Imaging

oltre la TC

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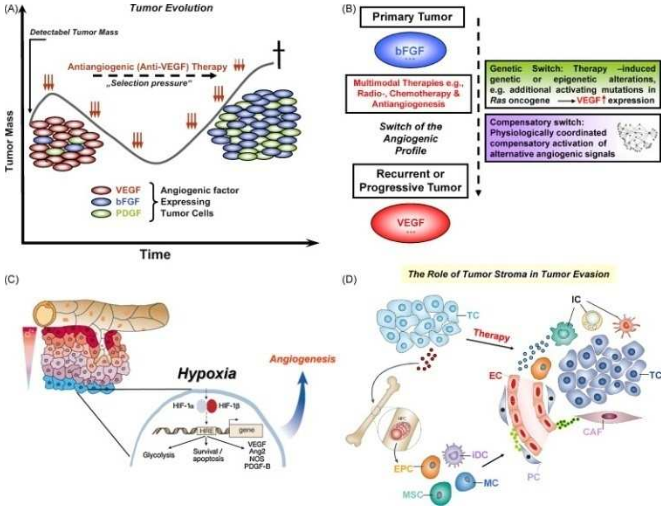
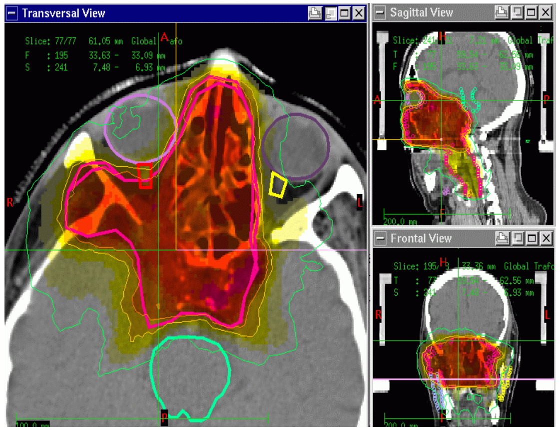
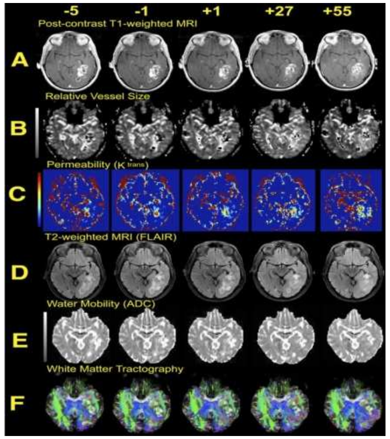
Evoluzione delle conoscenze biologiche





Evoluzione delle tecniche di radioterapia

Evoluzione tecnologica

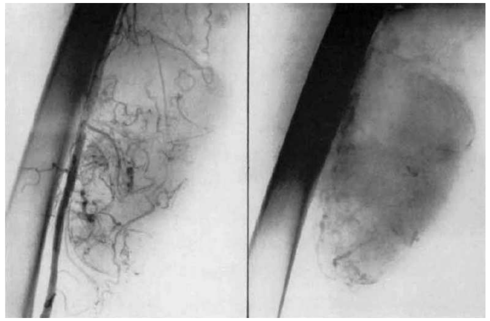


Evoluzione tecnologica

Evoluzione dell'imaging

Before the CAT-scan ?

- Roentgen Diagnostic Methods
  - Angiography
  - Lymphography
  - Tomography
  - Hysterography
- Isotope Methods
  - liver and renal scintigraphy
  - gammaencephalography

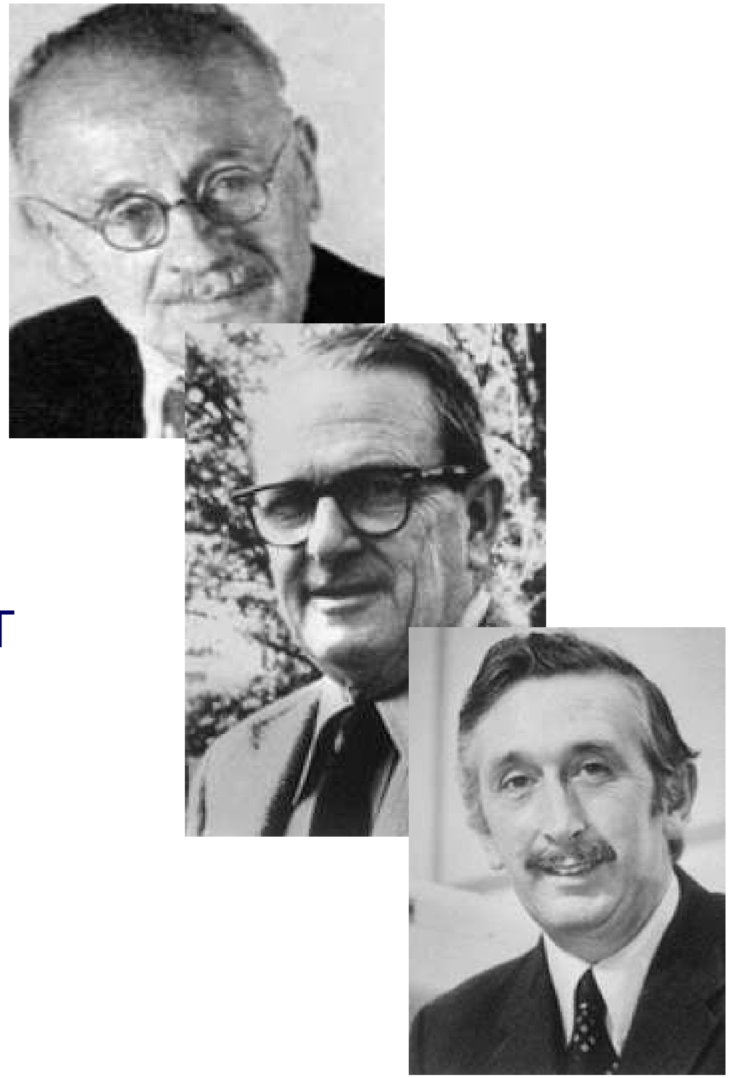


<u>Radioterapia 2D</u>

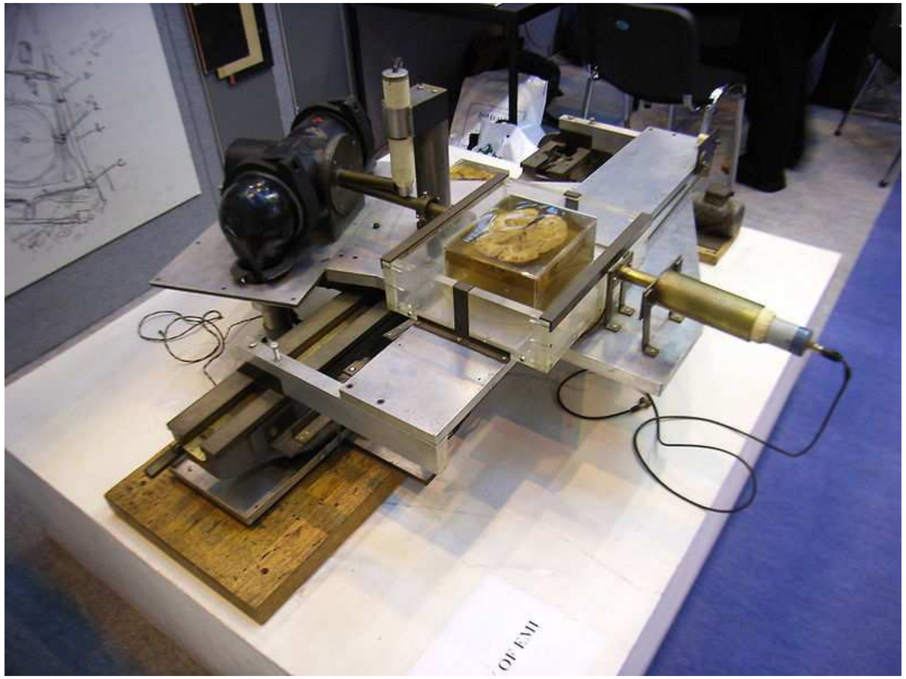
(Lingren M, Cancer, 1968)

CT pioneers:

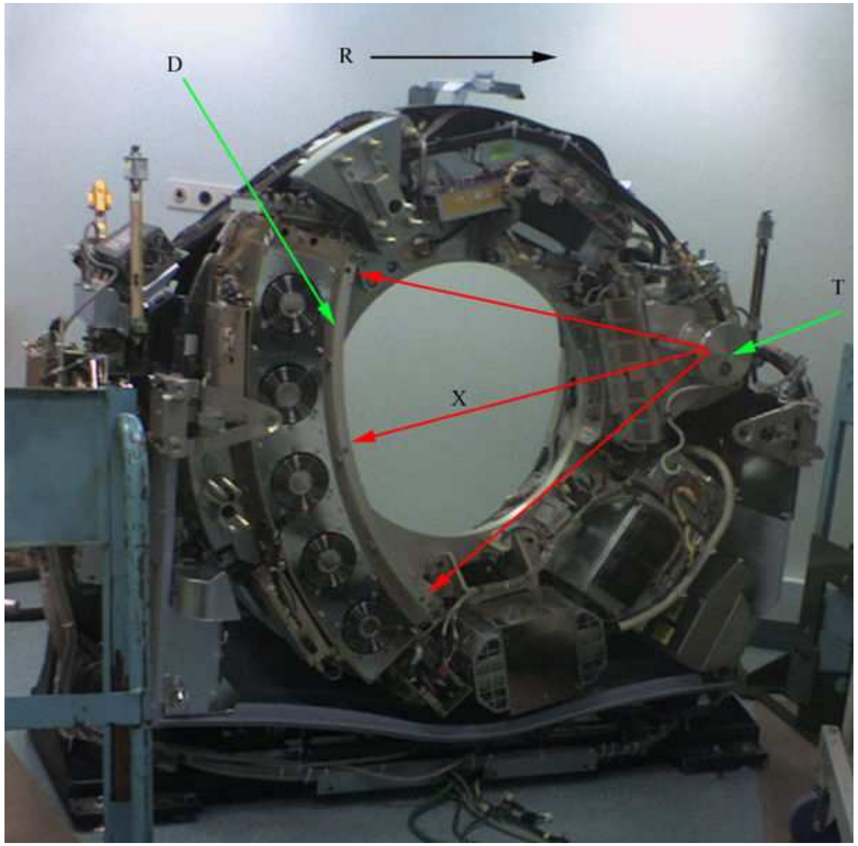
- 1917: Johann Radon establishes the mathematical framework for tomography, now called the Radon transform.
- 1963: Allan Cormack publishes mathematical analysis of tomographic image reconstruction, unaware of Radon's work, *studying tissue inhomogeneities for radiation therapy*.
- 1972: Godfrey Hounsfield develops first CT system, unaware of either Radon or Cormack's work, develops his own reconstruction method.
- 1979 Hounsfield and Cormack receive the Nobel Prize in Physiology or Medicine.



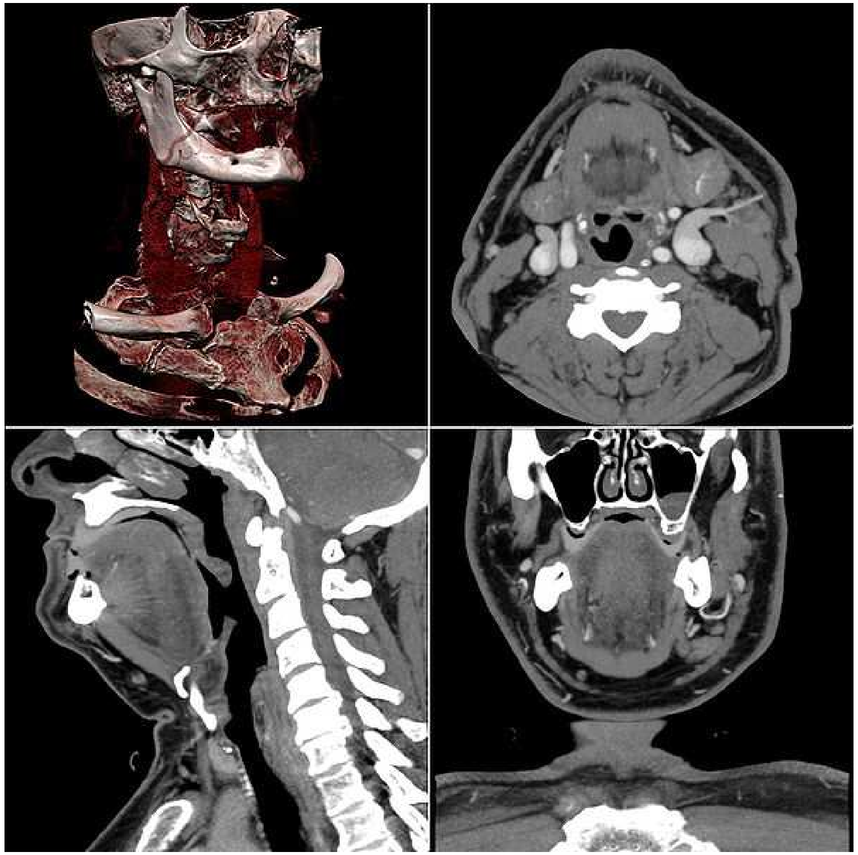
CT - scan



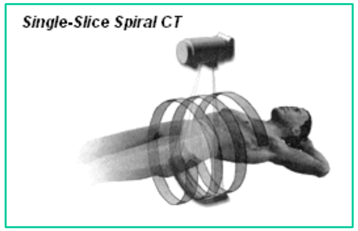
The very first ct scanner prototype. Invented by Houndsfield at EMI.



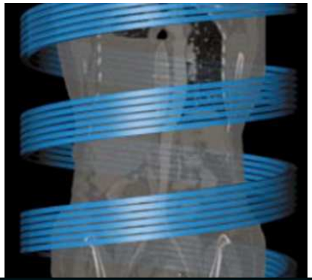
Old vs. new CT imaging



Evoluzione della TC



TC SPIRALE



TC MULTIDETTETORE
4 CANALI

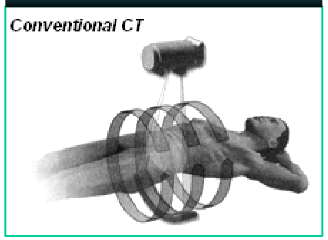
0,5 sec

TC MULTIDETETTORE
32-64-(256) CANALI

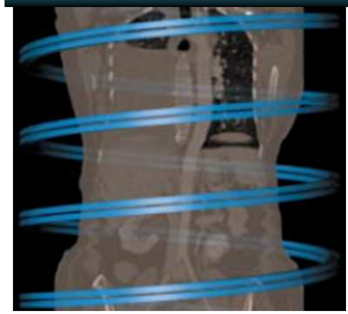
0,33 sec

1972……1989…..1991……..1998….2000/02….2005/07…..

INVENZIONE
DELLA TC



TC TWIN-SLICE



0,4 sec

TC MULTIDETTETORE
8-16 CANALI

DOSE REDUCTION

Historical papers on the use of CT for TP

- Radiology. 1975 Dec;117(3 Pt 1):613-4. The use of computed tomography for radiation therapy treatment planning. Chernak ES, Rodriguez-Antunez A, Jelden GL, Dhaliwal RS, Lavik PS.

- Belge Radiol. 1976 May-Jun;59(3):301-7.The use of computed tomography in radiation therapy treatment planning. Jelden GL, Chernak ES, Lavik PS, Dhaliwal RS, Rodriguez-Antunez A.

- Int J Radiat Oncol Biol Phys. 1977;3:27-33. The measurement of tissue heterodensity to guide charged particle radiotherapy. Goitein M.

Computed Tomography

- Elevata risoluzione spaziale
- Ricostruzione 3D
- Informazione su attenuazione delle radiazioni
- Strato sottile, piani multipli, ricostruzione 3D, mdc
- Adeguata identificazione N patologici
- Coinvolgimento osseo/cartilagineo
- Rapidità di acquisizione

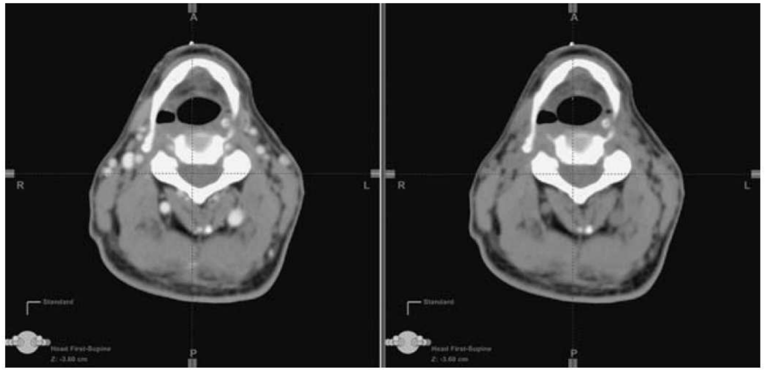
Journal of Medical Imaging and Radiation Oncology **53** (2009) 114–118

RADIOLOGY—ORIGINAL ARTICLE

Influence of CT contrast agent on dose calculation of intensity modulated radiation therapy plan for nasopharyngeal carcinoma

FK-H Lee, CC-L Chan and C-K Law

Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong SAR, China



Differences in nodal mean/median dose were statistically significant, but small (0.15 Gy for a 66 Gy prescription).

In the vicinity of the carotid arteries, the difference in calculated dose was also statistically significant, but only with a mean of approximately 0.2 Gy. We did not observe any significant correlation between the difference in the calculated dose and the tumor size or level of enhancement.

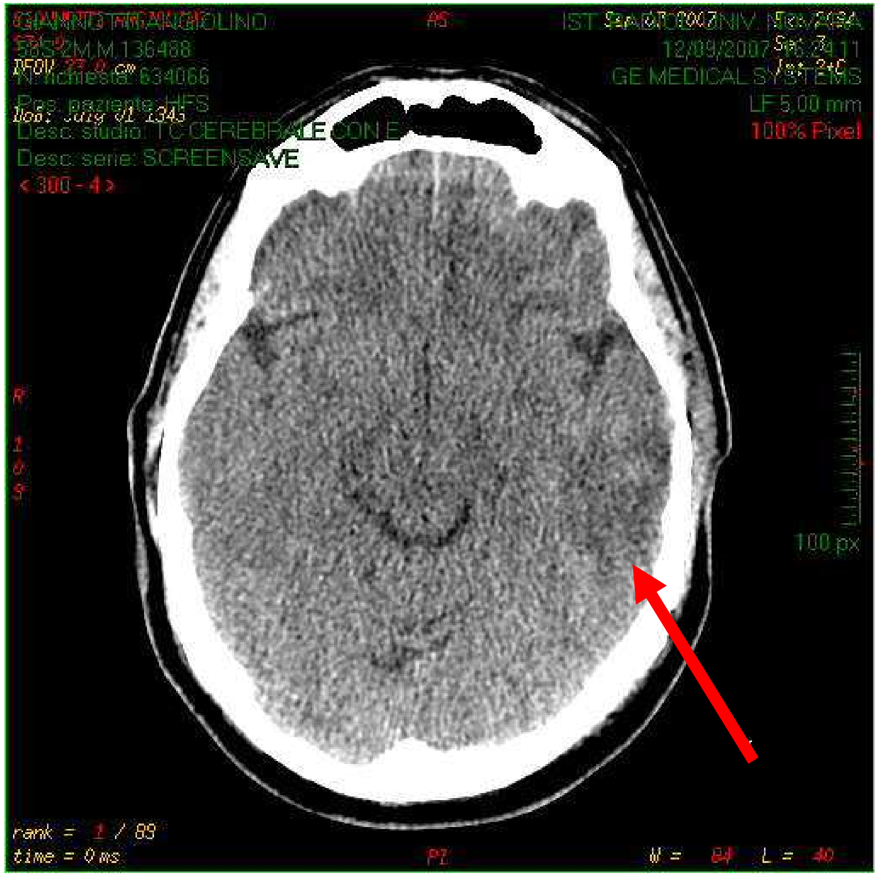
The results implied that the calculated dose difference was clinically insignificant and may be acceptable for IMRT planning.

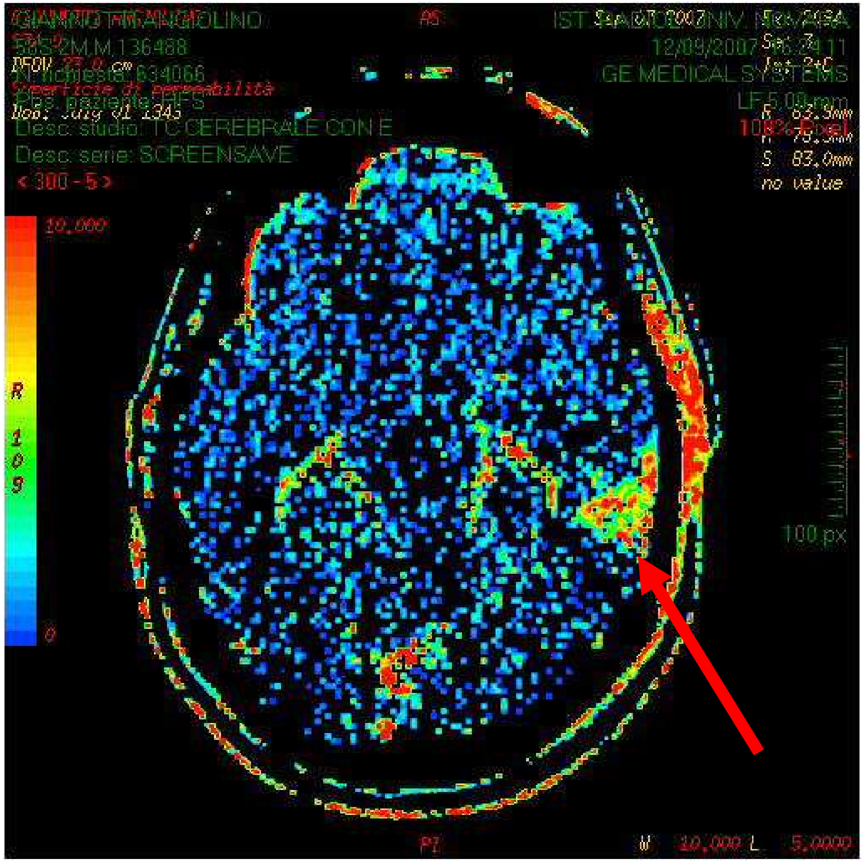
Contrast agents in CT for TP in H&N

Reference	Irradiation technique	No. head and neck cases studied	No. NPC cases studied	Results
Shibamoto et al.	**Parallel opposing beams**	**5**	**1**	0.09% increase in MU
Letourneau et al.	**IMRT**	**10**	**0**	Minimum dose to PTV varied by a maximum of 0.17 Gy. Maximum point dose to critical organs changed by a maximum of 0.12 Gy (brainstem).
Choi et al.	**IMRT**	**15**	**6**	Significant but small (<1%) dose difference in the irradiated targets. Non-significant difference shown in parotid glands and spinal cords.
Liauw et al.	**IMRT**	**5**	**1**	Dose difference <0.2% for irradiated targets and critical structures (parotid glands and spinal cord).

From Morphology to Function …

CT perfusion (CTP) in brain GBM





CT perfusion (CTP)

- **Diagnostic imaging measuring capillary perfusion associated to the anatomy or to pathologic tissue; correlation with <u>tumor neo-angiogenesis</u>.**

- **Used to analyze:**
  - **Cerebral Blood Volume (CBV) (ml/100 g/tissue),**
  - **Cerebral Blood Flow (CBF),**
  - **Mean Transit Time (MTT) of the contrast-agent.**
  - **Permeability Surface (PS)**

- **These parameters (in particular CBV and PS) are higher in tumor tissue and progressively decrease in the surrounding edema.**

Computed Tomography

- Scarsa risoluzione di contrasto tra il tumore e i tessuti sani
- Difficoltà nell'identificare strutture con simile attenuazione delle radiazioni
- Variazioni inter e intra-osservatore
- Artefatti da strutture metalliche
- Artefatti da movimento e respirazione

Magnetic Resonance

- Accurata definizione dell'estensione del T nei tessuti molli o nell'osso
- Minori variazioni inter intraosservatore
- Immagini anatomiche dettagliate

- Mancanza di caratterizzazione biologica della lesione (a parte la MRS)
- Non applicabile a pazienti con PM o strutture metalliche
- Distorsione geometrica

Rasch *et al. Radiation Oncology* 2010, **5**:21
http://www.ro-journal.com/content/5/1/21

RADIATION ONCOLOGY

Decreased 3D observer variation with matched CT-MRI, for target delineation in Nasopharynx cancer

Coen RN Rasch[1*], Roel JHM Steenbakkers[2], Isabelle Fitton[3], Joop C Duppen[1], Peter JCM Nowak[4], Frank A Pameijer[5], Avraham Eisbruch[6], Johannes HAM Kaanders[7], Frank Paulsen[8], Marcel van Herk[1]

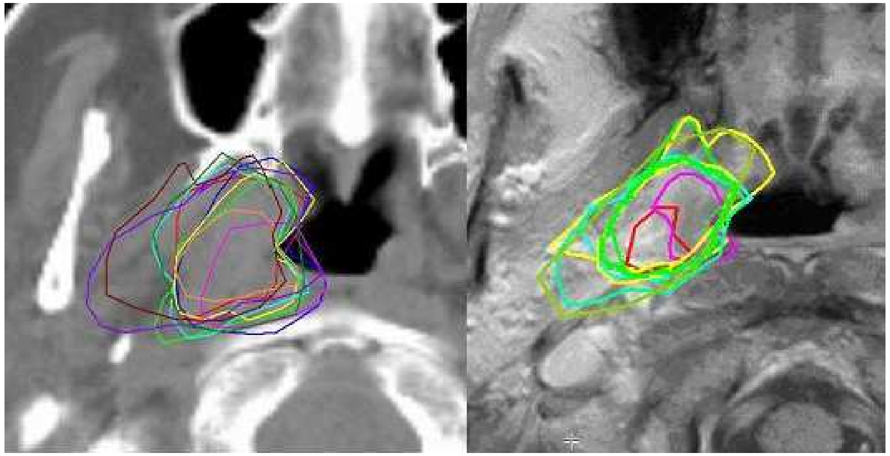
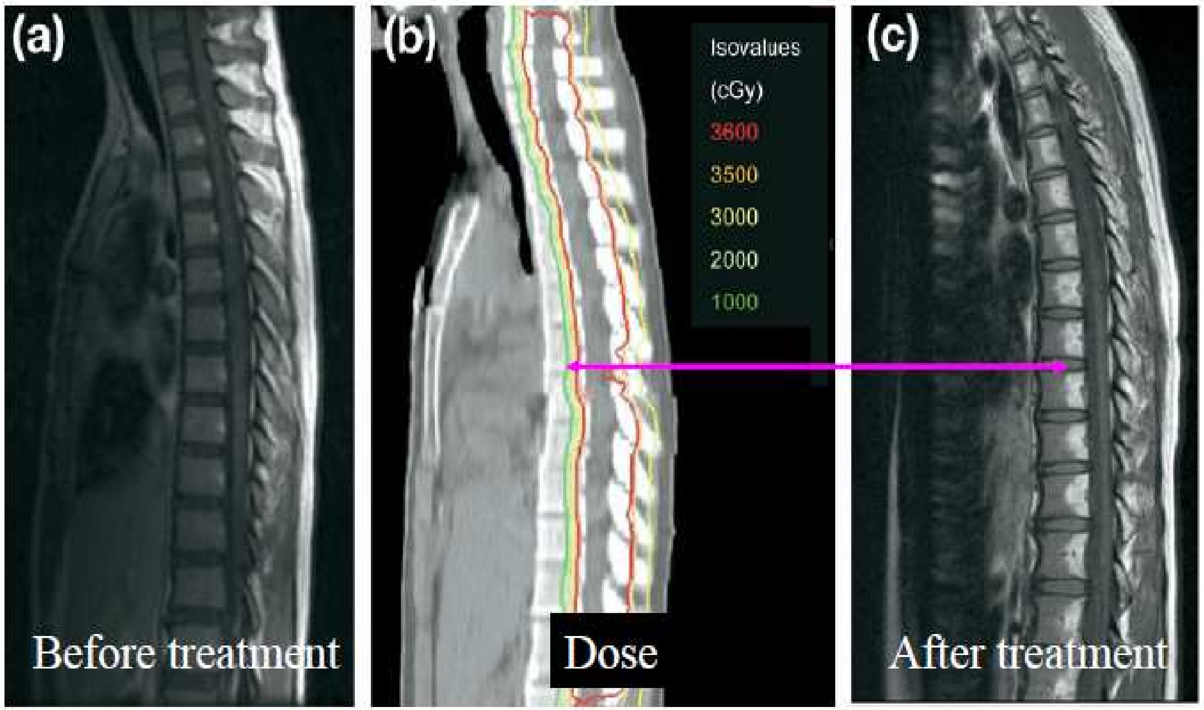
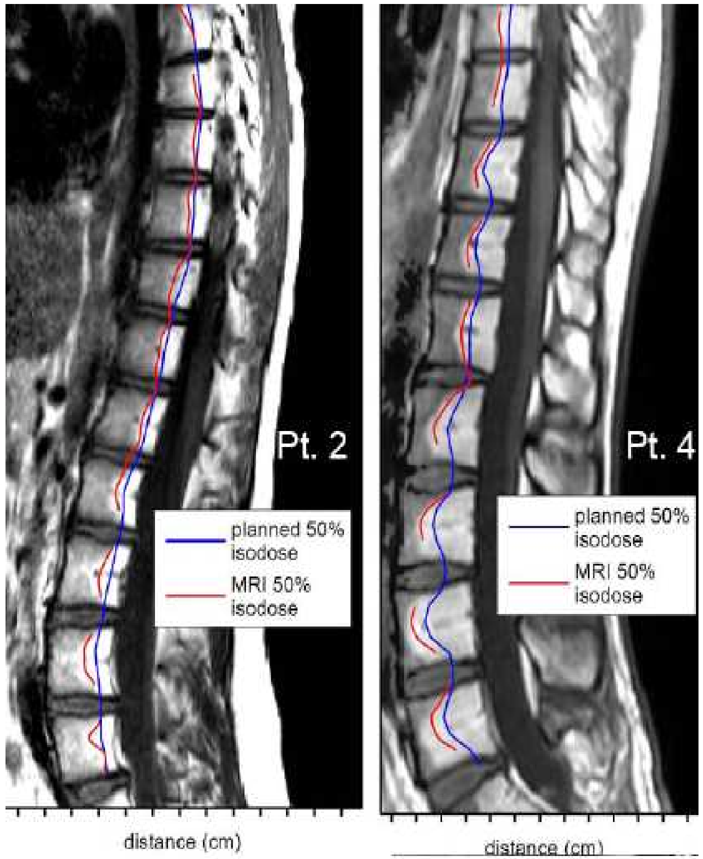


Table 3 Observer variation for the various CTV elective to normal tissue interfaces and the two delineation phases.

Anatomical regions	Phase 1		Phase 2	
	SD (mm)	Agreement (%)	SD (mm)	Agreement (%)
All regions	5.9	17	4.9 (p = 0.01)	59 (p = 0.004)
Dorsal - Bone	4.4	47	4.2 (n.s.)	75 (n.s.)
Dorsal - Invas.	5.1	9	4.5 (p = 0.02)	43 (p = 0.01)
Pterygoid	5.6	27	4.4 (p = 0.03)	58 (p = 0.02)
Parapharyngeal	5.7	15	4.9 (p = 0.04)	53 (p = 0.01)
Sphenoid	6.1	9	5.7 (p = 0.03)	51 (p = 0.04)
Nasoph. - Lat.	5.7	11	4.7 (n.s.)	66 (p = 0.02)
Nasoph. - Ant.	6.5	10	5.1 (p = 0.02)	70 (p = 0.01)
Caudal side	7.9	7	5.6 (p = 0.03)	47 (p = 0.005)



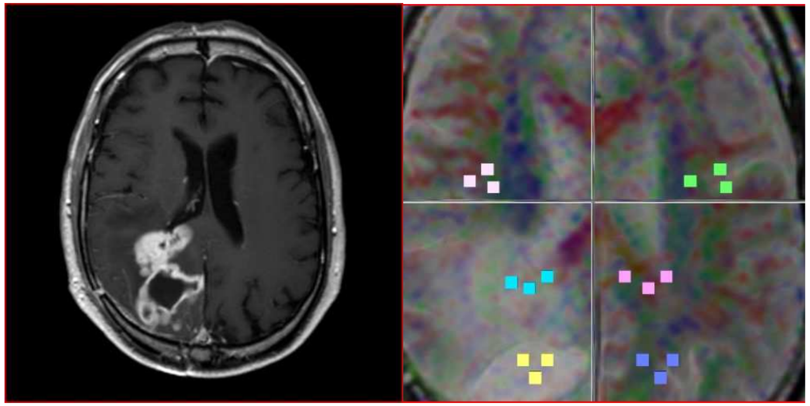


Reducing range uncertainties: Measurements by MR scan after treatment

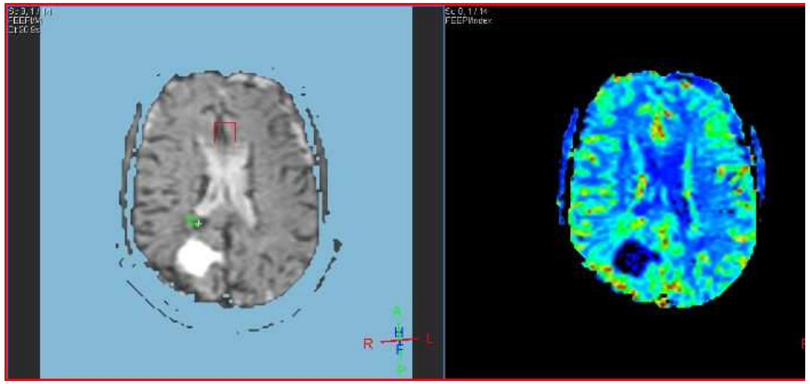
(Krejcarek, Yock, et al. IJROBP 2007;68:646-649)

Can imaging by PW and DW MR help in identification of radiation target ?

- 17 pts: 14 M, 3 F
- surgery+RT (60 Gy) + TMZ
- Timing of image acquisition:
  - MR DWI and MR PWI pre RT (**<u>T0</u>**)
  - MR DWI and MR PWI after RT (2 months) and during F/U (every 4 months)
  - @ PD: MR DWI and MR PWI (**<u>T1</u>**)



MR DWI @ T1



MR PWI @ T1

(Stecco et al. submitted, 2010)

MR DWI

Findings in the volume of recurrence (MRI @ **T1**)

	FA (mean +/- SD)	**ADC (x 10^{-3} m^2/sec) (mean +/- SD)**
ENH T1	0.25 +/- 0.09	1.41 +/- 0.48
CL – ENH T1	0.36 +/- 0.11	0.92 +/- 0.17
HYPER T1	0.21 +/- 0.06	1.63 +/- 0.58
CL – HYPER T1	0.39 +/- 0.10	0.92 +/- 0.14
NAWM T1	0.38 +/- 0.10	0.88 +/- 0.10
CL – NAWM T1	0.40 +/- 0.10	0.89 +/- 0.13

FA is significantly lower in the area with recurrence (ENH);
maximum value of ADC in the peritumoral edema area near ENH

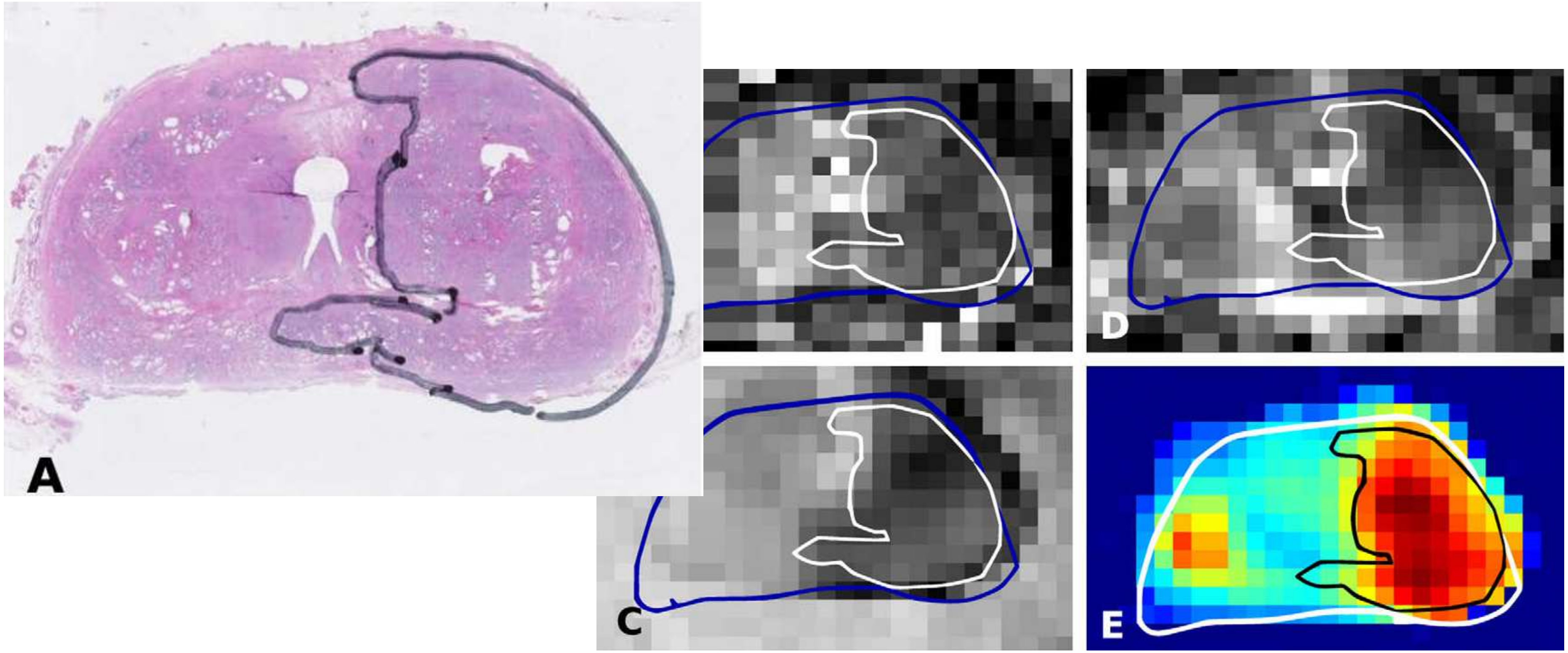
Similar results by: *Provenzale,* Radiology 2004; *Sinha,* AJNR 2002; *Sundgren*, Magnetic Imaging Resonance 2006

MR PWI

rCBV	T0 (mean +/- SD)	T1 (mean +/- SD)
ENH ENH @ T0 Non-ENH @ T0	0.44 ± 0.28 0.44 +/- 0.28 0.46 +/- 0.20	0.39 ± 0.28
CL – ENH	0.30 ± 0.17	0.48 ± 0.28
HYPER	0.32 ± 0.19	0.24 ± 0.24
CL – HYPER	0.34 ± 0.26	0.31 ± 0.22
NAWM	0.27 ± 0.16	0.32 ± 0.19
CL – NAWM	0.29 ± 0.13	0.45 ± 0.18

PREDICTIVE VALUE FOR RECURRENCE ?

DW-MRI and DCE-MRI in prostate cancer



Reasonable tumor coverage of about 85% and larger was found when applying a margin of 5 mm to the MR based tumor delineations.

(Groenendaal et al. R&O, in press)

TARGET VOLUME FOR IRRADIATION OF PELVIC LYMPH NODES IN HIGH-RISK PROSTATE CANCER

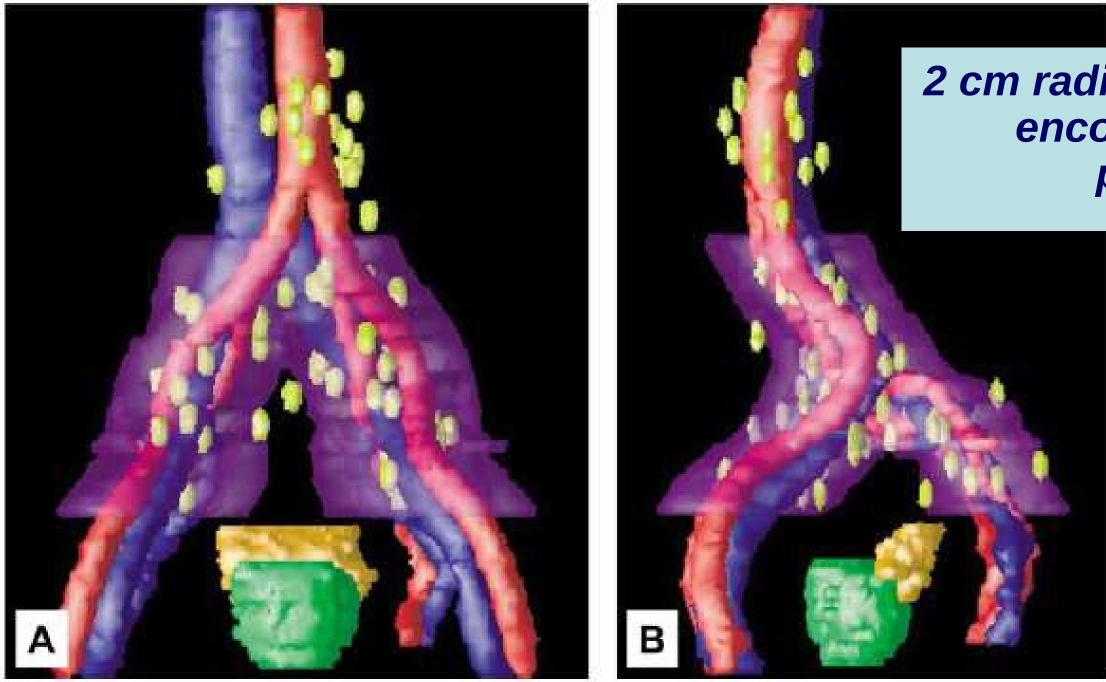
Table 3. Clinical target volume guidelines for high-risk pelvic nodal disease in advanced prostate cancer

Vessel region	Nodes (no.)	Length (cm)
Common iliac	6	2.5 cm superior to its bifurcation
External iliac	36	9.0 cm extending from common iliac bifurcation
Internal iliac	11	8.5 cm extending from common iliac bifurcation

Lymphotropic nanoparticle-enhanced MRI

Shih HA, et al.

IJROBP, 63:1262, 2005

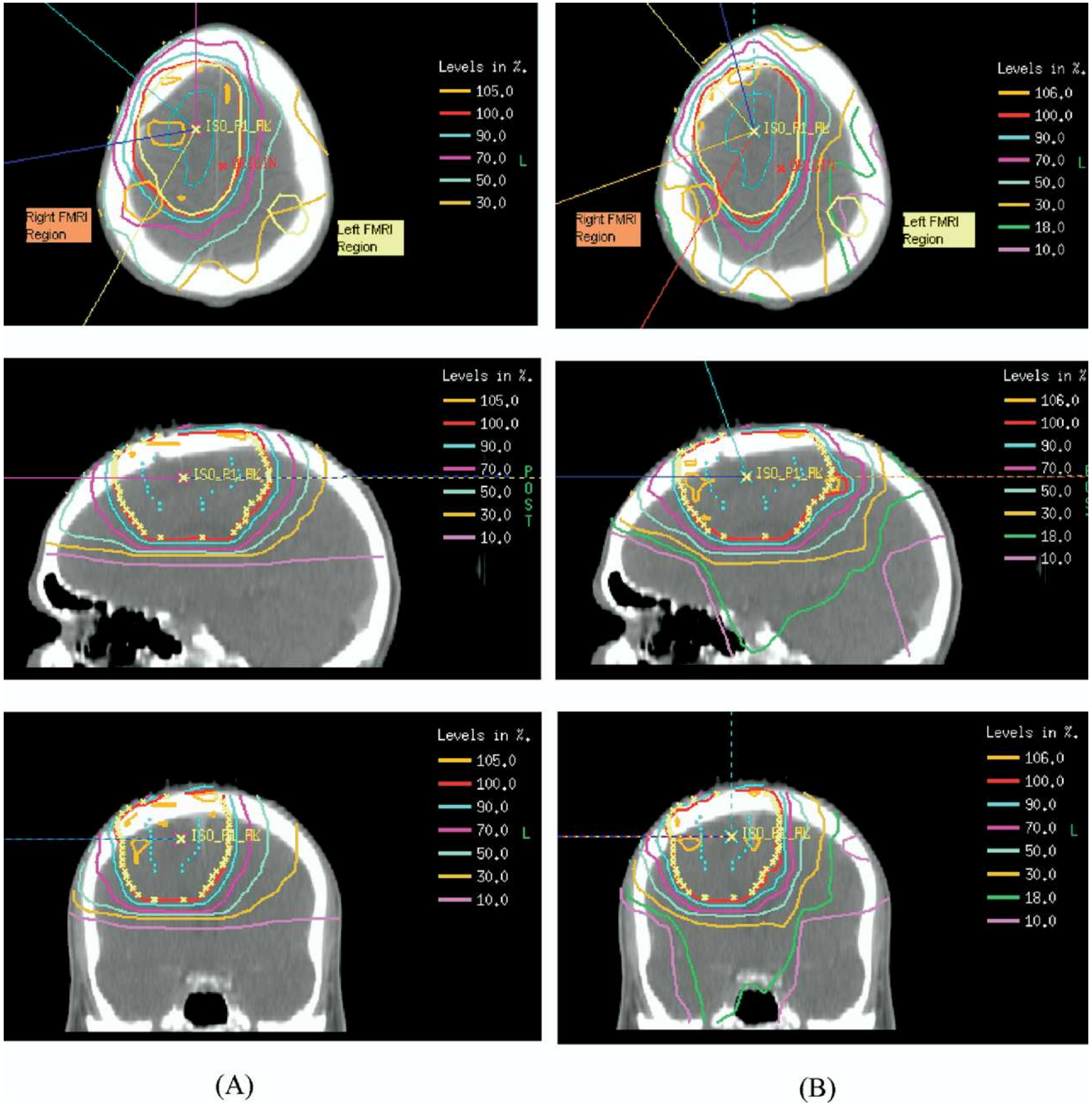


2 cm radial expansion can encompass 94.5% of pelvic nodes

Fig. 4. Metastatic nodes referenced to pelvic vessels with a 2.0-cm clinical target volume expansion to the region along pelvic vessels at greatest risk: (A) Anterior-posterior view. (B) Left lateral view.

IMRT using Brain Functional MRI

Chang J, Med Dos, 2008

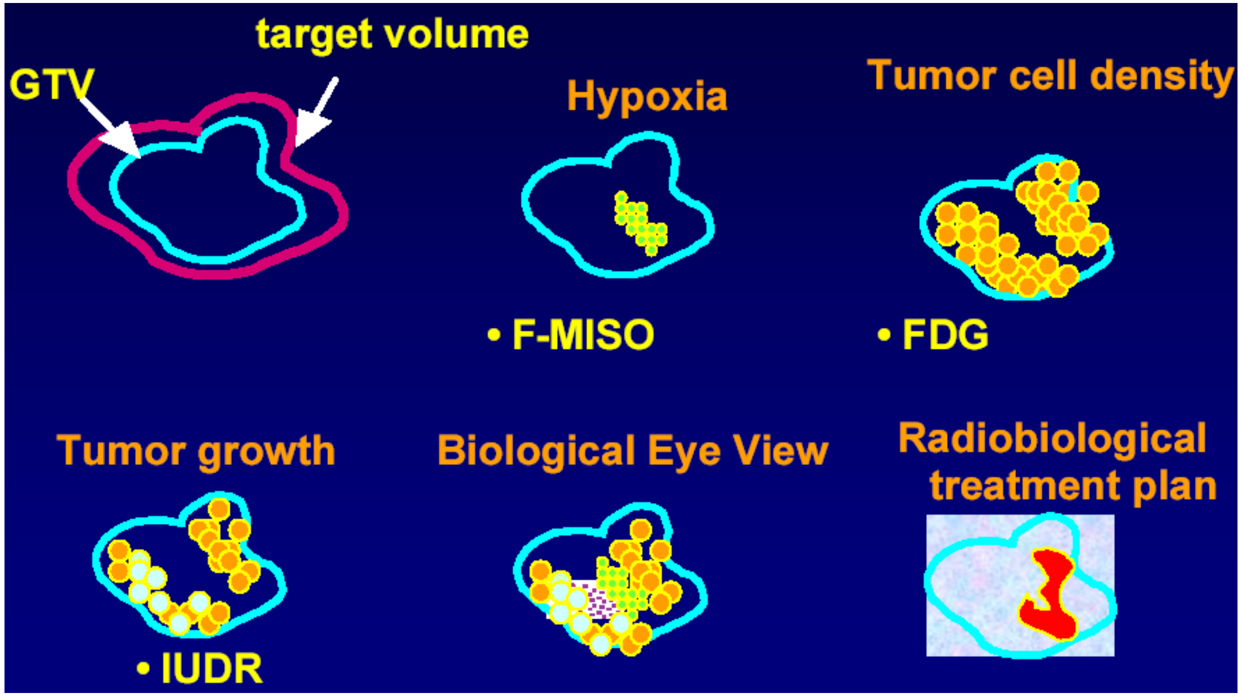


Treatment plans for patient no. 1 (A) without and (B) with the fMRI information

Limits of the Morphological/Functional Imaging for Radiation Therapy

- do not account for tumor heterogeneity
- do not show molecular targets
- are not predictive of short-term response
- are not sensitive to detect therapy-induced tumor cell kill
- may not distinguish between viable tumor and treatment effects in normal tissue

Bio-Molecular Imaging



(C. Ling, 2000)

- MRS
- SPECT
- PET

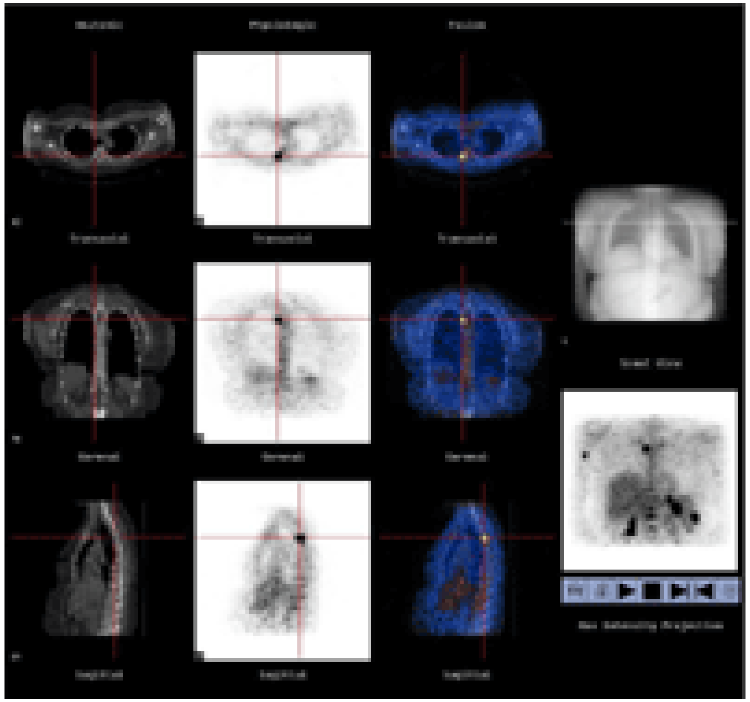
MR-Spectroscopy in volume definition

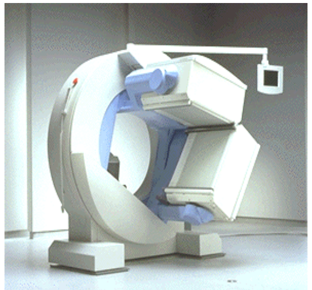
Kurhanewicz J, Radiology 198:795:805; 1996

MRS: voxel (8-10 mm3); < risoluzione spaziale vs TC e RM morfologica

Pirzkall A, New Technologies in Radiation Oncology; Springer 2006

SPECT with multiple detectors and SPECT/CT





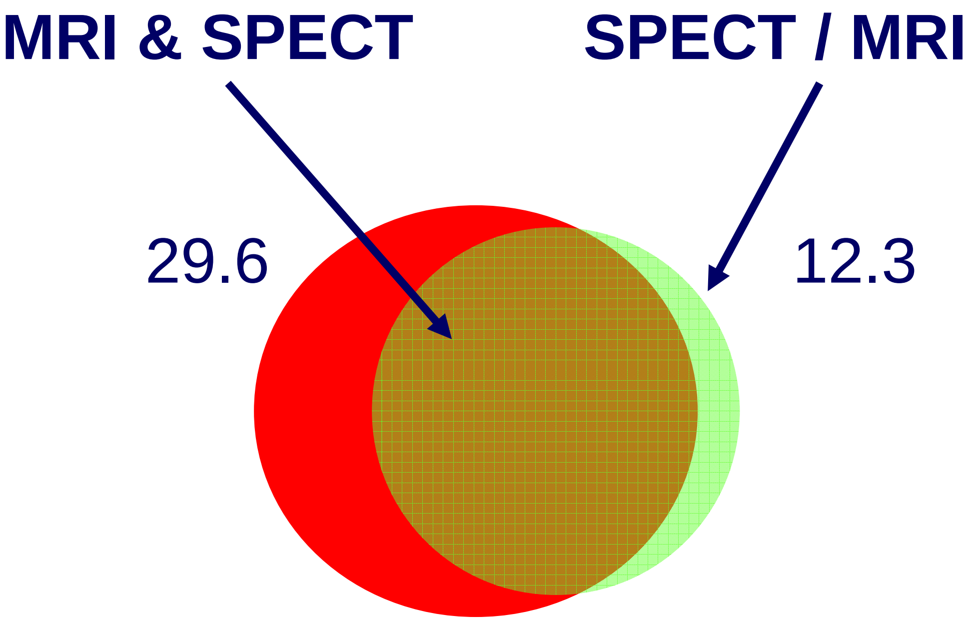
SPECT vs. PET

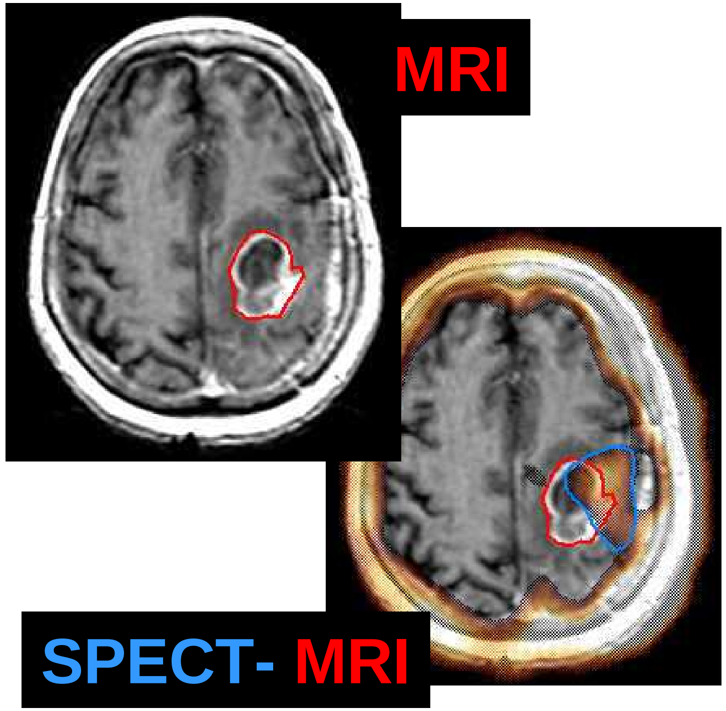
	SPECT	PET
Spatial Resolution	10 mm FWHM at center with Tc-99m and 30 cm orbit.	4.5-5 mm FWHM at center.
Radionuclides	Any with E from 60-200keV	Positron emitters only
Cost	About $500k for a twin-head system.	$1M-$2M

Strahlenther Onkol 2007;183:689–94

Delineation of Target Volume for Radiotherapy of High-Grade Gliomas by ^{99m}Tc-MIBI SPECT and MRI Fusion

Marco Krengli[1], Gianfranco Loi[2], Gianmauro Sacchetti[3], Irene Manfredda[1], Giuseppina Gambaro[1], Marco Brambilla[2], Alessandro Carriero[4], Eugenio Inglese[3]





In average, 13% of SPECT-GTV (BTV) was not included in MRI-GTV; this % was higher in operated pts

Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 4, pp. 1100–1104, 2006

POTENTIAL ADVANTAGE OF STUDYING THE LYMPHATIC DRAINAGE BY SENTINEL NODE TECHNIQUE AND SPECT-CT IMAGE FUSION FOR PELVIC IRRADIATION OF PROSTATE CANCER

Marco Krengli, M.D.,[*] Andrea Ballarè, M.D.,[*] Barbara Cannillo, Ph.D.,[†] Marco Rudoni, M.D.,[‡] Ervin Kocjancic, M.D.,[§] Gianfranco Loi, Ph.D.,[†] Marco Brambilla, Ph.D.,[†] Eugenio Inglese, M.D.,[‡] and Bruno Frea, M.D.[§]

20 PATIENTS

- intra-prostate trans-rectal injection of 115 MBq of ^{99m}Tc-nano-colloid

- Lymphoscintigraphy - SPECT

- SPIRAL CT-scan

- SPECT - CT images fusion

- TREATMENT PLAN (3D-CRT)

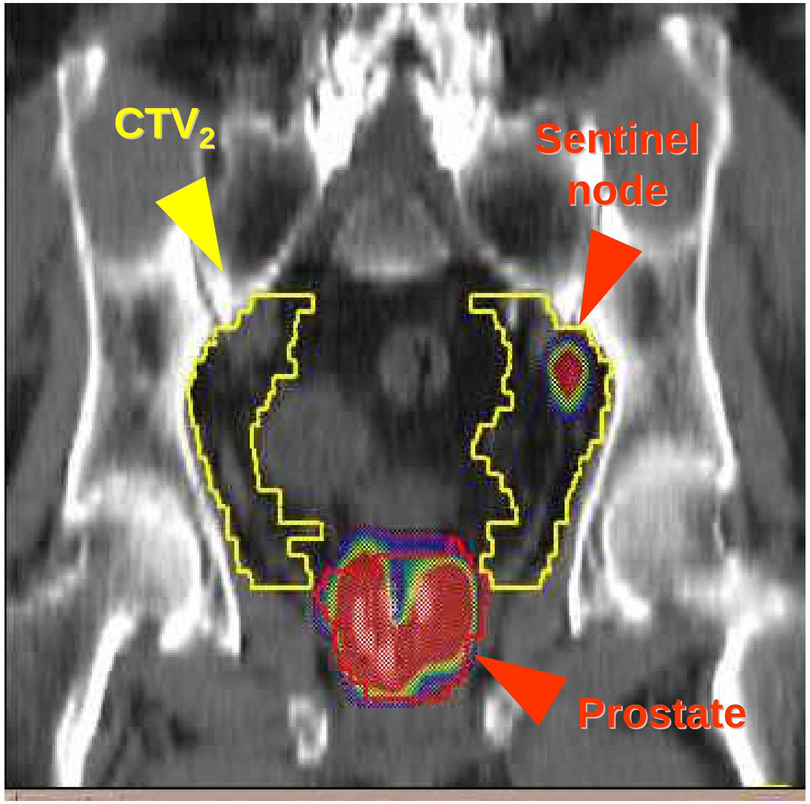
CTV_1 = prostate, seminal vesicles

CTV_2 = internal and external iliac nodes

- RESULTS

SN outside CTV2 in 4/20 (20%)

Other N outside CTV2 in 16/32 (50%)

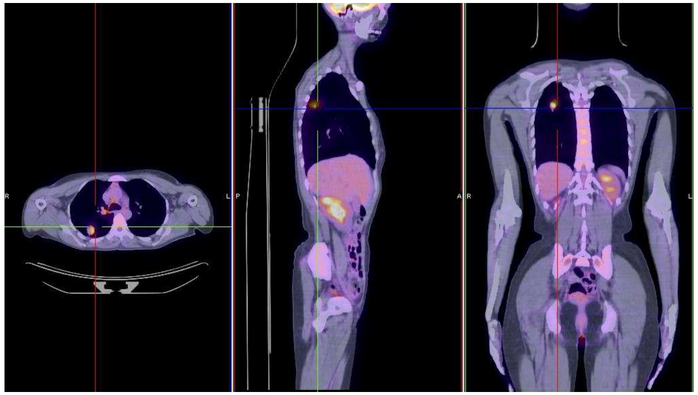


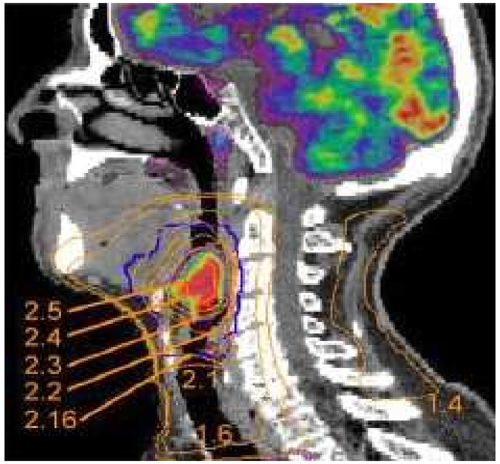
IMAGING MOLECOLARE: TRACCIANTI

• Glucose metabolism	[^{18}F]FDG
• Membrane function	[^{11}C]Choline
• Proliferation	[^{18}F]FLT
	[^{18}F]FMISO
• Hypoxia	[^{18}F]FAZA
	[^{64}Cu]ATSM
• Apoptosis	[^{18}F]Annexin V
• Angiogenesis	[^{18}F]NGR-peptide
• Neuroendocrine tumors	[^{110}In]Octreotate

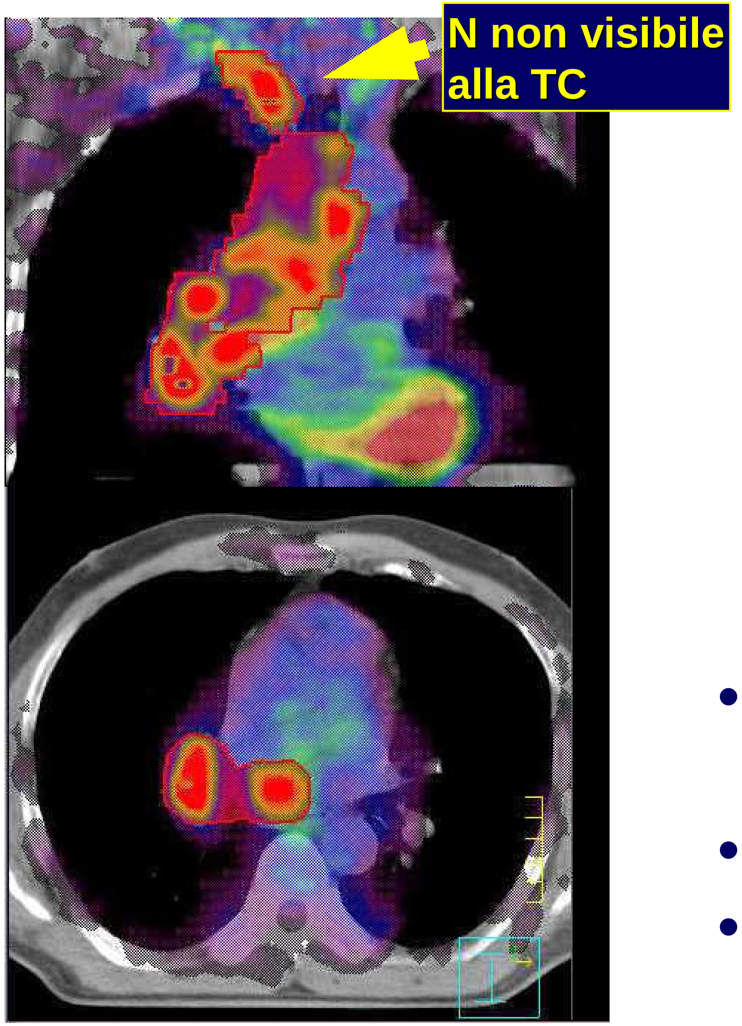
IMAGING MOLECOLARE: PET

- Stadiazione (selezione pazienti)
- Predizione risposta
- Identificazione e selezione del target volume
- Caratterizzazione biologica per dose painting
- Valutazione risposta al trattamento per adaptive therapy
- Identificazione precoce recidive
- Valutazione modificazioni nelle funzioni d'organo





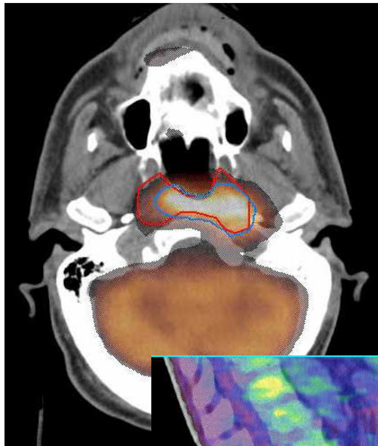
FDG-PET/TC in lung cancer

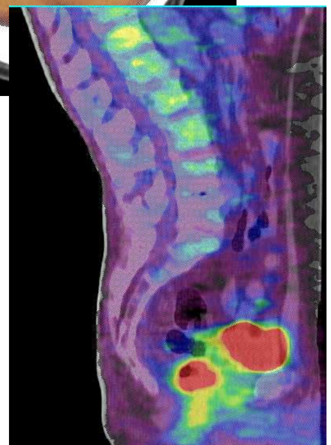


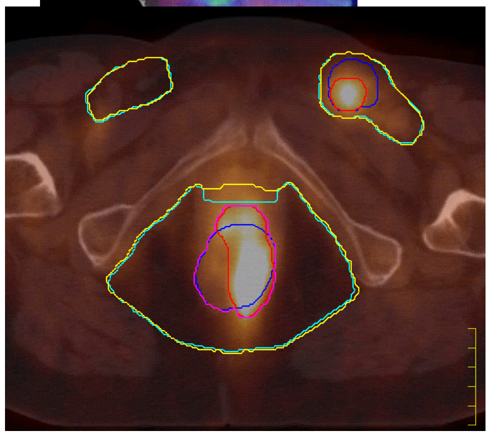
	CT	PET
Sensitivity	61%	85%
Specificity	79%	90%

- Change in treatment strategy in 25% of cases (Mah, 2002)
- Reduction in PTV in up to 70%
- Increase in PTV in up to 76%

FDG-PET/CT for Tumor Delineation







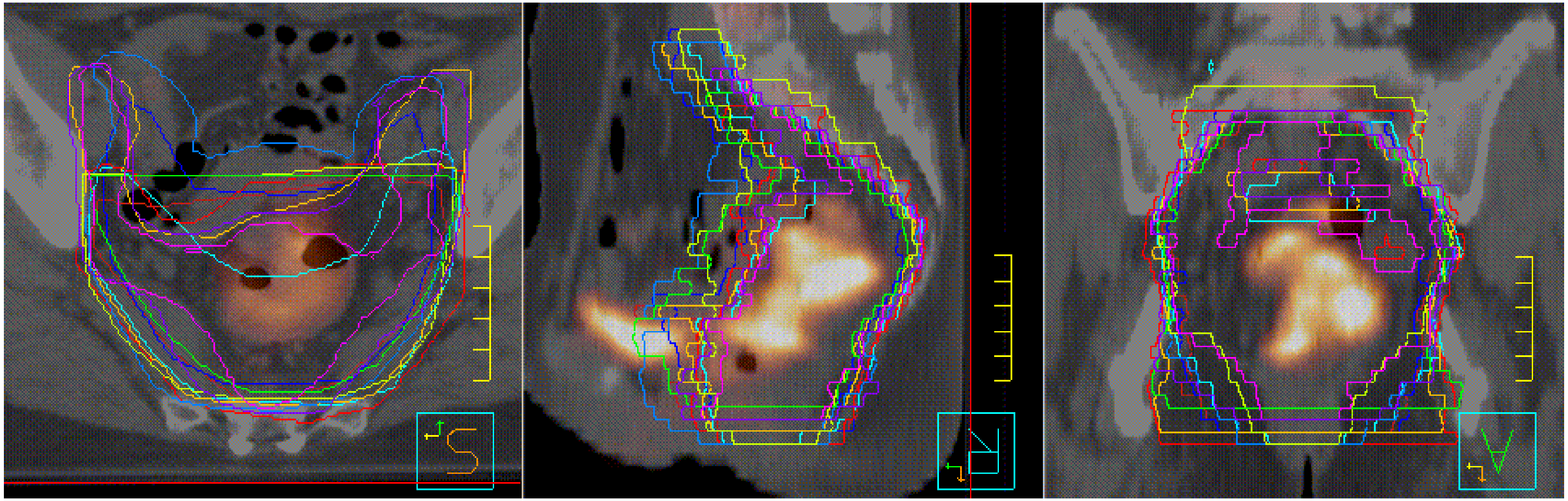
Head & Neck: 22 pts
Stage variation: 22%
Significant difference between PET/CT-GTV and CT-GTV ($p<0.0001$)
(Deantonio et al, Radiat Oncol 2008)

Rectum: 25 pts
Stage variation: 12%
Treatment strategy variation: 4%
Mean increase of GTV: 25%
Mean increase of CTV: 4%
(Bassi et al, IJROBP 2008)

Anal Canal: 27 pts
Stage variation: 19%
Treatment strategy variation: 4%
GTV and CTV changed in shape and in size based on PET/CT imaging
(Krengli et al, Radiat Oncol 2010)

Target Volume Delineation for Preoperative Radiotherapy of Rectal Cancer: Inter-Observer Variability and Potential Impact of FDG-PET/CT Imaging

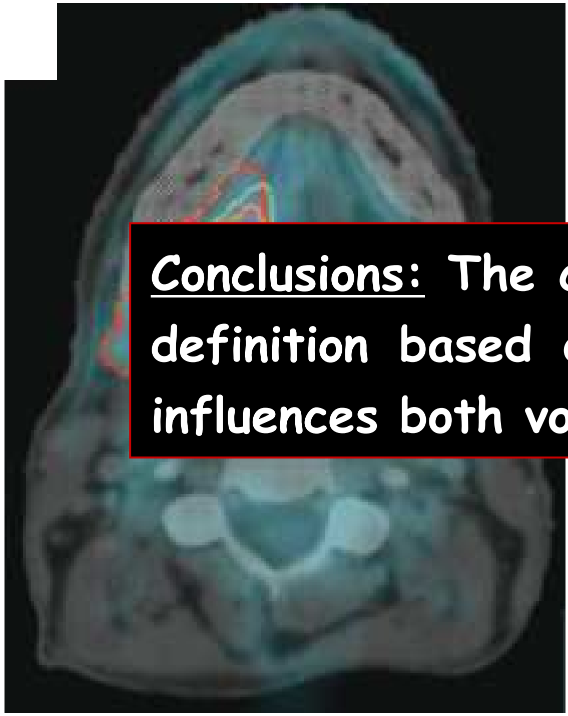
Technology in Cancer Research and Treatment
ISSN 1533-0346
Volume 9, Number 4, August 2010



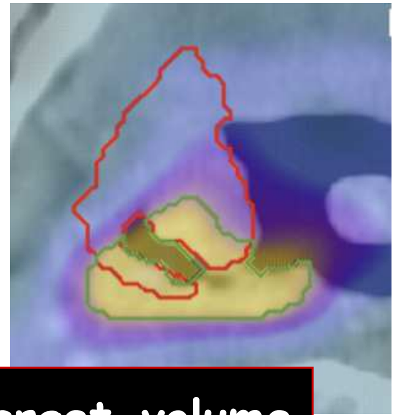
- **GTV variations were greater across the observers contouring on CT than across those contouring on PET/CT.**
- **CTV variations were related to a different clinical interpretation of risk of potential lymph node involvement.**

(Krengli et al.)

Definition of target volume with PET/CT: which method?



Results depend on segmentation method being used



CT:

Conclusions: The choice of segmentation tool for target-volume definition based on FDG-PET images is not trivial because it influences both volume and shape of the resulting GTV.

GTV_{visual}

$GTV_{40\%}$	20.1 cc (yellow)	semi-automated
GTV_{SUV}	32.6 cc (orange)	semi-automated
GTV_{SBR}	15.7 cc (blue)	semi-automated

COMPARISON OF FIVE SEGMENTATION TOOLS FOR ^{18}F-FLUORO-DEOXY-GLUCOSE–POSITRON EMISSION TOMOGRAPHY–BASED TARGET VOLUME DEFINITION IN HEAD AND NECK CANCER

2007 IJROBP

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From anatomical to biological target volumes: the role of PET in radiation treatment planning

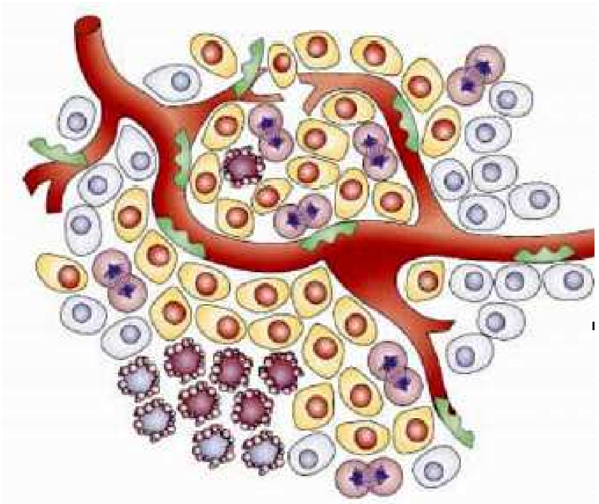
2006 International Cancer Imaging Society

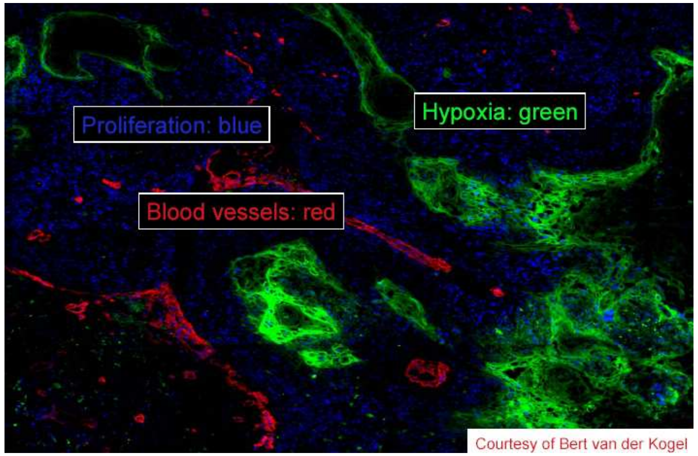
D A X Schinagl*, J H A M Kaanders* and W J G Oyen[†]

(courtesy of C. Iotti)

Oltre il contouring

- Il tumore è eterogeneo, alcune aree del GTV possono avere bisogno di una dose più elevata:
- Aree ipossiche
- Aree a più elevato indice di proliferazione
- Aree di neoangiogenesi
- Aree con cellule staminali tumorali



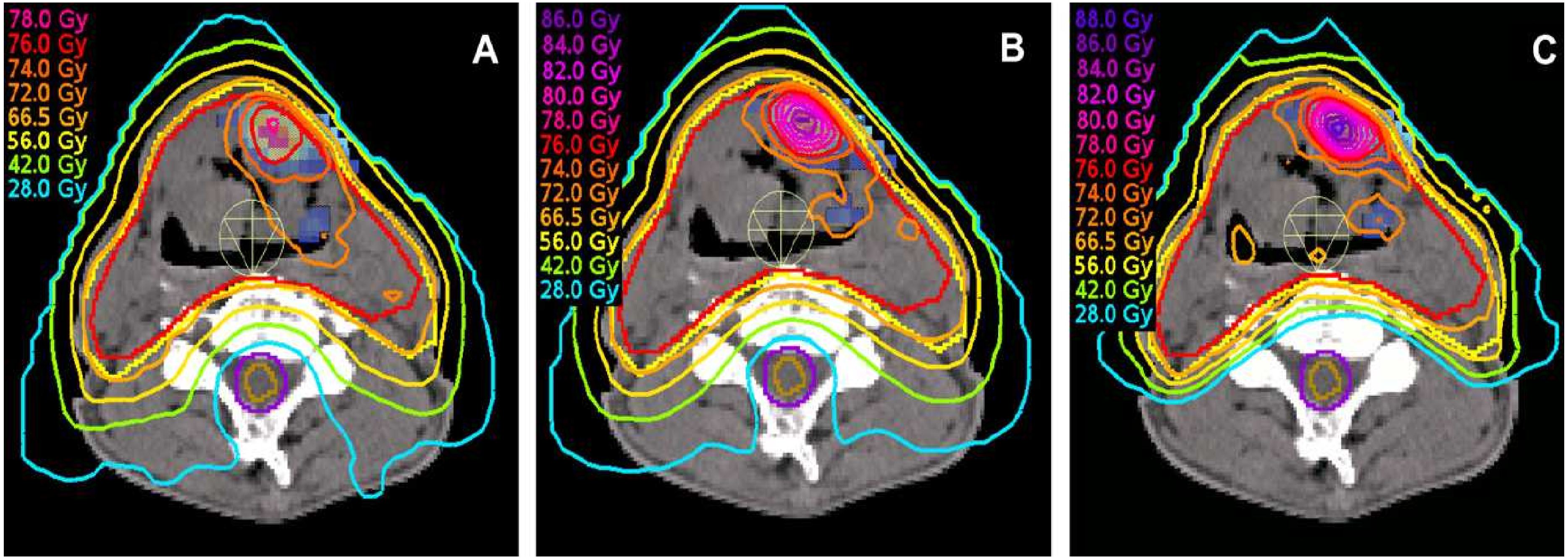


Courtesy of Bert van der Kogel

Dose painting with IMPT, helical tomotherapy and IMXT: A dosimetric comparison

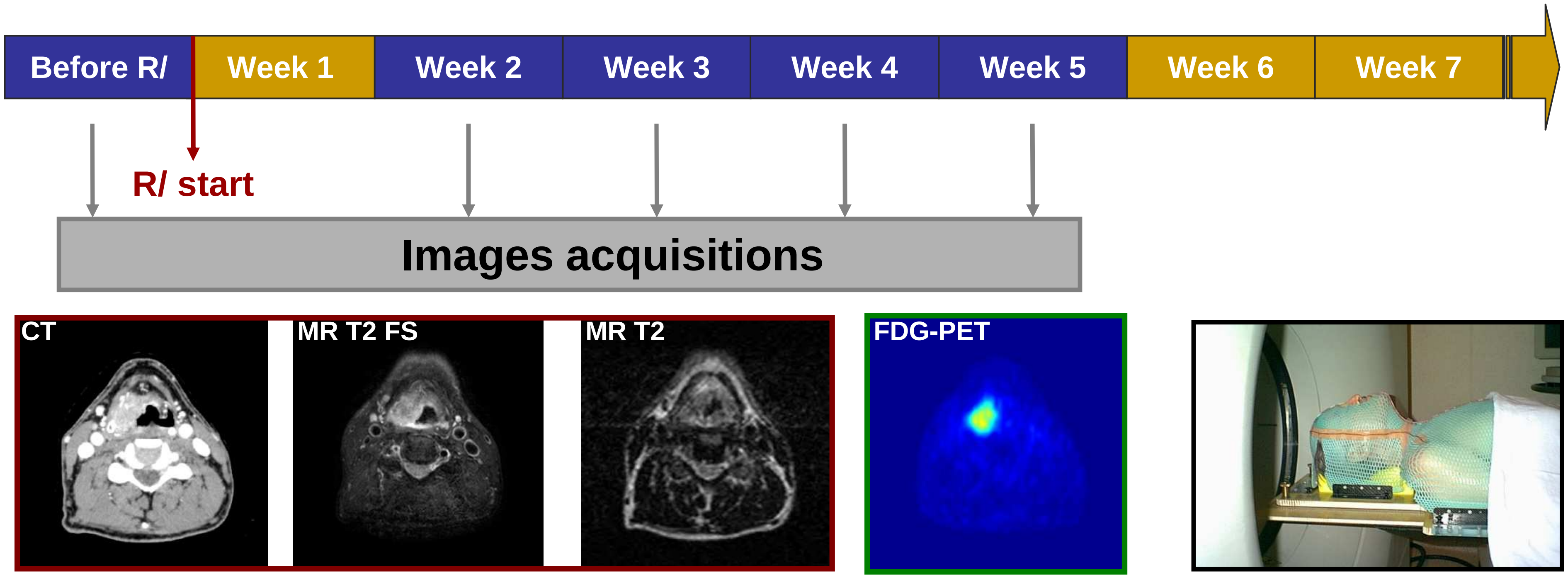
Daniela Thorwarth, Martin Soukup, Markus Alber

(Radiotherapy and Oncology 86:30–34, 2008)



IMXT **HT** **IMPT**

Biological adaptive IMRT



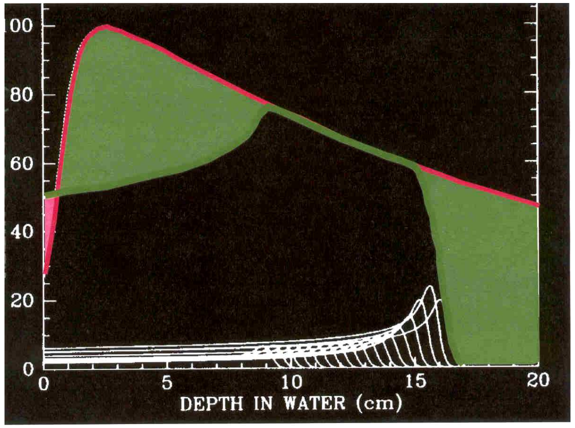
Anatomic imaging

Dynamic FDG-PET

- 10 patients with stage III-IV pharyngo-laryngeal SCC treated by CT-RT
- Images acquired before R/ and during RT after means doses of 14, 25, 35 and 45 Gy.

(Gregoire, 2009)

Adroterapia e Bio-Imaging

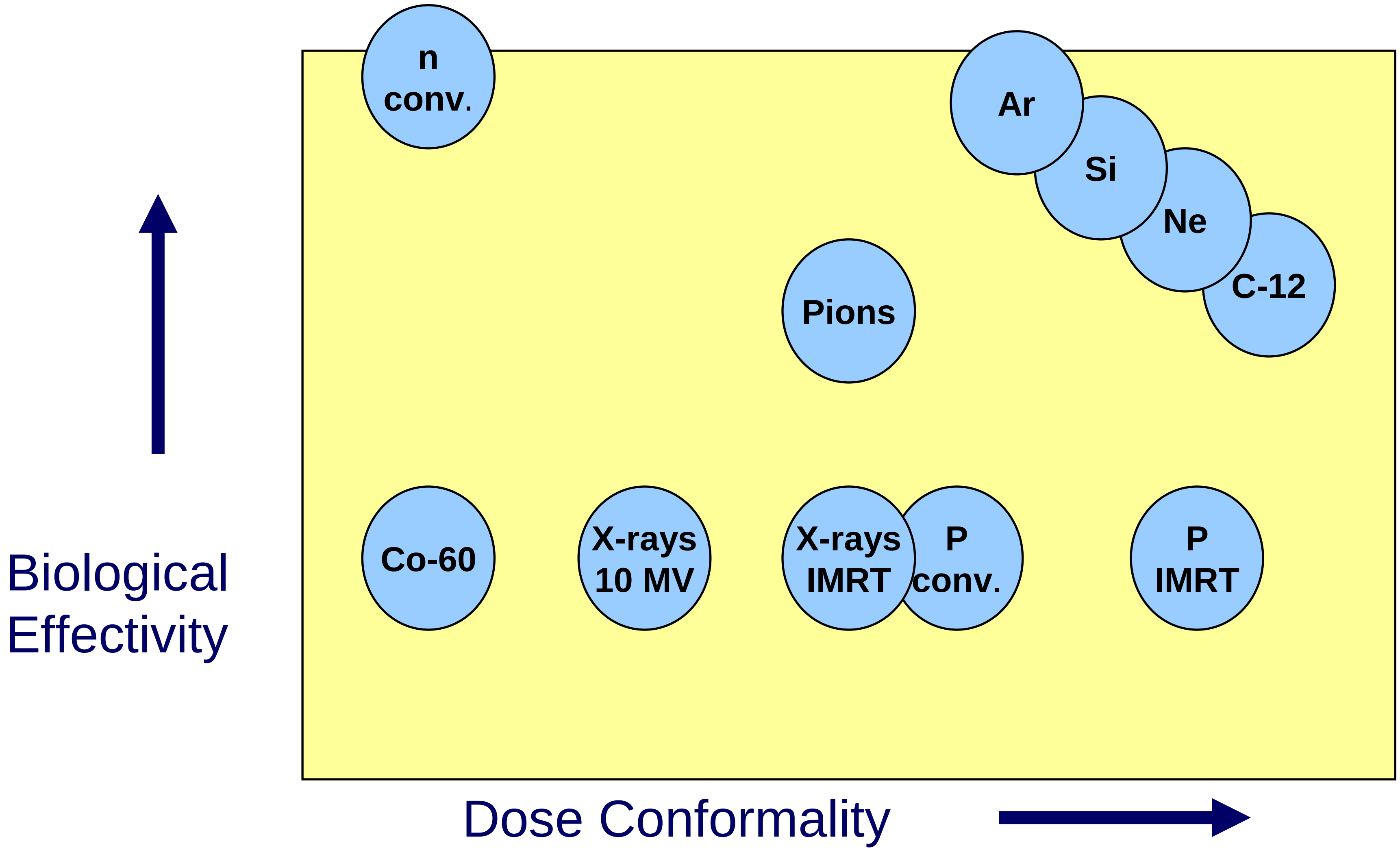


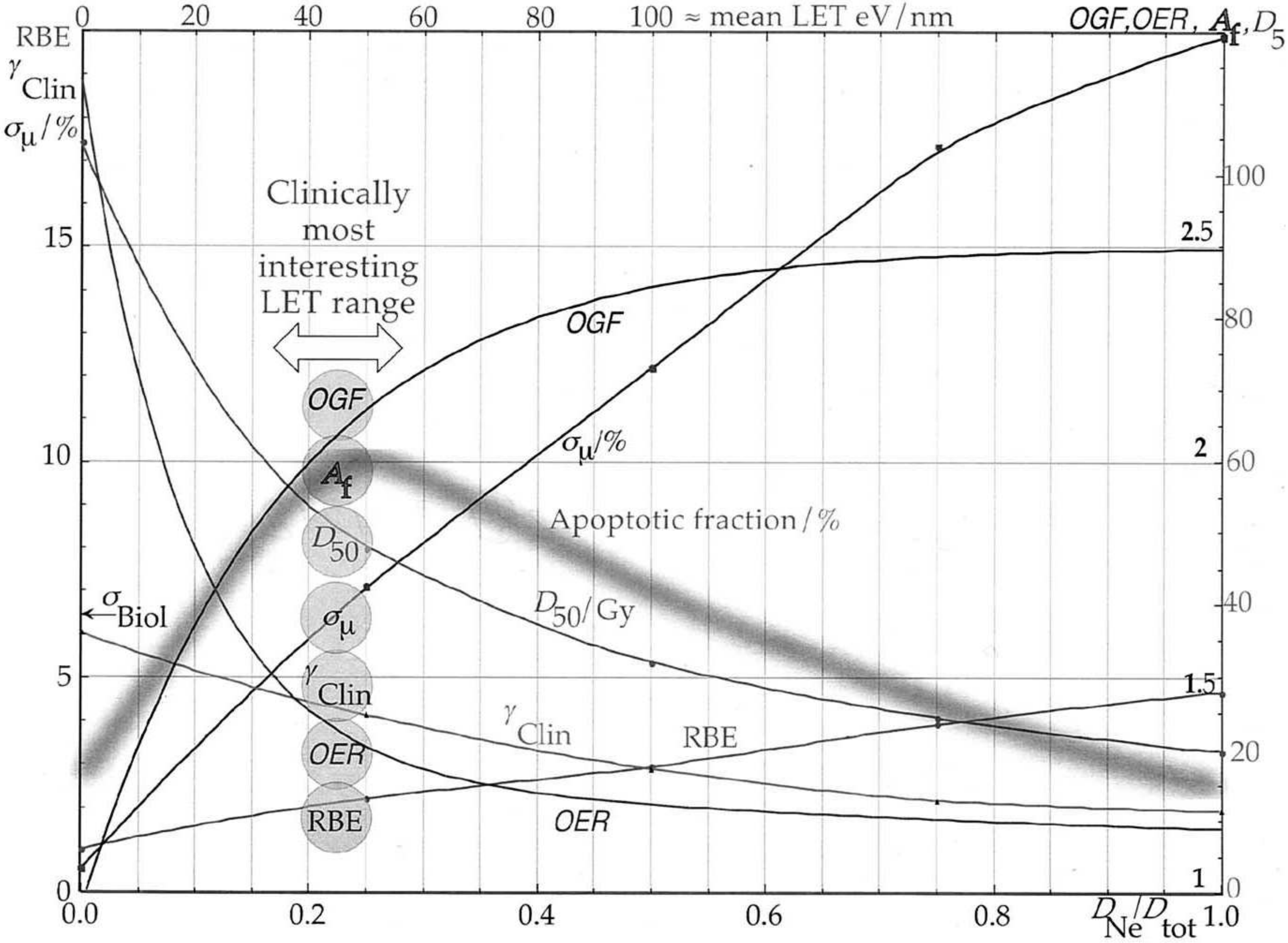
- Possibile uso di radiazioni con diverso EBR in base alle caratteristiche biologiche del tumore: from “dose painting” (IMRT) to *“biological dose painting” (“IMHT”)*

- Imaging PET nella verifica della sede di deposizione della dose (C-12, p+)

Particles in Radiation Oncology

Comparison of Protons, Neutrons, Pions, Ions and Photons

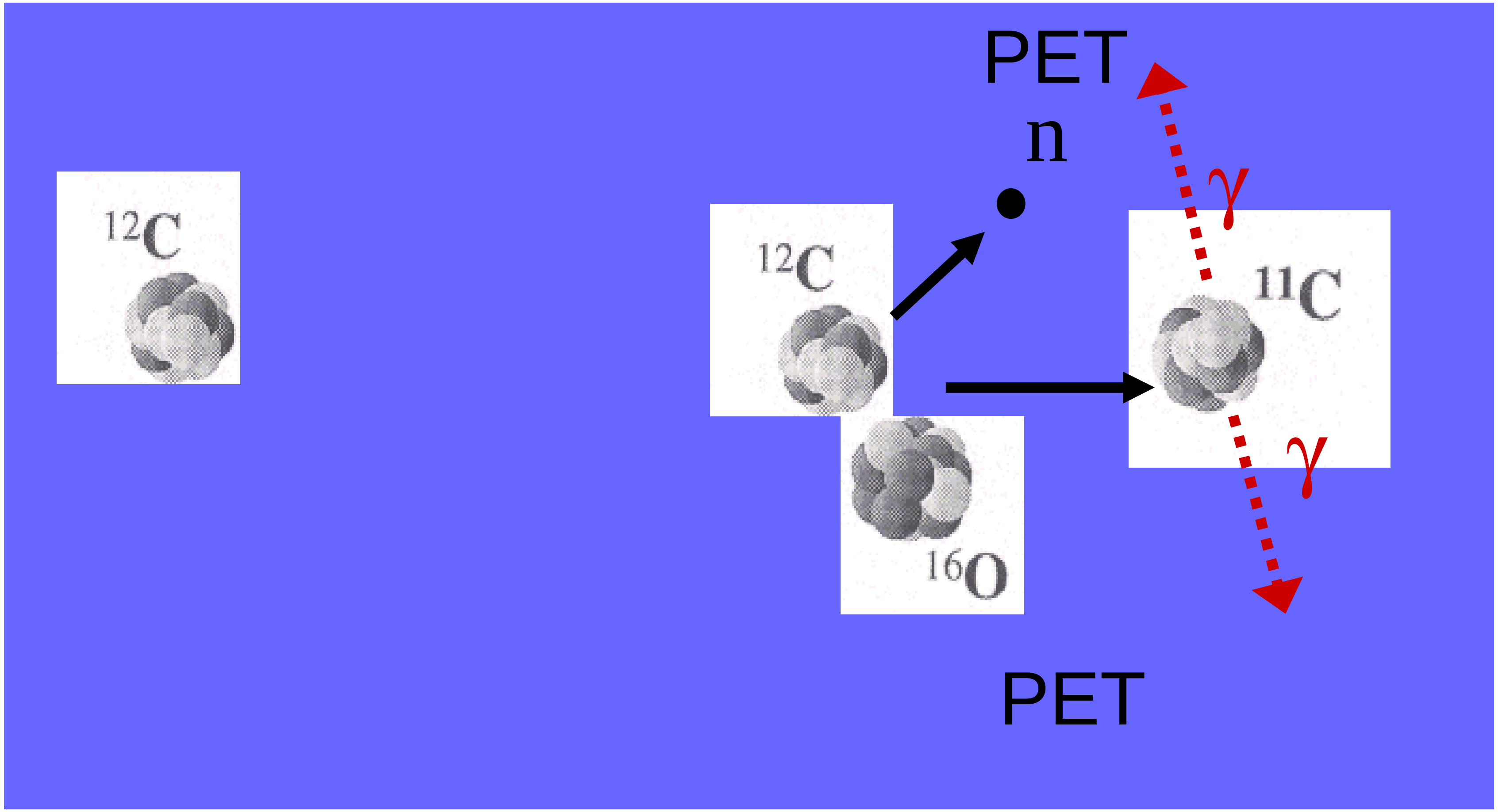




0 20 40 60 80 100 ≈ mean LET eV/nm
OGF,OER, Af, D5
RBE
γClin
σμ/%
Clinically most interesting LET range
OGF
Af
D50
σμ
γClin
OER
RBE
σμ/%
Apoptotic fraction/%
D50/Gy
σBiol
γClin
RBE
OER
15
10
5
0
100
80
60
40
20
0
2.5
2
1.5
1
0.0 0.2 0.4 0.6 0.8 1.0
DNe/Dtot

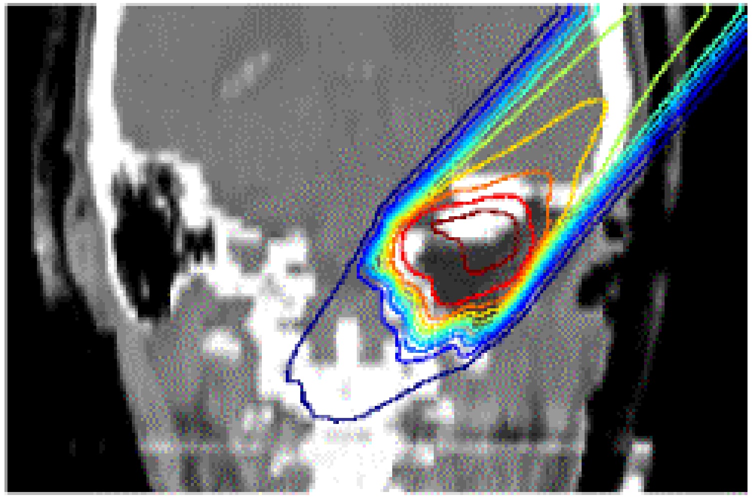
(Brahme 2004)

Tissue Activation by ^{12}C

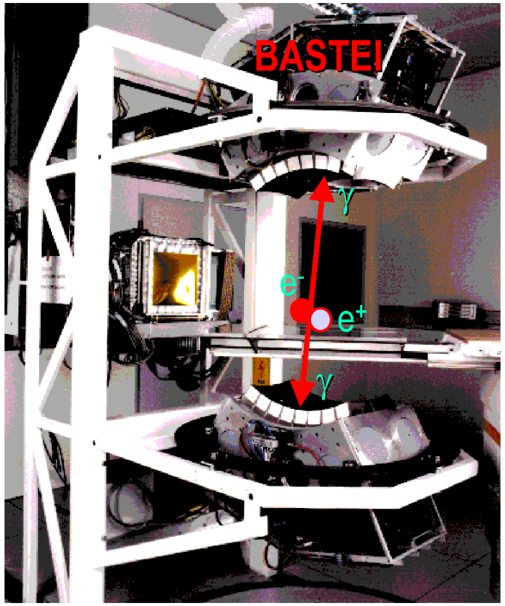


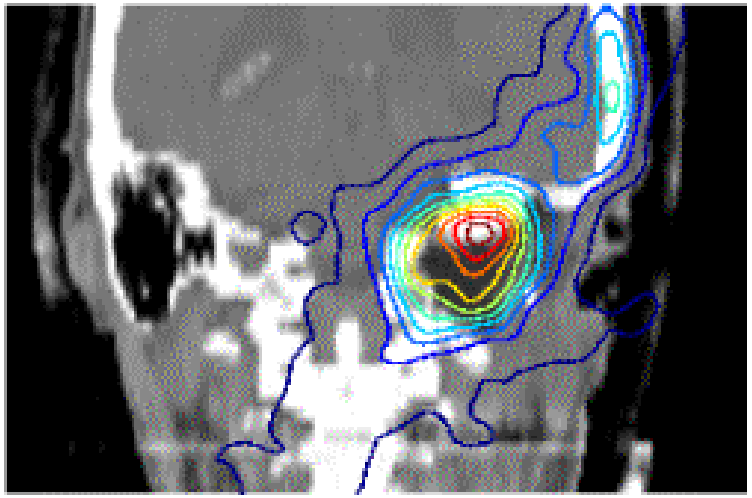
⇨ In Vivo-Monitoring of Irradiation

Carbon Ions
Verifying the position of the irradiation field by PET

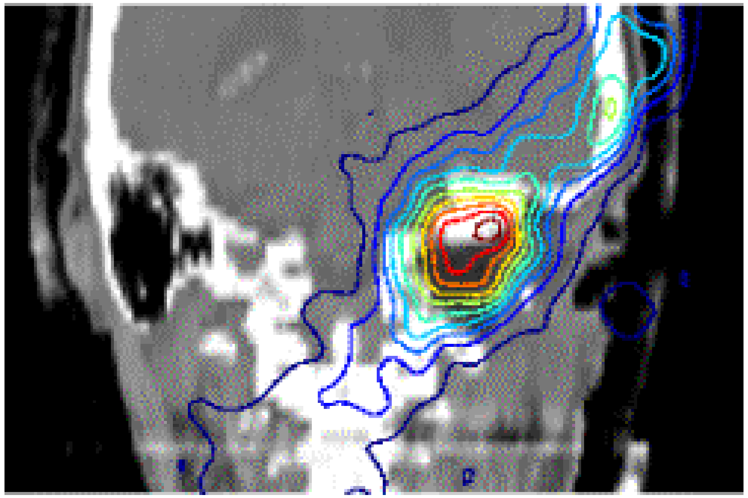


dose plan





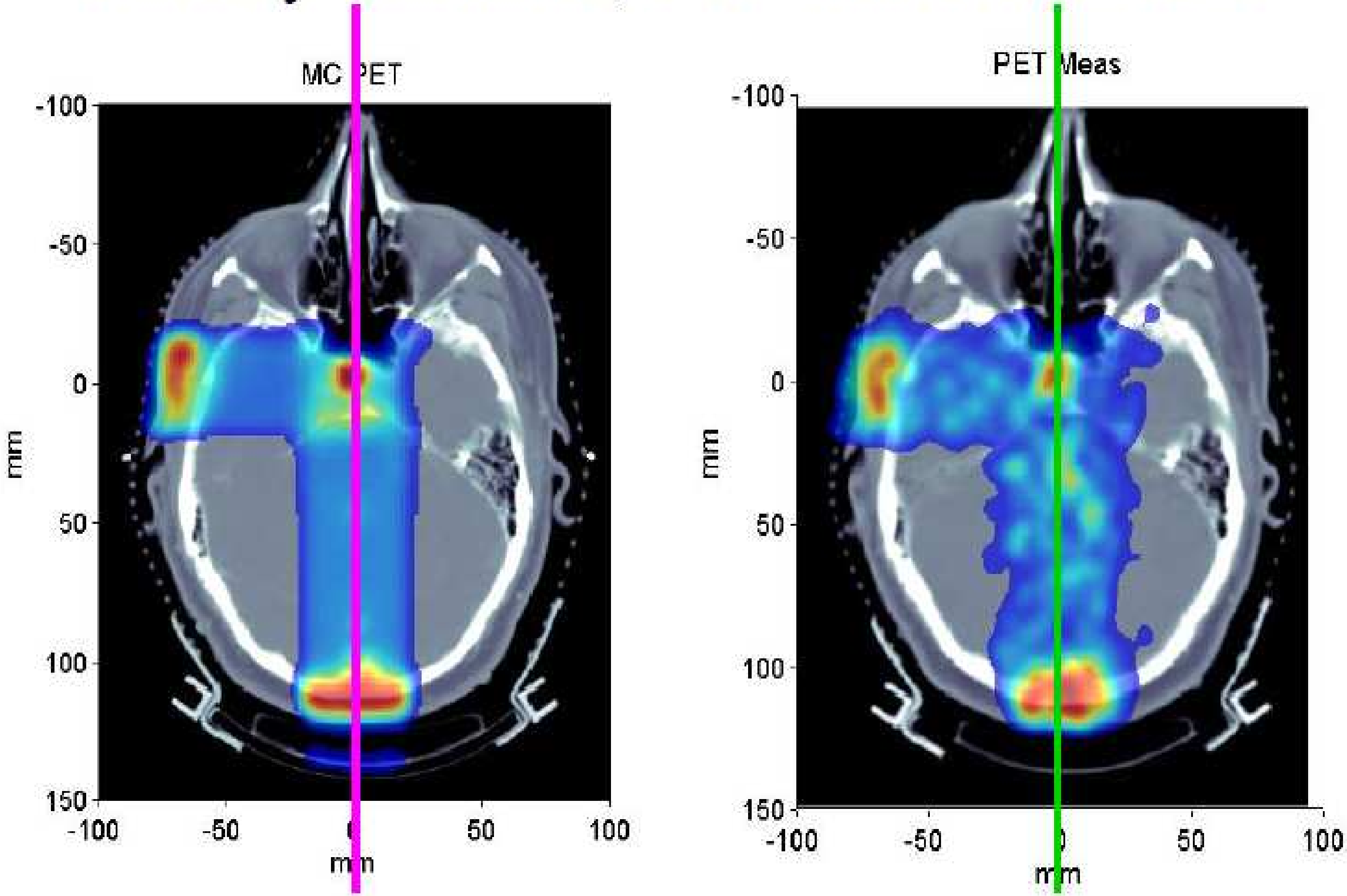
measured



simulated

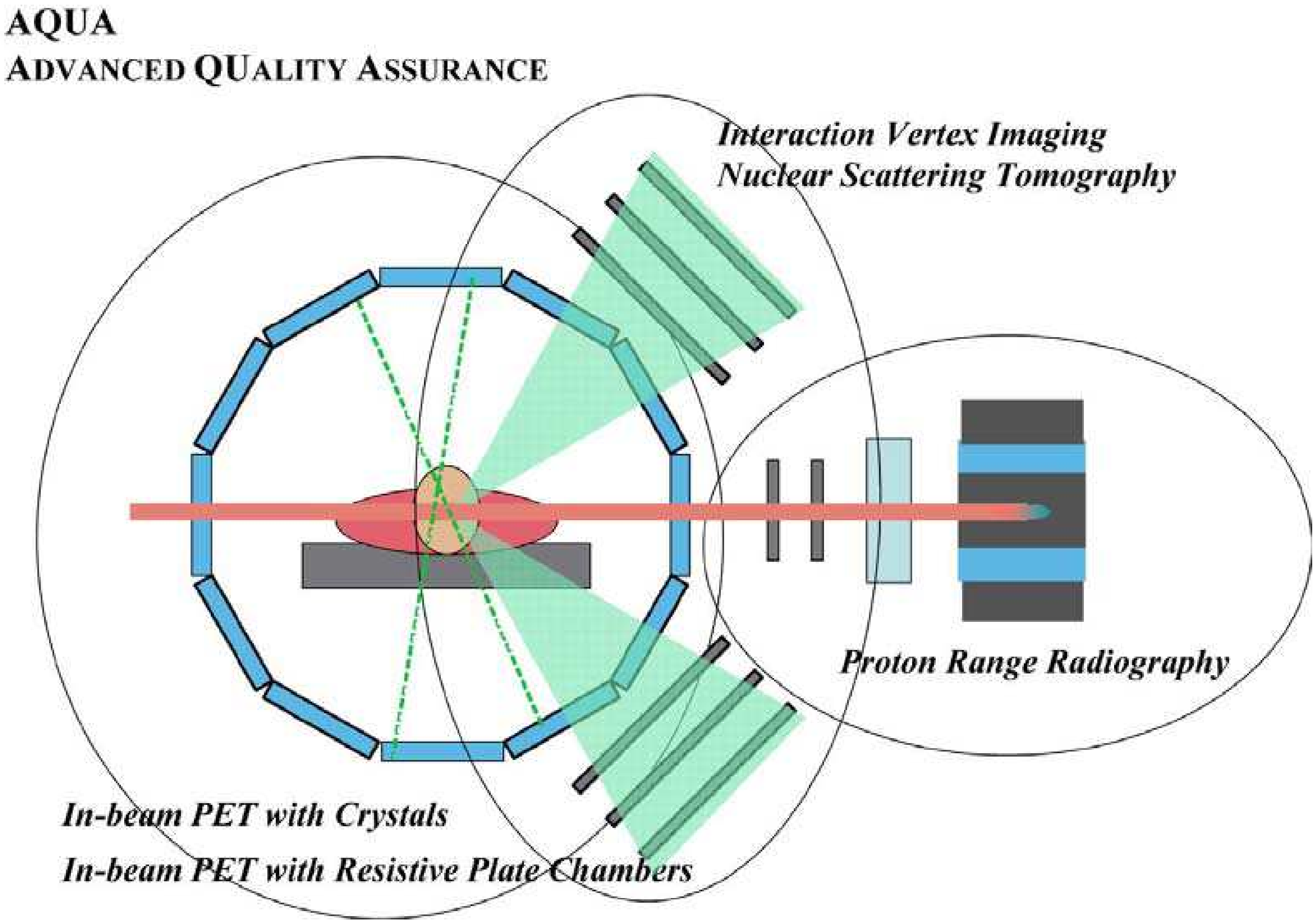
(W.Enghardt et al., FZR Dresden

Pituitary Adenoma, PET sim biol vs. PET



Mizuno et al. PMB 48:2269, 2003

In vivo PET verification at CNAO



Conclusioni I

- La TC rimane indispensabile per la pianificazione del trattamento in quanto consente di individuare la densità dei diversi tessuti.
- La TC con mdc consente una maggiore accuratezza nel riconoscimento dei volumi di interesse.
- La TC perfusionale apre prospettive nel campo della documentazione della vascolarizzazione e quindi della neo-angiogenesi.

Conclusioni II

- L’imaging funzionale e biologico sta modificando il modo di pianificare e di condurre la RT, ma è ancora da validare come modalità d’impiego.
- In alcune sedi in cui RM e PET sono state testate rispetto al gold standard (istologia) hanno dimostrato una maggiore accuratezza rispetto alla TC.

Conclusioni III

- Il concetto di dose painting, che potrà essere ottimizzato con l'impiego di radiazioni con diverso effetto biologico (adroterapia), necessità di disporre di un imaging capace di caratterizzare in modo dettagliato le varie componenti tumorali (proliferazione, ipossia, presenza di cellule staminali tumorali …) e di registrare le modificazioni che avvengono durante il trattamento.

Grazie!