest wall pain/rib fracture was higher in pts treated with SBRT ($p = 0.016$). Unexpectedly, the risk of RP/PF > 20% and the risk of AEs were correlated with a longer median time elapsed between first RT and re-RT (< vs > 17.5 months, $p = 0.043$ and $p = 0.005$ respectively). Possible confounding factors are currently under investigation.

Conclusions: lung re-RT is feasible and the toxicity profile is acceptable both with conventional fractionation and SBRT.

Table 1. Severe/fatal adverse events (AEs).

Study year [Accrual period]	1st Author/ Journal	Study type	N° of patients	Time elapsed since previous irradiation (median)	First-RT total dose/fractionation	Re-RT total dose/fractionation	Re-RT technique	Severe/Fatal AEs
2011 [1994-2004]	Peulen, Radiotherapy and Oncology	R	29	14	15 Gy x 3 (2) 15 Gy x 2 (12) 10 Gy x 4 (7) 10 Gy x 3 (2) 10 Gy x 2 (2) 8 Gy x 5 (5) 8 Gy x 4 (1) 8 Gy x 3 (1)	20 Gy x 1 (1) 15 Gy x 3 (6) 15 Gy x 2 (10) 11 Gy x 3 (1) 10 Gy x 4 (4) 10 Gy x 3 (1) 8 Gy x 5 (8) 8 Gy x 4 (1)	SBRT	3 G5 Bleeding 2 G4 Other (fistula, VCS fibrosis)
2012 [2004-2010]	Liu, Int. J. Radiation Oncology Biol. Phys	R	72	21	Conventional RT: median total dose 63 Gy (range 30-79.2 Gy)	12,5 Gy x 4 (all)	SBRT	1 G5 radiation pneumonitis
2013 [1993-2008]	Evans, Radiotherapy and Oncology	R	35	30	Conventional RT: median total dose 54 Gy (range 45–70 Gy)	Median total dose 60 Gy (range 30–70 Gy) Median dose/fraction 2.0 Gy (range 1.5–3.0 Gy)	/	2 G5 aortic toxicities
2013 [2004-2011]	Reyngold, Radiation Oncology	R	39	37	Median total dose 61 Gy (range 30–80 Gy)	Various fractionations BED10>100 (15) BED10<100 (24)	SBRT	1 G4 skin/connective tissue toxicity
2014 [2004-2013]	Griffioen, Lung Cancer	R	24	51	Median total dose 59.8 Gy (range 24–70 Gy); various fractionations	Conventional RT: median total dose 60 Gy (range 39–66 Gy)	IMRT	3 possible G5 bleeding (hematemesis or hemoptysis)
2014 [2001-2012]	Kilburn, Radiation Oncology	R	33	18	Median total dose all patients: 60 Gy (range 22.5–80.5 Gy) - EBRT (23 pts, 70%): 66 Gy (45–80.5 Gy) - SBRT (10 pts, 30%): 50 Gy (22.5–60 Gy)	Median dose all patients: 50 Gy (20–70.2 Gy) - EBRT (3 pts, 9%): 66-70,2 Gy - SBRT (30 pts, 91%): 50 Gy (20–54 Gy)	3D IMRT SBRT	1 G5 aorta-esophageal fistula
2014 [2004-2010]	Kruser, Am J Clin Oncol.	R	48	19.1	- NSCLC median 57 Gy (range 30–80.5 Gy) - SCLC median 45 Gy (range 12–54 Gy)	- NSCLC median 30 Gy (range 12–60 Gy) - SCLC median 37,5 Gy (range 25-45 Gy)	IMRT (92%) 2D, 3D	1 G4 late bronchostenosis
2014 [unknown]	Trovò, Int J Radiat Oncol Biol Phys.	R	17	18	50-60 Gy in 20-30 fractions	30 Gy in 5 (12) or 6 (5) fractions	SBRT	1 G5 radiation pneumonitis 1 possible G5 hemoptysis
2017 [2010-2015]	Chao, Journal of Thoracic Oncology	P, multi-institutional	57	19	Unknown	Median total dose 66.6 Gy (range 30–74 Gy)	Proton	3 G4 neutropenia 1 G4 pericardial effusion 1 possible G5 bronchopulmonary hemorrhage 1 possible G5 neutropenic sepsis 1 probable G5 anorexia 1 probable G5 pneumonitis 1 possible G5 hypoxic respiratory failure/pleural effusion 1 probable G5 tracheoesophageal fistula

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TOLERANCE OF ABDOMINAL ORGANS AT RISK TO ABDOMINAL RE-IRRADIATION: A SYSTEMATIC REVIEW

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Aims: Local recurrence of abdominal malignancies are common and can be associated with significant morbidity and mortality. Re-irradiation may represent a therapeutic choice, although it is often limited by dose constraints of surrounding organs, as small bowel. A systematic review regarding the feasibility of abdominal re-irradiation was performed, investigating the relative tolerance of abdominal organs at risk (OARs).

Methods: MEDLINE and EMBASE databases were used for a systematic search strategy. Terms related to re-irradiation and abdominal malignancies were included. The computer search was supplemented with hand searches of reference lists. The selected criteria were: full test English articles, published from January 1995 to December 2017, retrospectively and prospectively analysing, at least 10 patients, reporting toxicity and/or safety as outcomes. Re-irradiation fractionation and total dose and techniques used were analysed. Toxicity scales, types and incidences were examined.

Results: Forty-six articles were identified, of which 9 resulted appropriate for the inclusion criteria. Studies were small and data largely retrospective. In total, 203 patients have been reported, undergoing different prior abdominal irradiation techniques. Patients received several previous total (mean: 51 Gy) and fractionated doses (conventional fractionation in the majority of the studies). Time relapsed since previous irradiation and follow-up after re-irradiation resulted in median 19 months (range: 1-316 months) and 15.6 months (range: 1-77 months), respectively. Re-irradiation was mostly delivered by stereotactic (SBRT: 5 studies), followed by brachytherapy, proton external beam, 3D conformal and IMRT intensity modulated (IMRT) techniques. Few information was provided regarding organs at risk constraints adopted in the re-irradiation setting. Median follow-up was 13 months (range: 7.5-34.5 months). Globally, treatment was well-tolerated: 29 (14.3%) patients experienced mainly gastrointestinal acute or late episodes of grade 3-4 toxicities. The rate of acute and late toxicities has been paired to cumulative dose.

Conclusions: Based on preliminary results, abdominal re-irradiation seems to be safe and feasible, with acceptable acute and late toxicities rates. Statistical analysis is still ongoing and we are waited for final results. Considering the few studies available, prospective studies seem to be necessary to optimise future treatment approach.

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A SYSTEMATIC LITERATURE REVIEW OF ORGAN AT RISKS (OARS) TOLERANCE FOR PELVIC TUMORS RE-IRRADIATION

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Aims: Local recurrence of pelvic malignancies causes severe symptoms, which significantly impacts quality of life and patient prognosis. Re-irradiation could be effective for relieving symptoms and improving local control, but it is often not recommended because of the extremely high incidence of complications in normal tissues. A systematic review concerning re-irradiation of pelvic malignancies was performed, investigating the feasibility in term of acute and late toxicities and the relative tolerance of pelvic organs at risk (OARs).

Methods: A systematic search strategy was adopted using MEDLINE and EMBASE databases. The computer search was supplemented with hand searches of reference lists. The inclusion criteria were: full test English articles, published from January 1995 to December 2017, retrospectively and prospectively studies analysing at least 10 patients, reporting toxicity and/or safety as outcomes. Total dose and fractionation of re-irradiation and techniques adapted were analysed. Toxicity scales, types and incidences were examined.

Results: One hundred and eighty-three articles were identified, of which 36 resulted appropriate for the inclusion criteria. Studies were small and data largely retrospective. In total, 1209 patients have been reported, undergoing different prior pelvic irradiation, with photon external beam as stereotactic, intensity modulated, 3D conformal or 2D radiotherapy, proton external beam or electron ones. Dose and fractionation schedules are variable among studies. Time relapsed since pre-

vious irradiation resulted in median 27 months (range: 0-789 months) and follow-up after re-irradiation resulted different in these several studies, in median 20.65 months (range: 0-172). Little information is provided regarding organs at risk constraints adopted in the re-irradiation setting. Globally, treatment was well-tolerated: 316 (26.1%) patients experienced mainly genitourinary and/ or gastrointestinal acute or late grade 3 toxicities, 37 (3.1%) patients an episode of grade 4 and only 2 of grade 5 toxicity. The rate of acute and late toxicities has been paired to cumulative dose.

Conclusions: The review is still ongoing but, from the preliminary results, re-irradiation seems to be feasible and safe, with acceptable acute and late toxicities rates. Prospective studies seem necessary to optimise future treatment approach.

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HIGH-DOSE IONIZING RADIATION INDUCES GENE-EXPRESSION SIGNATURES IN PRIMARY BREAST CANCER CELLS

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Aims: In breast cancer (BC) care, radiation therapy (RT) is an efficient treatment to control localized tumor. However, BC is a heterogeneous disease at both clinical and molecular levels and the RT success is also related to specific molecular characteristic of BC subtypes, since approximately 90% of BC related deaths are linked to cancer metastatic progression. Moreover, radiobiological research is needed to understand molecular differences that affect radiosensitivity of different tumor subtypes and response variability. The aim of this study was to analyze gene expression profiles (GEPs) in primary BC cells following irradiation with 9 Gy and 23 Gy delivered by intraoperative electron radiation therapy (IOERT) in order to define gene signatures of response to high doses of ionizing radiation (IR), which affect the death/survival balance.

Materials and Methods: We performed GEPs by cDNA microarrays and evaluated cell survival after IOERT treatment in three primary BC cell cultures (a normal epithelial, an ER+/PR+/HER2− and a triple negative ER−/PR−/HER2− cell line). Real-time quantitative reverse transcription polymerase chain reaction (qRT-PCR) was performed to validate candidate genes.

Results: We selected a 4-gene and a 6-gene signatures, as new molecular biomarkers of radiation cell response in primary BC cell cultures after exposure at 9 Gy and 23 Gy respectively. Overall, the IR-induced GEPs and related pathways appear to be cell-line dependent and linked to the HR status.

Conclusions: Gene signatures activated by IR may predict response to RT and could contribute to defining a personalized biological-driven treatment plan.

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EFFECTS OF PELVIS RADIOTHERAPY ON PERIPHERAL BLOOD LYMPHOCYTE SUBPOPULATIONS IN PROSTATE CANCER PATIENTS: STANDARD FRACTIONATION VS MODERATE HYPOFRACTIONATION

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Aims: Radiotherapy (RT) is an important treatment in patients with localized prostate cancer. Unfortunately, during pelvis radiotherapy (PRT), radiations impair bone marrow activity, and cause peripheral leukocyte count decrease, particularly lymphocytes. The purpose of our study was to evaluate the changes in the different peripheral blood lymphocyte subpopulations after PRT in a group of patients irradiated for prostate cancer. We also studied the correlation between these changes and different radiotherapy techniques and dose-fractions.

Methods: Thirty-two patients (median age 76, 58-91) affected by prostate cancer were enrolled into the study. Sixteen of them (50%) had received hormonetherapy, none chemotherapy. PRT with radical (n. 22) or salvage (n. 10) intent was given. Nineteen patients underwent hypofractionation (2,7-3,1 Gy) using Rapid Arc (RA) technique, with a prescription dose to the planned target volume (PTV) of 73-78 Gy. In 13 conventional fractionations (1,8-2 Gy), using 3D conformal technique, prescription dose to PTV was 62-67,5 Gy. Absolute counts of white blood cells (WBC) and lymphocytes (ALC) were collected at baseline, at the end of RT and at follow-up, after three and six months. Lymphocyte subpopulations (total T, T CD4+, T CD8+, regulatory T cells - Tregs, NK and B cells) were analyzed, at the above-mentioned time points, by FACSCanto II flow cytometer (BD Biosciences) and 6-color antibody combination approach.

Results: We found that the absolute value of WBC, ALC and of all the lymphocyte populations (T, B, NK, Tregs, T CD4+, T CD8+) had significant variations (Kruskal.test < 0,05) during the 4 time points considered (Figure 1). In particular, ALC, Tregs, total T cells, T CD4+ and T CD8+ cell values at the end of PRT correlated (p value adjusted < 0,05) with fractionation, that is they were higher in the hypofractionation group.

Furthermore, we found no correlation between different techniques and lymphocyte values variations or acute/chronic gastro-intestinal and genito-urinary toxicities. However, there was a trend for a less cases with prolonged hematological toxicity better, in hypofractionation group respect to the conventional fractionation group, for WBC (27% vs 82%) and ALC (0% vs 36%) absolute values respectively.

Conclusions: These preliminary data show that a significant and durable decrease occurs in all lymphocyte populations, at the end of PRT. The RA technique and hypofractionation are able to reduce such a toxicity.

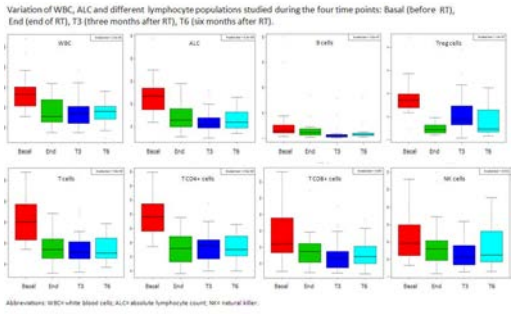

Figure 1.

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PROGNOSTIC AND PREDICTIVE CA 19-9 ROLE IN RADIOTHERAPY OF PANCREATIC CANCER: A REVIEW

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Aims: The role of CA19-9 as a prognostic and predictive biomarker in pancreatic adenocarcinoma (PAC) has been widely investigated and several results have been reported. Despite the increasing number of biomarkers studies, there is no well-established role for Ca19-9 in RT of PAC. Aim of this review was to collate the evidence and assess the prognostic and predictive impact of CA19-9 in PAC RT.

Methods: A review of literature was performed searching on PubMed "CA 19-9, pancreatic cancer, radiotherapy" without any time limits. Only articles with CA 19-9 evaluation as primary or secondary endpoint were considered. All patients underwent neoadjuvant or adjuvant or definitive chemo-radiotherapy (CRT).

Results: In pre-operative setting, CA 19-9 was found to be prognostic indicator for overall survival (OS), local control (LC) and distant metastases (DM) and predictive for effectiveness and response to neoadjuvant therapies. It is associated with "borderline resectable" features and response according to RECIST criteria. In patients treated with definitive CRT, low pre-treatment CA 19-9 predicts better response probability after CRT and/or RT, while a decrease after treatment was correlated to response, LC, prolonged time to DM and OS. A definitive cut-off has not been found. Most of the series were retrospective. To date, only one phase III trial was performed to assess the prognostic and predictive impact of CA 19-9.

Conclusions: CA 19-9 seems to have a predictive role in different settings of PAC RT. Therefore, it could be evaluated for inclusion in predictive model for this disease.

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IMPACT OF ANTHOCYANIN SUPPLEMENTATION ON THE SKIN SIDE EFFECTS OF RADIOTHERAPY IN PATIENTS WITH BREAST CARCINOMA: PRELIMINARY RESULTS (FP7 EUROPEAN UNION ATHENA PROJECT)

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Aims: The role of anthocyanins has been studied in the prevention of radiotherapy (RT) side effects. In a prospective randomized study, we verified the impact of anthocyanin supplementation on acute and medium-term skin side effects of RT in breast cancer (BC) patients.

Methods: A double-blind randomized clinical trial with 2 parallel arms (A and B) was designed. BC patients were randomized to assume a preparation containing 125 mg anthocyanins (3 times a day) versus placebo. Supplementation started 1 week before and lasted till the end of RT. One group of patients (MARA3) received 44 Gy simultaneous integrated boost (SIB) over 16 fractions in 3 weeks by an hybrid IMRT class solution; the other group (MARA4) received 60 Gy SIB over 25 fractions in 5 weeks. Patients used a moisturizing cream (® Atonderma) during RT. Clinical evaluation was performed at the end of treatment and skin toxicity was graded according to RTOG score.

Moreover, skin parameters, as elasticity (R0, R2 and R5 values), erythema (Mexa_Er) and pigmentation (Mexa_M), were measured in predefined areas of the irradiated breast and in the contra-lateral one through a specific device (Cutometer® dual MPA 580), before (T0), at the end (T1) and 1, 6 and 12 months after RT.

Results: 242 patients were eligible and 195 were randomized to groups A and B (Figure 1). Both clinical and cutometer evaluations failed to show differences in terms of skin toxicity (elasticity, erythema and pigmentation) between groups A and B. The elasticity parameters R0 (p=0.54) and R2 (p=0.27) similarly decreased from T0 in both arms, while Mexa_M (P=0.74) and Mexa_Er (P=0.25) similarly increased in both groups, suggesting no protective effect of anthocyanin supplementation. Neither RT protocol seemed to differently affect elasticity parameters. However, the increase in Mexa_M and Mexa_Er was greater in MARA4 (5 week RT) than in MARA3 (3 week RT) (p=0.0027 and p=0.0087, respectively). Comparing irradiated and contra-lateral breast no differences were observed for R0(p=0.48) and Mexa_M(p=0.14) variations from T0 to T1. On the contrary, decrease of R2 and increase of Mexa_Er were observed only in irradiated but not in contra-lateral breast (p<0.0001). Clinical toxicity RTOG data did not correlate with variations in parameters recorded by cutometer.

Conclusions: Preliminary data failed to demonstrate that an anthocyanin supplementation can effectively protect BC patients from skin side effects of two different RT regimens.

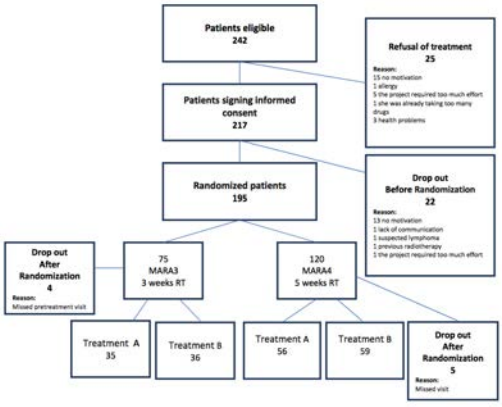

Figure 1. Study flow chart.

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PILOT STUDY ON IMMUNOMODULATION ROLE OF RADIOTHERAPY IN OROPHARYNGEAL CANCER: PRELIMINARY RESULTS

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Background: The discovery of the key role of the immune system in the pathogenesis of tumors prompted studies aimed at identifying immunological prognostic biomarkers. The encouraging results of immunotherapy in recurrent non-resectable head and neck cancer may indicate its potential efficacy, combined to conventional therapies, also as primary treatment. The aim of our study is to perform a comprehensive analysis of the circulating and intratumoral T cell compartments in patients affected by Oropharyngeal Squamous Cell Carcinoma (OSCC) to search for new prognosticators and to get insights on new possible immunotherapeutic strategies.

Methods: From May to November 2017 14 untreated patients affected by moderately to advance stage OSCC and treated by radiotherapy or chemoradiotherapy have been enrolled in the study; 6 healthy subjects have been included as control group. Analysis of the peripheral and intratumoral immunophenotype was performed by immunofluorescence and flow cytometry in order to analyze the frequency of CD4+ and CD8+ T cell subsets and to evaluate the expression of PD-1 and CTLA-4 immune checkpoints on T cells.

Results: Oncologic patients and controls showed, among circulating CD3+ T cells, comparable frequencies of CD8+ (42.0% vs 39.9%;p=0.99) and CD4+ (57.8% vs 59.5%;p=0.99) T cell subsets. With respect to control subjects, OSCC patients showed a reduction of naïve CD8+ (33.3% vs 47.5%;p=0.01) and effector memory CD4+ (22.3% vs 35.2%;p=0.01) T cells associated with an increase of terminal effector memory CD8+ cells (32.8% vs 12.1%;p=0.02) and central memory CD4+ (38.5% vs 21.5%,p=0.01) T cells. Moreover, the frequency of circulating CD3+PD-1+ T cells was significantly higher in cancer patients than in healthy subjects (29.8% vs 14.5%;p=0.04): interestingly, the frequency of CD3+PD-1+ and CD3+CTLA-4+ T cells was remarkably more elevated at the tumor site than in the circulation (86.6% vs 29.8% p<0.001 and 29.2% vs 8.8% p=0.002, respectively).

Conclusions: Our data, showing alterations of circu-

lating T cell subsets in OSSCC patients, corroborate the concept of the strong interplay between tumors and immune system. In this context, the significant increase of PD-1 expression by patients' T cells has a twofold relevance: it envisages tumor-driven expression of this immune checkpoint as a pathogenic mechanism for cancer development and progression, and pins point PD-1-specific immune checkpoint inhibition as a further therapeutic strategy in OSSC.

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RISK ADAPTIVE DOSE PRESCRIPTION IN CENTRALLY LOCATED EARLY STAGE NSCLC AND LUNG OLIGOMETASTASES

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Aims: Stereotactic ablative radiotherapy (SABR) is considered an effective and non-invasive approach in peripherally early stage non-small cell lung cancer (NSCLC) and lung oligometastases. Several experiences evaluated SABR in inoperable central (<2 cm from large bronchial tree) lung tumors located reporting unacceptable levels of severe lung toxicity. A "risk adaptive" dose prescription is considered a tool to minimize toxicity related to organs at risk (OAR) involvement. Aim of this study was to evaluate efficacy (local control) and tolerability of centrally located primary or metastatic central lung lesion, treated with a "risk adaptive" SABR approach.

Methods: Patients aged ≥ 18-years with a histological or radiological proof of single central early stage NSCLC or lung oligometastases were recruited. OAR were as follow: homo-controlateral lung, heart, spinal cord, esophagus, bronchial tree and chest wall. Total radiation dose was defined according to a "risk adaptive" approach. In the case of overlap between target and OAR, sparing of the OAR was favoured to target volume coverage. A number of daily fractions between 4 and 10 was prescribed. Radiological response was assessed according to RECIST, acute (<6 months) and late (≥ 6 months) clinical and radiological toxicities were scored using Ikezoe et al. criteria and Common Terminology Criteria for Adverse Events version 4.0, respectively.

Results: From January 2012 to December 2017, 30 patients with early stage or oligometastatic lung metastases received a SABR treatment. Median Biological equivalent dose prescription and fractions were: 105 Gy (range 96-119) and 10 (range 4-10), respectively. Median follow-up was 17 months. Local control was reported in 26 patients (87%), a local progression in 4 patients (13%). Early radiological abnormalities were identified as follows: no changes in 16 patients (53%), patch ground glass opacity in 9 (30%) and patchy consolidation and ground glass opacity in 5 (17%). Late radiological abnormalities were as follows: no changes in 6 cases (20%), scar-like pattern in 8 (27%), mass-like pattern in 10 (33%), not available in 6 cases (20%). Acute and late clinical pulmonary toxicity ≥ grade 2 were recorded in 2 out of 30 patients (7%) and 3 out of 24 patients (12%).

Conclusions: SABR "risk adaptive" prescription in inoperable central lung tumors seems to be a safe and efficacy treatment. Higher accrual and follow-up are necessary to confirm these prominsing data.

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SHORT-COURSE REGIMEN OF PALLIATIVE RADIOTHERAPY IN COMPLICATED BONE METASTASES: A PHASE I-II STUDY (SHARON PROJECT)

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Aims. Metastases with soft tissues invasion, impending fractures or spinal cord compression (complicated bone metastases) represent a common clinical problem in advanced cancers and frequently lead to deterioration of patients' quality of life (QoL). In this study we try to define the maximum tolerated dose (MTD) of a short-course radiotherapy and its efficacy in palliation of complicated bone metastases.

Methods. A phase I trial was designed with three dose-escalation steps: 16, 18, and 20 Gy. Total dose at each level was delivered in two days, twice daily. Eligibility criteria were painful complicated bone metastases and ECOG performance status < 3. The presence of acute toxicity > Grade 3 (RTOG scale) was considered the dose limiting toxicity. The MTD was used to plan a phase II trial with pain response as the primary outcome. Pain was recorded using a Visual Analogic Scale (VAS), and QoL using CLAS scales.

Results. Forty-five patients were enrolled in this trial. In phase I no Grade > 2 acute toxicities were recorded. Thus 20 Gy was established as MTD. In phase II, with a median follow-up of 4 months, rates of complete symptom remission, partial response, no symptomatic change, and symptoms progression were 32.0%, 52.0%, 8.0%, and 8.0%, respectively.

Conclusions. This RT protocol tested in our study is

effective and tolerable with comparable results to traditional RT treatments delivered in 5-10 daily fractions.

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HYPOFRACTIONATED RADIOTHERAPY (RT) AFTER CHEMOTHERAPY (CHT) IN LUNG CANCER (LC): A NEW STRATEGY TO OVERCOME RADIATION RESISTANCE IN STAGE III-IV LUNG CANCER PATIENTS

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Aims: Treatment for locally advanced LC still results in poor clinical outcome. Recently, RTOG0617 failed to demonstrate the superiority of dose escalated RT concomitant to chemotherapy in stage III Non Smalll Cell LC probably due excess toxicity, among other factors, but suggested that IMRT results in better outcome. Treatment acceleration seemed to improve results in a metaanalysis and moderate accelerated HRT is currently prospectively tested in RTOG1106. Aim of our analysis is to evaluate clinical outcomes and toxicity of HRT applied in pts with stage III-IV (oligometastatic) LC.

Methods: After obtaining ethics committee approval, we retrospectively analyzed 73 consecutive pts with LC referred to our Radiotherapy Unit and treated with HRT between 2009 and 2016. Fifty-two pts were male and 21 female. Mean and median age were 72,3 (range 47-90) and 70 years, respectively. All pts had histologic proof of LC (39 pts had Squamous Cell Carcinoma, 20 Adenocarcinoma, 13 Neuroendocrine carcinoma with only one case of pleomorphic lung carcinoma). Clinical stage was IIIB in 31 pts (42.4%), IIIA in 24 pts (32.8%), I-II in 10 pts (13.7%) and IV (oligometastatic) in 8. Mean PTV volume was 296 cc (21-861 cc). Sixty-three pts (86.3%) received systemic therapy before HRT in a sequential setting (59 platinum based, 4 Gemcitabine, 1 Gefitinib) and 8 of them received more than one regimen due to progression disease.

Results: All pts underwent HRT (range 39-66 Gy) with 42 pts receiving 39-51 Gy in 13-17 fractions (fx), while 30 pts received 61.6-66 Gy in 28-30 fx (2,2-2,7 Gy/die). Different techniques were used to deliver HRT: 39 pts underwent Tomotherapy, 17 pts VMAT, 16 pts 3DcRT, and only one static IMRT. At analysis after a median follow up of 14.2 months 12 pts were alive with a 1- and 3-year Overall Survival of 54,3%±5.4ES and 20%±4,9ES respectively. Median Progression Free Survival of the entire population was 5.5 months while 1- and 3-year local control were 41.3%±6.3SE and 18.2%±4.9SE. Patient, tumor and treatment feature variables were analyzed with univariate analysis for OS, PFS and LC. Particularly, histology, clinical stage and total RT dose seems to increase OS in favor of non-neuroendocrine histology ($p<0,02$), stage I-IIIA ($p<0,04$) and delivered dose superior than 60 Gy ($p<0,02$) respectively. Regarding toxicity, no G3 or more acute side effects were observed, while 1 case of G4 and 1 G5 radiation induced pneumonitis as subacute side effects were reported.

Conclusions: In selected pts affected by locally advanced and or oligometastatic LC, HRT seems to be feasible, well tolerated, effective and seems to represent an efficient treatment. Higher RT doses seem to confer better results. HRT needs further investigations through prospective clinical trials to confirm the real benefit induced by a shorter total treatment time concomitantly with higher dose per fx and to define appropriate dose volume constraints.

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BASELINE HEMOGLOBIN LEVEL AND XRCC1 POLYMORPHISM TO INCORPORATE CISPLATIN IN STANDARD CAPECITABINE-BASED NEOADJUVANT CHEMORADIOTHERAPY FOR RECTAL CANCER

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Aims: Optimal neo-adjuvant chemo-radiation (CRT) up to pathological complete response (pCR) may favor conservative surgical procedures for locally advanced rectal adenocarcinoma (RA). Cisplatin has rarely been used to enhance CRT response. .The present study aimed to evaluating whether baseline biochemical variables and genetic profiling of genes involved in DNA repair and chemotherapy metabolism identified patients who would benefit from the addition of Cisplatin to standard CRT for RA.

Methods: Consecutive patients with locally advantaged histologically confirmed RA were treated with standard pelvic radiotherapy (45 Gy/25 fraction plus boos 5 .4 Gy/) and concurrent capecitabine (825 mg/m^2 twice daily days 1 - 14 and 22 -35) plus cisplatin (40 mg/m^2 once every three weeks). Surgery was planned at 8-10 weeks after the end of CRT. Eight cycles of standard adjuvant, FOLFOX was offered to all patients. Common biochemical variables at baseline and germiline polymorphism in the following genes: GSTP1, XRCC1, ERCC1, UGT1A1, CYP3A5, MTHFR, werw analysed as potential predictors of pCR.

Results: Fifty-one patients (male:female, 35:16 pts, median age 63 years, range 41-77), were enrolled. Clinical stage was II –III. Radical abdominoperineal and abterior resection was performed in 36 and 12 patients, 3 patients underwent palliative sugery. pCR (regression AJCC grade 0) was documented in 7 patients, nearly complete response (AJCC grade 1) in 10 patients. There was a strong association between DFS and AJCC grade, with a 3 –year-DFS of 100%, 79% and 33% for AJCC grade 0-1, grade2 and grade 3, respectively, p 0.0047. High frequency of grade 3-4 toxicities, we observed (35% of patients). Among common cinical e biochemical variables, baselin hemoglobin (Hb) was significantly associated with pCR, p

0.027, meaning a 48% increasing chance of having a pCR for 1-unit increase in baseline Hb. As for pharmacogenomics analysis, XRCC1 rs25487 polymorphism was significatently associated with pCR, 70% vs 18%, for XRCC1 rs25487GG vs GA+AA, Odds Ratio 25.8, p 0.049. XRCC1 rs 25487 GG was also associated with higher baseline Hb levels.

Conclusions: Despite a good tumor AJCC regression rate, the high occurrence of grade 3-4 toxicities with CisCape CRT makes this regimen not suitable for larger phase III trials in all RC patients. Hower, baseline Hb and XRCC1 polymorphism may represent possible patients' criteria for this intensive treatment strategy.

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EARLY-SALVAGE RADIOTHERAPY TRIAL (EASY TRIAL) IN PATIENTS AT INTERMEDIATE RISK AFTER RADICAL PROSTATECTOMY

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Aims: To describe preliminary data about a protocol based on close PSA monitoring after radical prostatectomy and early salvage radiotherapy in no-metastatic patients at intermediate risk of biochemical and/or clinical relapse.

Methods: Selected histologically proven prostate cancer patients undergoing radical prostatectomy with or without lymphadenectomy and one of these pathological features: pT2-R1, pT3a-R0, pT3a-R1, pT3b-R0 and pN0 and undetectable PSA level after surgery were included. PSA test every two months was performed and 68Ga-PSMA PET/CT was planned in patients with increased PSA. Patients with two consecutive postoperative raised PSA or at least 1 postoperative PSA > 0.2 ng / ml and negative 68Ga-PSMA PET/CT for extrapelvic disease localization were treated with salvage radiotherapy. No hormonal therapy performed before or after prostatectomy was allowed.

Results: From October 2016 to May 2017, 150 patients < 80 years old were enrolled: 41, 67, 27, and 15 were pT2-R1, pT3a-R0, pT3a-R1, and pT3b-R0, respectively. To date only 10 case of biochemical relapse was recorded. After negative 68Ga-PSMA PET/CT, this patient underwent radiotherapy on prostate bed with 66 Gy in 30 fractions (2.2 Gy per fraction) and follow-up started.

Conclusions: Longer follow-up and larger series will allow to evaluate the role of early salvage strategy and its efficacy in terms of biochemical relapse free survival.

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CHEMO-RADIOTHERAPY FOLLOWED BY STEREOTACTIC BOOST IN UNRESECTABLE PANCREATIC CANCER PATIENTS. AN INNOVATIVE APPROACH

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Aims: to evaluate feasibility and toxicities of a stereotactic boost in unresectable pancreatic cancer patients previously submitted to external beam irradiation and chemotherapy.

Methods: From May 2016 to April 2018 we retrospectively analysed all patients affected by unresectable pancreatic cancer treated with radiotherapy (RT) in our centre. Among these we evaluated the records of patients submitted to stereotactic body (SBRT) boost after external beam RT.

Results: In the period of observation six unresectable pancreatic cancer patients were submitted to external beam irradiation. These patients had previous biopsy with histological diagnosis of pancreatic adenocarcinoma; nobody underwent surgery. At the time of primary diagnosis staging was cT4, cN0/1, cM0. All patients received neoadjuvant chemotherapy (4/6 GEM+ABRAXANE; 2/6 GEM) followed by external beam radiotherapy (V-MAT 4 patient; IMRT 2 patient) delivering a median total dose of 50.6 Gy (range 50-51.25 Gy). Two patients had early progressive disease with liver metastases; two patients currently are submitted to external beam; two patients were treated with consecutive stereotactic boost delivering a median total dose of 11Gy/1 fraction (range 10-12 Gy). Patients treated with boost showed no significative acute toxicities: 1/2 patient had nausea G1 and diarrhea G1. 1/2 patients had nausea and vomit G2. Up-to-date the two stereotactic patients are alive: one 12 months with local recurrent disease, and one three months without sign of clinical recurrence.

Conclusions: No data exists on the sequential use of SBRT after EBRT. The very preliminary data observed in our study seems to indicate that this kind of therapy

could be emerge as a novel therapeutic option in this clinical scenario. More data are necessary to verify this hypotheses.

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ABSTRACT WITHDRAWN

P334

RADIUM-223 DICHLORIDE FOR METASTATIC CASTRATION RESISTANT PROSTATE CANCER PATIENTS. A RETROSPECTIVE EXPERIENCE

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Aims: Radium-223 (Ra-223) dichloride is an α-emitting radiopharmaceutical currently approved for treatment of metastatic castration-resistant prostate cancer (mCRPC) patients with symptomatic bone metastases. Ra-223 is the only bone targeted agent which showed to provide significant survival benefit in this setting if compared with placebo. In the current series, we retrospectively collected and reviewed data about patients treated in our institution with Radium-223 dichloride, exploring safety and clinical benefit outcomes in a real world scenario.

Methods: We collected data from clinical records of 16 consecutive mCRPC patients treated with Ra-223 at our institution since June 2016 to April 2018. All patients were evaluated by a radiation oncologist from our department and deemed suitable for this treatment strategy on the basis of presence of progressive metastatic disease with castration testosterone levels and predominance of symptomatic bone metastatic lesions. Data about clinical benefit in terms of symptoms palliation measured with Numerical rating scale (NRS), skeletal related events (SRE) and tolerability were reported.

Results: Average follow up was 8.7 months. All patients received at least 1 previous line of systemic therapy for mCRPC, and 9 out of 16 patients (56.2%) had been treated with at least 1 previous line of chemotherapy (Docetaxel, Cabazitaxel). Thirteen patients (81.3%) were alive at last follow up visit. Of note, 9 patients had at least one cardiovascular coexisting comorbidity. Nine out of 16 patients (52.6%) had a significant improvement in pain symptoms measured with NRS scale (at least one point reduction after treatment if compared to baseline), and no pain deterioration was reported. Two patients are currently still on treatment (2 and 1 cycle received, respectively), and average number of cycles administered in the rest of population is 4.3 (range 1-6). Unfortunately, 9 patients (52.6%) did not manage to complete all the 6 planned injections due to >G2 anemia. No SRE were reported.

Conclusions: Clinical benefit of Ra-223 treatment was confirmed in this heavily pretreated and fragile population, despite the low number of patients completing the whole planned treatment. mCRPC patients should be evaluated earlier for this treatment strategy in order to maximize clinical benefit.

P335

ZINC-L-CARNOSINE (HEPILOR) PREVENTS DYSPHAGIA IN LOCALLY ADVANCED BREAST CANCER PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY: RESULTS OF PHASE III RANDOMIZED TRIAL

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Aims: Irradiation of level III and IV draining nodes in breast cancer patients is often associated with dysphagia, requiring treatment with FANS and/or steroids. The present randomized phase III trial determined whether Zinc-L-Carnosine (ZLC, Hepilor), prevents or delays the onset of dysphagia in these patients.

Methods: December 2015-October 2017: 40 breast cancer patients undergoing radiation therapy (RT) to the breast or chest wall and level III and IV lymph-nodes were randomized to receive ZLC or placebo. All underwent RT with Tomotherapy at a total dose of 50 Gy in 25 fractions. 11/40 (27,5%) women who had received conservative surgery were given a 10 Gy boost to the tumor bed, using a simultaneous instantaneous boost technique. The primary end-point was no dysphagia, as evaluated by the CTCAE v 4.0 and EAT-10 questionnaire. The trial was approved by the Regional Ethics Committee and all patients gave signed informed consent. The Chi-square and Mann-Whitney tests analyzed differences between ZLC and placebo arms. The Kaplan-Meier test estimated the cumulative incidence of dysphagia and the log-rank test compared results. Univariate Cox regression analysis tested relations between toxicity and prognostic factors.

Results: All patients completed RT. Treatment arms were matched for age, chemotherapy (CT) and administration of trastuzumab and hormonal therapy (HT). Overall, the median age was 56 years (range 28-82); 93% received CT before RT, 35% and 70% received, respectively, Trastuzumab and HT during RT. The esophagus median maximum dose (Dmax) was significantly higher in the placebo arm (p=0.005). The median dose to the esophagus was similar in both groups (p=0.76). Nine (45%) patients in the ZLC arm and 20 (100%) receiving placebo developed G1-G2 dysphagia during RT (p<0.0001). No patient developed >G2 dysphagia. Five ZLC patients (25%) and 17 (85%) pla-

cebo patients with dysphagia required steroid treatment. ZLC was associated with a later onset and lower risk of G1-G2 dysphagia during RT (cumulative incidence 55.2%, 95%CI: 29.4-81.1 vs 100%, 95%CI: 85.4-100, p<0.0001) . Univariate analysis showed esophagus Dmax was not a significant risk factor for dysphagia.

Conclusions: In our phase III trial ZLC significantly prevented or delayed the incidence of dysphagia in breast cancer patients undergoing RT to the draining nodes. Consequently, the need for steroid therapy was significantly reduced.

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VI-RT-US PROJECT: HOW TO EXPLORE ETHICAL ISSUES IN RADIATION ONCOLOGY

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Aims: The physician who treats cancer patients is particularly exposed to ethical problems in his daily routine. The aim of this review was to explore ethical dilemmas related to Radiation Oncology.

Methods: The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two authors did a review of citations from PubMed. The search was conducted using the matching "Ethics in radiotherapy" or "Ethical dilemmas in radiotherapy" or "Ethical dilemmas in radiation oncology"or "Ethical challenges in radiotherapy" or "Ethical challenges in radiation oncology" or "Ethics in radiation oncology" or "Ethical issues in radiotherapy" and "Ethical issues in radiation oncology". Exclusion criteria included: articles not written in English, duplicates and not pertinent.

Results: Our systematic search yielded 1928 potentially relevant abstracts and titles from PubMed. Of these, 1885 articles were immediately excluded according to the reported criteria and a further 17 were excluded after review. A total of 26 appropriate articles (1.3%) were included. Of this number 42% were discussions in medical and scientific journal articles, 27% were reviews and 19% were surveys. The United States produced the majority of the ethical research (77%), followed by Europe (15%). A significant increase of interest in ethics and radiotherapy occurred from 2000 with a rise of the number of published articles during a 20 years period. Although the majority of articles addressed more than one of ethical issue, the most common topic was the ethics of clinical research and it's applications with new technologies.

Conclusions: From this review the key points of the ethical debate emerge in the field of radiation oncology. Awareness of these issues, open discussion and training will help the radiation oncologist to treat patients in the best possible way.

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PRELIMINARY RESULTS OF A PHASE II STUDY OF INDUCTION FOLFIRINOX FOLLOWED BY RADIOCHEMOTHERAPY IN BORDERLINE RESECTABLE OR UNRESECTABLE LOCALLY ADVANCED PANCREATIC CANCER

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Aims: The aim of this study was to evaluate the safety and efficacy of induction FOLFIRINOX followed by a high weekly dose of gemcitabine-based radiochemotherapy in patients with borderline resectable or unresectable locally advanced pancreatic cancer.

Methods: This trial was performed as a single-center one-armed phase II study. From January 2015 we evaluated twenty-two patients with borderline resectable or unresectable pancreatic cancer (characteristics of patients are summarized in Table 1). A pre-treatment staging was performed with CT scan, 18FDG PET-CT scan and laparoscopy. Patients with metastatic disease were excluded. Suitable patients received chemotherapy with Folfirinox (four cycles every 14 days). Patients without disease progression after restaging received conformal radiation therapy with concurrent gemcitabine at the dose of 600 mg/mq weekly.

Table 1.

Characteristic	No of patients (N = 22)	%
Age (years)		
Median	63.5	
Range	48-79	
Sex		
Male	10	45,5
Female	12	54,5
ECOG performance status		
0	22	100
1	0	0
CA 19-9 at diagnosis, U/mL		
Median	4219	
Range	<2–8945	
Tumor localization		
Head	18	81,8
Body/Tail	4	18,2
Resectability status		
Borderline resectable	6	27,3
Locally advanced unresectable	16	72,7

Results: Further to the results of the pre-treatment workup, nine patients (40,9%) were excluded from the protocol because of the evidence of metastatic disease, and thus a total of thirteen patients were consequently enrolled. Five patients (38,5%) had a progression of disease after induction chemotherapy. Eight patients (61,5%) completed radiochemotherapy. Of these, four patients underwent surgical radical resection (30,8%).

At the present, the median Overall Survival was 13,8 months and the median Progression Free Survival was 18,9 months. For the entire cohort of patients the treatment was well tolerated. Only haematological grade 3-4 toxicities were observed.

Conclusions: Altough the follow-up time is limited, these preliminary data of the protocol treatment show promising results for patients with borderline resectable and unresectable pancreatic cancer. The enrollment is actually ongoing. Continued optimization in multimodality therapy and an accurate patient selection are crucial for the appropriate treatment of patients.

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A PROSPECTIVE COHORT STUDY EXPLORING ACUTE CARDIAC TOXICITY IN RADIOTHERAPY FOR STAGE III NON-SMALL CELL LUNG CANCER

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Aims: The aim of this study is to estimate the overall and the individual incidence of any early cardiac events in patients treated by radiochemotherapy (RCT) for stage III NSCLC.

Materials and Methods: This trial is a prospective, observational cohort-study. The inclusion criteria are: patients aged >18 years with histology or cytology proven NSCLC, with stage III or intra-thoracic relapse after surgery, who required RCT. We have excluded all patients with previous thoracic radiotherapy and metastatic disease. At the beginning of treatment, all patients have been undergone screening tests including clinical history, physical examination, blood chemistry (including lipid dosage, cardiac markers as TnI, NTproBNP, CKMB, myoglobin, and C-reactive protein), 12-leads ECG, transthoracic echocardiogram and cardiac MRI. A weekly evaluation has been detected during treatment with ECG and cardiac marker assays (early evaluation) and another evaluation at 1 month and 3 months after the end of RCT by performing ECG, cardiac markers, echocardiograms and cardiac MRI (late evaluation).

Results: The enrollment of the trial is ongoing. At the present time, 6 patients with stage III NSCLC have been enrolled, all males and smokers. Four of them had cardiovascular risk factors. Three patients concluded the treatment, the others are ongoing. No acute cardiac event was detected during treatment. Only one patient presented increased cardiac markers in the absence of symptoms and alterations to the ECG. With a median follow-up of 8 weeks, four patients had a partial response, two patients developed a progression of disease. Five patients are alive.

Conclusions: These preliminary data shown that no acute cardiac events have been reported in patients undergoing RCT for stage III NSCLC. Therefore in the next future we may have data that allow us to estimate the overall and individual incidence of any early cardiac event in these patients and to identify any variables that cause an increased risk of acute cardiac events.

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EFFICACY AND SAFETY OF STEREOTACTIC BODY RADIATION THERAPY SBRT WITH CONCURRENT TRABECTEDIN IN METASTATIC SOFT-TISSUE SARCOMA PATIENTS. A SINGLE INSTITUTION EXPERIENCE

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Aims: The aim of this observational monocentric study is to assess the efficacy and safety of Trabectedin administered concurrently with stereotactic body radiation therapy (SBRT) in patients with metastatic soft-tissue sarcomas (STS).

Methods: Twelve metastatic STS patients treated with SBRT to metastatic sites and concomitant Trabectedin between 2009 and 2017 were retrospectively analyzed. Trabectedin dose was 1.5 mg/m^2 in 24-hour infusion every 3 weeks. SBRT was performed within 5 weeks from last Trabectedin infusion with Volumetric Modulated Arc Therapy (VMAT); dose prescription was prescribed depending on tumor site and size. Overall response rate was assessed using Response Evaluation Criteria in Solid Tumors version 1.1.For clinical evaluation, we used Numerical Rating Scale (NRS)for pain response, Common Terminology Criteria for Adverse Events scale version 4.03 and RTOG Common Toxicity Criteria for radiation adverse events.

Results: The median age at diagnosis was 47.5 years (range 19-68). Histopathologic subtypes were leiomyosarcoma (33.3%), spindle and pleomorphic sarcoma (25%), synovial sarcoma (8.3%), pleomorphic liposarcoma (8.3%), pleomorphic sarcoma (8.3%), spindle sarcoma (8.3%), malignant peripheral nerve sheath tumor (8.3%). Eight (66.7%) patients underwent neoadjuvant and/or adjuvant treatments, 4 (33.3%) patients had metastatic disease at diagnosis. Mean number of prior chemotherapy lines for metastatic disease was 1 (range 0-2). The median number of cycles received before SBRT was 2.5 (range 0-9). Metastases sites treated included bone (50%), soft tissue (25%), lung (16.7%), lymph nodes (8.3%); in seven patients (58.3%) lesions were painful and the mean NRS before SBRT was 5.28 (range 2-8). Anemia was the most common ≥3grade hematologic toxicity (25%) followed by thrombocytopenia (8.3%) and elevated transaminase (8.3%). Incidence of ≤2grade radiation dermatitis was of 16.6%; no≥3 grade radiation toxicities were reported. Onepathologic bone fracture was experienced. At a median follow-up of 39.4 months, 9 patients (75%) had a stable disease (SD) and 3 patients (25%) had a progressive disease (PD). The median time to progression (TTP) was of 34 months. At clinical evaluation three months after SBRT the median NRS was

1.85 (range 0-4).

Conclusions: Our experience demonstrated that SBRT associated with trabectedin, in patients with metastases from STS, increase the local metastases control with a favorable safety profile.

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HYPOFRACTIONATED IRRADIATION IN ADVANCED BREAST CANCER PATIENTS WITHOUT SURGERY

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Aims. Hypofractionated whole breast irradiation (HF-WBI) has been proved effective and safe and with even better results as for acute or late toxicity. Moreover it improves patient convenience, quality of life and it is advantageous in the medical care system because of reducing the costs. Many guidelines state that hypofractionation is the gold standard in some types of patients with well defined characteristics. The aim of this study is to report the results, in terms of tolerance and local control, of a medium-high whole breast hypofractionated regimen, in patients with locally advanced or local recurrent breast cancer.

Methods. From January 2017 a medium-high whole breast hypofractionated regimen (34 Gy/10 fr, 4 fr per week) in patients with locally advanced or local recurrent breast cancer, without previous radiation treatment was adopted in our Department. 12 patients were treated with 3D conformal radiotherapy (3D-CRT), 4 of them presented with local recurrence, the others with locally advanced disease. All of them underwent chemotherapy, before (9 patients) or after (3 patients) the treatment. Two of them underwent immunotherapy. All of them had pain symptoms, requiring specific medications. None of them underwent surgery.

Results. All patients completed the treatment with immediate benefit on objective and subjective symptoms. The tolerance was very good, in presence of acute skin toxicity not higher than G2 and, in the 2 cases with ulceration, resolution in 4 and 6 weeks, respectively. All of them presented a benefit on the pain, with reduction or interruption of specific therapy. As for late toxicity no indurations were observed nor pulmonary or cardiac symptoms. With a median follow up of 7,4 months all patients are alive and locally free from disease.

Conclusions. Hypofractionated whole breast irradiation has been proved effective and safe. In our experience this medium-high regimen was well tolerated and showed to improve the quality of life and to maintain the timing of systemic treatment, in patients with locally advanced or recurring breast cancer. Studies on a wide scale will be needed to confirm these initial evidences.

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HEMATOLOGIC PARAMETERS AS PREDICTIVE BIOMARKERS IN NON-SMALL CELL LUNG CANCER (HERMES-LUNG) FOR EARLY RESPONSE TO INDUCTION TREATMENT

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Aims: Systemic inflammatory response has been confirmed to have prognostic value in several types of cancer, including lung cancer. This study was aimed to investigate the utility of circulating inflammatory parameters in predicting early response to induction treatment (assessed by 18F-FDG PET-CT) in locally advanced non-small-cell lung cancer (LA-NSCLC) patients treated with a multimodality approach.

Methods: We retrospectively reviewed the medical records of patients with stage IIIA/IIIB NSCLC underwent multimodality approach, including surgery. Peripheral complete blood count were collected at baseline and after two cycle of induction treatment [2 cycles of platinum-based chemotherapy administered concurrently to LDRT (CT-LDRT, 40 cGy twice daily, 1-2 and 8-9 day)]: absolute neutrophil count (ANC), absolute platelet count (APC), absolute lymphocyte count (ALC), Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR). Patients were dichotomized according to the median value for each parameter. OS was estimated using the Kaplan-Meier method and logistic regression model was used for multivariable analysis.

Results: 53 patients [38 (71.7%) male, median age 67] with stage IIIA/IIIB NSCLC, treated between March 2009 and October 2016 were enrolled. In the overall population, median OS e median progression free survival were respectively 14 and 13 months. Kaplan-Meier survival analysis suggested that patients who experienced baseline high-APC, in comparison with low-APC, showed significant reduction in OS ($p=0.02$) and those with high-ANC, in comparison with low-ANC, showed only marginally reduction in OS ($p=0.05$). At univariate analysis, patients classified as early responders showed significant better OS ($p=0.0003$) than patients classified as non-responders. Using a logistic regression model we observed that increasing absolute platelet count (APC) at baseline

(p=0.046) and decreasing NLR at baseline (p=0.0186) were significant independent markers predictive of a early response to induction treatment (Area under the curve: 0.767; 95% CI: 0.6405-0.894 (DeLong)).

Conclusions: Lower baseline NLR might correlate to early response to induction treatment in NSCLC. Higher baseline APC, maybe in contrast with literature data might be used as a predictive biomarker but its role needs further evaluation. These findings allow to select patients, according to different risk group, for intensified local treatment and personalized therapy.

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IT AIN'T OVER TILL THE FAT LADY SINGS: A RETROSPECTIVE STUDY ON RHEUMATOID ARTHRITIS AND RADIOTHERAPY

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The purpose of this study was to evaluate whether radiotherapy in a cancer patient with rheumatoid arthritis is able to worse his symptomatology. From January 2005 to December 2015, 29 patients with rheumatic arthritis received radiotherapy for a cancer. The median age was 74 years and 68.9% were female. The average DAS28 before radiotherapy was 2,25±0,4. Radiation was prescribed for different cancer treatment and was delivered in 24 patients with a conventional daily dose (1.8-2Gy). Radiotherapy was well tolerated among patients, only four patients (13.8%) experienced a grade 3 acute toxicity. At 24 months, no grade 3 or higher late toxicity was observed. Six (20.7%) relapses occurred, all but one occurred within the first six months. The 6 and 12 months relapse-free survival were 82.8% and 79.3%, respectively. In conclusion, radiotherapy can increase rheumatoid arthritis relapses, especially when delivered with daily dose ≥ 5 Gy or when delivered with chemotherapy. Prospective studies are needed to confirm these results.

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INTER-OBSERVER VARIABILITY IN ORGANS AT RISK CONTOUR DELINEATION IN BREAST CANCER TREATMENT

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Aims: To compare contour delineation of organs at risk (OARs) in breast cancer treatment, performed by senior radiation oncologist (SRO), junior radiation oncologist (JRO), fellow radiation oncologist (FRO) and clinical specialist radiation therapist (CSRT).

Methods: The four operators contoured independently the following OARs on planning computer tomography (CT) datasets of 10 patients undergoing complementary radiotherapy treatment after a monolateral conservative quadrantectomy and sentinel lymph node biopsy: breast, esophagus, heart, kidney, left anterior descending artery (LAD), liver, spinal cord, stomach and trachea. The variability of contoured volumes between the four operators has been measured using the Dice Similarity Coefficient (DSC), with a threshold value of 0.7 considered as minimum level of good concordance and the Center of Mass Distance (CMD). The raw data were submitted to an Analysis of Variance (ANOVA) test. The significance P-value threshold was set to 0.01.

Results: Good results in terms of overlap were obtained for all considered OARs but LAD, for which mean DSC was 0.34 (±0.17, standard deviation), and esophagus, for which mean DSC was 0.66 (±0.06, standard deviation). For stomach, spinal cord and trachea, DSC was about 0.8 (±0.06, standard deviation), whereas for heart, liver, breast and kidney mean DSC was 0.88-0.93. Mean DCM was less than 1 cm for all organs and the standard deviation was higher that ±0.01 only for LAD and stomach. Considering couples of operators, mean DSC was superior to 0.7 in all cases and mean DCM inferior to 1 cm. The best mean overlap was obtained between JRO and CSRT (DSC: 0.82; DMC: 0,49 cm) and between SRO and JRO (DSC: 0.80; DCM: 0,51 cm).

Conclusions: Despite the study shows a significant variability in the contoured volumes by operators, with differences from patient to patient and between different organs, there is a good concordance between all operators, particularly between SRO, JRO and CSRT while FRO shows the highest variability when compared to the other operators. Despite the short training dedicated to contour delineation of OARs in breast cancer treatment (100 hours approximately), CSRT has obtained a good concordance with its training tutor, JRO. Similarly, JRO showed a good concordance with its instructor, SRO. The results about LAD show a remarkable variability in its delineation due to the narrow volume and difficulty of visualization and recognition on CT imaging.

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BRAIN STRUCTURAL NETWORKS TOPOLOGICAL ALTERATIONS FOLLOWING FRACTIONATED STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH PRIMARY BENIGN BRAIN TUMORS: A PROSPECTIVE PILOT STUDY

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Aims: To investigate whether fractionated stereotactic radiotherapy (FSRT) on primary benign brain tumors leads to a topological rewiring of structural brain networks.

Methods: Inclusion criteria to be eligible in the present study are: age<55 years, no previous history of hypertension, metabolic, traumatic, neurological disorders or brain surgery. All patients have to perform magnetic resonance imaging with a 1.5 T scanner following a standardized protocol including a 3D T1-weighted sequence and diffusion tensor imaging. Images have to be acquired before start of FSRT and one year after completion of FSRT. Diffusion images are preprocessed to perform high angular resolution whole-brain probabilistic tractography, while T1 images have to be co-registered to the diffusion images and parcellated in cortical and subcortical structures. Structural connectivity matrices will be computed considering the internodal number of streamlines as edges and the brain structures as nodes of the network. This study has been approved by our Ethical Committee.

Results: To date, we recruited two patients with primary benign brain tumors (one acoustic neurinoma and one petro-clivus meningioma). Topological network features have been computed across a range of threshold preserving one connected component in the structural networks. At the global level both patients exhibited preserved small-world characteristics. In general, the characteristic path length and clustering coefficient of whole-brain structural network were slightly reduced in the patient who underwent FSRT. More significantly altered network metrics were obtained from hemisphere network analysis than that from the whole-brain network analysis. Indeed, the hemisphere ipsilateral to the FSRT target showed increased modularity, clustering coefficient and closeness centrality. As regard the hub analysis, most of the hub nodes were distributed in the same location in the two patients. However, some cortical and subcortical nodes showed different hub properties after FSRT.

Conclusions: Our preliminary findings suggest alterations in global and local network topology in patients with primary benign brain tumors following FSRT. Taking into account that the underlying pathophysiology of radiation-related altered brain connectivity has not been well characterized and that communication across close and far brain regions is fundamental for high order motor and non-motor functions, further investigations should be fostered.

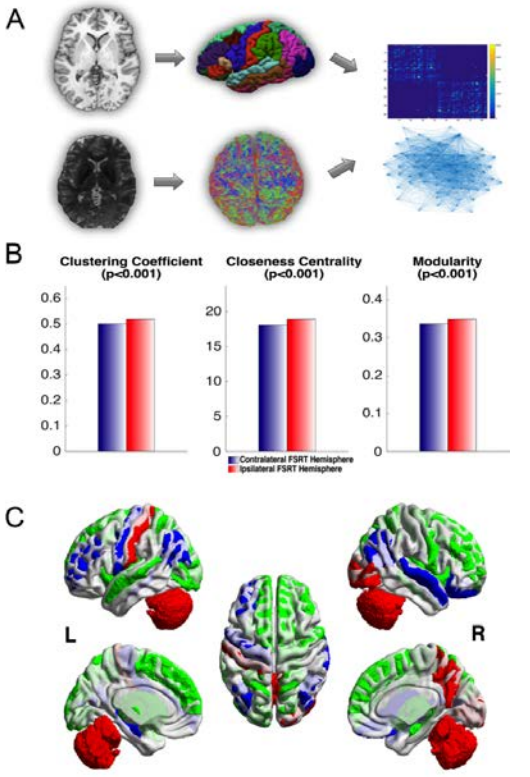

Figure 1. A) Brief summary of the fundamental steps to construct a tractography-based structural connectivity matrix. After initial pre-processing operations, the diffusion signal is modelled in order to perform a high angular resolution whole brain probabilistic tractography. The T1 images are co-registered to the diffusion MRI and then parcellated in cortical and subcortical structures according to the Desikan-Killiany Atlas. Finally, the pairwise internodal number of streamlinesisestimated and fitted into a weighted connectivity matrix, whichcan besubsequentlythresholded and binarized.B) Barplots show thepreliminary result on the intrehamispheric structural networks following FSRT. The Clustering Coefficient is a measure of segregation which evaluates the cross-interaction between the first neighbours of each node in the network. The clustering coefficient together with the characteristic path length are used to calculate the small-worldness of a network. Structural brain networks have a small-world behaviour being characterized by high average clustering coefficient and low characteristic path length: this supports a good trade-off between wiring costs and information transfer. The Closeness Centrality is an indicator of node centrality assessing how close a node is toall the others in the network. The Modularity evaluates the possible existence of segregated modules within the network: high modularity indicates that the modules tend to interact densely within them selves but sparsely or not at all between each other. C) Lateral, medial and axial views of a glass brain showing the brain regions acting as hub-nodes. Green colour indicates the brain structures identified as hub-nodesboth before and after FSRT; in bluecolour, the brain regions identified as hub-nodesonly in the network reconstructed before FSRT; in red colour,the brain regions identified as hub-nodesonly in the network reconstructed after FSRT.

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LONG TERM SURVIVAL IN A PATIENT WITH SCLC: A CASE REPORT

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Aims: In this study we demonstrate that the decrease of the cycles of chemotherapy and so the early start of the radiotherapy in a shorter time on the lung at a higher dosage, reduce the toxicity and improve the outcome of the patient

Methods: we have examined an 55-year-old male with the diagnosis of a SCLC. On 23/07/2007, he performed a total body TC for staging that showed only the pulmonary involvement with a solid tumor formation of about 85 x 53 mm of diameter. In August 2007, chemotherapy was initiated with CDDP 130 mg and VP16 170 mg, the patient received 4 cycles of chemotherapy. On November, the patient began the radiant treatment, the mediastinum was the first part of his body subjected to irradiation with 44 Gy in 22 fractions of 200 cGye and then until 60 Gy. Finally, encephalic prophylaxis was performed with a dose of 30 Gy in 10 sessions of 300 cGy. The patient performed checks over time until 2017 which highlighted the disappearance of the disease (Figure 1).

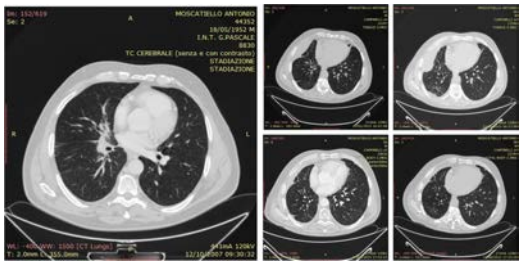

Figure 1.

Results: In this work we show that the radiotherapy treatment before doing only 4 cycles of chemo instead of 6 cycles can determine a better result. The total treatment with higher dosage of gray is well tolerated and gives excellent results in countering the regional recurrence. Given the high incidence of brain metastases in the SCLC, the prophylactic irradiation of the brain is an integral part of the therapeutic strategy in patients who responded to first line therapy. This method has proven to be able to significantly reduce intracranial relapses. The patient treated with radiotherapy and chemotherapy is alive 11 years after diagnosis, with no evidence of further relapse. The patient provided informed consent to the publication of the case details and associated images.

Conclusions: The results are encouraging because the patient was in good health until March 2018 when there was the recurrence of the disease and he died on April 2018. The importance of this work is that it is one of the few studies that shows a remission from SCLC for 11 years and this study emphasizes the healing capacity of the combined CT / RT treatment and we highlight how perfect timing programming and higher dose radiation therapy involve fewer side-effects and it's associated with improved survival.The results of this treatment program appear superior to any previously reported ones and compare favorably to those in the literature at large.

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EFFICACY AND SAFETY OF A 3D HALF BODY IRRADIATION (HBI) IN PATIENTS WITH MULTIPLE BONE METASTASES

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Aims: To evaluate in a large population of multiple bone metastases cancer patients the efficacy on pain relief and the safety of an Half-body irradiation (HBI) short course hypofractionated treatment delivered by a "modern" radiotherapy technique.

Methods: Patients with widespread symptomatic bone metastases and no previous history of large field radiotherapy were enrolled. The pain score, the drug score and the visual analog scale (VAS) for pain were used to record and monitor pain. Data on pain status and dosage/frequency of analgesic consumption were recorded before treatment (baseline evaluation) and during follow-up. HBI encompassed the lower half body (pelvic bones, lumbo-sacral vertebrae and upper third of femurs). Skeletal metastases received accelerated HBI (3 Gy fractions twice daily, 6–8 h apart, on 2 consecutive days, up to 12 Gy) using multiple fields (box technique) three-dimensional conformal RT (3DCRT).

Results: From August 2003 to February 2016, 180 patients (M/F 57/123; median age: 61.3; range 33-95) completed the treatment. After HBI, a significant reduction of pain, as evaluated by VAS, was recorded (pre-treatment versus post- treatment mean VAS: 5.3 versus 2.7; p=0.0001). Overall, 59 of 159 (37.1%) patients with VAS non-zero showed complete pain relief, while 113 of 159 (71.0%) showed a partial response (i.e. > 2 point Pain Score reduction). The pain score analysis evidenced that two third of patients showing high pain score before RT had a significant reduction after treat-

ment. The drug score analysis evidenced that more than one third of patients (40.2%) with high pain score before RT had a significant reduction of drug assumption after treatment. Nearly 49.4% of patients exhibited no treatment related complications, and an additional 49,4% experienced only mild or moderate transitory toxicity. As a whole, severe toxicity was seen in 2 patients (1.2%). Thirty-eight patients (21.1%) presented pain flare's phenomenon. The 12-, 24- and 36 months pain progression free survival were 77.0%, 63.4% and 52.7% respectively. With a median follow-up of 9 months (range 1-131) 30 patients (16.7%) underwent retreatment on the same site (N°=19) or on a smaller volume inside previous HBI field (N°=11). The median retreatment time was 15.9 months (range 2-126).

Conclusions: HBI delivered with 3DCRT technique is safe and effective, providing long lasting pain reduction in patients with multiple bone metastases.

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IMPACT OF EATING HABIT ON ACUTE TOXICITY DURING PELVIC RADIOTHERAPY: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY

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Aims: Aim of the study was to analyse the impact of eating habit on acute toxicity during pelvic radiotherapy (RT) for prostate and gynaecological cancers. Here we report preliminary data on time-trends in symptoms development during RT.

Methods: RT was delivered in 22-35 fractions with dose/fraction of 1.8-2.7 Gy. We recorded the incidence of specific symptoms (lack of appetite, nausea, vomit, gastric pain, abdominal cramps, diarrhea, swelling, flatulence, constipation, costiveness, taste and smell alterations) in the three moments during the RT (1st day = T0, halfway through RT = T1, end of RT = T2). Statistical analysis was performed using the chi-square test to compare the incidence of any symptom at different time points. In this preliminary analysis we considered only symptoms reported by almost 25% of patients.

Results: Forty patients (22 males and 18 females, median age 70.7 years, range 45-86) were included. Twenty-two patients received postoperative RT (10 for gynecologic cancer, 12 for prostate cancer) and to seven female patients concurrent chemotherapy was prescribed. All evaluated symptoms showed statistically significant variations during RT. Flatulence was the most frequent symptom in T0, T1, and T2. Diarrhea, flatulence and lack of appetite increased progressively from T0 to T2, with some difference between individual patients. For diarrhea we recorded a statistically significant increase in T0-T1, T1-2 and T0-T2 (p=0.01, 0.004, 0.02, respectively), for lack of appetite in T0-T1 and T1-T2 (p=0.02, 0.01, respectively) but not in T0-T2, for flatulence in T1-T2 and T0-T2 (p=0.02 and 0.01, respectively), but not in T0-T1. The presence of nausea was constant but with significant differences between all evaluation (T0-T1: p=0.0003, T1-T2: p=0.000004, T0-T2 p=0.01). Cramps and swelling were more frequent in T1 with differences in T1-T2 and TO-T2 (p=0.002, p=0.03, respectively) for cramps, and in T1-T2 (0.001) for swelling.

Conclusions: As expected, during pelvic RT several symptoms affects patients with increasing frequency. Interestingly, the time-trend of the different symptoms was variable, with some symptoms more frequent at the end of the treatment and other symptoms more frequent halfway through treatment. A detailed analysis of this trends together with the evaluation of eating habits would improve the possibility of a tailored supportive therapy for these patients.

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BOOST ON THE DOMINANT INTRAPROSTATIC LESION (DIL) IN PROSTATE CANCER RADIOTHERAPY: A SYSTEMATIC REVIEW

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Aims: Local recurrence has been shown to originate within the initial tumor in prostate cancer (PCa). Modern imaging allows identification of dominant intra-prostatic lesions (DIL). Evidence suggests that higher radiotherapy (RT) doses result in increased biochemical control, but dose escalation to the whole pro-

state is limited by the surrounding normal tissues tolerance. Therefore, a systematic review was conducted to analyse the current evidence of RT boost to DIL and assess toxicity and biochemical outcome.

Methods: PubMed Electronic database was searched through 9th April 2018 for clinical studies on DIL boost irradiation published in English. Established inclusion criteria were: ≥ 15 number of patients, localized PCa, and only clinical studies with planned boost to the DIL.

Results: Thirteen studies with a total of 1044 patients (range: 15-239) reported on a boost to DIL. In all studies, functional imaging was used in DIL delineation to correlate with the histopathological findings. Boost RT to DIL-PTV was delivered using hypofractionated image-guided RT techniques. In series where boost RT was delivered by IMRT-SIB, median dose to DIL was 82.0 Gy (range: 74.0 -83.2 Gy), while in series with BRT boost, median total dose was 78.0 Gy (range: 56.0-96.0 Gy). Median acute G ≥ 3 GU and GI toxicities were 2.0% (range: 0.0-7.0%) and 0.0% (0.0-5.0%), respectively. Median Late G ≥ 2 GU and GI toxicities reported were 7.5% (0.0-39.0%) and 6.3% (0.0-21.0%), respectively. Median 5-year bDFS was 94.0% (range: 70.5-98.0%).

Conclusions: Based on our analysis, the strategy of boosting the DIL is correlated with reasonable toxicity and excellent results in terms of bDFS.

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VERY-LOW DOSE RADIOTHERAPY FOR SYMPTOMATIC SPLENOMEGALY IN HEMATOLOGICAL DISORDERS: A PROMISING APPROACH

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Aims: Splenic irradiation (SI) is a palliative treatment for symptomatic splenomegaly occurring in patients (pts) with hematological disorders and malignancies. The aim of the study is to analyze the role of very-low dose SI in terms of feasibility, efficacy and toxicity.

Methods: We retrospectively analyzed a series of consecutive pts with congestive symptomatic splenomegaly. Very-low dose SI consisted of 4 fractions of 0.5 Gy delivered twice a week to a total dose of 2 Gy to the entire spleen. Treatment efficacy was assessed 14 days after SI and was evaluated in terms of symptomatic improvement, decrease of spleen size and haematological response. Toxicity was scored according to the CTCAE 4.0 scale.

Results: A total of 14 pts, 6 males and 8 females, were identified for this analysis. Mean age was 59.5years and ECOG-PS was 0, 1 and 2 in 5 (35.7%), 6 (42.9%) and 3 (21.4%) pts, respectively. Mean spleen longitudinal diameter was 17.5 cm. Clinical presentation is summarized in Table 1. Overall, 13/14 pts (92.6%) completed the planned treatment. One patient died after one fraction for splenic rupture. Long term relief of abdominal distension, abdominal pain, nausea, vomiting and anorexia were observed in 7/8(87.5%), 8/10(80%), 3/5(60%), 4/5(80%) and 3/4(75%) pts, respectively. A reduction in size of the spleen was demonstrated by palpation or images in 8 pts (57.1%). Haemoglobin, white blood cells and platelet counts improved in 9(64.2%), 4(28.6%) and 7(50%) pts as compared to the initial value. Toxicity of SI was limited to a single case (7.1%) of grade 3 thrombocytopenia. No other worsening in blood counts or gastrointestinal toxicity were reported. Among non responders, 3 pts (21.4%) were rescued by re-irradiation with standard dose.

Conclusions: SI with very-low dose radiotherapy was feasible, well tolerated and provided effective palliation for the majority of pts. These encouraging results need to be confirmed in a larger population trial.

Table 1. Clinical presentation.

Total patient number 14		n	%
Diagnosis			
• MDP			
	• Primary myelofibrosis	2	14.3
	• Polycythemia vera	2	14.3
	• CML	1	7.1
• CLL		2	14.3
• Lymphoma		7	50
Symptoms			
• **Abdominal distension**			
	• G0	6	42.9
	• G1	0	0
	• G2	8	57.1
• **Abdominal pain**			
	• G0	4	28.6
	• G1	1	7.1
	• G2	4	28.6
	• G3	5	35.7
• **Nausea**			
	• G0	9	64.3
	• G1	2	14.3
	• G2	3	21.4
• **Vomiting**			
	• G0	9	64.3
	• G1	3	21.4
	• G2	2	14.3
• **Anorexia**			
	• G0	10	71.5
	• G1	1	7.1
	• G2	2	14.3
	• G3	1	7.1
• **Anemia**			
	• G0 (Hb > LLN)	4	28.6
	• G1 (Hb<LLN-10 g/dl)	5	35.7
	• G2 (Hb<10-8 g/dL)	3	21.4
	• G3 (Hb<8-6.5 g/dl)	2	14.3
• **Leukopenia**			
	• G0 (WBC> LLN)	6	42.9
	• G1 (WBC<LLN-3.000/mm^3)	3	21.4
	• G2 (WBC<3.000-2.000/mm^3)	2	14.3
	• G3 (WBC<2.000-1.000/mm^3)	3	21.4
• **Thrombocytopenia**			
	• G0 (Plt> LLN)	7	50
	• G1 (plt<LLN-75.000/mm^3)	3	21.4
	• G2 (plt<75.000-50.000/mm^3)	2	14.3
	• G3 (plt<50.000-25.000/mm^3)	2	14.3
Splenomegaly grade according to Hackett classification			
	• Grade 2	2	14.3
	• Grade 3	6	42.8
	• Grade 4	4	28.6
	• Grade 5	2	14.3

MDP, myeloproliferative disorder; CML, chronic myeloid leukemia; CLL, chronic lymphocytic leukemia; Hb, hemoglobin; WBC, white blood cells; LLN, lower limit of normal; Plt, platelets.

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MODERATE HYPOFRACTIONATED POST-PROSTATECTOMY VOLUMETRIC ARC THERAPY WITH IMAGE GUIDANCE (VMAT-IGRT): FEASIBILITY AND ACUTE TOXICITY

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Aims: Moderate hypofractionated radiotherapy (hypoRT) in a post-prostatectomy setting may allow a reduction of treatment time but the risk of toxicity may be increased. Aim of this analysis is to evaluate acute toxicity in patients (pts) treated with post-operative volumetric modulated arc therapy (VMAT) for prostate cancer (PC)

Methods: From March 2011 to February 2018, 195 pts received post-operative hypoRT; 91 in adjuvant setting and 104 with salvage intent at biochemical relapse, or in 16 cases for a clinical relapse. Median age was 68 years old; all the pts had 0-2 ECOG performance status. One hundred thirty one pts were treated only on prostate bed whereas 64 also on pelvic lymph nodes. One hundred four pts underwent to some hormonal manipulation. Patients were treated with VMAT (RapidArc) and Simultaneous Integrated Boost (SIB) in 30 fractions for a total dose of 66 or 67.5 Gy to the tumor bed (2.2-2.25 Gy/fraction), and 51 or 54 Gy to the lymph node volume (1.7-1.8 Gy/fraction), respectively. Genitourinary and gastrointestinal toxicities were scored according to CTCAE version 3.0. Urinary symptoms were also evaluated with IPSS questionnaire at baseline and at the end of RT in 173 patients.

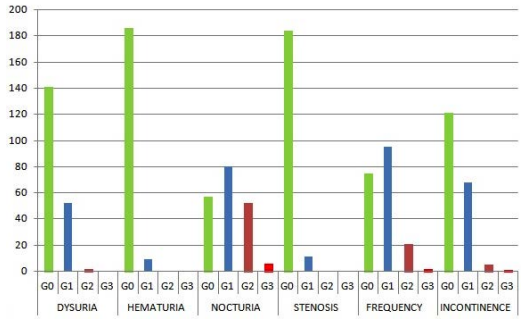

Figure 1.

Results: All the pts completed the planned treatment. Acute gastrointestinal and rectal toxicity was mild with G2 as a maximum grade in 13 patients (6.7%), and none G3. The maximum acute genitourinary toxicity was G3 in 7 patients (3.6%), of these 5 pts were treated in adjuvant and 2 in salvage setting. G2 acute genitourinary toxicity were observed in 60 pts (30.8%). Analyzing each G3 symptom we recorded urinary frequency in 2 pts , urinary incontinence in 1 patient and nocturia in 6 pts . Maximum grade of dysuria and spasm was G2 in 2 pts . None hematuria or stenosis greater than G1 were observed. We also evaluate IPSS score pre and post RT in 173 pts and we calculate a Δ (delta). Mean variation was Δ= - 1.03 points (range: [-10]-[+18]) In 35 pts we didn't record any variation between baseline and the end of treatment; 43 pts had an improvement of IPSS score (7 with Δ≥ 5 points – 4.05%) while 95 had a IPSS deterioration (18 with Δ≥ 5 points - 10.4%).

Conclusions: According to our results, moderate postoperative hypofractionated RT (VMAT-IGRT) seems to be feasible and safe, with a good acute toxicity profile, without unacceptable detrimental effects, also for patients treated with large volumes.

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VESSEL-SPARING PROSTATE VOLUMETRIC MODULATED ARC THERAPY WITH SIMULTANEOUS INTEGRATED BOOST TO DOMINANT INTRAPROSTATIC LESION

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Aims. New evidences suggested a vascular etiology for sexual impotence after prostate radiotherapy. Internal pudendal arteries (IPA), corpora cavernosa (CC) and penile bulb (PB) were identified as critical structures related to erectile function. We explored the potential of VMAT to spare the critical erectile structures with a SIB to the dominant intraprostatic lesion (DIL)

Methods. Twelve patients were selected for this study. DILs were defined using T2-weighted, dynamic contrast-enhanced and diffusion-weighted MRI (multiparametric MRI). Vascular structures were contoured and expanded by a uniform 2 mm margin. The seminal vescicles, the prostate and DIL were expanded

uniformly by 5 mm to create the planning target volumes (PTVsv, PTVpr and PTVdil, respectively). PTVsv, PTVpr and PTVdil dose prescription was 56.3, 67.5 and 70 Gy, respectively, in 25 fractions. The doses were prescribed to cover >95% of PTVs. All VMAT plans were generated in a dual-arc modality for a VersaHD linac. Original clinical plans (ST-VMAT) were created to fulfil targets coverage and Quantec constraints for non vascular OARs (NV_OARs: rectum, bladder and femoral heads). For each patient, a new plan (SS-VMAT) based on the approved ST-VMAT plan was created. IPA, CC and PB were considered OARs related to sexual impotence (V_OARs). All objectives for PTVs coverage and NV_OARs sparing were left unchanged. New objectives were added for V_OARs, with priority to minimize mean doses to IPA, CC and PB. A Wilcoxon signed-rank test was used to compare the two optimization techniques.

Results. For all plans, targets coverage was well within the predefined objectives for all metrics (D95, D98, Dmean). In particular, D98% was >95% of prescribed doses for all targets, patients and techniques. No significant differences were found in sparing rectum, bladder and femoral heads for all considered metrics (Dmean, V50, V60, V70). With regard to V_OARs sparing, SS_VMAT plans provided a major reduction of dose irradiation. Mean doses for IPA, CC and PB were reduced by 32.4% (11.2 Gy, p=0.002), 22.7% (4.2 Gy, p=0.006) and 10.1% (4.7 Gy, p=0.010), respectively. V30 decreased from 61.1% to 21.4% (p=0.02) for IPA and from 27.2% to 14.8% (p=0.04) for CC.

Conclusions. We showed that a significant dose sparing for IPA, CC and PB using VMAT-SIB strategy is feasible, allowing vessel-sparing and highly conformal plans, dose escalation to DIL and fast treatment delivery.

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IMPACT OF A MULTIDISCIPLINARY METHOD IN THE CLINICAL MANAGEMENT OF DIFFICULT CASES OF PROSTATE CANCER: THE IRCCS GIOVANNI PAOLO II PRELIMINARY EXPERIENCE

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Aims: The high incidence of prostate cancer in patients older than 65 years, combined with the complexity of disease clinical management and the improvement of life expectancy and patients survival, requires an adequate multidisciplinary assessment (MDA) to identify men at risk, optimize treatment pathways and manage comorbidities and late iatrogenic toxicities. Also international guidelines consider MDA as a fundamental part of diagnostic and therapeutic process (DTP). The aim of this study is to report our preliminary results in the multidisciplinary management of difficult cases of prostate cancer.

Methods: Between September 2015 and December 2016 our Multidisciplinary Team for urological cancers (which met twice a week) evaluated 63 not-routinary clinical cases that included 18 patients with prostate cancer (age between 52-82 years). As first phase, patients were selected by an oncologist, urologist or radiation oncologist beacause of the presence of clinical complexity criteria (i.e. comorbidities and contraindications for specific therapeutic approaches, atypical histology or other neoplasms). The specialist physicians involved in the second phase – the MDA – and in subsequent DTP were the urologist, oncologist, radiation oncologist, radiologist, pathologist, nuclear specialist and the nurse. As third phase, the referring specialist physician discussed with each patient over the team joint proposal for his personalized DTP. The evaluation criteria of the proposed MD method were: effectiveness of MDA in clinical management (obtained by interpreting a database which collects the discussed clinical cases); total time required for the completion of the DTP and patient compliance (obtained by the feedback from the referring specialist physicians, as reported in a questionnaire).

Results: The therapeutic goals were: oncological radicality for 11 patients, adequate palliation for 7 patients. The proposed strategies (diagnostic investigation/staging, surveillance, surgery, radiotherapy, hormone therapy or second-line therapies) were well tolerated by patients. The MDA showed a positive impact on the overall times required for the completion of the DTP (compatibly with waiting lists) and on patient compliance. References to the literature consulted in specific cases have been collected in the database.

Conclusions: Our good subjective and objective results confirm the usefulness of MDA to manage difficult cases of prostate cancer.

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IMPACT OF IALURIL SOFT GEL® ON ACUTE URINARY TOXICITY IN THE POSTOPERATIVE MODERATE HYPOFRACTIONATED RADIOTHERAPY FOR PROSTATE CANCER

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Aims: Acute genito-urinary (GU) toxicity represents a

crucial issue in the postoperative treatment of patients with prostate cancer, as it is often related to the probability of late adverse events. In this series we evaluated the potential benefit of Ialuril Soft Gel® caps (hyaluronic acid, quercetin, curcumin, chondroitin-solfate) in 70 patients who underwent postoperative radiotherapy for prostate cancer.

Methods: Thirty-five patients educated at the use of daily Ialuril Soft Gel® caps during radiotherapy were evaluated in a comparison with a matched group of 35 control subjects. Ialuril caps were administered 1 cp/die starting from day one of treatment to 15 days after the end of RT. All 70 patients were treated with Helical Tomotherapy in the adjuvant (n=34) or salvage (n=36) setting delivering 63.8 Gy in 29 fractions to prostate bed alone in 28 cases and 63.8 Gy and 47.3 Gy in 29 fractions to prostate bed and pelvic lymph nodes with simultaneous integrated boost in 42 patients. Acute GU toxicity was weekly investigated during treatment and for the first 3 months from the end of radiation therapy. Adverse events were scaled using CTCAE v4.0 criteria. Chi-square tests were conducted to evaluate any potential difference between the treatment arms, assuming a $p \leq 0.05$ for statistically significative.

Results: Median age was 69 (range, 47-81), most frequent comorbidity was hypertension, observed in 38 cases. Pre-RT urinary incontinence was present in 54 patients. Acute GU toxicity rates were: G0 in 13, G1 in 19, G2 in 3 in the control sample, and G0 in 23, G1 in 11, G2 in 2 in the Ialuril arm; no G≥3 observed. Most common adverse event was urinary tract pain in both groups (16 and 9, respectively). A statistical difference between the two groups was detected for of G≥1 toxicity (p=0.016), however no statistically significant difference was found in terms of G≥2 toxicity (p=1).

Conclusions: Despite the small sample size, in our series the daily assumption of Ialuril Soft Gel® during treatment shows a beneficial impact on the onset of acute urinary toxicity in patients treated with postoperative moderate hypofractionated radiotherapy for prostate cancer.

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IMRT-SIB ON PELVIC AND/OR PARA-AORTIC PET-POSITIVE LYMPH NODES IN PROSTATE CANCER: A FEASIBILITY STUDY

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Aims: The treatment of patients with pelvic and para-aortic positive lymph nodes in prostate cancer is still debated. Traditionally, they were treated with hormone therapy. In our center, from 2012, these patients receive an Intensity-Modulated Radiation Therapy (IMRT) treatment on pelvic +/- para-aortic lymph nodes, with Simultaneous Integrated Boost (SIB) on prostate and seminal vesicles (or prostatic bed in operated patients) and on coline-PET positive lymph nodes (pelvic and/or para-aortic). Purpose of this analysis is to report the preliminary results of this treatment.

Methods: Twenty-nine patients (median age: 70; range 55-78) with prostate cancer (T2: 6 patients, T3: 20 patients, T4:3 patients) and positive lymph nodes (pelvic: 29 patients, para-aortic: 6 patients) received definitive (15) or salvage (14) treatment in 25 fractions. Pelvic +/- para-aortic nodes received 54 Gy with IMRT. A SIB was delivered to prostate and seminal vesicles (67.5 Gy), and on pelvic +/- para-aortic nodes (60 Gy) with SIB technique. The dose prescribed to the prostatic bed in operated patients was 66 Gy.

Results: No Grade ≥ 3 acute gastrointestinal and genitourinary toxicities were recorded. Three patients presented grade ≥ 2 late genitourinary toxicity and no cases of grade ≥ 2 late gastrointestinal toxicity were observed. With a median follow-up of 26 months (range: 2-50), 3 patients showed biochemical relapse with a 2-year biochemical relapse-free survival rate of 85.4%.

Conclusions: Preliminary results in terms of toxicity and biochemical relapse-free survival are encouraging.

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COMBINING FRACTIONATED STEREOTACTIC RADIOTHERAPY PRE-BOOST WITH VOLUMETRIC MODULATED ARC THERAPY FOR ATYPICAL MENINGIOMA: RADIOBIOLOGICAL CONSIDERATIONS

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Aims: Atypical meningiomas represent a common primary intracranial neoplasm with higher recurrence and mortality rate compared to benign meningioma. Despite it has been demonstrated that postoperative radiotherapy is likely to ameliorate local control and overall survival, it is not clear yet whether either external beam radiation therapy (EBRT), stereotactic radiotherapy (SRS) and/or fractionated stereotactic radiotherapy (FSRT) could be more effective when administrated alone or in combination. In our Center, until 2015, different techniques and/or fractionation schemes have been used to treat atypical meningioma according to volume and location lesion (EBRT 54-60Gy/2Gy; SRS

14.5Gy/1Fx; FSRT 25-27.5Gy/5Fx or FSRT 24Gy/3Fx). We report our experience regarding to a combined approach with a "FSRT-pre-boost" followed by a volumetric modulated arc therapy (VMAT) in patients with atypical meningioma.Methods: We retrospectively evaluated postoperative recurrence of atypical meningioma treated from September 2015 to March 2018 in our center. All patients underwent surgical resection at the time of initial diagnosis and tumor grading was performed according to the 2007 WHO grading criteria for grade III meningioma. All patients underwent a "FSRT-pre-boost" with a prescription dose of 15 Gy in 3 fractions (median prescription isodose line was 78.5% (range 72-85) followed by a VMAT 46Gy in 23 fractions. Assuming the alfa/beta value to 3 for atypical meningioma. We calculated the biological equivalent dose sum (BED3SUM) of the proposed fractionation scheme ("FSRT-pre-boost" and of VMAT) in respect to the BED3 values of the traditional fractionation schemes used in our Center.Results: The results of the novel combined therapeutic approach were BED3=76.67 Gy for VMAT and BED3=40.00Gy for "FSRT-pre-boost" with BED3sum=116.67Gy. The BED3 values achieved for the previously used techniques/fractionation schemes were respectively: BED3EBRT=90-100Gy, BED3SRS=84.4Gy, BED3FSRT=66.7-88Gy. In all patients we obtained BED2<100Gy for normal tissue. The BED3 values achieved with the proposed combined approach seems to result superior than the previously fractionation schemes. To date, all patients show local control and any acute and late toxicities ≥G2 have been observed. Conclusions: Our patients with atypical meningioma recurrence have benefit from a "FSRT-pre-boost" followed by VMAT. Combining two different highly conformal techniques together with a hypo-fractionation scheme permits to achieve a BED3 > 100Gy. Such approach seems to be a feasible and safe therapeutic option in patients with atypical meningioma. However, prospective randomized clinical studies should be encouraged to confirm our hypothesis.

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PREOPERATIVE RADIO-CHEMOTHERAPY (RT-CT) IN LOCALLY ADVANCED RECTAL CANCER (LARC) USING TWO DIFFERENT DOSES; PRELIMINARY FINDINGS OF A MONOISTITUTIONAL EXPERIENCE

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Aims: FColorectal cancer (RC) is the most common gastrointestinal (GI) malignancy. More than half patients (pts) affected by RC consist in LARC and preoperative RT-CT followed by total mesorectal excision (TME) is the standard treatment in these pts. The aim of this study was to evaluate prognostic factors and toxicities in pts affected by LARC underwent neoadjuvant RT-CT using two different doses.

Methods: From January 2014 to January 2018 we analyzed 27 pts affected by LARC treated with neoadjuvant RT-CT followed by TME surgery. Sixteen pts (Group 1) received 55 Gy in 28 FF (45 Gy to the pelvis and 55 Gy to the T, N+ and mesorectum in SIB technique) + Capecitabine 1650 mg/mq/day; 11 pts (Group 2) received 50.4 Gy to the pelvis in 28 FF + Capecitabina 1650 mg/mq/day. We evaluated clinicopathological characteristics of Tumour (T), Nodal (N), grading, margins, N-down-staging, T-down-staging, toumor regression and sphincter preservation. According to CTCAE vs 5 scale acute and late toxicity was evaluated.

Results: After a median follow-up of 38 months the PFS at 2 and 3 years was 93,2% and 82,%, respectively. At histological examination 5 pts (18,5%) had a T- complete response (CR), 17 pts (62.9%) had N-CR and 4 pts (14.8%) had both T and N-CR. There was no statistically differences between two groups (p-value > 0,05). Tumour down-staging was observed in 17 (62.9%) pts (68,8% Group 1 and 63.5% Group 2; p-value 0,78). Nodal down-staging was reached in 86, 6% of pts (100% in Group 1 and 77% in Group 2; with a trend in favor of Group 1, p-value= 0,082). Three pts had disease progression (1 pt in Group 1 and 2 in Group 2). Of them two pts had lung metastases and one pt had locally and distant metastases. All pts underwent systemic treatment. Overall sphincter preserving was reached in 78% (93, 5% Group 1 and 65% Group 2; p-value 0,026). Finally, GI and GU G2/3 acute toxicity was observed in 6 pts (22%): 2/16 (12,5%) Group 1 and 3/11 (27,2%) Group 2.

Conclusions: Neoadjuvant RT-CT with SIB technique and TD of 55 Gy/28ff (45 Gy to the pelvis + 10 Gy boost to mesorectum, T and N+) showed an advantage regarding N-down-staging and sphincter preserving compared to standard RT treatment (50.4 Gy/28ff). Acute and late toxicity was acceptable with no statistically differences between two groups. Randomized trials with higher number of pts and longer follow-up are needed to confirm our results.

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ACUTE RADIATION PNEUMONIA EVENTS IN LOCALLY ADVANCED LUNG CANCER PATIENTS: A COMPARISON BETWEEN 3D-CRT AND VMAT TECHNIQUE

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Aims: To compare the rate and degree of observed acute pulmonary toxicity among locally advanced lung cancer patients treated with 3DCRT technique or VMAT

technique and concurrent chemotherapy.

Methods: Locally advanced lung cancer patients underwent concomitant radio-chemotherapy using 3D or VMAT technique. During treatment, weekly CT scans and clinical evaluations were performed and, if occurred, radiation pneumonitis was graded according to the National Cancer Institute Common Toxicity Criteria (vers. 4.02).

Results: From January 2016 to December 2017, 91 patients [median age 66 years (range 43-85)] underwent concomitant radio-chemotherapy: 41 patients [21 male (51%), 20 female (49%), histologically 15 adenocarcinoma (37%), 10 squamous cell (24%), 10 small-cell lung cancers (24%), 6 without histological diagnosis (15%)] underwent concomitant radio-chemotherapy with 3D-CRT technique; 50 patients [35 male (70%),15 female (30%), histologically 33 adenocarcinoma (66%), 11 squamous cell (22%), 6 small-cell lung cancers (12%)] underwent concomitant radio-chemotherapy with VMAT technique. Mean radiotherapy dose delivered was 52,36 Gy in 3D-CRT technique group and 50,25 Gy in VMAT technique group. Acute pulmonary toxicity (CTCAE scale G =2) was reported in 3 patients (7%) treated with 3D-CRT technique; acute pulmonary toxicity (CTCAE scale G ≥2) was reported in 3 patients (6%) treated with VMAT technique, in particular 2 grade 2 (4%) and 1 grade 5 (2%) acute pulmonary toxicities occurred.

Conclusions: Concomitant radio-chemotherapy in locally advanced lung cancer patients is a well tolerated treatment both with 3D-CRT technique and VMAT technique. In order to spare organs at risk and obtain a better target coverage, VMAT can be used with encouraging clinical results.

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CLINICAL APPROACH, SPECIALIZED ASSESSMENT AND USE OF DVH AS A PREDICTOR OF ACUTE SKIN TOXICITY IN BREAST CANCER RADIOTHERAPY

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Aims: The correlation between acute cutaneous toxicity and homogeneous dosimetry in breast cancer radiotherapy is now certain. For this reason, using the 3D conformational technique, we recorded the acute cutaneous toxicity and we reviewed the dosimetry and DVH of each patient.

Methods: from September 2017 to April 2018, 204 patients with breast cancer underwent 3D conformal radiotherapy on the breast. Tangential latero-medial technique, 6 MV photons, also using dynamic filters, two treatment schedules: single dose. 2.65 up to 42.40 Gy or single dose 2 to 50 Gy plus boost with single dose electrons. 2.5 up to 10 Gy. Both during and after treatment, the onset, the location, and the degree of cutaneous toxicity were recorded. So we evaluated the DVHs of each treated patient.

Results: 56 patients (27%) reported acute G2 / G3 toxicity in the ipsilateral axillary area and submammary line, 21 patients in the toxicity group recorded (10% of total) G2 toxicity but the whole breast. The use of more aggressive topical therapy was necessary. The evaluation of the DVH and of the dosimetry of each patient regardless of the fractionation used showed the presence of hot spots with respect to the prescribed dose for 51/56 of the aforesaid patients even in the presence of normal dosimeters for the remaining parameters that are considered. In any case, the presence of hot areas only in some points did not allow us to understand the onset of toxicity on the whole mammary area. Reviewing the outlines made it was possible to highlight that the presence of such dose peaks may be due to various factors such as the size or shape of the breast. No patient discontinued treatment. The post-treatment cosmetic result at a median follow-up of 4 months did not result in radiotherapy outcomes.

Conclusions: The 3D conformational technique used by us has allowed a decrease in toxicity compared to the data reported in the literature, but does not always allow homogeneity of the treatment. The combination of clinical and radiotherapy techniques knowledges allows the identification of new methodological approaches to avoid functional imperfections and limitations, limited to the duration of treatment. The possibility of having an instrument such as DVH to predict acute toxicity also allows to put in action for selected patients those actions useful to avoid the toxicity onset, first of all with the use of new treatment methods (IMRT) able to limit the number of hot spots. Even the continuous use of topical supportive therapy should not be underestimated.

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INTEROBSERVER AND INTERFRACTION VARIABILITY USING FREE-BREATHING CBCT FOR SBRT OF THE UPPER ABDOMEN

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Aims: To evaluate the interobserver and interfraction setup error with the use of cbCT in stereotactic treatment of tumors of the upper abdomen. We analyzed also wheter the actual PTV expansion (ITV + 4 mm) is adequate to compensate for the variability.

Methods: cbCT data sets from 10 patients who completed SBRT for tumors of the upper abdomen were chosen. Matching data of each cbCT from 11 observers (7 radiation oncologists, 2 radiologists and 2 radiotherapists) experienced in the treatment of tumors of the upper abdomen were prospectively collected. CbCT were matched in all 3 translational directions and obser-

vers were allowed to adjust window width. In this study we will analyze interobserver variability as well as difference between fractions.

Results: We evaluated a total of 484 cbCTs in 10 patients. Significant variability was seen in the matching of liver lesion with the use of fiducials and without, respectively: median cranio-caudal (CC) 4 mm (range, 2-18 mm) versus 13 mm (range 4-33mm) (p 0.02), median latero-lateral (LL) 3 mm (range, 2-7) versus 6 mm (range, 3-13 mm) (p n.s.), median anterior-posterior (AP) 3,5 mm (range, 2-8 mm) versus 7 mm (range, 1-15 mm) (p n.s.). Median variability for kidney tumors was: CC 4 mm (range, 3-7mm), LL 4 mm (range, 3-7), AP 4 mm (range, 3-5mm). Pancreatic tumor was as follows: CC 9 mm (range, 3-10 mm), LL 2 mm (range, 2-4 mm), AP 3 mm (range, 3-4 mm) and for adrenal metastases: CC 10.5 mm (range, 7-20 mm), LL 4 mm (range, 3-6 mm), AP 4 mm (range, 3-4 mm).

Conclusions: major variability between observers was seen without the positioning of fiducial markers for liver lesion in the CC direction. Interobserver variability must be taken into account when creating treatment margins.

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TOXICITY OUTCOME IN POSTOPERATIVE INVERSE PLANNING IMRT BREAST CANCER PATIENTS

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Aims: To evaluate results in terms of acute/sub-acute and late toxicity using IMRT postoperative radiation therapy (PORT) in stage II-III breast cancer patients (pts).

Methods: From October 2012 to April 2017, at Radiation Oncology of San Francesco Hospital, 28 pts with median age 59 (range 28-83) who received intensity modulated PORT to whole breast/chest wall and supraclavicular fossa were retrospectively reviewed .Twenty-one of them received also axillary node irradiation while 2 were treated also in internal mammary nodes. Thirty-five pts (79%) received OT with Tamoxifen or aromatase inhibitors in association or not with LH-RH analogue, 89% received adjuvant/neo-adjuvant chemotherapy (Anthracyclines and/or Taxans) and 6% Trastuzumab. Seven-nine fields inverse planning IMRT started 4 weeks after chemotherapy completion and total dose was 50 Gy/25 fr to chest wall or breast and nodes; 7 pts received 10 Gy simultaneous or sequential boost to the tumor bed. Pts were examined once a week during radiation treatment, after 1, 3, 6 and 9 months then every 6 months up to 5 years. Radiation pneumonitis (RP) were evaluated within 6 months with chest X-ray and/or CT scan. Toxicity was graded using Radiation Therapy Oncology Group / European Organization for Research and Treatment Cancer (RTOG/EORTC) criteria.

Results: The following median constraints were obtained: PTV: D95% = 93% (range 93-96), V95% = 94% (range 90-98), D1% = 105.5% (range 103 -108); ipsilateral lung Dmean = 13 Gy (range 12-17) and V20 Gy = 24% (range 13-28); Heart: Dmean = 6 Gy (range 2 -7) and V25 Gy = 3% (range 1-7). See Table 1. Median follow up was 18 months (range 2-59); at the end of RT there were 6 G1 acute skin toxicity (21%), 17 G2 (61%) 3 of them treated with bolus), 4 G3 (14%) all of them with bolus; after 3 months 18 G1 skin toxicity (64%), 4 G2 (15%). After 12 months 3 G1 (10%). Acute dysphagia at the end of RT was 7 G1 (25%), 5 G2 (18%); After 9 months no residual toxicity was observed. Lung toxicity 6 months after the end of RT was 2 G1 (7%), 1 G2 (3.5%). No heart toxicity was noted in 16 valuable pts.

Conclusions: Inverse planning IMRT allowed a good PTV coverage and reduces volumes receiving greater than 107%. Despite homogeneity of dose we checked an excess of skin toxicity probably due to the large volume, chemotherapy and use of bolus. No relevant lung toxicity and cardiac toxicity was observed. IMRT PORT is feasible and safe but a longer follow-up could be necessary.

Table 1.

Dosimetric parameters	Median value
Ipsilateral lung volume	
D_{mean}	13,25
V_{20}	23,85
V_{30}	16,1
Contralateral lung volume	
D_{mean}	4
V_{20}	0
Total lung	
D_{mean}	8,6
V_{20}	12
V_{30}	7,35
Heart	
D_{mean}	5,95
V_{25}	3,7
Esophagus	
D_{mean}	14,1
V_{35}	11,8
PTV coverage	
V_{95}	93,94
D_{95}	94,35
D_1	105,5
Contralateral breast	
D_{mean}	3,1

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IS IT FEASIBLE A REDUCTION OF RADIATION DOSE IN PATIENTS AFFECTED BY GLIOBLASTOMA UNDERGOING RADIO-CHEMOTHERAPY ACCORDING TO MGMT PROMOTER METHYLATION STATUS WITHOUT JEOPARDIZING SURVIVAL?

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Aims: To explore therapeutic results of different radiotherapy (RT) dose schedules combined to Temozolomide (TMZ)-RT treatment in newly diagnosed glioblastoma (GB), according to the MGMT methylation status.

Materials and Methods: Patients with newly diagnosed GB received either standard (60-59,4 Gy) or reduced (54 - 52Gy) dose radiation therapy (RT) with concomitant and adjuvant TMZ between June 2010 and October 2016. We retrospectively evaluated the therapeutic effectiveness of the RT ranges schedules in terms of Overall Survival (OS) with univariate and multivariate analysis, after analyzing the MGMT methylation status.

Results: One hundred and nineteen patients were selected for the present analysis out of 146 total treated patients accrued. Sixty-eight out of the selected cases received the standard RT-TMZ course (SDRT-TMZ) whereas the remaining 51 underwent the reduced dose schedule (RDRT-TMZ). The analysis according to the MGMT promoter methylation status showed that, in methylated-MGMT GB patients, SDRT-TMZ and RDRT-TMZ groups did not show different median OS (p=ns) according to the two RT schedules, independently by the extent of surgical resection. Instead, a difference in survival outcomes was confirmed in unmethylated-MGMT GB patients with a better survival for patients undergoing to SDRT, particularly in sub-total resection.

Conclusions: In our experience, a reduction of radiation dose schedule seems does not jeopardize survival in methylated-MGMT patients independently by the extent of resection.

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CONSERVATIVE BREAST RECONSTRUCTION: ANALYSIS OF OUTCOMES AFTER 146 CONSECUTIVE CASES OF PRE-PECTORAL, SUBCUTANEOUS IMPLANT-BASED BREAST RECONSTRUCTION IN A SINGLE INSTITUTION SERIES

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Aims. To evaluate factors related to acute and late toxicity among breast cancer (BC) patients who underwent pre-pectoral breast reconstruction (BR).

Methods. We performed a retrospective analysis of BC patients who underwent therapeutic or prophylactic mastectomy from October 2012 to May 2016 at our Center. We recorded data for each patient related to individual parameters (age, BMI, smoke-history, comorbidity, BRCA-carrier), and to other BC-related treatments (axillary surgery, adjuvant radiotherapy (RT), chemotherapy, endocrine therapy and use of trastuzumab). Toxicity profile was evaluated in terms of complications related to BR; we recorded acute and late toxicity data and prosthesis/implant explant events.

Results. We analyzed 146 BC patients treated with subcutaneous BR, 117 therapeutic and 29 prophylactic mastectomies. 37 patients received postmastectomy RT. The significant factors related to acute toxicity were: previous RT (34.5% vs 8.5%; p=0.001, previous RT and not, respectively), BMI (31.3% vs 8.8%; p=0.003, BMI >25 and <25, respectively), previous breast surgery (22.2% vs 8.7%; p=0.027, breast surgery before mastectomy or not, respectively), and diabetes (100% vs 11.9%; p=0.002, diabetes or not, respectively). Factors significantly correlated to implant/prosthesis explant were current or previous exposition to cigarette smoking (13.8% vs 2.6%; p=0.029, smoker or not, respectively), and primary systemic therapy (18.8% vs 3.5%; p=0.022, primary systemic therapy and not, respectively); axillary lymph node dissection was significantly related to late toxicity (5.7% vs 0%; p=0.04, axillary surgery or not, respectively). At a 3-year median follow up, three deaths, five local recurrences (LR) and fourteen distant metastasis (DM) occurred among 117 patients treated by therapeutic mastectomy. Overall survival was 78.1%, LR free survival was 95%, and DM free survival was 71.6%. Postmastectomy RT was not significantly related to acute, late toxicity, and explant occurrence.

Conclusions: Pre-pectoral subcutaneous implant-based BR is a safe and effective approach, with low rates of toxicity and of prosthesis explants. The risk of acute toxicity increases in patients previously treated with RT or surgery, and in case of diabetes or BMI >25. Axillary lymphadenectomy seems to be the only factor significantly related to late toxicity; postmastectomy RT is not associated to higher rate of toxicity.

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IMPLICATIONS OF ADOPTING MONTE CARLO TREATMENT PLANNING FOR SBRT-VMAT OF LUNG METASTASES

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Aims: Clinical implementation of Monte Carlo lung SBRT planning is challenging due to the difficulty of reinterpreting historical outcome data calculated with older dose algorithms. We investigated the consequences of the transition from a type-a dose calculation algorithm (pencil beam, PBC) to more advanced type-b (collapsed cone convolution, CCC) and type-c (MonteCarlo, MC) for SBRT of lung lesions treated with VMAT technique.

Methods: 27 lung SBRT patients that underwent SBRT for lung metastases were re-calculated with CCC and MC. This last is the XVMC dose engine implemented in the Monaco TPS (Elekta). Historical PBC plans were optimized using a full 6MV coplanar VMAT arc. The prescribed dose (PD) to the PTV ranged from 20Gy to 30 Gy in a single fraction. A 1mm MLC block margin was adopted in order to increase the dose fall-out and intensify the dose within the GTV. The PTV was also separated into components in tissue (GTV) and air (PTVair) to better understand the impact of air amount in PTV on dose distributions. Plans were compared using V100, D95, D98 and Dmean for the PTV and the GTV. For lung, Dmean and various Vx% were calculated. Based on changes in D95 and D98, the prescription dose was converted from PBC to CCC and MC.

Results: The median PTV size was 26.3 cc (range, 5.6–101.3). PBC plans caused large PTV underdosage, mainly at the target periphery. Average V100 significantly decreased from 96.1% to 42.3% and 53.2% for PTV, and from 100% to 83.9% and 92.1% for GTV when PBC plans were re-calculated with CCC and MC ($p < 0.01$). Similarly, D95 significantly decreased from 101.7% to 84.7% and 87.0% for PTV, and from on 114.2% to 101.2% and 103.6% for GTV. Compared with MC and CCC, PBC overestimated D98% by an average of 15.5% and 18.0% to the PTV, and by an average of 11.1% and 13.6% to the GTV. Dmean, V5, V10 and V20 to lung strongly correlated among the three algorithms ($R2>0.99$). With respect to MC, CCC shows deviations <3% for all metrics, with a tendency to an over-correction. Based on the mean reduction in D95 and D98, the PBC dose in our last escalation level (1x30Gy) should be converted to a MC prescription dose equal to 1x25Gy.

Conclusions: Type-a SBRT lung plans considerably overestimate target coverage for all patients. Our aim was to adjust the MC prescription dose for lung metastases in order to approach our current dose level, because our clinical outcomes provided an high local tumor control and low toxicities with PBC planning.

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PRONE POSITIONING IN INTENSITY MODULATED RADIATION THERAPY OF PELVIC MALIGNANCIES: WHO CAN BENEFIT?

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Aims: It has been shown in previous studies that a high maximum point dose (more than 55 Gy) to the small bowel can increase the risk of severe late toxicity, including small bowel obstruction. Even when using high conformal techniques, such as intensity modulated radiotherapy, there may be some cases where the small bowel loops cannot be completely spared due to their close proximity to the target volume. The aim of this study was to evaluate if the prone positioning can gain some advantages over the supine and if there are any predictive factors to select patients who can mostly benefit. Here we present preliminary data.

Methods: In order to select the best set-up for radiation treatment, patients with pelvic malignancies treated in our center between February and May 2018 with doses higher than 55 Gy, routinely underwent two simulation computed tomography (CT) scans both in the supine and prone positions. Small bowel loops (SBL) within the pelvis were contoured from the level of the sacrum promontory to the rectum plane. A margin of 7 mm was added to the clinical target volume (CTV) to obtain the planning target volume (PTV). The volume of the small bowel overlapping the PTV was prospectively collected together with many other clinical variabilities, such as gender, age, body mass index, tumor type and previous surgery.

Results: Thirty-one patients are available for the analysis (8 men and 23 women, median age 59, range 24-84 years). Tumor sites included prostate (22.5%), rectum (25.8%), endometrium (29.0%), uterine cervix

(35.5%), vagina (3.2%) and anus (3.2%). Twenty-two (70.9%) patients had received previous surgery to the pelvis. The median volume of SBL within the pelvis was 342 (range 0-770 cc) and 305 cc (0-640 cc) in the supine and prone position respectively ($p<0.05$). The median volume of SBL overlapping the PTV was 2 cc (range 0-66 cc) and 0 cc (range 0-44 cc) in the supine and prone position respectively ($p<0.01$). A greater proportion of patients had lower volume of SBL overlapping with the PTV among elderly, female, and patients who had received surgery ($p=0.02$, 0.01, 0.05, respectively).

Conclusions: In the overall population prone positioning allowed for a better small bowel sparing as compared to supine positioning. Prone positioning was particularly advantageous in elderly, female, and in patients who had received surgery.

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MODELING DOSIMETRIC PARAMETERS FOR UPPER GASTRO-INTESTINAL TUMORS TREATMENT TOXICITY REDUCTION

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Aims: Upper gastro-intestinal (GI) toxicity is a limiting factor in radiation therapy for abdominal neoplasms. Constraints for treatment planning in abdominal radiotherapy mostly derive from scientific publications of pelvic tumors. The aim of this study is to evaluate dosimetric and clinical parameters regard to toxicity outcome in upper GI cancer radiotherapy patients.

Methods: We retrospectively analyzed patients with upper GI cancer treated since 2009 to 2018 with 3D-conformal or intensity modulated radiotherapy, with concurrent chemotherapy or not, and after abdominal surgery or not operated. During the treatment, acute upper GI toxicities such as nausea, vomit and weight loss were reported and have been coded according CTCAE v4.03 scale. In all patients bowel bag (BB), liver, stomach (if present), were delineated by radiation oncologists on simulation CT. Dose Volume Histograms (DVH) of the delivered treatment were extrapolated and analyzed for detecting the VDose related to organs at risk (OARs) and the impact of other clinical factors that better predict the toxicity rising during the treatment.

Results: The records of 199 patients have been analyzed, median age was 66 years (range 35-84), 115 (57.8%) resected and 84 (42.2%) not resected. Primary tumors were located in the following subsites of upper GI tract: gallbladder 8 (4%), junction 9 (4.5%), pancreas 102 (51.3%), stomach 48 (24.1%), biliary tract 32 (16.1%). Median prescription dose was 50.4Gy (range 30-55.8) with median fractionation 1.8Gy (range 1.8-3.0). Linear quadratic correction for mildly hypofractionated treatments was not applied because the observed outcome was the acute toxicity, less influenced by fraction size and more by total dose. The DVHs of GI organs at risk were analyzed against the outcome (CTCAE toxicity grade) by fitting univariate logistic regression on Vdoses calculated at step of 0.1 Gy from 5 Gy to 50 Gy. The model showing in each case the lowest Akaike Information Criterion was selected for choosing the best VDoses. Upper GI CTCAE toxicity Grade >= 1 and Grade >= 2 best VDoses were V24Gy on BB, while Grade = 3 VDose on BB was V30Gy. Other OARs Vdoses didn't return significant results. Results of multivariate analysis are summarized in table 1. Found VDoses are the best predictors of toxicity.

Conclusions: Our analysis shows a strong correlation between toxicity grade and VDoses on BB. The most significant result is given by the model using V24Gy for CTCAE toxicity grade >= 2.

Table 1.

CTCAE 4.03 >= G1
Coefficients:

	Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	-0.2568968	0.2980920	-0.862	0.388795	
Sex male	-1.2108082	0.3265919	-3.707	**0.000209**	***
Bowel Bag V24	0.0017095	0.0003615	4.729	**2.26e-06**	***

CTCAE 4.03 >= G2
Coefficients:

	Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	-0.9019019	0.3903444	-2.311	0.02086	*
Sex male	-0.9157190	0.3576855	-2.560	**0.01046**	*
Chirurgia	-0.9146087	0.3405086	-2.686	**0.00723**	**
Gastropatia	1.6596762	0.5930665	2.798	**0.00513**	**
Bowel Bag V24	0.0015871	0.0003552	4.468	**7.89e-06**	***

CTCAE 4.03 = G3
Coefficients:

	Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	-2.2434914	0.4310007	-5.205	1.94e-07	***
Chirurgia	-0.6410994	0.4257032	-1.506	0.1321	
Gastropatia	1.1565195	0.5974689	1.936	**0.0529**	.
Bowel Bag V30	0.0011093	0.0004964	2.235	**0.0254**	*

Results of multivariate analysis: three models are defined for three different levels of toxicity. Significant covariates are shown in **bold**. P-Values are in the rightmost column.

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ROLE OF INTERNAL MAMMARY LYMPH NODE IRRADIATION IN BREAST CANCER: A SINGLE CENTER EXPERIENCE

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Aims: The routinary inclusion of internal mammary lymph node irradiation (IMLN RT) in the traditional nodal targets in patients (pts) affected by locally advanced breast cancer (BC) is still a matter of debate. Literature reported different and controversial results regarding the balance between the improved outcomes and acceptable toxicities. That's why the aim of our study was to retrospectively, evaluate the outcome and

major toxicities related to the irradiation of IMLN.

Methods: We retrospectively analyzed 105 pts affected by locally advanced BC, staging IIB-IIIC according to TNM 7th edition, from February 2013 to November 2017. Median age was 54 (range 32-80).

Infiltrative ductal carcinoma histology was evidenced in most of patients (82%). Most of pts had a 3 tumor grading (G3) (55%) and 12% had triple negative receptor status. Eighty-two pts (78%) underwent mastectomy and 22% conservative surgery, followed respectively by conventional 3D conformal RT at the level of thoracic wall (50 Gy) and at the level of whole breast (50 Gy) with a boost of 10 Gy on surgical bed. All pts underwent RT at the level of regional lymph nodes: 65% underwent IMLN-RT. Comparison between two groups, one with pts who underwent IMLN RT and one with pts who did not, was performed in terms of disease-free survival (DFS) as main outcome and acute and late toxicity. Kaplan-Meier analysis and log-rank test, with p value significance <0.05, were used for statistical analysis.

Results: Median follow up was 32 months. Ten pts (9%) developed distant metastases, 2 pts at the level of IMLN. After 3 years we didn't evidence statistically significant differences between the two groups in terms of DFS (p=0.3): at 3 years we assessed 88.8% of DFS with IMLN RT and 82.8% of DFS without IMLN RT. Acceptable lung and heart toxicities were evidenced also in pts who underwent IMLN RT.

Conclusions: Our results didn't find improved survival in terms of DFS with the irradiation of IMLN with just a partial but not statistically significant advantage with IMLN RT. An interesting result is that, according to literature, we evidenced a potential but not statistically significant advantage with IMLN RT in triple negative patients (3-year DFS of 59% with IMLN RT vs a 3-year DFS 40% without IMLN RT). A more numerous sample of pts and a longer follow up is needed in order to assess the real effectiveness of IMLN RT and to select the subgroup of pts who may benefit from irradiation of IMLN.

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INTEROBSERVER VARIABILITY IN TUMOR BED CONTOURING IN WOMEN UNDERWENT BREAST CONSERVATIVE SURGERY: COMPARISON BETWEEN RADIATION ONCOLOGIST AND RADIATION THERAPIST

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Aims: To evaluate the interoperator variability between radiation oncologist (RTO) and radiation therapist (RTT) in tumor bed (TB) contouring for patients (pts) with early breast cancer.

Methods: We retrospectively analyzed pts undergoing breast conservative surgery (BCS) who received a boost on the TB. The RTT contoured the TB independently of the RTO after a training course. In the group 1 CTV boost was the surgical bed, defined by adding 1 cm to the surgical clips placed in the lumpectomy cavity during surgery. In the group 2 the boost CTV was defined on the evaluation of preoperative mammography, medical history, intraoperative data and ultimate histological description. Moreover in this group the seroma cavity or a metallic find on the scar were used to identify the CTV boost. The CTVs were three dimension expanded of 0.5 cm creating a planning target volume (PTV). We compared the contours in terms of volume, number of slices, and DICE similarity coefficient (DSC).

Results: Forty pts were evaluated. Twenty pts had surgical clips (group 1), the other twenty had no clips (group 2). For each pts of group 1, no difference in the number of contoured slice was found between the two operators, but a statistically significant difference was found in terms of volumes, being RTT TB on average ~ 45% smaller than RTO TB (9.5±5.5 cm3 vs. 17.4±10.5 cm3). For group 2, random variations between the two operators were found in terms of contour location, number of contoured slices, and volumes, with mean values of 24.7±16.3 cm3 and 26.7±17.1 cm3 for RTT TB and RTO TB, respectively. The TB delineated for this group were significantly bigger ($p<0.05$) than those delineated by the RTT for group 1. A difference was obtained by comparing the TB volumes delineated by both the operators in each group: 13.4±9.2 cm3 in group1 vs. 25.7±16.5 cm3 in group 2. The mean DICE value between RTO TB and RTT TB was 0.69±0.07 (range 0.53-0.81) in group1 and 0.37±0.18 (range 0-0.58) in group2 ($p<0.05$).

Conclusions: This study showed a decrease of the interoperator variability in the TB contouring with the use of surgical clips. The reduction of the volumes in the group with clips is closely related to the possibility of decrease side effects like fibrosis. The RTT following an appropriate training may become an important figure in the radiotherapy multidisciplinary team, able to support the RTO also in the contouring phase of the radiotherapy treatment.

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VARIABILITY OF CLINICAL TARGET VOLUME DELINEATION FOR RECTAL CANCER PATIENTS PLANNED FOR NEOADJUVANT RADIOTHERAPY WITH THE AID OF THE PLATFORM ANATOM-E

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Aims: Delineation of treatment volumes is a major source of uncertainties in radiotherapy. This is also true for rectal cancer patients undergoing neoadjuvant radiation, with a potential impact on treatment quality. We investigated the role of the digital platform Anatom-e (Anatom-e Information Sytems Ltd., Houston, Texas) in increasing the compliance to follow a specific treatment protocol in a multicentric setting.

Methods: Two clinical cases of locally advanced rectal cancer were chosen. The 2 clinical cases are described in Figure 1A (Figure 1A). Participating were instructed to follow the 2009 Radiation Therapy Oncology Group (RTOG) consensus atlas and asked to manually segment clinical target volumes (CTVs), for both patient 1 and 2, on day 1 with and without the use of Anatom-e. After one week (day 2), the same radiation oncologist was asked to contour again, with and without Anatom-e, the same 2 CT series. Anatom-e nomenclature of target volumes is reported in Figure 1B (Figure 1B). Intraobserver (Intra-OV) and interobserver (Inter-OV) variability were evaluated with the Dice similarity coefficient (DSC), the Hausdorff distance (HD) and mean distance to agreement (MDA). Delineated volumes for clinical case 2 are shown in Figure 1C (Figure 1C).

Results: For the clinical case 1, no significant difference was found for both Intra-OV and Inter-OV. For the clinical case 2, no significant difference was found for Intra-OV but a statistically significant difference was found in terms of Inter-OV for DSC when using or not the platform. Mean DCS was 0.65(SD:+0.64;range:0.58-0.79) for day 1 vs reference volume without Anatom-e and 0.72(SD:+0.39; range:0.67-0.77) (p=0.03) with the platform. Mean MDA was lower with Anatom-e(3.61;SD:+1.33; range:2.85-4.78) than without(4.14;SD:+2.97; range:2.18-5.21), with no statistical significance (p=0.21) The use of Anatom-e decreased the SD from 2.97 to 1.33. Mean HD was lower with Anatom-e(26.06;SD:+2.05;range:24.08-32.62) but without statistical significance (p=0.14) compared to that without (31.39;SD:+1.31; range:26.14-48.72).

Conclusions: The use of Anatom-e decreased the inter-observer variability in the delineation process of CTVs for locally advanced rectal cancer patients with a complex disease presentation planned for neoadjuvant RT.This system may be potentially helpful in increasing the compliance to follow shared guidelines and protocols.

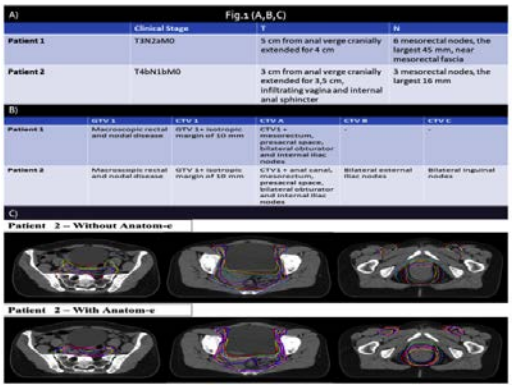

Figure 1.

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A RETROSPECTIVE ADAPTIVE RADIATION APPROACH IN LUNG CANCER TO CALCULATE ITV MARGIN

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Aims: The aim of this work is to evaluate if the standard ITV (Internal Target Volume) which was adopted by physician for patients with lung cancer, has a sufficient margin to maintain an optimal coverage of GTV (Gross Target Volume) during all treatment course. This in order to decide if re-planning is necessary.

Methods: We considered 7 patients affected by adenocarcinoma lung cancer, treated in the Department of Radiation Oncology of Ferrara between 2013 and 2014. GTV and CTV (clinical target volume) was contoured by the physician and a non-personalized ITV was defined (with an expansion of 1cm in cranium-caudal direction and 0.5 cm in other direction from CTV).For each patient 3D plan was available and several CBCT (from 7 to 9).Using MIM-MAESTRO software (MIM Software, Inc., Cleveland, OH, USA) the radiotherapist propagated GTV and PTV contours from pCT (planning CT) to each CBCT.To obtain accumulated DVH we first generated deformed dose and contours of pCT on CBCT, then we propagated contours and dose from the planned CT to the last CBCT.

Results: To decide if replan might be necessary we evaluated mean coverage of GTV on accumulated DVH related to pCT (we considered the 95% of prescription dose). In 6 of 7 cases the difference in coverage was less than 2%; only in one patient is around 3%. For PTV, the differences in coverage was less than 5%.

Conclusions: We could say that CBCT set up verification and correction for these kind of patients is enough to control GTV coverage. This is due to the fact that the security margin adopted for standard ITV is corrected. In adenocarcinoma lung cancer adaptive radiotherapy could not be necessary.

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DEFINITION OF STRUCTURES AIMED TO URINARY CONTINENCE AND SEXUAL POTENCY USING 3 TESLA-MRI: AN ANATOMO-RADIOLOGICAL STUDY OF THE MALE PELVIC FLOOR

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Aims: Radiotherapy (RT) is widely used in prostate cancer. Urinary incontinence and erectile dysfunction are possible toxicities RT related. 3 Tesla (3T) MRI ensures an optimal anatomical definition of prostate and pelvic floor structures and it is therefore useful in RT treatment planning. The purpose of this preliminary study was to identify and contour critical structures aimed to urinary continence and sexual potency, on 3T-MRI. An anatomo-radiological study of the male pelvic floor was performed.

Methods: We selected structures of interest involved in urinary continence and sexual potency after a literature review. A prostate diagnostic MRI was performed on a 3Tesla scanner. On T2 sequences using axial, coronal and sagittal planes radiation oncologists jointly with radiologists identified and contoured critical structures.

Results: Structures identified were penile bulb (PB), corpus spongiusum (CS), corpus cavernosum (CC), bladder neck (BN), preprostatic sphincter (PS), prostate-membranous sphincter (PMS) and neurovascular bundles (NVBs). PB was contoured jointly with the CS since there is no visible distinction on MRI. Cranially it is a iperintense structure anterior to the rectum and posterior to CC. Caudally, CS constitutes the penis surrounding the urethra, posterior to CC (Figure 1a). CC appears as a iperintense structure delimitated by a ipointense membrane, on T2 sequences, extending from the penis root to its free edge, in anterior position respect to the CS (Figure 1b). BN is well represented on sagittal plane as the ipointense lower portion of the bladder above the prostate (Figure 1c). PS, visible on coronal plane, is located in the ipointense lower tract of the bladder neck, in continuity to the detrusor muscle (Fig 1d). PMS is a ipointense structure surrounding the membranous portion of the urethra, between the apex of the prostate and the bulb of the urethra (Figure 1e). NVBs run posterolaterally to the prostate, at hours 5 and 7. On axial T2 MRI sequences they appear as tiny ipointense structures in the contest of a region of iperintense fibrous tissue, delimited laterally from lateral pelvic fascia, medially from prostatic fascia and posteriorly from the fascia of Denonvilliers (Figure 1f). In addition, we delineated also levator ani, internal anal sphincter and external anal sphincter (Figure 1g-1l).

Conclusions: Diagnostic 3T-MRI was indispensable in identifying and contour male pelvic floor structures aimed to the urinary continence and sexual potency.

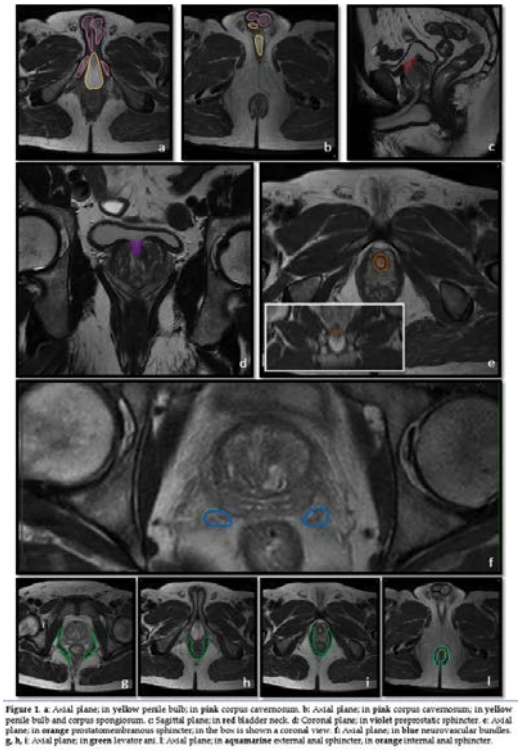

Figure 1. a: Axial plane; in yellow penile bulb; in pink corpus cavernosum. b: Axial plane; in pink corpus cavernosum; in yellow penile bulb and corpus spongiosum. c: Sagittal plane; in red bladder neck. d: Coronal plane; in violet preprostatic sphincter. e: Axial plane; in orange prostatomembranous sphincter; in the box is shown a coronal view. f: Axial plane; in blue neurovascular bundles. g, h, i: Axial plane; in green levator ani. l: Axial plane; in aquamarine external anal sphincter, in orange internal anal sphincter.

Figure 1.

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POSTMASTECTOMY RADIOTHERAPY DOSE DISTRIBUTION ON TISSUE EXPANDERS: DOES THE INFLATION STATUS REALLY MATTER?

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Aims: Different pattern practice exist about the inflation/deflation status of tissue expanders (TE) and postmastectomy radiotherapy (PMRT). This study compares PMRT dose distribution to the chest wall and to organs at risk (OARs) on three different TE inflation status to find the best condition.

Methods: From May 2013 to November 2014 six patients (pts) addressed to PMRT on TE were studied. They were given a CT simulation immediately after surgery with empty TE (eTE). Once obtained definitive expansion two other CT studies were achieved: one with TE fully enflated (fTE) and the other after its deflation (dTE). A 3D-conformal radiotherapy (RT) using two opposite tangential photon fields was planned for each of the three conditions and delivered by a LINAC. Dose prescription to the target volume was 50.4 Gy/28 fractions with respect to OARs dose constraints according to AIRO guidelines.

Results: Four pts had right breast cancer stage IIIb and two had left side stage IIIc. Median age was 60 (range 39-74). Dose volume histograms were conducted to highlight the best situation in terms of target coverage and OARs respect. Concerning planning target volume (PTV) coverage for the chest, median value of V95% was 98.6% (range 97.6;99.4), 98.2%(range 96.2;99.2) and 98.3% (range 95.3;99.0) for the eTE dTE and fTE, respectively. Dose constraints for OARs have been always respected. For lungs the best values of V20Gy< 20% were in the fTE condition being 11.8% to the right lung and 12.5% to the left one. For the heart the mean dose < 5Gy was considered and was always respected. We identified fTE condition as the status that minimized the dose to OARs with the only exception for contralateral breast, where D1%< 5Gy were found to be 2,23Gy and 1,9Gy for the fTE and eTE status, respectively. RT was always delivered in the fTE configuration.

Conclusions: Even if very limited, this study has shown no differences on dose distributions given the three different TE inflation status. Due to unnecessary deflation of the TE, supported by adequate treatment plannings, our policy is to treat pts with TE fully inflated, also according to recent published data where maximal inflation is suggested as the option that minimizes RT related complications.

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MRI–CT CO-REGISTRATION FOR VOLUME DELINEATION IN RADICAL RADIOTHERAPY OF PROSTATE ADENOCARCINOMA: VOLUMETRIC AND DOSIMETRIC EVALUATIONS

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Aims: To assess the role of magnetic resonance imaging (MRI) in treatment volume delineation for radical radiotherapy of prostate cancer.

Methods: Thirty patients (pts) candidates to radical radiotherapy were enrolled in this study. Median age was 73.5 (range: 64-80), median Performance Status was 90 (range: 80-100), median Gleason score was 7 (range: 6-9) and median PSA was 21 (range: 5.9-125). According to D'Amico classification system, 4 pts were "low risk", 6 pts were "intermediate risk" and 20 pts were "high risk". All pts underwent pelvic CT and contrast MRI for tumor staging and radiotherapy planning. T2-weighted MR images were co-registered with CT simulation images. The clinical target volume (CTV) was contoured on CT images (CTV-CT) and on CT/T2-weighted MRI dataset images (CTV-MRI). Two treatment plans were calculated for the two CTV datasets. All pts were treated with intensity-modulated therapy (IMRT) or volumetric modulated arc therapy (VMAT). The PTV prescribed dose was 76 Gy for low-risk pts and 78 Gy for intermediate and high-risk pts.

Results: The mean CTV-CT was 41.51 cc (range 25.24-73.61), and the mean CTV-MRI was 33.62 (range 16.14-81.90). The CTV-MRI mean value was 8.9% smaller than that defined by CTV-CT, corresponding to a CTV-MRI mean reduction of 7.89 cc (range 0.1-22.45). Dosimetric parameters of 15/30 pts have been analyzed thus far: a significant reduction of penile bulb V50 (-25.17) and D50 (-38.24%) and a significant reduction of rectum V60 (-2.08%) and V40 (- 4.2%) were observed. Other parameters (bladder V50, bladder V65) are under evaluation

Conclusions: The use of MRI fusion imaging showed a reduction in treatment volumes and dosimetric parameters for organs at risk (OARs) compared to CT images alone. Thus, our findings point to a key role of MRI in the planning of radiotherapy treatment, showing a reduction in target volumes and significant OARs sparing in the planning phase.

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NODAL SALVAGE RADIOTHERAPY IN PATIENTS PREVIOUSLY IRRADIATED ON PROSTATIC BED: A REPORT OF TWO CASES

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Aims. Salvage radiotherapy (RT) of nodal failure after RT of prostate or prostate bed is challenging. Traditionally, treatment was based on hormonal therapy. Here we report two cases of pelvic nodes RT after adjuvant or salvage RT on prostate bed.

Methods. Both patients were diagnosed with prostate cancer and underwent radical prostatectomy in 2010. One patients with very high risk cancer (GS 7, pT3b, NX) was treated with adjuvant 3D conformal radiotherapy on the prostatic bed (70 Gy/35 fractions). The other patient, with intermediate-risk cancer (PSA: 2.55, GS: 7 and pT2a, N0), underwent salvage intensity modulated radiation therapy (IMRT) on the prostatic bed for local relapse 44 months after surgery (66 Gy/30 fraction). An increased value of PSA with a doubling time ≤ 6 months was recorded in both patients after 52 and 14 months from RT, respectively. Patients underwent 11C-Choline PET and multiple pelvic lymph nodes metastasis were diagnosed (common iliac + external iliac + internal iliac nodes and para-rectal + internal iliac + common iliac nodes, respectively). Hormonal therapy with LH-RH analogue (3 years) and salvage pelvic lymph nodes RT were prescribed to both of them. Prescribed dose, delivered with IMRT-SIB, was 54 Gy to standard nodal pelvic target and 60 Gy to positive nodes in 25 fractions, respectively.

Results. Both patients did not show severe toxicity (G ≥ 3 acute toxicity or G ≥ 1 late toxicity). The worse toxicity was G2 nicturia in the first patients 9 months after the end of salvage RT.In both patients, 22 and 26 months after salvage RT, respectively, PSA value is 0.01 ng/ml.

Conclusions. In conclusion, these two cases seem to suggest the feasibility of salvage pelvic nodes RT after irradiation of the prostatic bed.

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T2 AND DIFFUSION-WEIGHTED MRI SEQUENCES FOR GROSS TUMOR VOLUME DELINEATION IN RECTAL CANCER: AGREEMENT BETWEEN RADIOLOGIST AND RADIATION ONCOLOGIST AND IN VOLUMES

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Aims: T2 weighted Magnetic Resonance Imaging (MRI) imaging is currently considered the gold standard for rectal cancer staging and is often used in addition to Computed Tomography (CT) scan for rectal cancer radiotherapy planning. Functional Diffusion-weighted MRI (DWI) images are able to improve lesion detection and could represent a valid instrument for an accurate delineation of Gross Tumor Volume (GTV) in rectal cancer, as reported in several studies. The aim of this study was to evaluate the inter-observer agreement between a radiologist and a radiation oncologist, and the difference in volumes, in T2 and diffusion weighted (DWI) MRI of GTV delineation, in locally advanced rectal cancer patients.

Methods: Two observers, one radiologist and one radiation oncologist, both with specific experience in rectal cancer diagnosis and treatment, delineated GTV of 50 rectal cancer patients on T2 weighted MRI (T2GTV) and echo planar b1000 DWI (DWIGTV). Observer agreement was assessed using DICE index, Bland-Altman analysis and intra-class correlation coefficient (ICC). Student t test was used for GTV comparison.

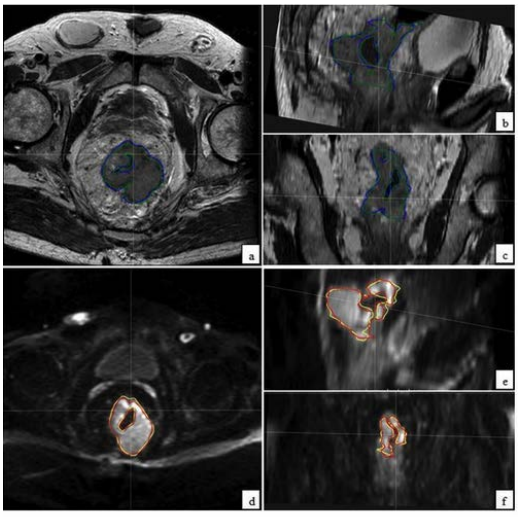

Figure 1 Graphic representation on axial (Panels a), sagittal (Panels b) and coronal (Panels c) planes for $T2_{GTV}$ and on axial (Panels d), sagittal (Panels e) and coronal (Panels f) for DWI_{GTV} volumes. Green and blue contours represent $T2_{GTV}$ for radiologist and radiation oncologist, respectively. Red and yellow contours represent DWI_{GTV} for radiologist and radiation oncologist, respectively.

Figure 1.

Results: Median T2GTV and DWIGTV volumes were 17.09±14.12 cc (1.92-62.03) and 12.79±12.31 cc (1.23-62.25) for radiologist, and 16.82±13.66 cc (1.78-65.9) and 13.72±12.77 cc (1.29-69.75) for radiation oncologist. T2GTV were significantly larger compared to DWIGTV ($p<0,001$ and $p<0,001$, for both observers). An example of agreement for both observers in T2GTV and DWIGTV delineation is shown in Figure 1. Mean DICE index for T2GTV and DWIGTV were 0.80±0.07 and 0.77±0.06. The mean difference between the two observers were 0.26 cm3 (95%CI: -5.36 to 5.88) and -1.13 cm3 (95%CI: -5.70 to 3.44) for T2 and DWI volumes. The ICC for T2 volumes was 0.989 (95%CI: 0.981-0.994) ($p<0.001$) and 0.992 (95%CI: 0.986-0.996) ($p<0.001$) for DWI volumes.

Conclusions: DWI resulted in smaller volumes delineation compared to T2 weighted MRI. Substantial and almost perfect agreements were reported for DWIGTV and T2GTV between radiologist and radiation oncologist. Due to the fact that DWI could be considered a simple technique for volume delineation for radiation oncologist, DWI could be used to improve quality in radiation planning for an accurate and smaller boost volume delineation when a dose escalation is investigated.

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PARTIAL IRRADIATION OF A BULKY SARCOMA WITH A HIGH-SINGLE-DOSE: A CASE REPORT

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Aims: The objective of this case is to report the excellent results of using an unconventional radiotherapy schedule consisting of a high dose Partial IrradiaTion of a bulky lesion targeting the Hypoxic tumor segment (PITH, Tubin *et al*.) which in early studies has shown to possibly induce both abscopal and bystander effects.

Materials and Methods: In January 2018, a 57-year-old male was referred to our Radiotherapy Unit for severe uncontrolled pain (NRS=10) due to a bulky tumor mass (15 cm maximum diameter) mass in the left pelvis extending from the muscle ileopsoas to the adductor complex. A biopsy demonstrated a poorly differentiated malignant fibrosarcoma. The patient received the PITH treatment consisting of a single radiotherapy fraction of 10 Gy to the 70% isodose line encompassing a subtle 3 mm rim around the central necrotic core of the lesion (defined as the hypo-metabolic tumor volume showing no contrast enhancement on an integrated positron emission and computed tomography scan) with no margin. PITH was delivered using a volumetric modulated arc technique on a Linear accelerator equipped with an on board cone beam computed tomography (Edge, Varian)

Results: Three days after the treatment the patient experienced a partial pain relief (NRS 4) that allowed for a reduction of the opioid medication. One month after treatment, in February 2018, a CT scan showed a marked reduction of the size of the mass (maximum diameter 8 cm), the patient was free from opioid medication and reported only a mild pain (NRS 2). No side effects were observed.

Conclusions: A novel unconventional simple 1-day-treatment have demonstrated high effectiveness, with no toxicity in a case with a bulky radio-resistant tumor mass. This successful result deserves further investigations in clinical studies.