Adroterapia
Evidenze Cliniche

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XXIV CONGRESSO NAZIONALE
AIRO 2014
Padova, 18-11 Novembre 2014
Improvement in Technology

Improvement in Dose Distribution
Improved Dose Distribution

Technology

• Smaller volume
• Higher dose

Inverse Square Law

• > LC & Survival
• < Toxicity
• Shorter treatment
Hadrons. A new dimension ......
Physical Selectivity

- Inverted depth dose profile (Bragg peak)
- Defined penetration depth
- Less lateral scattering ($^1\text{H} \neq \text{C}_{12}$)
- Reduction of integral dose
Radiobiology of particles
Which tumors might benefit of high LET particles?

**Radioresistant for genetic alteration**
- Up-regulated oncogenes
- Mutated tumor suppressor genes
- Dis-regulated apoptosis

**Radioresistant for intratumoral micromilieu**
- Deprivation of oxygen
- High angiogenetic potential
- Up-regulated defense system

**Radioresistant for proliferation status**
- High content of quiescent cell clones
- Slow proliferation activity
Worldwide Access to Hadrons
Union of Light Ion Centres in Europe

The ULICE project is co-funded by the European Commission under FP7 Grant Agreement Number 228436.
Loma Linda University Medical Center

First hospital based protontherapy centre (1992)

Optivus Ltd. commercialises this centre
Protontherapy: a market exists ...
Coming up: single room facility
Literature survey
In-silico studies
Cancer Registry

Standard Indications

Recommends to treat

Recommends to investigate

Improved Local Control

Reduced Side Effects

Reduced Second Tumors
Standard Indications
<1% of RT
Eye, Pediatrics, Base of skull

Improved LC
3% of RT
Intracranial, H&N, Urologic, Lung, Sarcoma, Reirradiation

Reduced Side Effects
12% of RT
Intracranial, H&N, Urologic, Lung, Breast, GI, Lymphoma, Sarcoma, Gynecological

Reduced Second Tumors
2% of RT
Breast, Lymphoma, Testis
UVEAL MELANOMA

- More than 10,000 patients treated
  (MGH/HCL Boston, PSI Villingen, Nice & Orsay, Clatterbridge)
- 5y-LC rate >95%
- Eye preservation >90%
- Visual acuity >45%
PT in Skull Base Chordomas and Chondrosarcomas
<table>
<thead>
<tr>
<th>Reference</th>
<th>Institution</th>
<th>Pts</th>
<th>Histo-logy</th>
<th>RT</th>
<th>GTV</th>
<th>Dose , mean (CGE)</th>
<th>% LC</th>
<th>F-up (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hug et al, 1999</td>
<td>LLUMC</td>
<td>58</td>
<td>C (33) CS (25)</td>
<td>X+p</td>
<td>(9%): 0 to ≤15 mL (12%): &gt;15 to ≤25 mL (79%): &gt;25 mL</td>
<td>71.9 (66.6-79.2)</td>
<td>3 yrs: 67 (C) 5 yrs: 59</td>
<td></td>
</tr>
<tr>
<td>Munzenrider et al, 1999</td>
<td>MGH</td>
<td>290</td>
<td>C</td>
<td>X+p</td>
<td>NA</td>
<td>72 (70 – 75.6)</td>
<td>5 yrs: 73 (C) 5 yrs: 98 (CS)</td>
<td></td>
</tr>
<tr>
<td>Igaki et al, 2004</td>
<td>Tsukuba</td>
<td>13</td>
<td>C</td>
<td>X+p</td>
<td>(5) P only (8)</td>
<td>Median 72.0 (63.0 -95.0)</td>
<td>3 yrs: 67.1 (C) 5 yrs: 46.0 69.3 (14.6-123.4)</td>
<td></td>
</tr>
<tr>
<td>Noel et al, 2005</td>
<td>CPO</td>
<td>100</td>
<td>C</td>
<td>X+p</td>
<td>23 cm3 (1 - 125 cm3)</td>
<td>Median 67.0 (60.0-71.0)</td>
<td>2 yrs: 86 (C) 4 yrs: 53</td>
<td></td>
</tr>
<tr>
<td>Noel et al, 2004</td>
<td>CPO</td>
<td>26</td>
<td>Cs</td>
<td>X+p</td>
<td>NA</td>
<td>Median 67.0 (22-70)</td>
<td>3 yrs: 91 (CS) 3 yrs: 34 (3-74)</td>
<td></td>
</tr>
<tr>
<td>Ares C et al, 2009</td>
<td>PSI</td>
<td>42</td>
<td>C (42) CS (22)</td>
<td>p</td>
<td>≤25 mL n=24 (C) , n= 15 (CS) &gt; 25 mL n=18 (C) , n= 7 (CS)</td>
<td>73.5 for C (67-74) 68.4 for CS (63-74)</td>
<td>3 yrs: 87 (C) 5 yrs: 81</td>
<td></td>
</tr>
</tbody>
</table>

**5-y Local Control**

Chordoma 59-81%
Chondrosarcoma 79-98%
<table>
<thead>
<tr>
<th>Ref</th>
<th>Institutio n</th>
<th>Pts</th>
<th>Histo</th>
<th>RT</th>
<th>GTV Mean</th>
<th>Dose, mean (CGE)</th>
<th>% LC</th>
<th>Fu (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schulz-Ertner D et al, 2007</td>
<td>GSI</td>
<td>96</td>
<td>C</td>
<td>CRT</td>
<td>80.3 ml (13.9-594.2)</td>
<td>Median 60 (60-70)</td>
<td>80 % at 3 yrs 70 % at 5 yrs</td>
<td>Mean 31 mo (3-91)</td>
</tr>
<tr>
<td>Schulz-Ertner D et al, 2007</td>
<td>GSI</td>
<td>54</td>
<td>CS</td>
<td>CRT</td>
<td>57.2 mL (range, 13.1–255.7 mL)</td>
<td>Median 60 (57-70)</td>
<td>96.2 % at 3 yrs 89.8 % at 4 yrs</td>
<td>Median 33 months (3-84 mo.)</td>
</tr>
<tr>
<td>Mizoe et al, 2009</td>
<td>NIRS</td>
<td>39</td>
<td>C</td>
<td>CRT</td>
<td>51 cm³ (2-328)</td>
<td>60 % at 5 for 48-57.6 Gy E</td>
<td>95 % at 5 for 60.8 GyE</td>
<td>Mean 53 mo. (8-129)</td>
</tr>
<tr>
<td>Hasegawa *, 2010</td>
<td>NA</td>
<td>12</td>
<td>CS</td>
<td>NA</td>
<td>48-57.6 (2) 60.8 (10)</td>
<td>100 % at 5y</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Up-dated analysis at international meeting*
# Proton therapy for Atypical and Malignant Meningiomas


<table>
<thead>
<tr>
<th>Parameters/Results</th>
<th>Atypical Meningioma (AM)</th>
<th>Malignant Meningioma (MM)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photon RT only</td>
<td>4/15 (27%)</td>
<td>11/16 (73%)</td>
<td>—</td>
</tr>
<tr>
<td>Combined Proton/Photon RT</td>
<td>11/15 (73%)</td>
<td>5/16 (31%)</td>
<td>—</td>
</tr>
<tr>
<td>Mean RT Target Doses (Gy/CGE)</td>
<td>62</td>
<td>58</td>
<td>—</td>
</tr>
<tr>
<td>Range</td>
<td>50–68</td>
<td>40–72</td>
<td>—</td>
</tr>
<tr>
<td>Local Control</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>At 5 years (actuarial)</td>
<td>7/15 (47%)</td>
<td>6/13 (46%)*</td>
<td>—</td>
</tr>
<tr>
<td>At 8 years (actuarial)</td>
<td>3/8 (19%)</td>
<td>2/8 (17%)</td>
<td>—</td>
</tr>
<tr>
<td>Failure site</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>In-field</td>
<td>6/8 (75%)</td>
<td>7/7 (100%)</td>
<td>—</td>
</tr>
<tr>
<td>Marginal</td>
<td>1/8</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>1/8</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>RT Target Dose</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>≥60 versus &lt;60 Gy/CGE</td>
<td>90% vs. 0%</td>
<td>100% vs. 0% (at 5 years)</td>
<td>0.025 (AM)</td>
</tr>
<tr>
<td>Distant Metastasis</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>Survival</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>Alive</td>
<td>14/15 (93%)</td>
<td>6/16 (38%)</td>
<td>—</td>
</tr>
<tr>
<td>no evidence of disease</td>
<td>10/15 (67%)</td>
<td>6/16 (38%)</td>
<td>—</td>
</tr>
<tr>
<td>with disease</td>
<td>4/15 (37%)</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Dead of disease</td>
<td></td>
<td></td>
<td>—</td>
</tr>
<tr>
<td>of intercurrent disease</td>
<td>1/15 (07%)</td>
<td>10/16 (63%)</td>
<td>—</td>
</tr>
<tr>
<td>At 5 years (actuarial)</td>
<td>89%</td>
<td>51%</td>
<td>0.02</td>
</tr>
<tr>
<td>At 8 years (actuarial)</td>
<td>89%</td>
<td>51%</td>
<td>0.02</td>
</tr>
<tr>
<td>RT dose ≥60 vs. &lt;60 Gy/CGE</td>
<td>—</td>
<td>87% vs. 15% (at 5 years)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

*excludes 3 pts. who died at or shortly after XRT; Gy = Gray; CGE = Cobalt Gray Equivalent.*
Malignant Melanoma
57.6 GyE/16fr/ 4 wks

Pre RT

53 months

Carbon ion RT at NIRS
Malignant Melanoma in the Left Maxillary Sinus
(Target volume = 151.9 ml)

64 GyE/16 frs.
## Malignant mucosal melanoma in head and neck

<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>Tumor location</th>
<th>Treatment modalities</th>
<th>5-year OS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilligan</td>
<td>28</td>
<td>Sinonasal</td>
<td>Radiotherapy</td>
<td>18</td>
</tr>
<tr>
<td>Shibuya</td>
<td>28</td>
<td>Upper jaw</td>
<td>Radiotherapy +/- surgery</td>
<td>25</td>
</tr>
<tr>
<td>Shah</td>
<td>74</td>
<td>Head and neck</td>
<td>Surgery +/- radiotherapy</td>
<td>22</td>
</tr>
<tr>
<td>Chaudhry</td>
<td>41</td>
<td>Head and neck</td>
<td>Surgery +/- radiotherapy +/- chemotherapy</td>
<td>17</td>
</tr>
<tr>
<td>Lund</td>
<td>58</td>
<td>Sinonasal</td>
<td>Surgery +/- postoperative radiotherapy +/- chemotherapy (BCG, melphalan)</td>
<td>28</td>
</tr>
<tr>
<td>Pandey</td>
<td>60</td>
<td>Head and neck</td>
<td>Surgery +/- radiotherapy +/- chemotherapy</td>
<td>28*</td>
</tr>
<tr>
<td>Chang</td>
<td>163</td>
<td>Head and neck</td>
<td>Surgery +/- radiotherapy +/- chemotherapy</td>
<td>32</td>
</tr>
<tr>
<td>Patel</td>
<td>59</td>
<td>Sinonasal and oral</td>
<td>Surgery +/- postoperative radiotherapy +/- chemotherapy</td>
<td>35</td>
</tr>
<tr>
<td>Stern</td>
<td>42</td>
<td>Sinonasal and oral</td>
<td>Surgery +/- radiotherapy +/- chemotherapy +/- immunotherapy</td>
<td>40</td>
</tr>
<tr>
<td>Guzzo</td>
<td>48</td>
<td>Head and neck</td>
<td>Surgery +/- radiotherapy +/- chemotherapy +/- immunotherapy</td>
<td>21</td>
</tr>
<tr>
<td>Wada</td>
<td>31</td>
<td>Head and neck</td>
<td>Surgery +/- radiotherapy +/- chemotherapy</td>
<td>33*</td>
</tr>
<tr>
<td>NIRS-1(9602)</td>
<td>100</td>
<td>Head and neck</td>
<td>Carbon ion radiotherapy</td>
<td>36</td>
</tr>
<tr>
<td>NIRS-2(0007)</td>
<td>82</td>
<td>Head and neck</td>
<td>Carbon ion radiotherapy +/- chemotherapy</td>
<td>62</td>
</tr>
</tbody>
</table>
Carbon ion RT at NIRS

**Bone and soft-tissue sarcoma**

Pre CIRT  70.4 GyE/16fs/4 wks  5 years
Table 4. Comparisons of overall survival and local control of sarcomas of the adult head and neck

<table>
<thead>
<tr>
<th>Institution (year)</th>
<th>Histology</th>
<th>Treatment</th>
<th>n</th>
<th>MOP (mo)</th>
<th>5-year LC (%)</th>
<th>5-year OS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMH (21) (1944–1988)</td>
<td>Soft-tissue sarcoma</td>
<td>Surgery ± X-ray ± chemo</td>
<td>103</td>
<td>50</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>MGH (22) (1972–1993)</td>
<td>Soft-tissue sarcoma</td>
<td>Surgery ± X-ray ± chemo</td>
<td>46</td>
<td>50</td>
<td>69</td>
<td>74</td>
</tr>
<tr>
<td>NIRS (current study) (2001–2008)</td>
<td>Bone and soft-tissue sarcoma</td>
<td>Carbon ion RT</td>
<td>27</td>
<td>37.0</td>
<td>80.4</td>
<td>57.6</td>
</tr>
</tbody>
</table>

Abbreviations: LC = 5-year local control rate; MOP = median observation period; MSCMCC = M. Sklodowska-Curie Memorial Cancer Center; NCI = national cancer institute; NIRS = National Institute of Radiological Sciences; OS = 5-year overall survival; RMH = Royal Marsden Hospital; UCSF = university of california san francisco

Jingu K et al IJROBP, 2012

CLINICAL INVESTIGATION

CARBON ION RADIATION THERAPY IMPROVES THE PROGNOSIS OF UNRESECTABLE ADULT BONE AND SOFT-TISSUE SARCOMA OF THE HEAD AND NECK


From the *Research Center for Charged Particle Therapy, National Institute of Radiological Sciences (NIRS), Chiba, Japan; †Department of Radiation Oncology, Tokai University School of Medicine, Isehara, Japan; ‡Department of Oral Medicine, Tokyo Dental College, Ichihara, Japan

Purpose: To evaluate the safety and efficacy of carbon ion radiotherapy (C-ion RT) with 78.4 GyE for unresectable bone and soft-tissue sarcoma of the adult head and neck.

Methods: Twenty-seven patients (mean age, 46.2 years) were enrolled in this prospective study on C-ion RT with 78.4 GyE/16 fractions (8 GyE/fraction) between April 2001 and February 2008. The primary end points were acute and late reactions of normal tissues, local control rate, and overall survival rate. The secondary end point was efficacy of the treatment in comparison to historical results with 87.6 or 64.8 GyE/16 fractions.
Carbon ion RT at NIRS

ACC 57.6GyE/16fr/4 wks

Pre RT

24 Months
ACC in the Maxillary Sinus (Target volume = 189 ml)

Dose distribution

Pre-treatment

Post 76 months

Pre-treatment

Post 76 months

57.6 GyE/16 frs.
5-year LC rate

Overall 68 %

MMM 75 %

ACC 73 %

Adenoca. 73 %

Papillary Adenoca. 61 %

SCC 61 %

Sarcomas 24 %
(with Max 64 GyE)

Mizoe J et al, Radiother Oncol, 2012
IMRT & Parotid Sparing
The potential benefit of radiotherapy with protons in head and neck cancer with respect to normal tissue sparing: a systematic review of literature

Groningen & Maastricht, The Netherlands

• 14 in silico planning comparative (ISPC) studies

• Protons have the potential for a significantly lower normal tissue dose, while keeping similar or better target coverage

• Probability of reducing >25% salivary flow with IMRT is 22%, and with IMPT 9%

• Probability of reducing grade 2-4 swallowing dysfunction is reduced by 8.8% with IMRT, and by 17.2% with IMPT

The results of these ISPC studies should be confirmed in properly designed clinical trials
1982-1995, T3-T4, 67.2 Gy vs 75.6 Gy

Shipley, IJROBP, 1995

MGH

Boston

PBT-History

- MGH Phase III results:
  - Decreased local failure in all patients treated with PBT. Reached statistical significance in Gleason 8-10 tumors only.
  - Increased rectal bleeding (primarily grade 1) in high-dose group.
  - No difference in survival.

Prostate Cancer
First Phase III randomized trial
Zietman AL et al, JAMA, 2005
Update at 10 years
b-NED
High Dose 83.7%
Conventional Dose 64.7%
(P=0.0001)

Same results of MD Anderson
phase III trial (70 vs 78 Gy)
with photon EBRT

Pollack A et al, IJROBP, 2002
Efstathiou J, Bekelman J (MGH, Uni Penn).
Phase III Randomized Trial of Protons vs IMRT (79.2 Gy) for low or low-intermediate risk Prostate Cancer

*Primary endpoint* *EPIC* bowel scores at 6 months

350 patients randomized

*EPIC: Expanded Prostate Cancer Index Composite*
Treatment Method by Risk

Low Risk:
T-stage ≤ T2a and PSA < 20.0 and GS ≤ 6

Intermediate Risk:
PSA < 20.0 and T-stage = T2b or GS = 7

High Risk:
T-stage = T3 or PSA ≥ 20.0 or GS ≥ 8

C-ion RTx w/o ADT

C-ion RTx with Short term ADT (6m)

C-ion RTx with Long term ADT (>24m)

ADT; Androgen Deprivation Therapy
Dose Constraint with Rectum DVH

Dose Constraints

OARs

Constraints

Rectum

- $D_{\text{max}} \leq 66\text{GyE}/20\text{f}
- V_{50} < 8\text{cc}

Bladder

- $D_{\text{max}} \leq 66\text{GyE}/20\text{f}
- V_{50} < 50\text{cc}$

Reference DVH: Average DVH of the patients with grade 0~1 rectal toxicity

To make a new plan in order that rectal DVH is below the reference DVH at high dose level.
Biochemical relapse free and Cause-specific survival according to risk factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>No. pts.</th>
<th>5-year rates (%)</th>
<th>*bNED</th>
<th>p-value</th>
<th>#CSS</th>
<th>p-value</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1/2</td>
<td>614</td>
<td>94.0</td>
<td></td>
<td>0.0000</td>
<td>100</td>
<td></td>
<td></td>
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<tr>
<td>T3</td>
<td>247</td>
<td>84.1</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>PSA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20</td>
<td>595</td>
<td>92.1</td>
<td></td>
<td>0.0678</td>
<td>99.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 20</td>
<td>266</td>
<td>88.7</td>
<td></td>
<td></td>
<td></td>
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<td>Gleason score</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>≤ 6</td>
<td>206</td>
<td>92.3</td>
<td></td>
<td>0.0072</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 7</td>
<td>412</td>
<td>94.3</td>
<td></td>
<td>0.0004</td>
<td>99.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 8</td>
<td>243</td>
<td>83.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Integral Dose
3 times higher for all photon’s techniques

Weber DC et al, Radiat Oncol, 2009; 4:34
Comparative analysis of second malignancy in patients treated with proton therapy versus conventional photon therapy.
50 th ASTRO Meeting, Boston, 2008

“treatment with photon therapy was significantly associated with an increased risk of a second malignancy (1.87 to 3.98, p<0.0001)”
New Indications

- NSLCC (Early & Advanced)
- Breast (PBI & Locoregional treatment)
- GI (liver, pancreas, rectum)
- GU (prostate, kidney)
Lomax AJ et al (Villigen & Geneva, Switzerland).
Potential role of intensity-modulated photons and protons in the treatment of the breast and regional nodes.
IJROBP, 55: 785, 2003

- ... only the 2-field, energy-modulated proton plan had the potential to preserve target dose homogeneity while simultaneously minimizing the dose delivered to both lungs, heart, and the contralateral breast.
**Case: 72yrs male, rt. S² adenoca. cT2NoM0 c-stage IB**

- **Lung function**

<table>
<thead>
<tr>
<th></th>
<th>%VC</th>
<th>FEV\textsubscript{1.0} %</th>
<th>%DLCO</th>
<th>PaO\textsubscript{2} (room air)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005.02.08</td>
<td>95.4</td>
<td>49.3</td>
<td>47.7</td>
<td>64.2</td>
</tr>
<tr>
<td>15 mo. after CIRT</td>
<td>104.9</td>
<td>57.3</td>
<td>43.4</td>
<td>62.4</td>
</tr>
<tr>
<td>30 mo. after CIRT</td>
<td>92.1</td>
<td>58.8</td>
<td>46.0</td>
<td>68.9</td>
</tr>
</tbody>
</table>

- **34.0GyE/1fr.**

- 2005.02.08
<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary gland tumors</td>
<td>34</td>
</tr>
<tr>
<td>Reirradiation of head and neck tumors</td>
<td>25</td>
</tr>
<tr>
<td>Mucosal melanoma</td>
<td>7</td>
</tr>
<tr>
<td>Chordoma</td>
<td>119</td>
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<tr>
<td>Chondrosarcoma</td>
<td>23</td>
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<tr>
<td>Sarcoma</td>
<td>32</td>
</tr>
<tr>
<td>Retreatment local recurrence rectal cancer</td>
<td>1</td>
</tr>
<tr>
<td>HCC</td>
<td>1</td>
</tr>
<tr>
<td>Local advanced pancreatic cancer</td>
<td>1</td>
</tr>
</tbody>
</table>
CLINICAL CASE
SKULL BASE CHORDOMA: Proton therapy

10 months F-up
Sacral chordoma, male, 69 years old
After one year hypoesthesia at the left foot: G1 toxicity, marked improvement in urinary and rectal continence, and pain, patient can sit and can walk for 15-20 minutes.
Clinical case

53 year old male

ACC in parafaringeal region with estention on clivus and petrous bone

07/2013 Nasopharinx biopsy: El adenoideo cistic carcinoma

15/10/2013 -- 07/11/2013 CIRT 68.8 Gy [RBE]
Toxicity at the end of CIRT: erythema G1, mucositis G1
Partial Remission and Acute Toxicity G0 after 3 months

PET metionine: significant decrease in MET uptake after 4 months
Clinical case

75 year old men

March 2013: endoscopic surgery R2

No CT for age and coomorbidity

CIRT:
68.8 Gy [RBE] / 16 fractions
FOLLOW-UP 9 AND 12 Months

tox G1 - CR
Improvement in Technology

Improvement in Dose Distribution
Technology Transfer in Clinics

Clinical Results !!!!!!!
Patient Treatment Plan Comparison

Photons vs Hadrons

TCP/NTCP
Small or absent

TCP/NTCP
Moderate or questionable

TCP/NTCP
Major in favour of P+

Randomized Clinical Trial

Photons

Hadrons
Grazie !!!

”Il progresso è reale solo quando i vantaggi di una nuova tecnologia diventano disponibili a tutti”