Appropriatezza nell'Imaging per il Planning Radioterapico in funzione della Tecnica di Trattamento e dei Volumi Radioterapici

Gabriella Macchia

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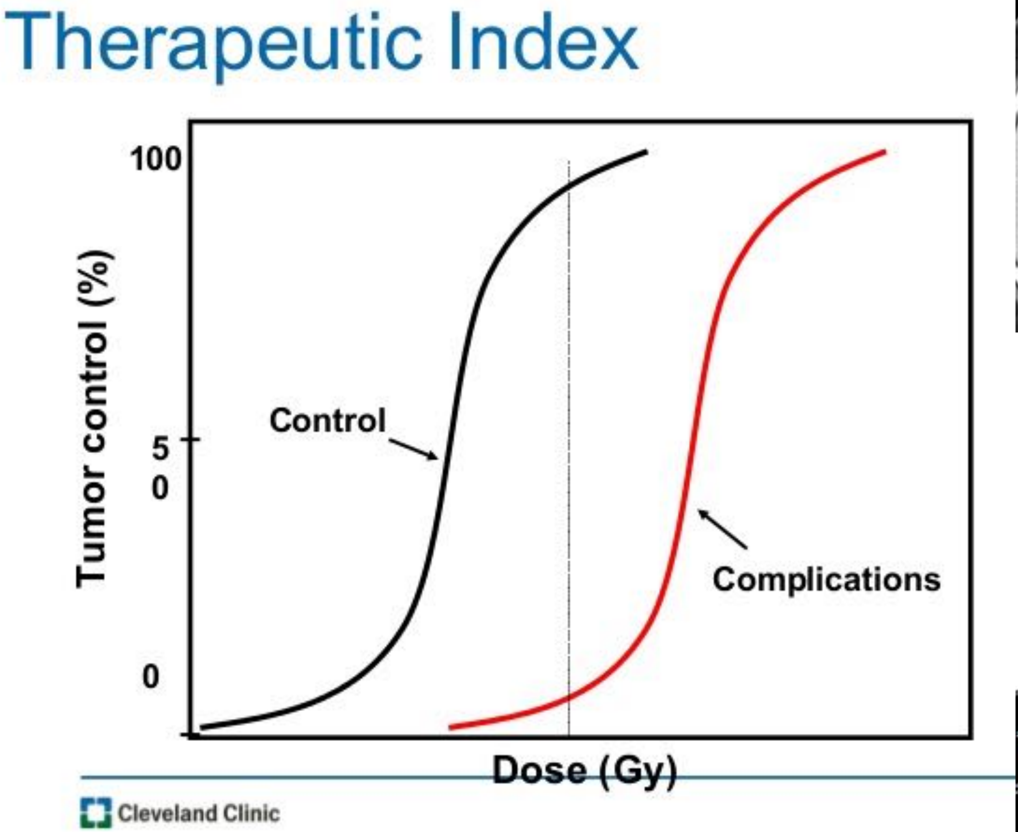
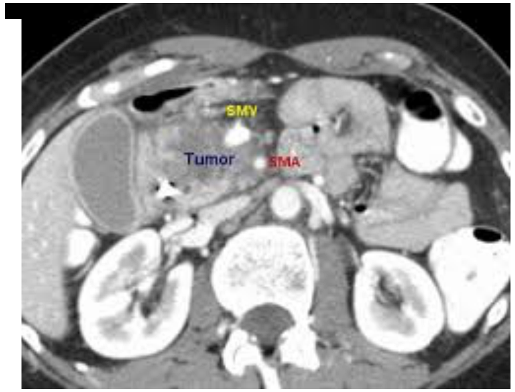
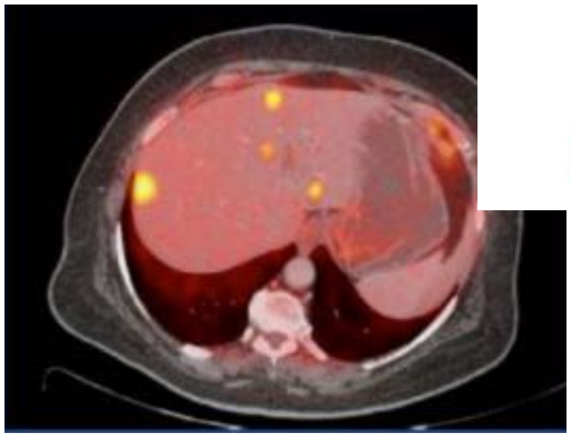
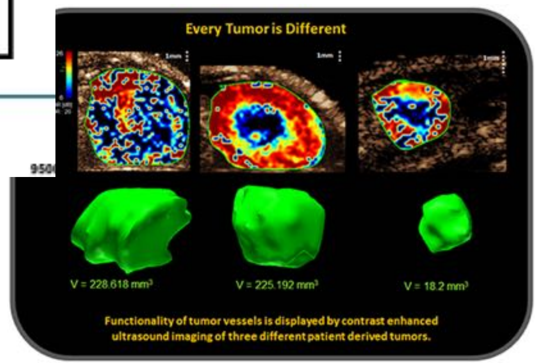
Radiologist & Radiation Oncologist: an unmarried couple!!!

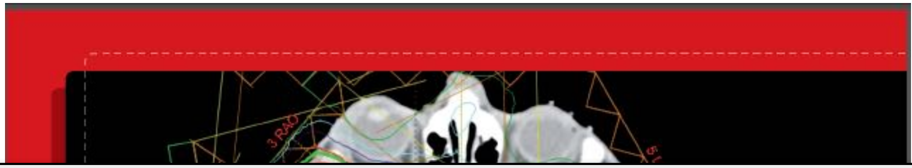
8 novembre 1894







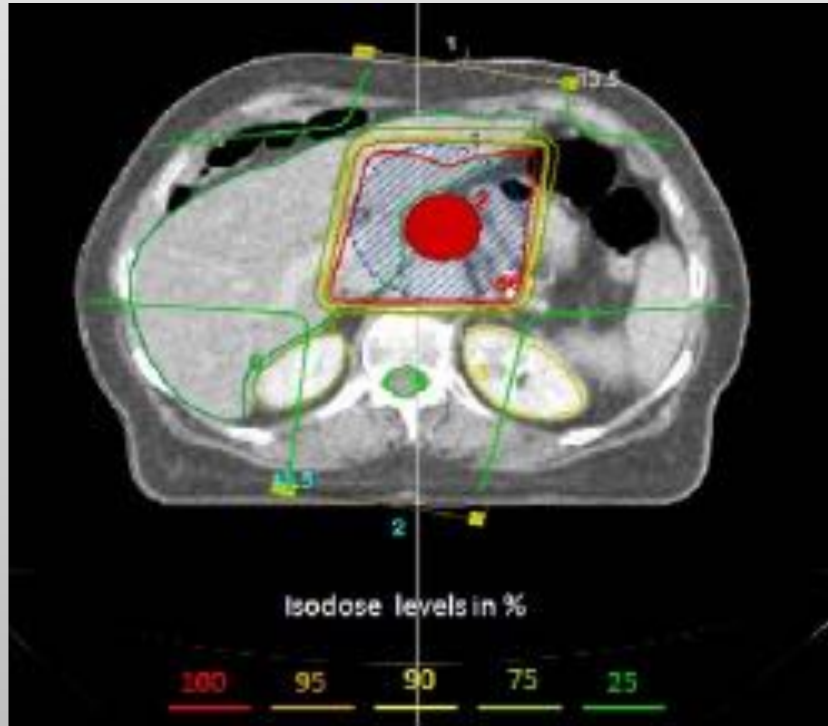




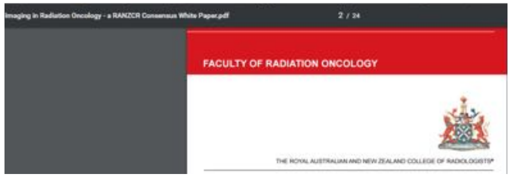
IMAGING IN RADIATION ONCOLOGY

Appropriateness criteria for each site listed under 4 headings:

- Diagnosis and staging
- Treatment planning
- Treatment delivery
- Response assessment

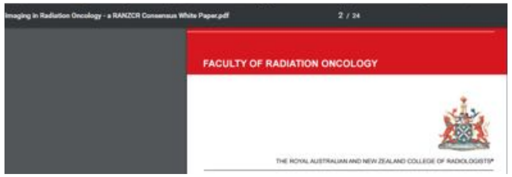


IMAGING IN RADIATION ONCOLOGY - A RANZCR (THE ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF RADIOLOGISTS®) **CONSENSUS WHITE PAPER**


Imaging in Radiation Oncology - a RANZCR Consensus White Paper.pdf
2 / 24
FACULTY OF RADIATION ONCOLOGY
THE ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF RADIOLOGISTS

Criteria of Appropriateness

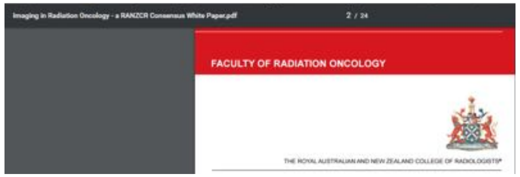
- **diagnostic accuracy** of an imaging modality (spiral multidetector CT in PC),
- **influence on clinical practice** (set-up CT with i.v. contrast →contouring),
- **impact on the patient's clinical outcome** (daily cone beam CT to reduce margin and increase dose)
- **assessed in most part based on high-level evidence** in published literature and supplemented by **expert opinion** (es. AIRO GI guidelines).



Appropriateness criteria for diagnosis and staging

DIAGNOSIS & STAGING					
Tumor Sites	Imaging Modalities				
	USS	CT	MRI	FDG PET	BONE SCINTIGRAPHY
PANCREAS	APPROPRIATE	APPROPRIATE	POTENTIALLY APPROPRIATE	POTENTIALLY APPROPRIATE	APPROPRIATE

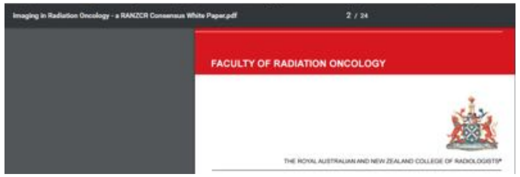
CT with IV contrast (pancreatic CT protocol). Endoscopic ultrasound. ERCP. Bone scan if symptomatic.	MRI with contrast. 18FDG PET for M staging.



Appropriateness criteria for Treatment localization and delivery

TREATMENT LOCALISATION AND DELIVERY			
Tumor Sites	Imaging Modalities		
	ORTHOGONAL (kv/MV)	VOMULETRIC (kV/MV)	USS
PANCREAS	APPROPRIATE	APPROPRIATE	INAPPROPRIATE

Operator dipendency
Ultrasound waves disrupted by air or gas
Large patients


Imaging in Radiation Oncology - a RANZCR Consensus White Paper.pdf 2 / 24

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Appropriateness criteria for Response assessment

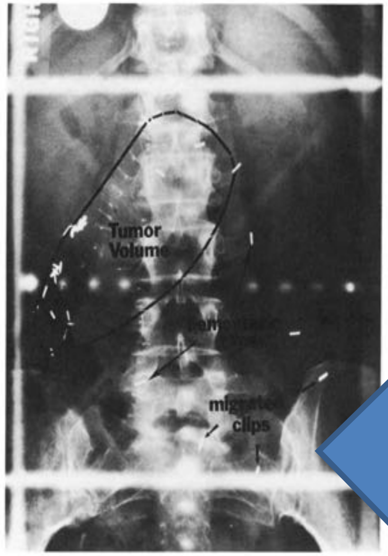
RESPONSE ASSESSMENT				
Tumor Sites	Imaging Modalities			
	USS	CT	MRI	FDG-PET
PANCREAS	INAPPROPRIATE	APPROPRIATE	INAPPROPRIATE	INAPPROPRIATE

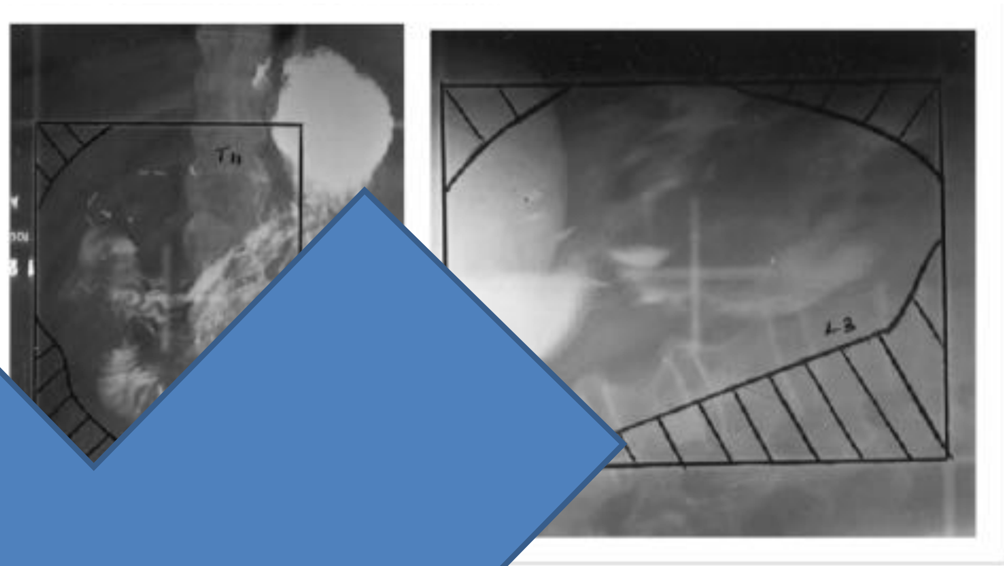
Additional Comments
1. 18FDG PET may be considered in high risk patients to detect extrapancreatic disease prior to definitive treatment. 2. MRI is used as problem solving tool for indeterminate features relating to pancreas or liver on CT.

IMAGING IN RADIATION ONCOLOGY

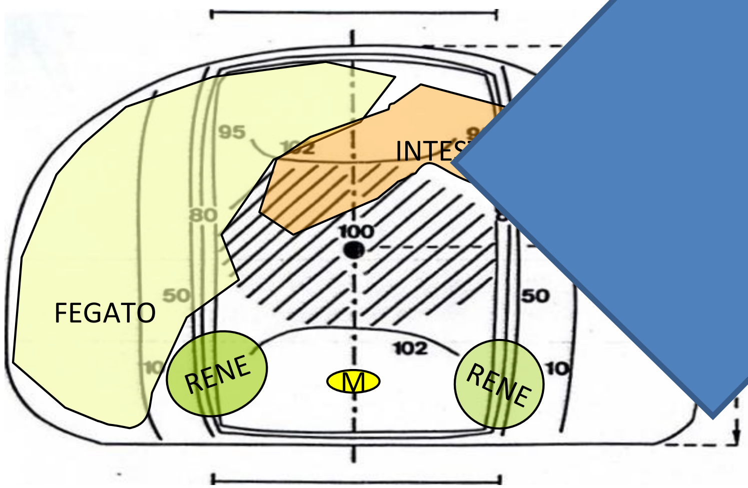
Appropriateness criteria for Treatment planning

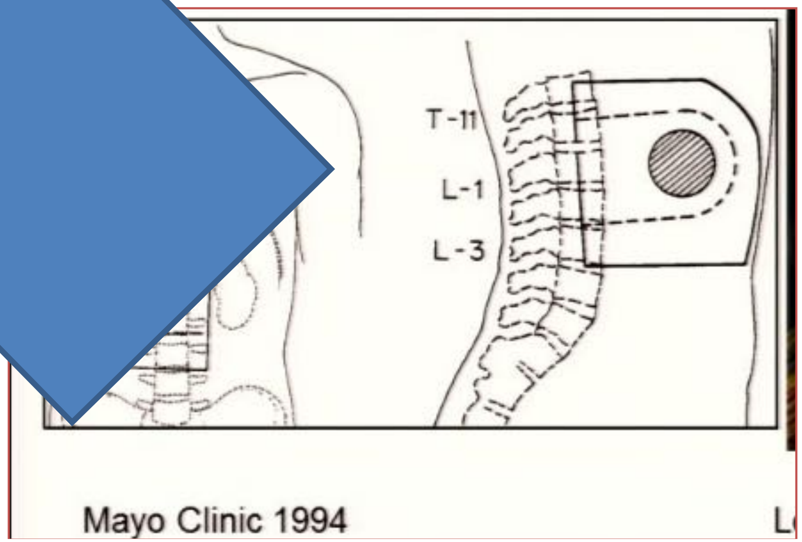
Appropriateness criteria for treatment planning



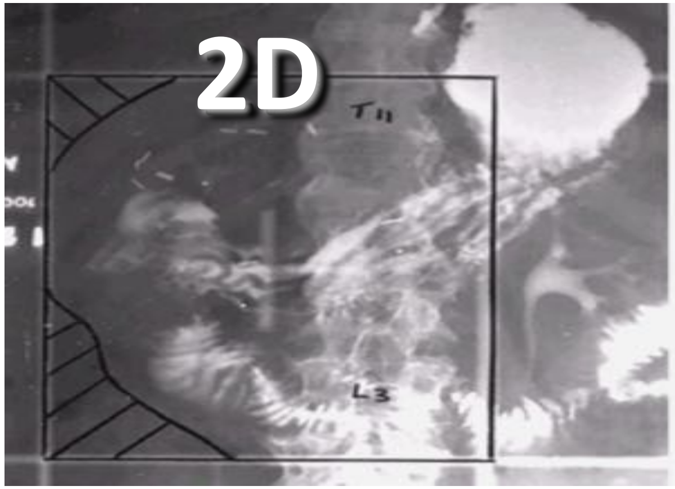


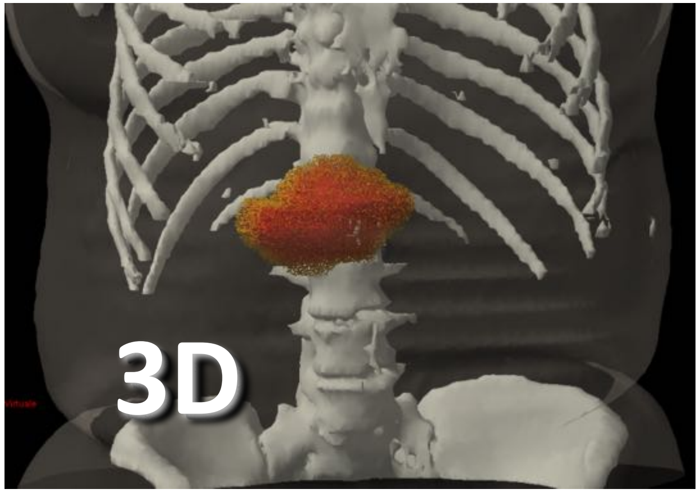
20 Gy - split - 20 Gy (… 1999, ESPAC-1 2004)

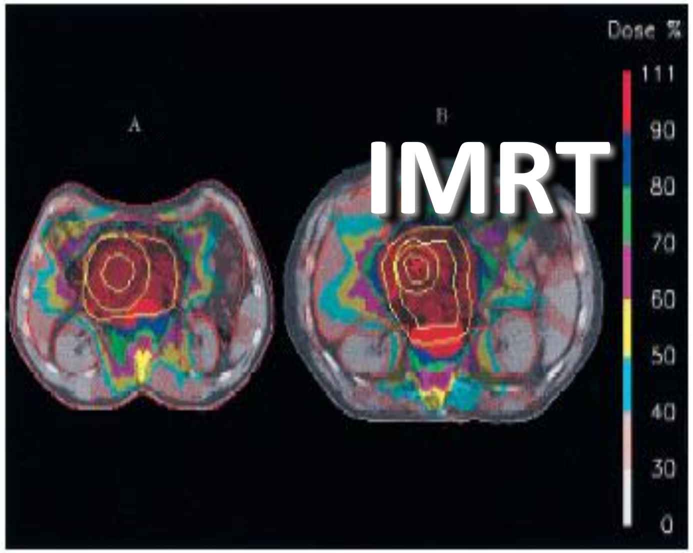


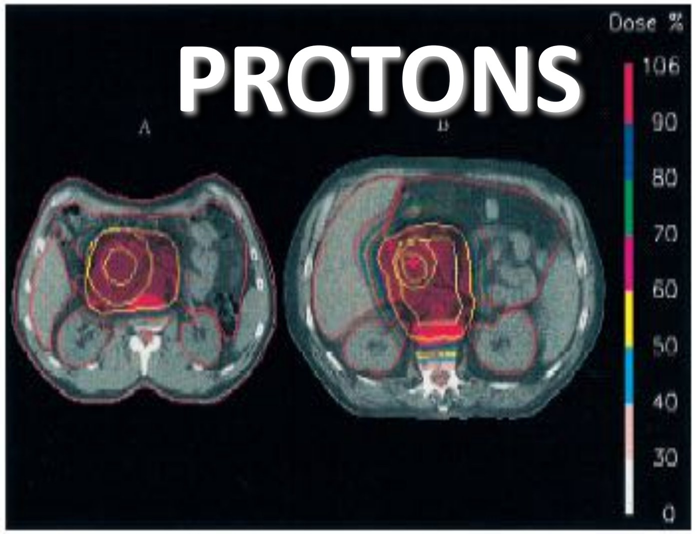


Pancreatic cancer techno-evolution: any improvement?

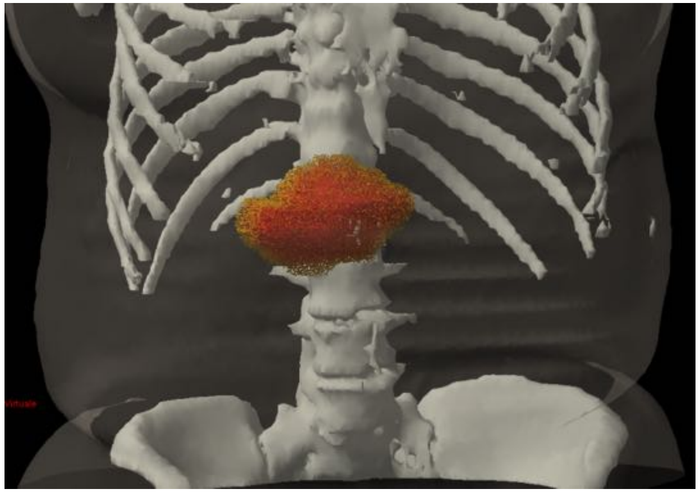




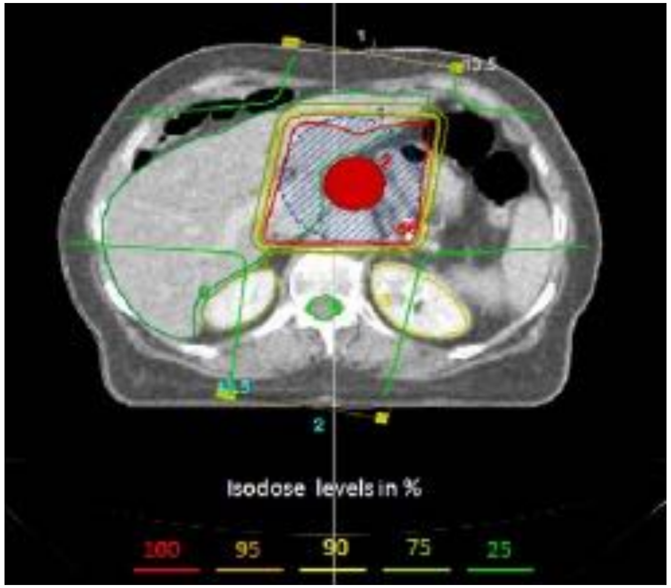




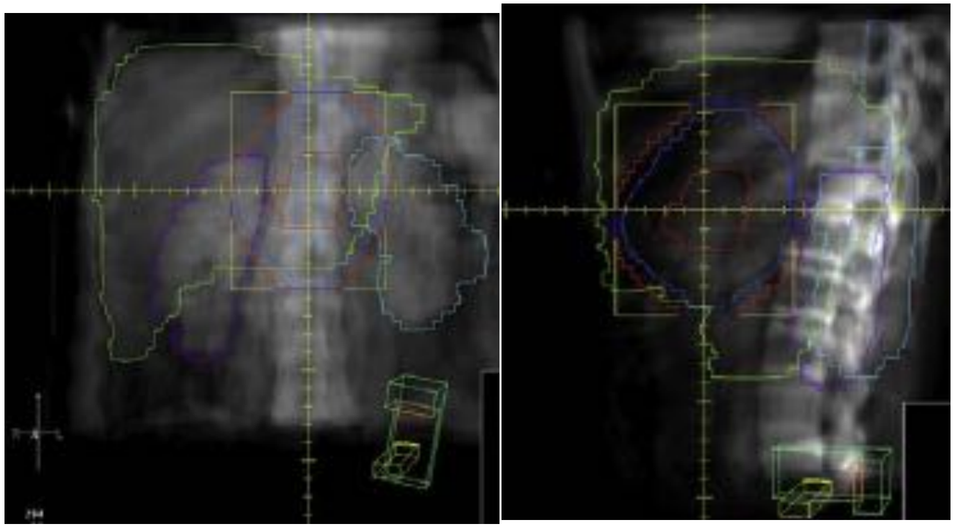
CT scan



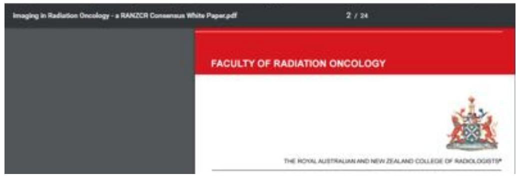
Better **knowledge** of the target volume and critical normal organ position



Platform upon which three-dimensional (3D) dose **calculations** can be made.



Radiation field apertures be **customized** to conform to an individual patient’s target volumes (i.e., conformal radiation therapy [CRT])



Appropriateness criteria for Treatment planning

TREATMENT SIMULATION AND PLANNING

Tumor Sites	Imaging Modalities			
	CT	MRI	FDG-PET	4D CT
PANCREAS	APPROPRIATE	INAPPROPRIATE	INAPPROPRIATE	POTENTIALLY APPROPRIATE

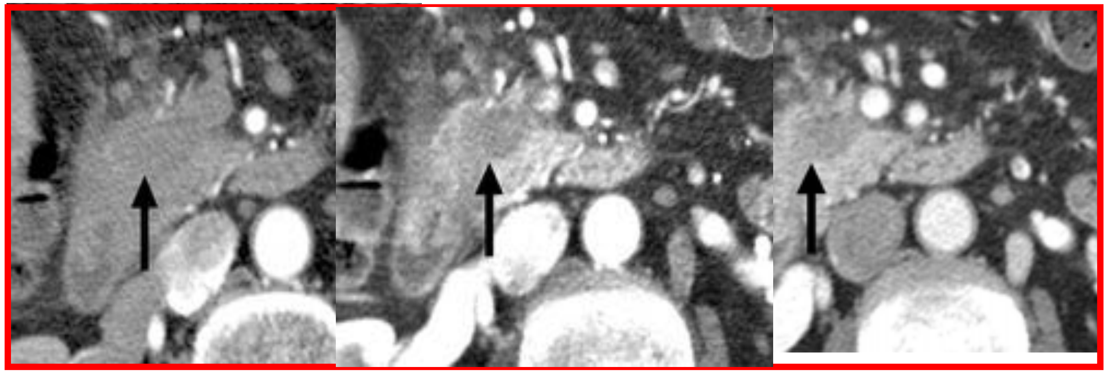
Technical requirements

Thin section

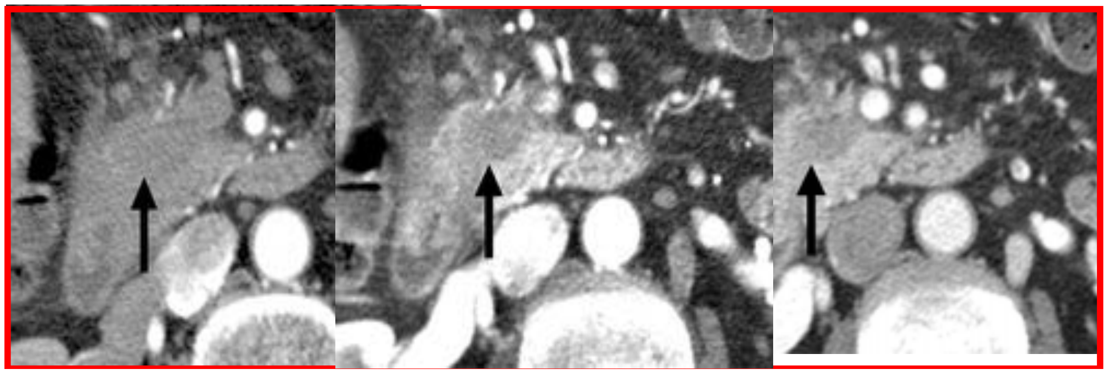
Multidetector spiral

IV contrast

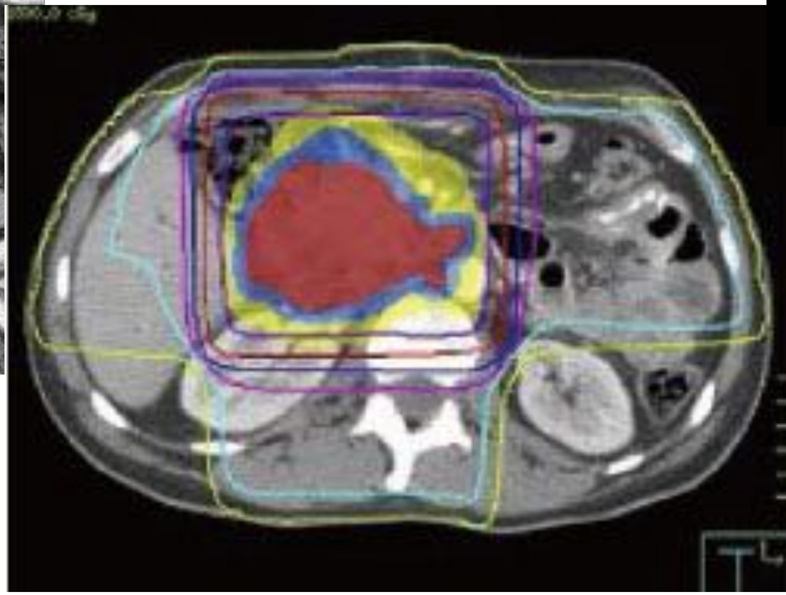
Coronal planes

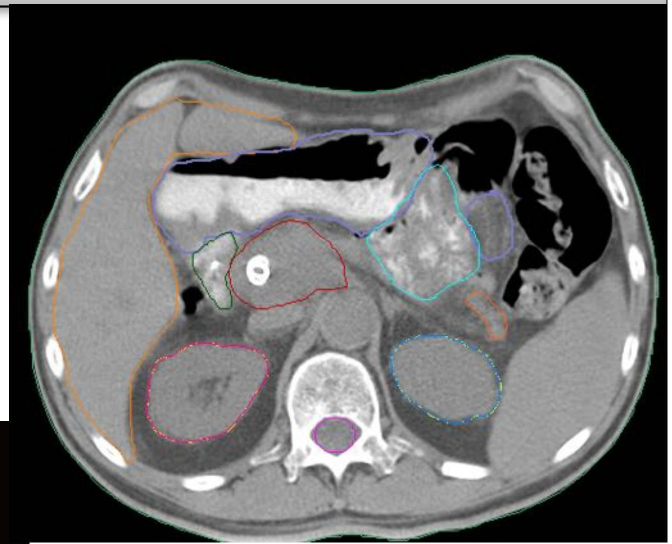


Diagnostic



3D-CRT→CT scan





Set-up

Radiotherapy Technical Considerations in the Management of Locally Advanced Pancreatic Cancer: American-French Consensus Recommendations

Florence Huguet, M.D., Ph.D.,* Karyn A. Goodman, M.D.,[†] David Azria, M.D., Ph.D.,[‡] Severine Racadot, M.D.,[§] and Ross A. Abrams, M.D.[¶]

IJROBP 2012

The planning CT scan should be obtained with **both intravenous and oral contrast medium** to adequately delineate the primary

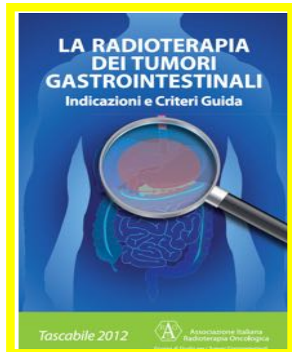
vel. If

c MRI

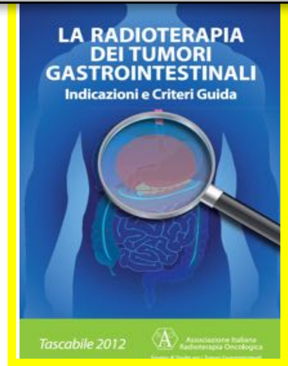
ne full

Simulazione TC:

Somministrazione di Gastrografin (½ litro di acqua con diluiti 2 cc di mdc) per la visualizzazione dell'intestino tenue 30 min prima dell'esecuzione dell'esame. L'infusione di m.d.c. per via endovenosa è raccomandata.
Paziente in posizione supina con braccia oltre la testa; fortemente raccomandato è l'utilizzo di sistemi di immobilizzazione e di tatuaggi di allineamento. L'uso delle tecniche 4D (gating respiratorio, tracking, compressione addominale) è consigliato soprattutto in caso di metodica SBRT/IMRT.



Appropriateness criteria for treatment planning



- Tools available:

Caravatta et al. Radiation Oncology 2012, 7:86
http://www.ro-journal.com/content/7/1/86

RADIATION ONCOLOGY

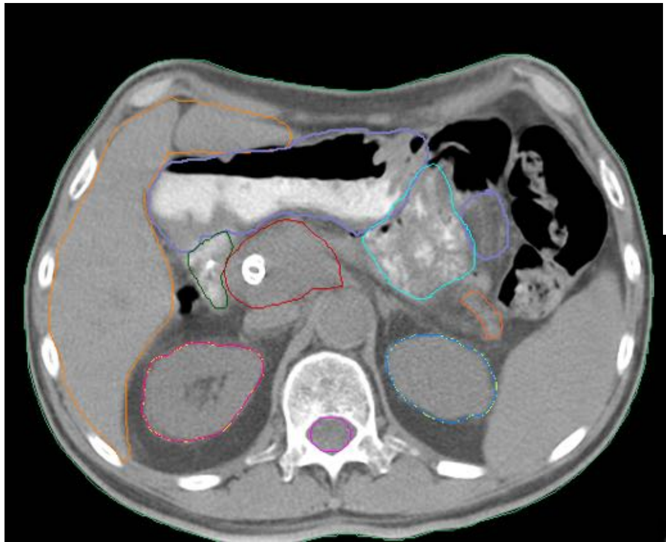
METHODOLOGY Open Access

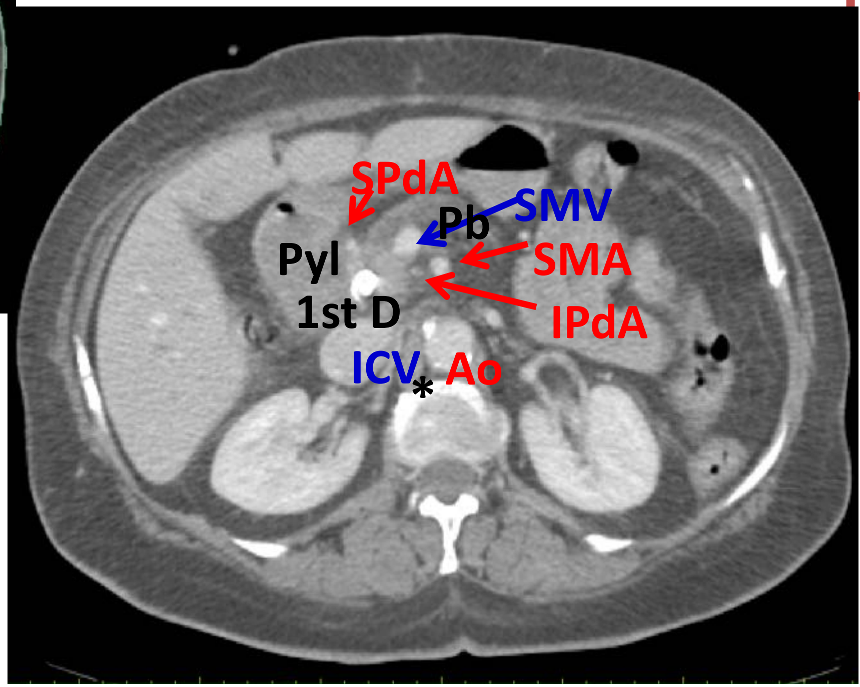
Clinical target volume delineation including elective nodal irradiation in preoperative and definitive radiotherapy of pancreatic cancer

Luciana Caravatta[1], Giuseppina Sallustio[2], Fabio Pacelli[3], Gilbert DA Padula[4], Francesco Deodato[1], Gabriella Macchia[1*], Mariangela Massaccesi[1], Vincenzo Picardi[1], Savino Cilla[5], Alfonso Marinelli[1], Numa Cellini[6], Vincenzo Valentini[6] and Alessio G Morganti[1,6]

CONSENSUS PANEL CONTOURING ATLAS FOR THE DELINEATION OF THE CLINICAL TARGET VOLUME IN THE POSTOPERATIVE TREATMENT OF PANCREATIC CANCER

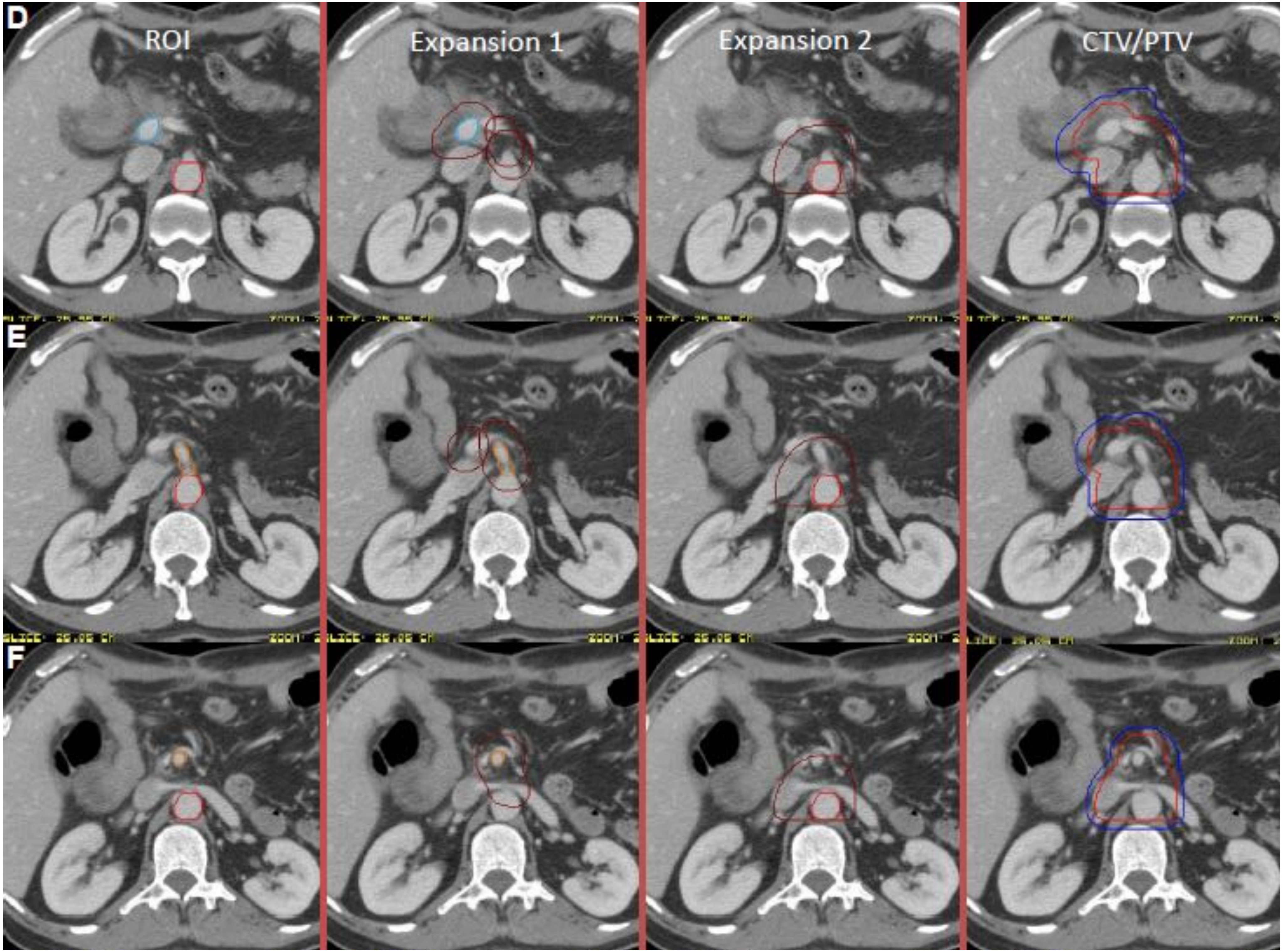
RTOG
RADIATION THERAPY ONCOLOGY GROUP

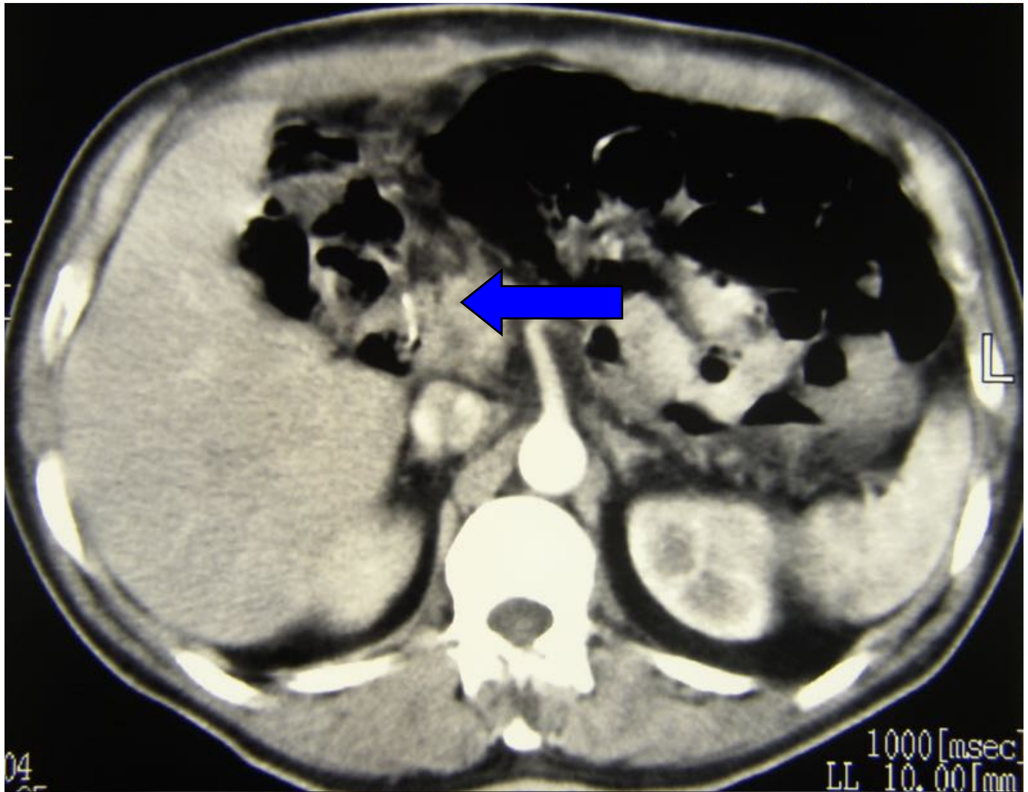


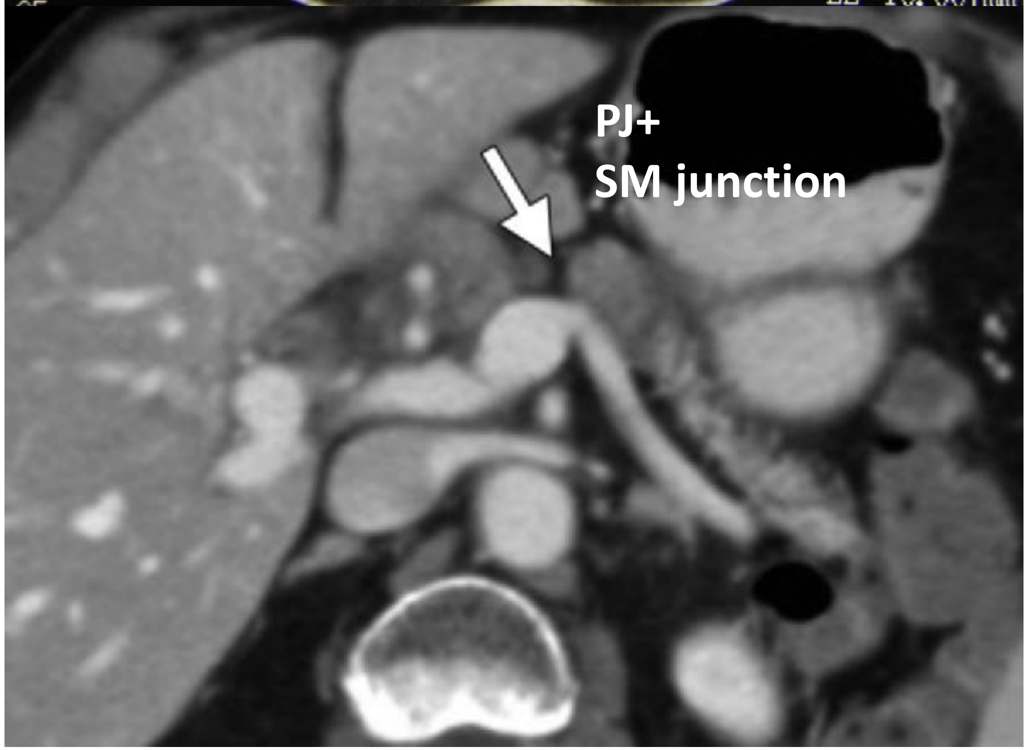


Delineate

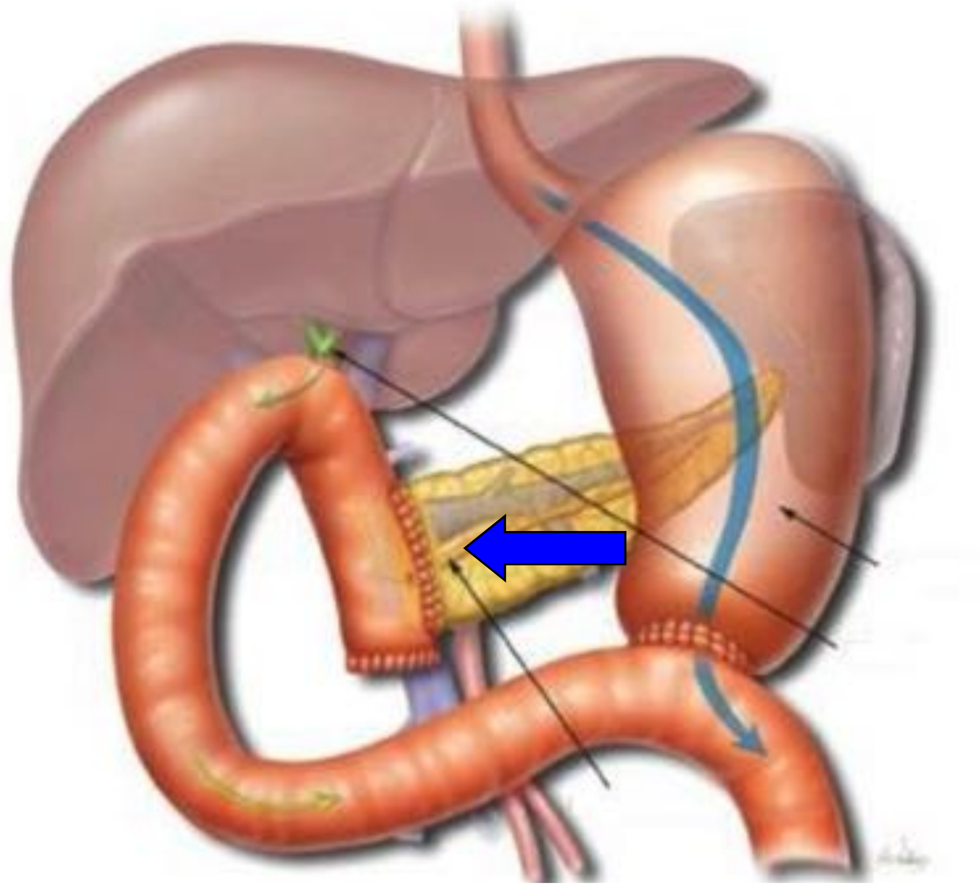
anatomical ROI's
vascular ROI's
OARs


D
ROI
Expansion 1
Expansion 2
CTV/PTV
E
F



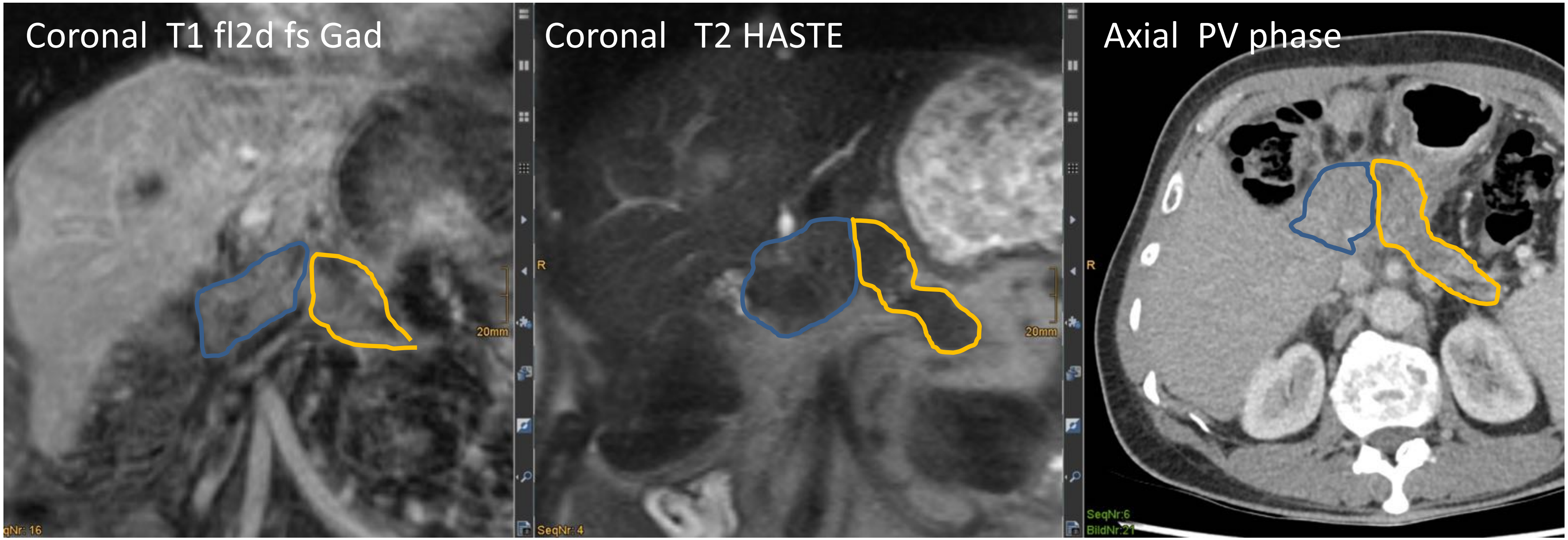


Pancreaticojejunostomy



Yamauchi FI. RadioGraphics 2012;
32:743–764

Postoperative anatomy: Pancreaticojejunostomy



Appropriateness criteria for treatment planning

ONCOLOGY REPORTS 34: 382-390, 2015

Patterns of radiotherapy practice for pancreatic cancer: Results of the Gastrointestinal Radiation Oncology Study Group multi-institutional survey

GABRIELLA MACCHIA[1], ALDO SAINATO[2], RENATO TALAMINI[3], GIOVANNI BOZ[4], ALMALINA BACIGALUPO[5], LUCIANA CARAVATTA[6], MICHELE FIORE[7], MARIA LUISA FRISO[8], VINCENZO FUSCO[9], MARCO LUPATTELLI[10], GIOVANNA MANTELLO[11], GIAN CARLO MATTIUCCI[12], NAJLA SLIM[13], PIERA SCIACERO[14], LUCIA TURRI[15], VINCENZO VALENTINI[12], ALESSIO GIUSEPPE MORGANTI[1,16*] and DOMENICO GENOVESI[17*]

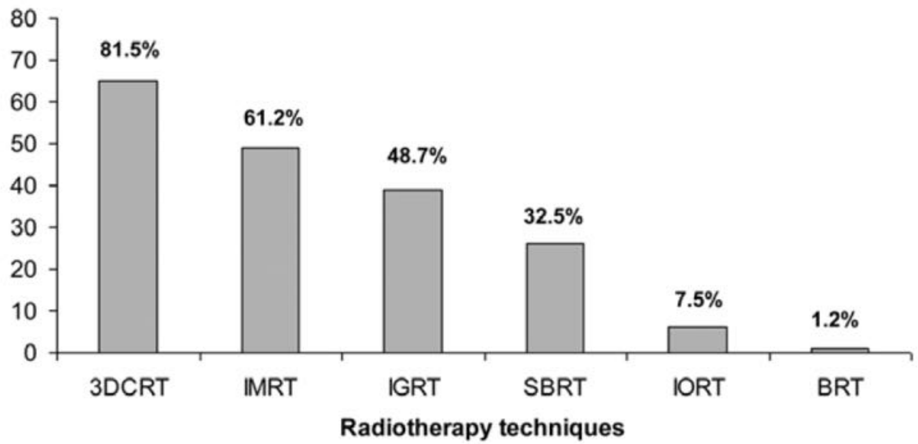
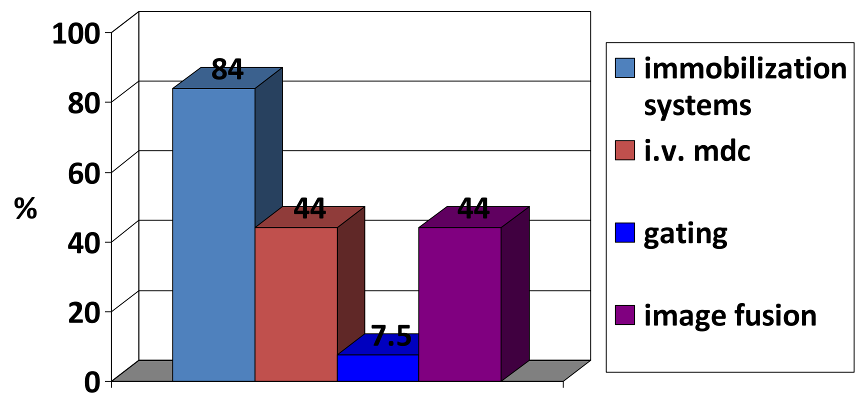
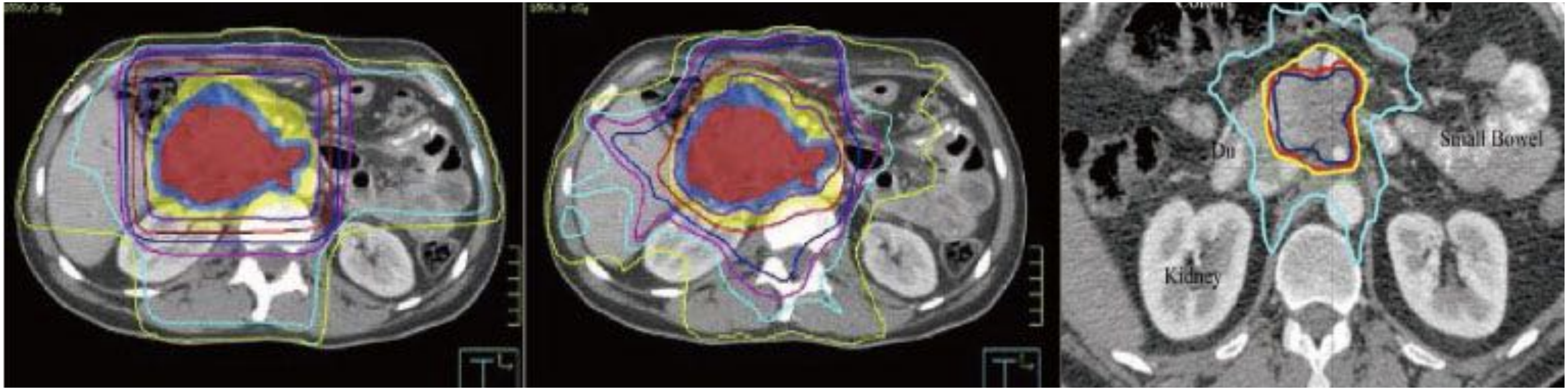


Figure 5. Number of centres using the reported radiotherapy techniques.



3D-CRT & IMRT are recommended techniques

Huguet F. IJROBP 2012



Reduces the dose to OARs and acute and late side effects allowing hypofractionation/dose escalation/both

BUT

High missing target risk (→expecially without IGRT)

IMRT & IGRT: an unmarried couple

ELSEVIER

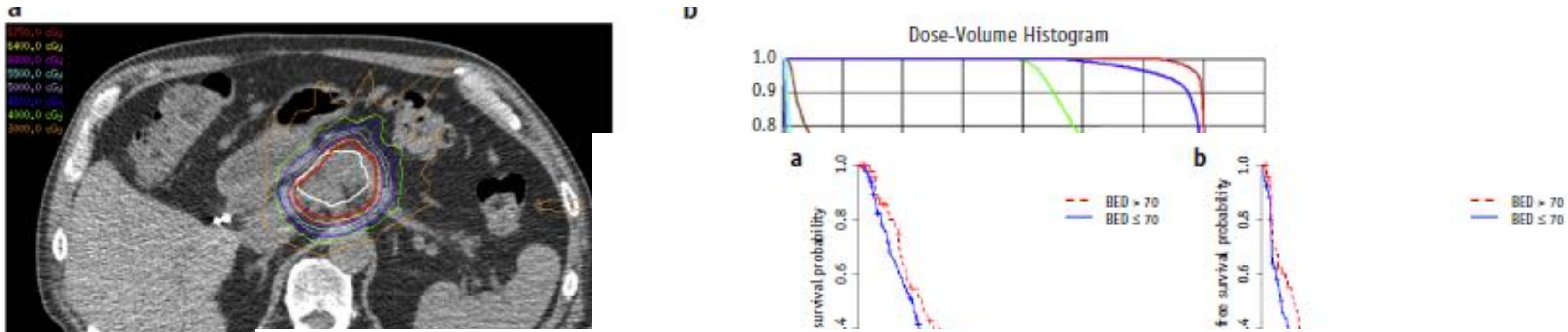
Seminars in RADIATION ONCOLOGY

Utilization of Intensity-Modulated Radiation Therapy and Image-Guided Radiation Therapy in Pancreatic Cancer: Is It Beneficial?

Adam S. Reese, MD, MS, Wei Lu, PhD, and William F. Regine, MD

The recent development of intensity-modulated radiation therapy (IMRT) and improvements in image-guided radiotherapy (IGRT) have provided considerable advances in the utilization of radiation therapy (RT) for the management of pancreatic cancer. IGRT allows for the reduction of treatment volumes, potentially less chance of a marginal miss, and quality assurance of gastrointestinal filling, while IMRT has been shown to reduce both sudden and late side effects compared with 3-dimensional conformal RT. Here, we review published data and provide essential recommendations on the utilization of IMRT and IGRT for the management of patients with pancreatic cancer.

Semin Radiat Oncol 24:132-139



Volume 94 • Number 4 • 2016

Clinical evaluation and treatment

All patients were evaluated by a medical oncologist and a radiation oncologist. Selected patients were subsequently seen by surgical oncologists. All patients were subjected to a dedicated pancreatic cancer protocol contrast-enhanced dual phase abdominal and pelvic CT scan. Pretreatment

Fig. 1. A representative plan of a patient treated with
Axial isodose plots and (b) dose-volume histogram corre
daily by mapping soft-tissue anatomy and isodose lines
simulation and (d) a computed tomography scan obtaine
isodose lines indicate 67.5 Gy, blue 45 Gy, and green 40 C
in an increased dose to the stomach wall. *Abbreviations:*

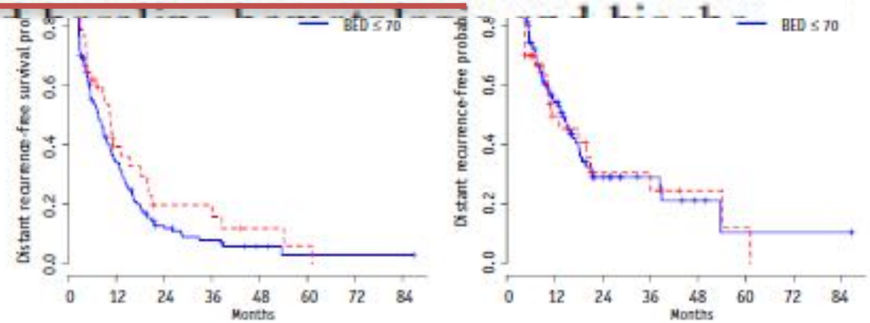


Fig. 2. Kaplan- Meier plots. (a) overall survival, (b) recurrence-free survival, (c) local-regional recurrence-free survival, (d) time to local-regional recurrence, (e) distant recurrence-free survival, and (f) time to distant recurrence by biologically effective dose (BED).

Krishnan et al. IJROBP, V94, N4,

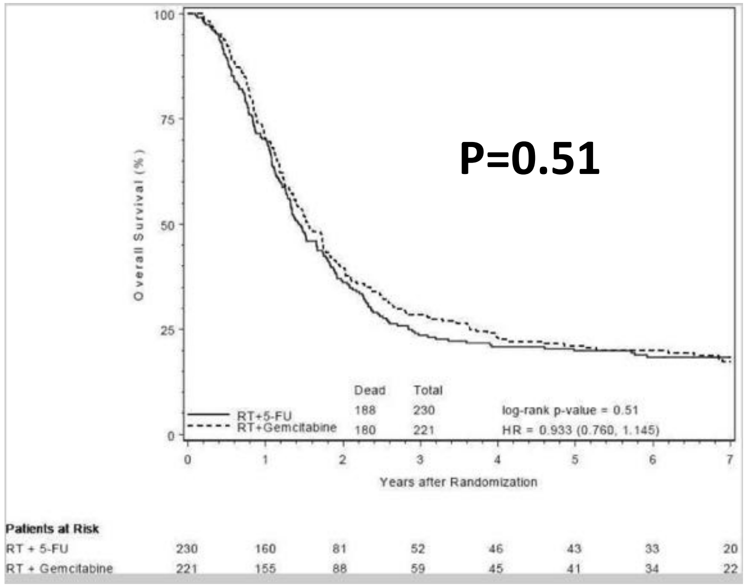
Int J Radiat Oncol Biol Phys. 2012 Feb 1;82(2):809-16. doi: 10.1016/j.ijrobp.2010.11.039. Epub 2011 Feb 1.

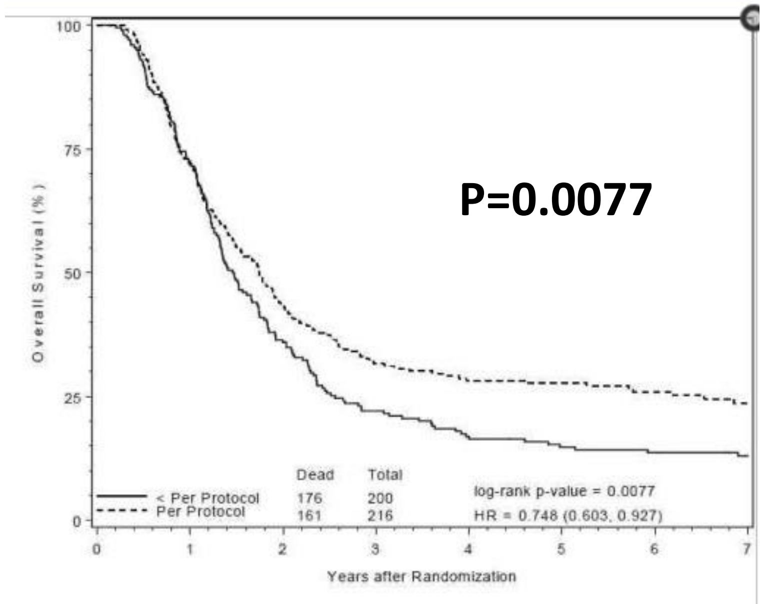
Failure to adhere to protocol specified radiation therapy guidelines was associated with decreased survival in RTOG 9704--a phase III trial of adjuvant chemotherapy and chemoradiotherapy for patients with resected adenocarcinoma of the pancreas.

Abrams RA[1], Winter KA, Regine WF, Safran H, Hoffman JP, Lustig R, Konski AA, Benson AB, Macdonald JS, Rich TA, Willett CG.

416 pts

216 PP 200 <PP





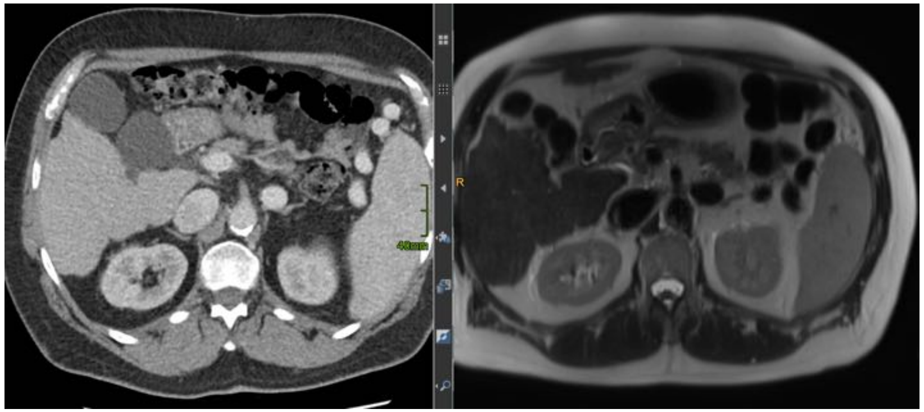
CONCLUSIONS: This is the first Phase III, multicenter, adjuvant protocol for pancreatic adenocarcinoma to evaluate the impact of adherence to specified RT protocol guidelines on protocol outcomes. Failure to adhere to specified RT guidelines was associated with reduced survival and, for patients receiving gemcitabine, trend toward increased nonhematologic toxicity.

Radiotherapy Planning using MRI

Maria A Schmidt and **Geoffrey S Payne**
Cancer Research UK Cancer Imaging Centre, Royal Marsden Hospital and the Institute of Cancer Research, Downs Road, Sutton, Surrey, SM2 5PT, UK

Abstract

The use of Magnetic Resonance Imaging (MRI) in Radiotherapy (RT) planning is rapidly expanding. We review the wide range of image contrast mechanisms available to MRI and the way they are exploited for RT planning. However a number of challenges are also considered: the requirements that MR images are acquired in the RT treatment position, that they are geometrically accurate, that effects of patient motion during the scan are minimised, that tissue markers are clearly demonstrated, that an estimate of electron density can be obtained. These issues are discussed in detail, prior to the consideration of a number of specific clinical applications. This is followed by a brief discussion on the development of real-time MRI-guided RT.



Phys Med Biol 2015

Recommendations for MRI-based contouring of gross tumor volume and organs at risk for radiotherapy of pancreatic cancer

H.D. Heerkens MD[1], W.A. Hall MD[2], X.A. Li Ph.D[2], P. Knechtges MD[3], E. Dalah Ph.D[2], E.S. Paulson Ph.D[2], C.A.T. van den Berg Ph.D[1], G.J. Meijer Ph.D[1], E.J. Koay MD Ph.D[4], C.H. Crane MD[4], K. Aitken MD[5], M. van Vulpen MD Ph.D[1], B.A. Erickson MD[2].

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[2] *Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI 53226, USA*
[3] *Department of Radiology, Medical College of Wisconsin, Milwaukee, WI 53226, USA*
[4] *Department of Radiation Oncology, MD Anderson Hospital, Houston, Texas*
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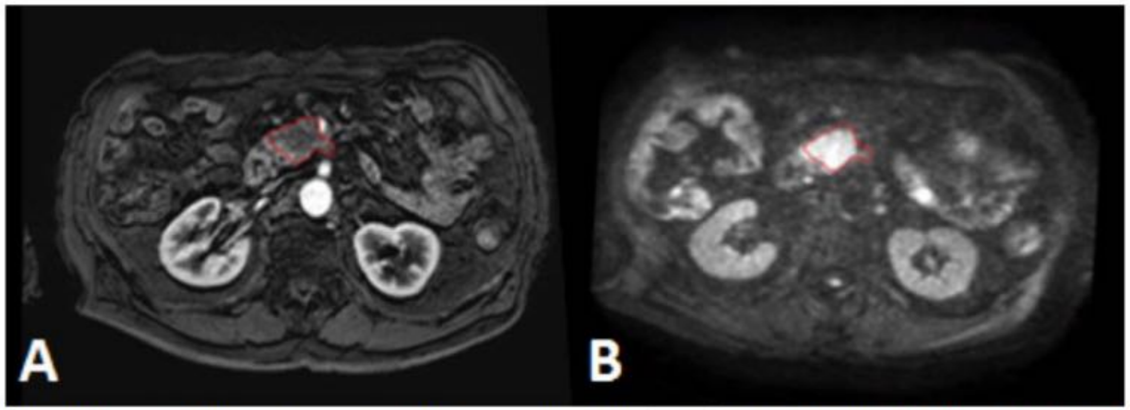


Figure 5: Unresectable pancreas case with contouring of tumor on arterial T1-weighted image (A) and on DWI (B). Red line: GTV. Note the hypointense area on the T1-weighted image and the diffusion restriction on the DWI.

How to integrate MRI in RTP?

- MRI in RT treatment position/same day
- Reproducible filling of the OARs
- Motion management strategies (e.g. the same respiration phase in order to minimize registration issue)
- Fiducial markers (for registration & IGRT)
- A slice thickness of ≤ 3 mm for MRI simulation for GTV contouring

MRI-based contouring: tips and tricks

1. Contour the GTV in conjunction with, or after discussion with, an **experienced radiologist**

2. **Start** contouring, the **T1**-weighted sequence **without IV gadolinium**→ include in the GTV the hypointense or dark area (Figure 6)

3. Subsequently, the **T1 series with IV gadolinium** are used to confirm or optimize the GTV

4. When in doubt about areas of involvement with tumor, we suggest looking at the high b-value DWI images and corresponding apparent diffusion coefficient (ADC) maps

5. Contouring of vessels is best performed on arterial and venous phases of the contrast-enhanced T1-weighted images

6. The organs at risk →on the T2-weighted images

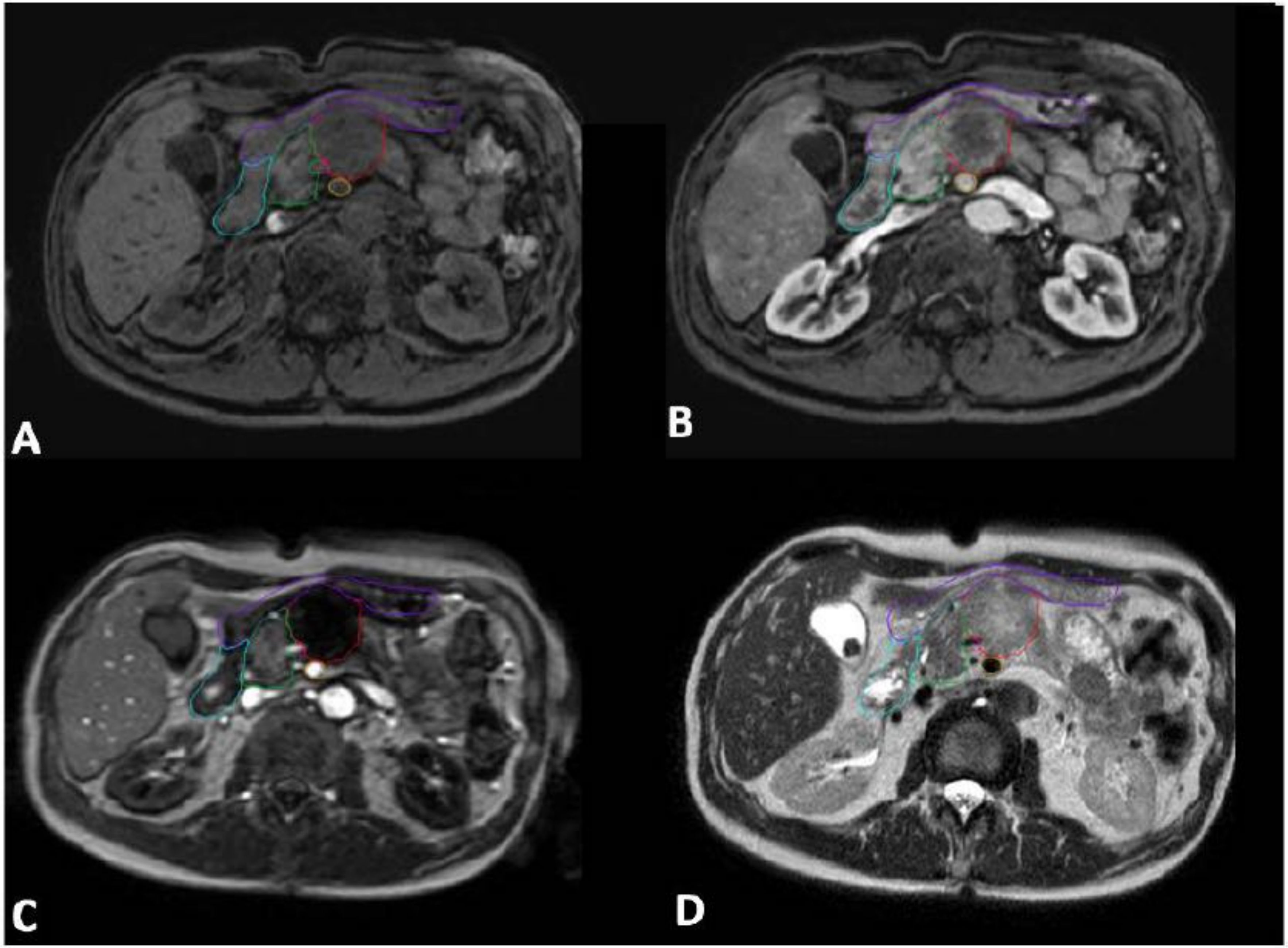


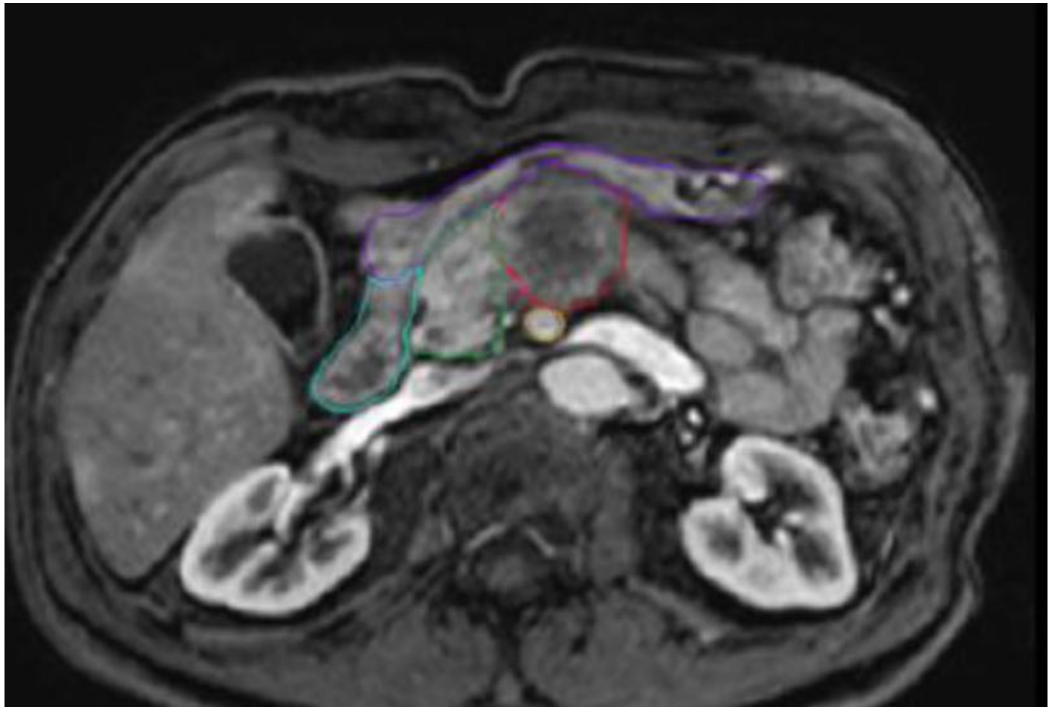
Figure 6: Contouring of an unresectable pancreatic tumor in the pancreatic body on pre contrast T1-weighted (A), arterial T1- weighted (B),T1- weighted (C), T2- weighted (D). Red: GTV, turquoise: duodenum,dark green: pancreatic head, purple: stomach.

MRI in Treatment planning

Pros

Superior soft tissue contrast

Less Rx exposure



Cons

Cost of MRI in addition to a CT

Patient discomfort

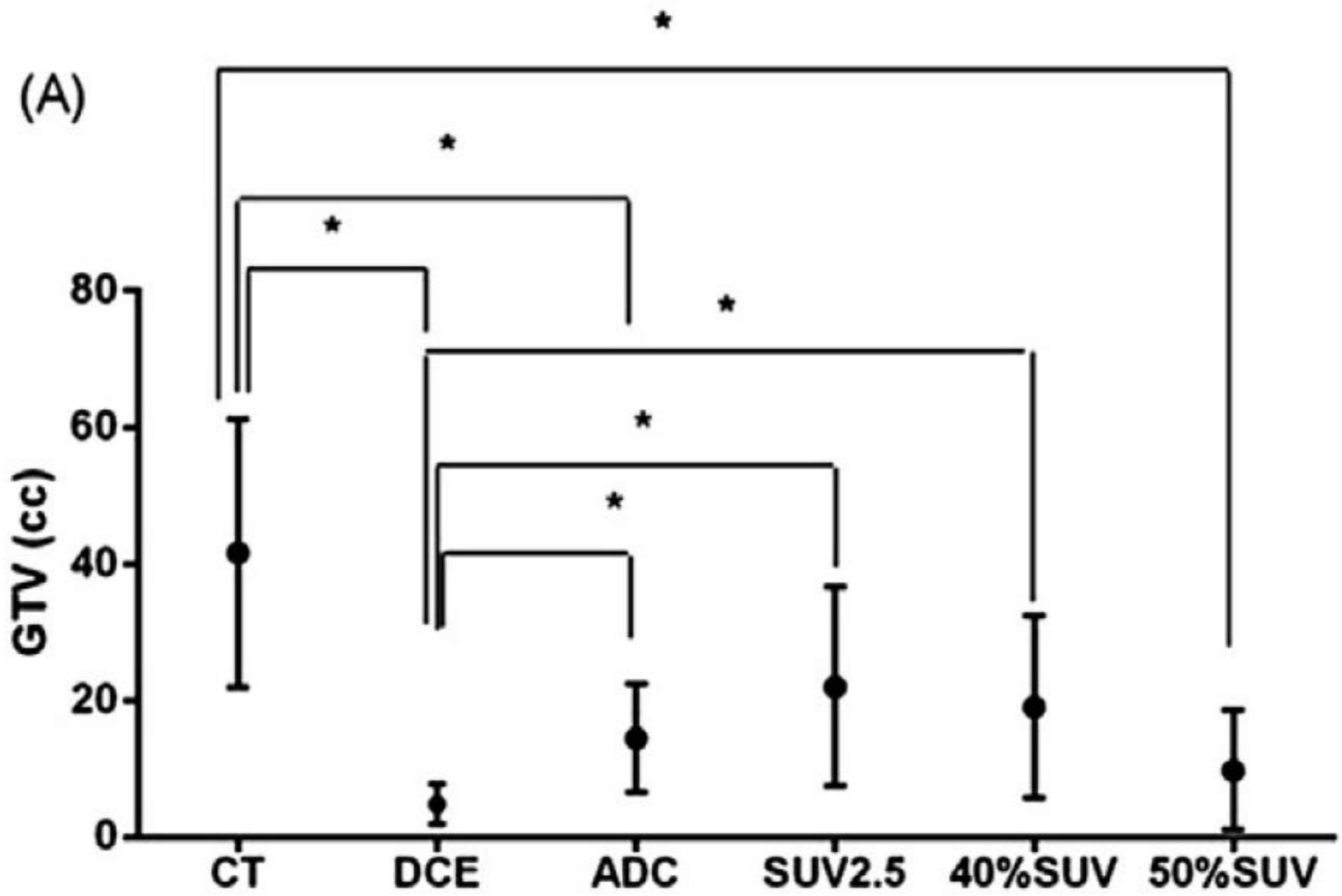
Extra time for fusing and contouring

CT is currently still needed for dose calculations in present radiotherapy practice

Results: Twenty-two patients (62.9%) had an MRI incorporated into GTV-delineation and 13 patients (37.1%) had a CT alone. 10 (28.6%) patients had BR tumors while 25 (71.4%) had LAPC. There was a median tumor size of 3.5cm (range 1.4-5.6). 5 (14.3%) patients underwent upfront CRT while 28 (80.0%) patients underwent induction chemotherapy followed by CRT. Chemotherapy agents used in CRT included infusional 5-fluorouracil (11.4%), gemcitabine (37.1%), oral capecitabine (42.9%) and other agents (5.7%). Median RT dose was 50.4 Gy (range 36-55.8) and 74.3% had fractionation of 1.8 Gy. 17 patients (48.6%) had an in-field boost incorporated into the treatment plan. 7 (20.0%) patients received standard IMRT while 28 (80.0%) patients underwent VMAT. Mean PTV expansion was 1.3cm for the CT group and 1.6cm for the CT-MRI group (p = 0.2). Median follow-up was 11.9 months for the CT-MRI group and 15.4 months for the CT group. Overall local control rate was 68.6% (24/35 patients). Local control rates were 46.2% (6/13) in the CT group and 81.8% (18/22) in the MRI group (p = .028). On stepwise logistic regression, lack of MRI use was the only predictor of local failure (adjusted OR 5.95 [95% CI = 1.22-28.95]; p = .027) with an AUC of 70%.

Conclusions: Incorporation of an MRI into GTV-delineation for radiation therapy treatment planning is associated with significantly higher local tumor control rates than seen with CT only-based planning among patients undergoing IMRT for borderline or unresectable pancreatic cancer.

Appropriateness criteria for treatment planning



ukee,

Fig. 2. (A) Mean and standard deviation of gross tumor volumes (GTVs) from 3-dimensional/4-dimensional CT, late arterial-phase dynamic contrast-enhanced (DCE), apparent diffusion-coefficient (ADC), positron-emission tomography standardized uptake value (PET-SUV)2.5, PET-40% SUVmax, and PET-50% SUVmax for the patents studied. (B) Mean and standard deviation of differences in DCE, ADC, and PET GTV relative to CT GTV (B). ∗Statistically significant differences.

Dalah E IJROBP 2014

Appropriateness criteria for treatment planning

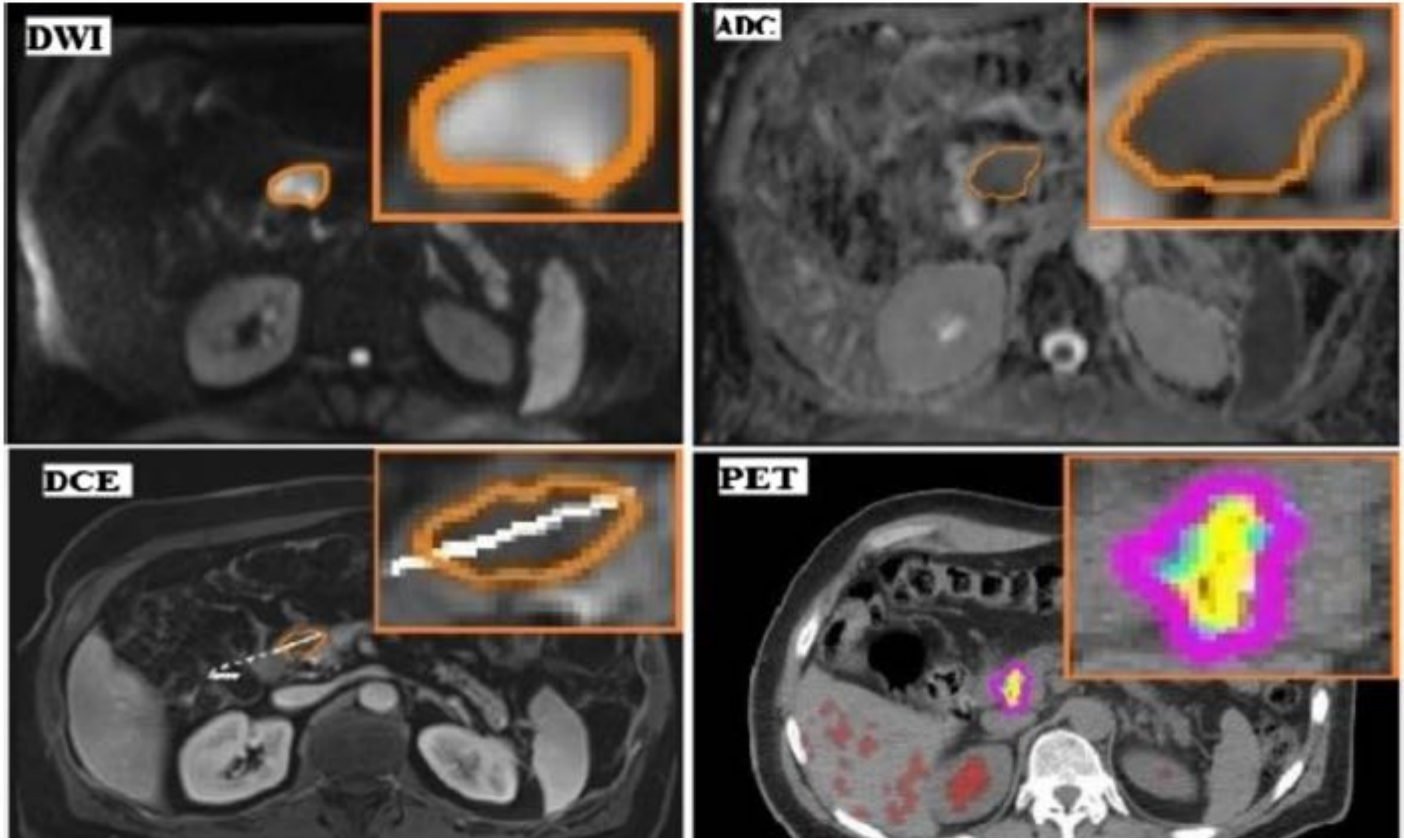


Fig. 3. Illustration of gross tumor volume contours on diffusion-weighted imaging (DWI) (b = 1000 s/mm^2) (top left), apparent diffusion-coefficient (ADC) map generated from DWI (top right), late arterial-phase dynamic contrast-enhanced (DCE) (bottom left), and positron-emission tomography (PET) using standardized uptake value (SUV)2.5 (yellow), 40% SUVmax (magenta), and 50% SUVmax (cyan) (bottom right). The upper right corner inset in each panel is an enlarged view. A color version of this Figure is available at www.redjournal.org.

Appropriateness criteria for treatment planning

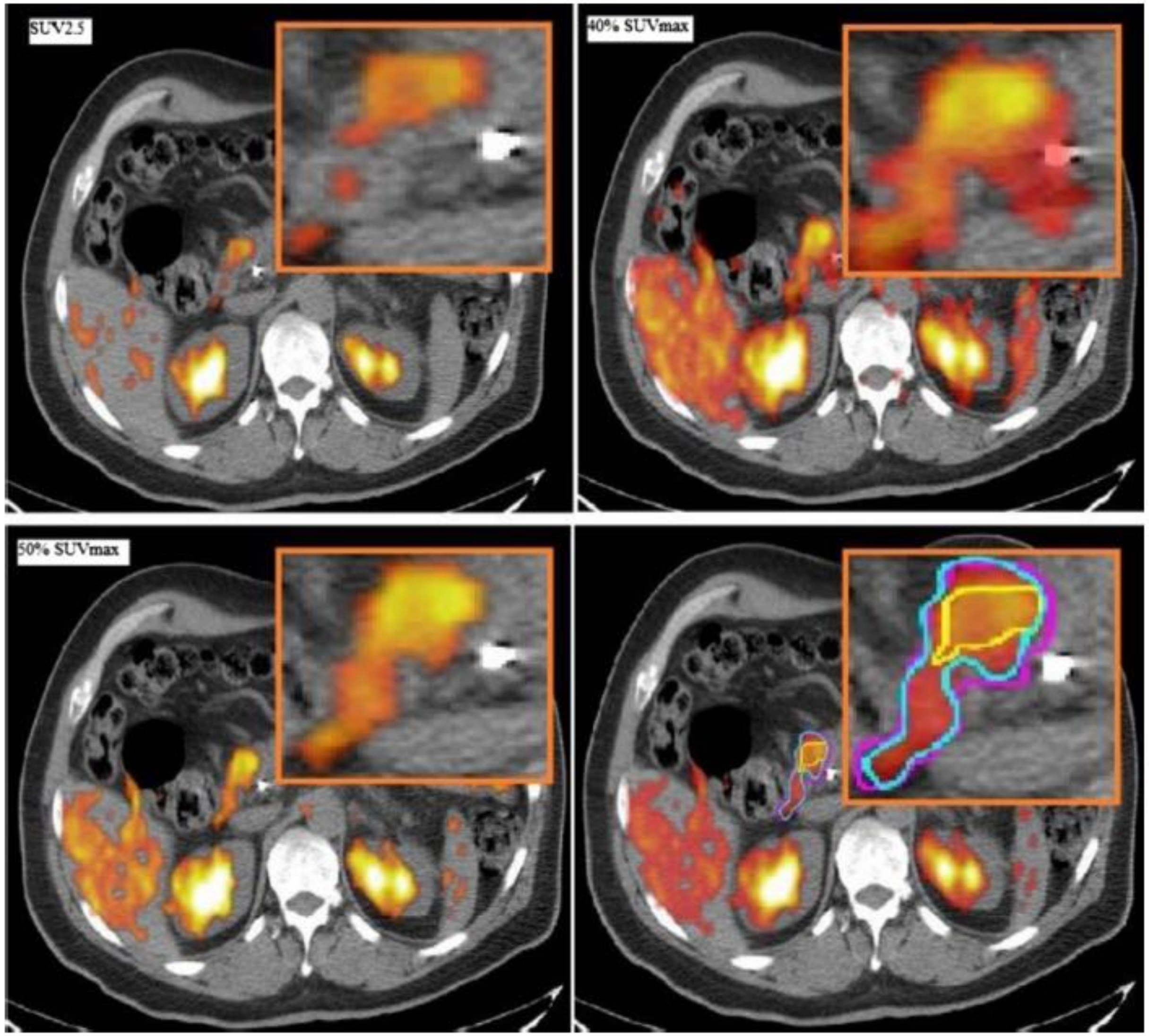


Fig. 4. Illustration of thresholded positron−emission tomography images based on standardized uptake value (SUV)2.5 (top left), 40% SUVmax (top right), 50% SUVmax (bottom left), and gross tumor volume contours from SUV2.5 (yellow), 40% SUVmax (magenta), and 50% SUVmax (cyan) (bottom right). The upper right corner inset in each panel is an enlarged view. A color version of this Figure is available at www.redjournal.org.

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14 patients with **unresectable LAPC**

3DCRT plans were made using the CT and PET-CT fusion data sets

Changes in GTV delineation 36% (5 pts) on PET-CT information.

The average increase in GTV was 29.7%, due to the incorporation of additional N+ and extension of the primary tumor beyond that defined by CT.

The GTVCT versus GTVPET-CT was 92.5 cc versus 104.5 cc ($p = 0.009$).

Conclusion

Co-registration of PET and CT information in unresectable LAPC may improve the delineation of GTV and theoretically reduce the likelihood of geographic misses.

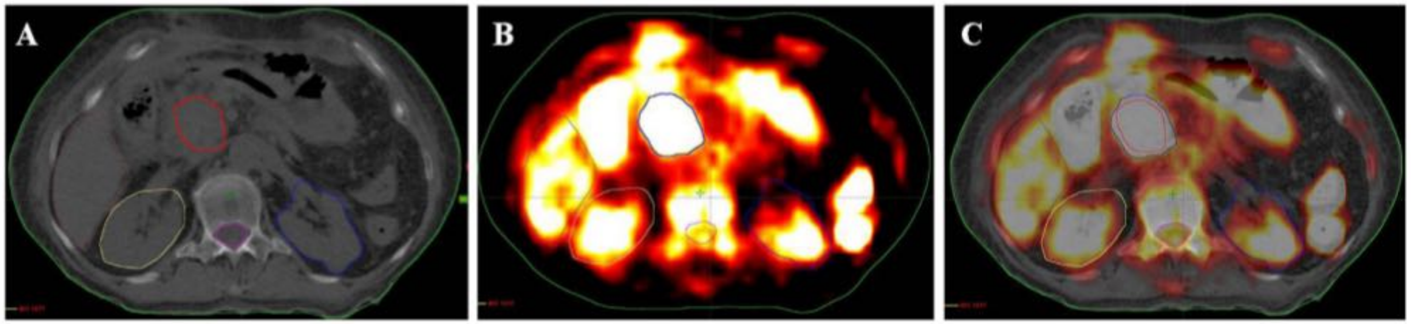
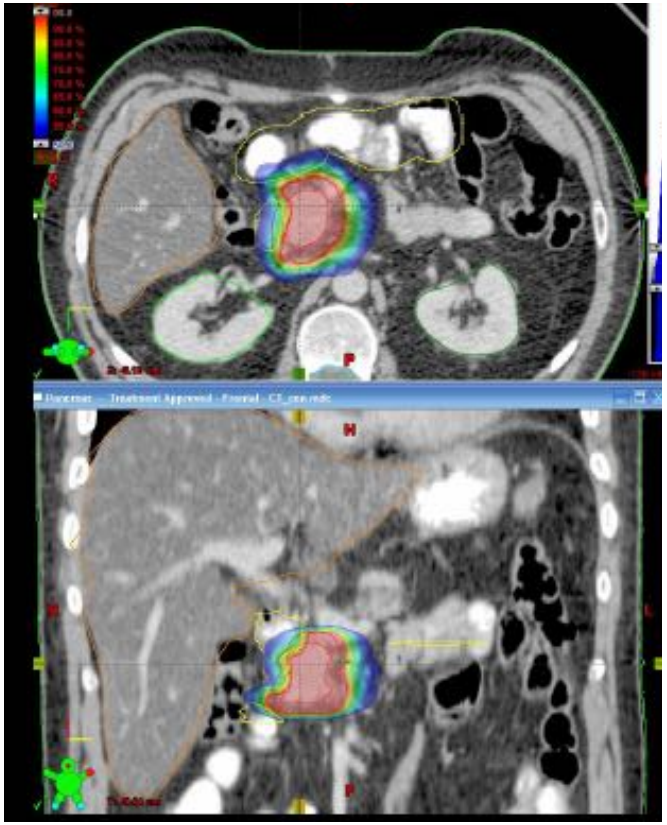


Figure 1
Representative image of a patient with different GTV delineations; CT (A), PET (B), and co-registered PET-CT.

Topkan et al. J of Exp & Clin Cancer Res 2008

SBRT

Conformity and rapid dose fall-off associated with SBRT offer the potential for dose escalation



2-year local control (LC) rates ranged from 50–92%

2-year OS rates following SBRT ranged from 29–74%

Acute and late grade ≥ 3 toxicity of 0–12.5% and 0–22.3%

Brunner T, R&O 2015
De Bari B, Critical Rev Oncol/Hematol 2016
Kim SK, J Gastroint Oncol 2016

2491

Triphasic Bolus Tracking Computed Tomography Simulation for Stereotactic Body Radiation Therapy of Locoregionally Advanced Pancreatic Cancer

D.J. Godfrey, B.N. Patel, J. Adamson, J.K. Salama, and M. Palta; *Duke University Medical Center, Durham, NC*

175 ml of Isovue 300 at 5 ml/sec.

following aortic enhancement

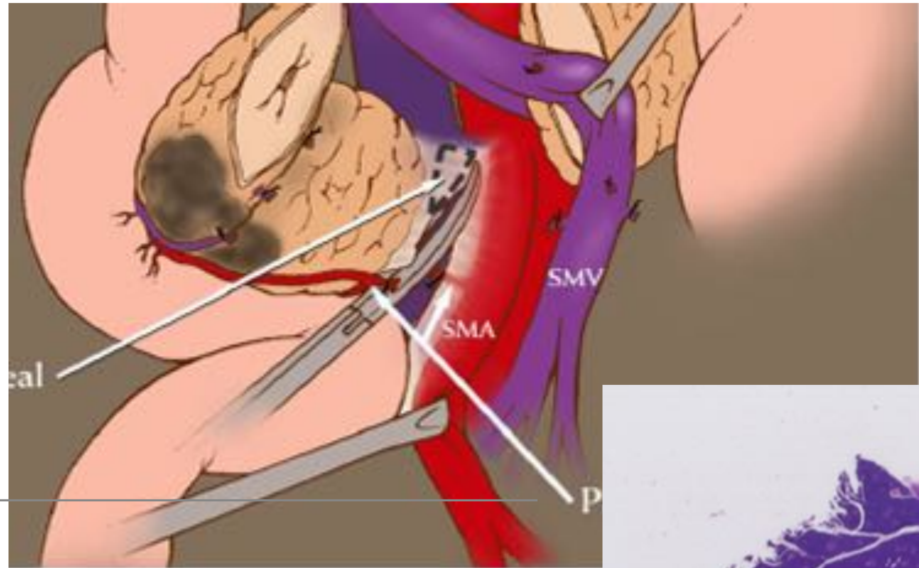
15s→ parenchymal enhancement (PP),
45s→ portal venous phase (PV),
165s→ delayed phases (DP

Conclusion: Triphasic CT simulation scanning was well tolerated and consistently yielded improved tumor conspicuity in the PP and PV phases relative to both the DP phase and the previously used conventional radiation therapy CT contrast protocol. The DP phase does not appear to provide useful information for precise tumor contouring. Given the variability of GTVs drawn on the PP and PV phases, it appears that each phase may capture unique perfusion physiology, and thus combined GTVs from a multiphasic CT simulation are recommended for pancreas SBRT.

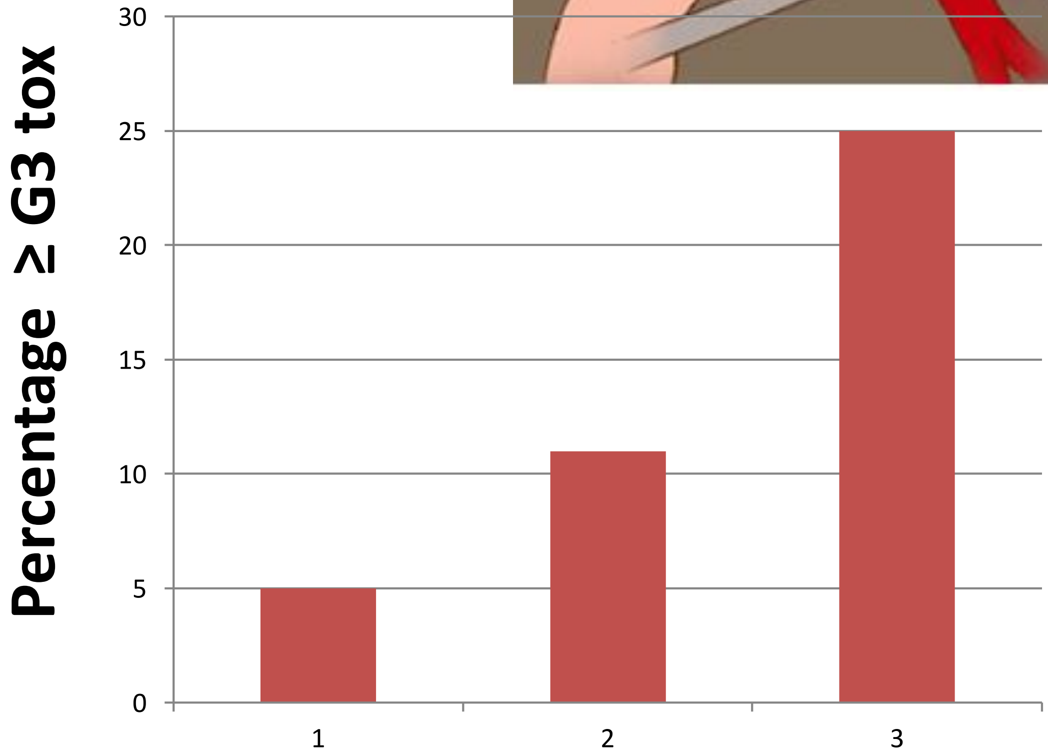
IJROBP V96 N2S, Supplement 2016

Challenges of SBRT to pancreas

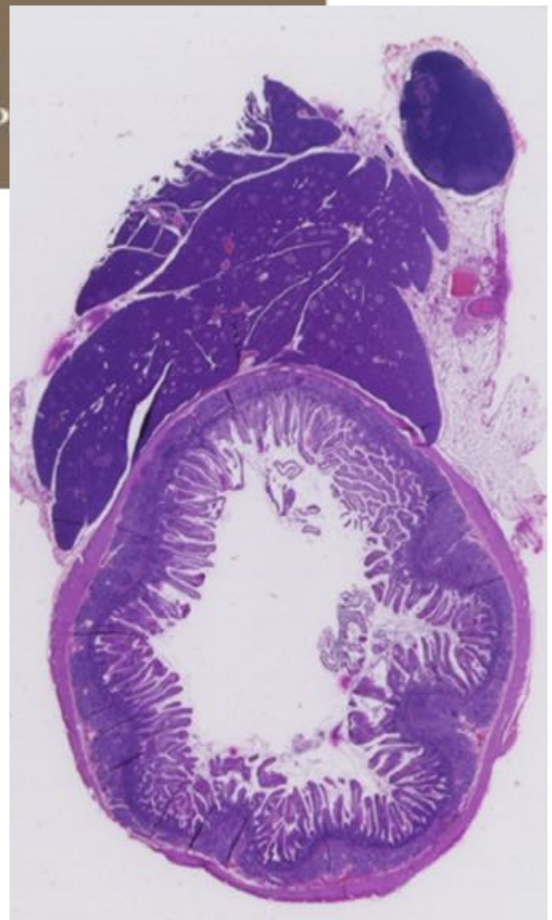
Proximity of pancreas to duodenum and SB:
high risk of late stenosis, ulceration, bleeding and perforation



tox rate is expected to be even higher with improved mOS



Chang et al. Cancer 2008

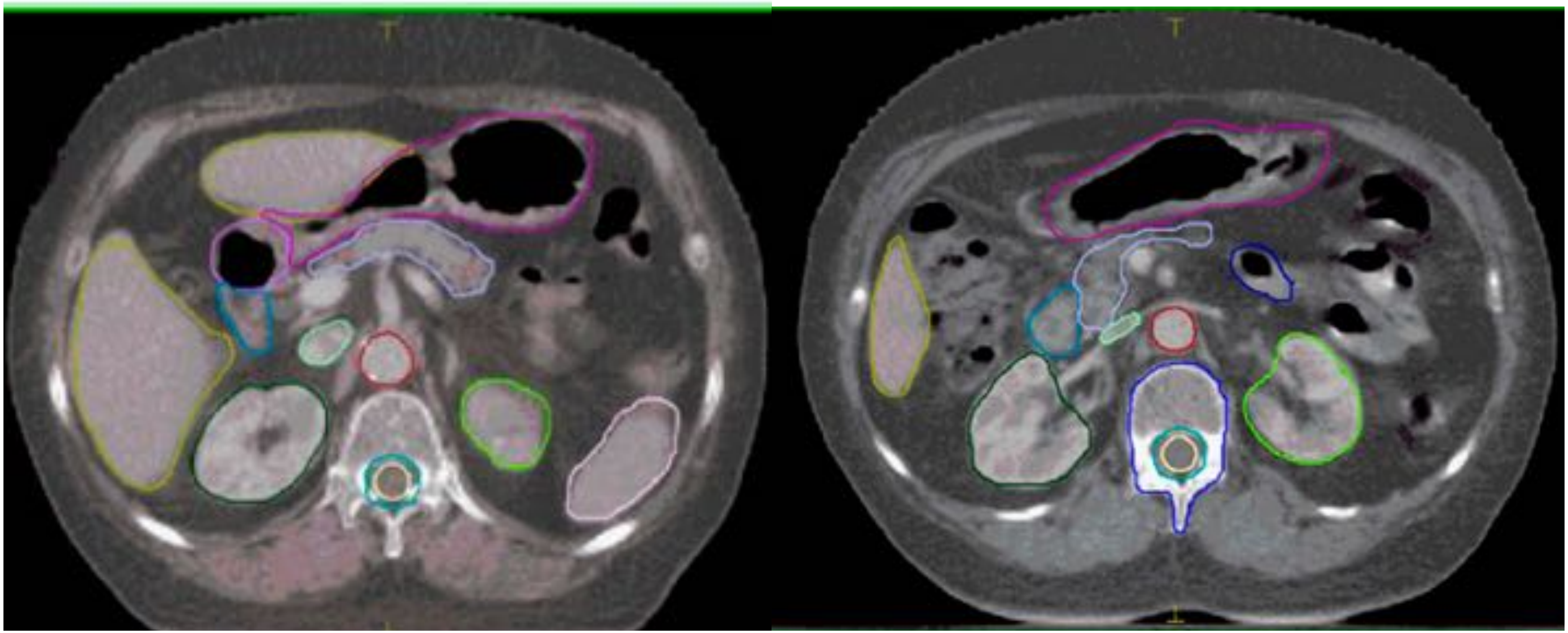


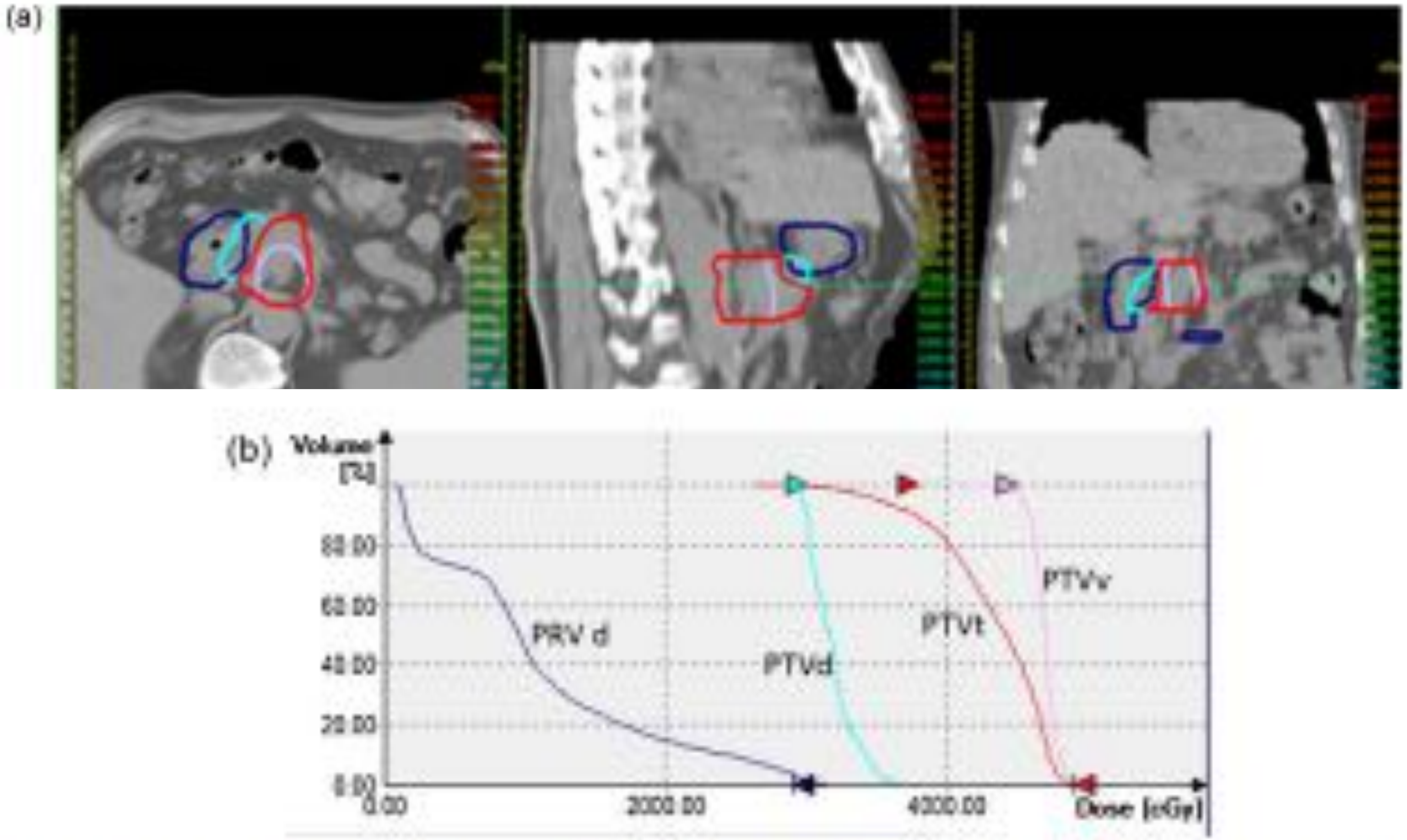
PICTORIAL REVIEW

Simple diagrammatic approach to delineate duodenum on a radiotherapy planning CT scan

[1]TEJINDER KATARIA MD, DNB, [1]DEEPAK GUPTA MD, [1]TRINANJAN BASU MD, [2]SHIVANI GUPTA MD, [1]SHIKHA GOYAL MD, DNB, [1]SUSOVAN BANERJEE MD, [1]ASHU ABHISHEK MD, [1]SHYAM S BISHT MD and [1]KUSHAL NARANG MD

Kataria BJR 2015





– (a) Axial, sagittal and coronal slice isodose distribution of SBRT (IMRT-SIB) respecting all constraints (
nd D_{mean}). The following volumes are shown: Duodenum (blue), PTVd (clear blue), PTVt (red) and PTVv
volume histogram for PRVd, PTVd, PTVt, PTVv of the same patient respecting all constraints (OARs, PT

FINAL REMARKS ON APPROPRIATENESS OF IMAGING IN TREATMENT PLANNING:

Multimodality imaging: an opportunity

MDCT with IV contrast→recommended

PET-CT/MRI-CT coregistration→helpful

MRI contouring→
PET-MRI→ the near future
RTP using MRI→