USP Hospital San Jaime
Torrevieja-Alicante

Jornada Inaugural PET-CT

Torrevieja, 27 de Septiembre 2006

Contribution of PET/CT in Radiotherapy Planning

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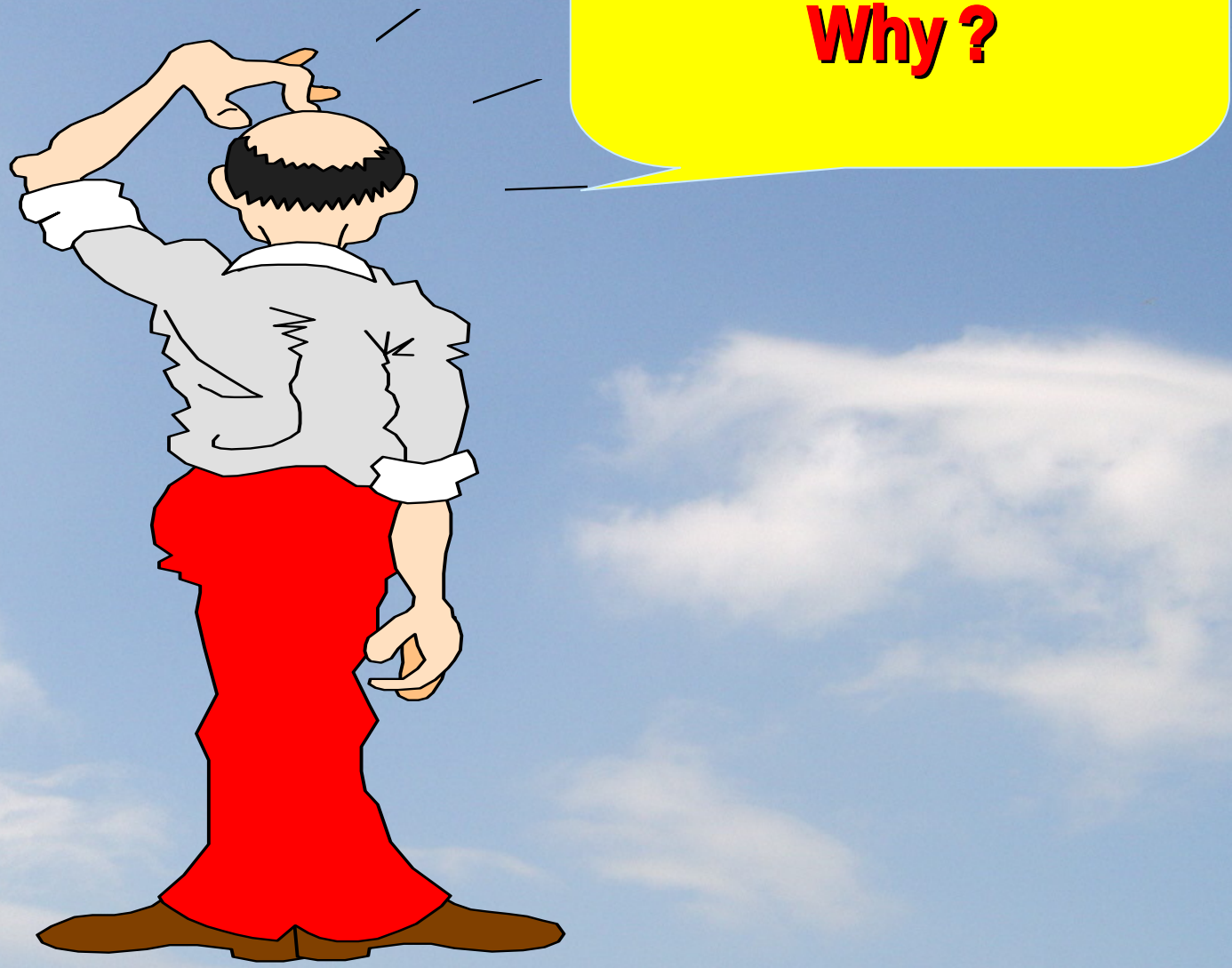
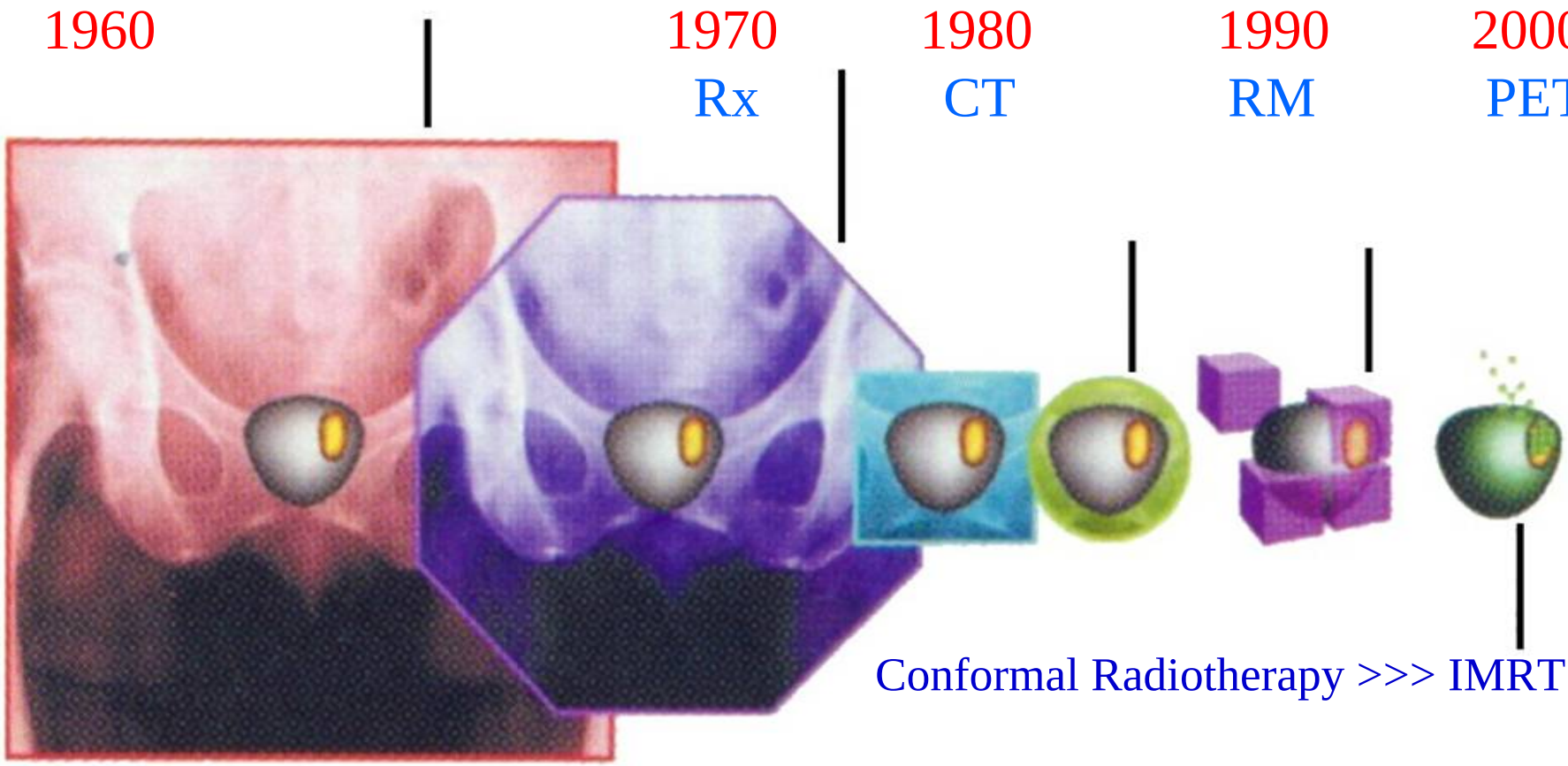
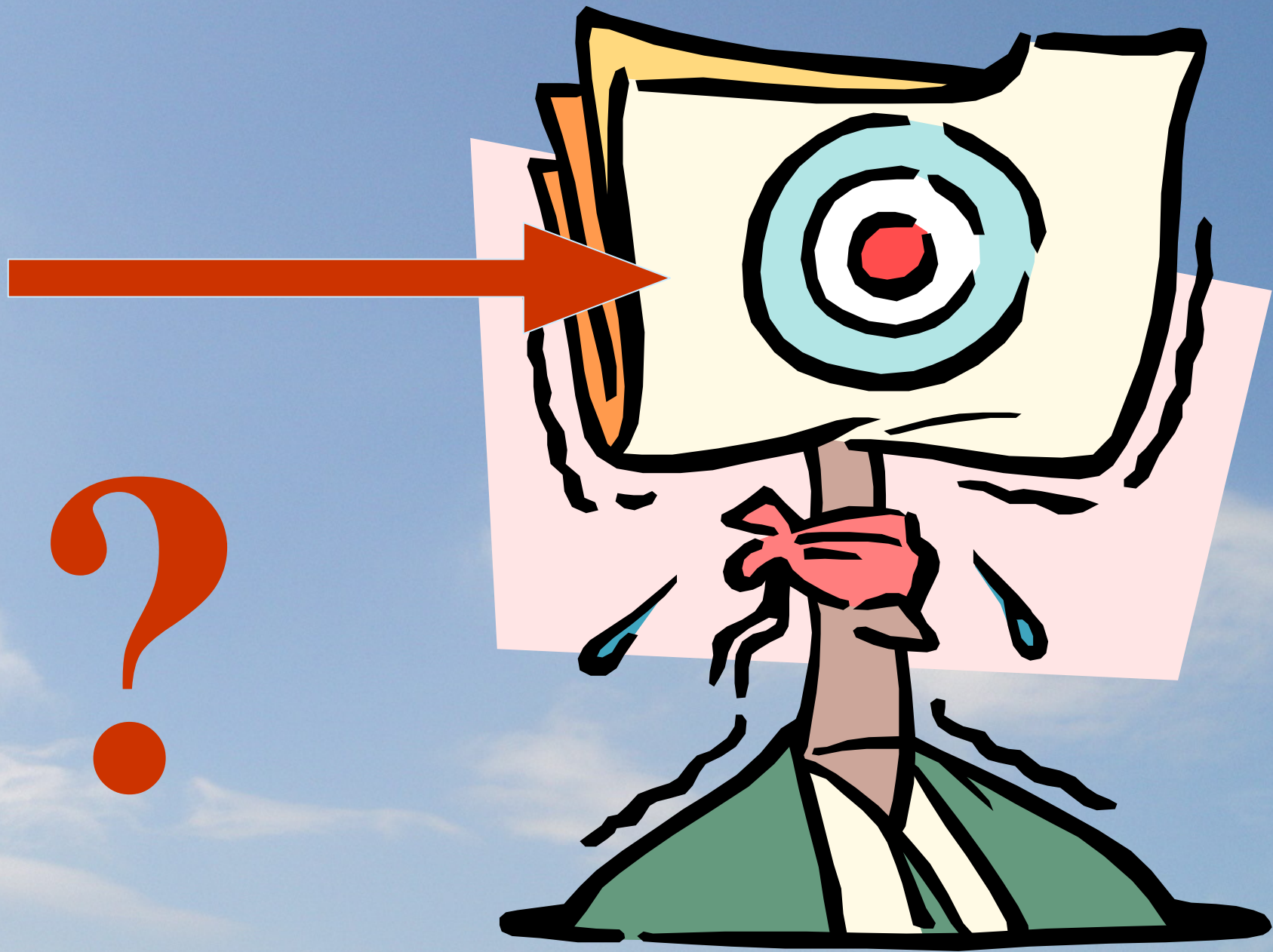

PET and Radiotherapy ?
Why ?

Development of Radiotherapy

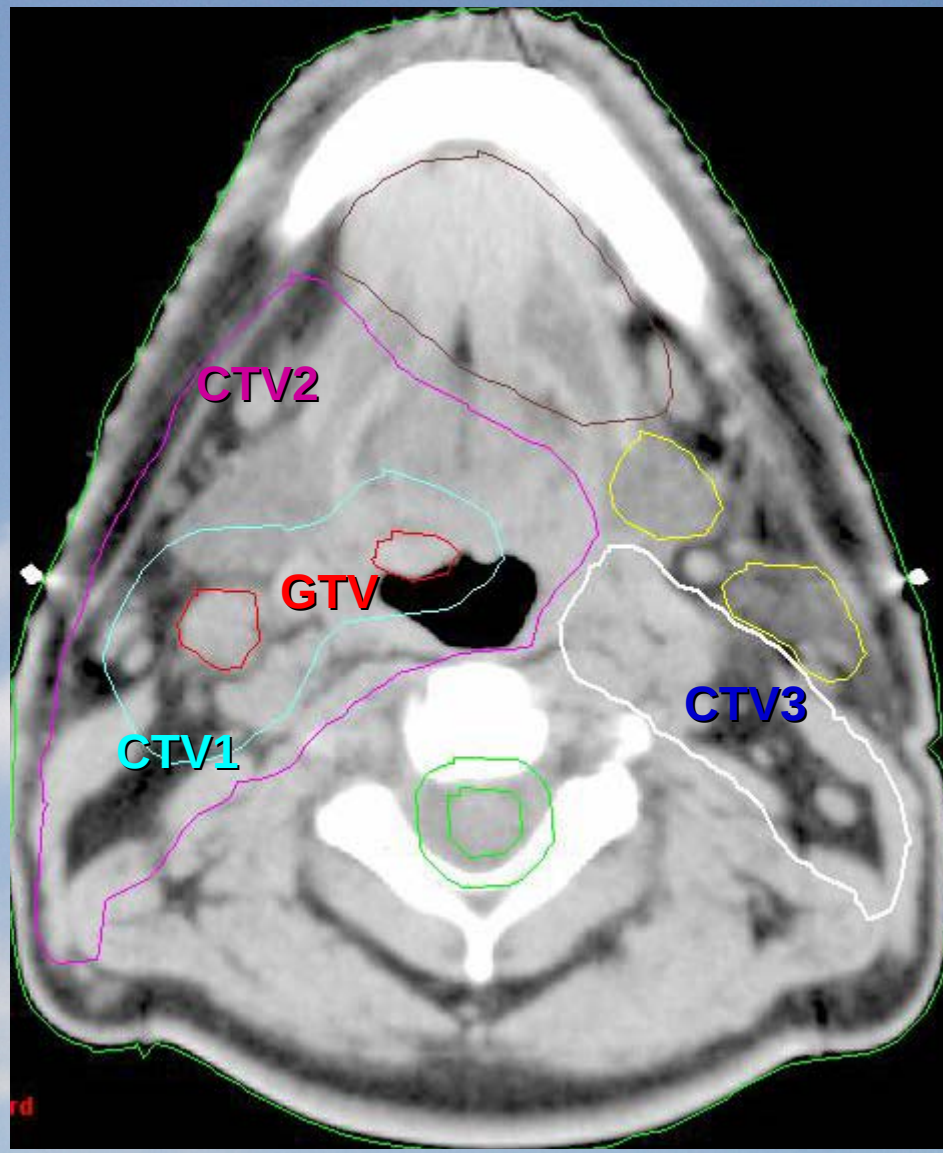


The error in target volume delineation may be the biggest error in the entire radiotherapy chain

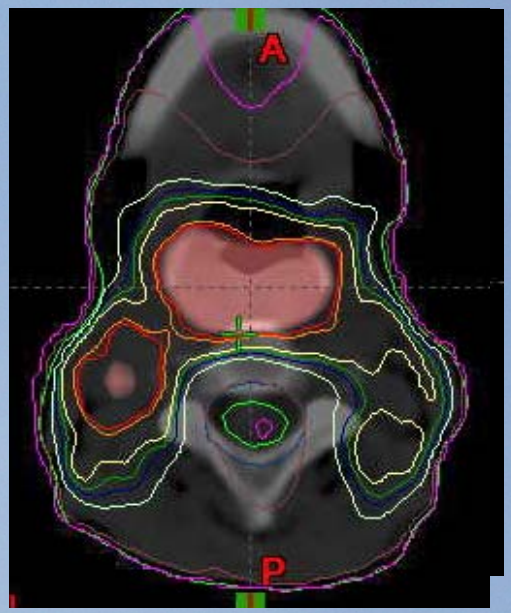


• geographic missing of the tumor → *reduction of local control probability*

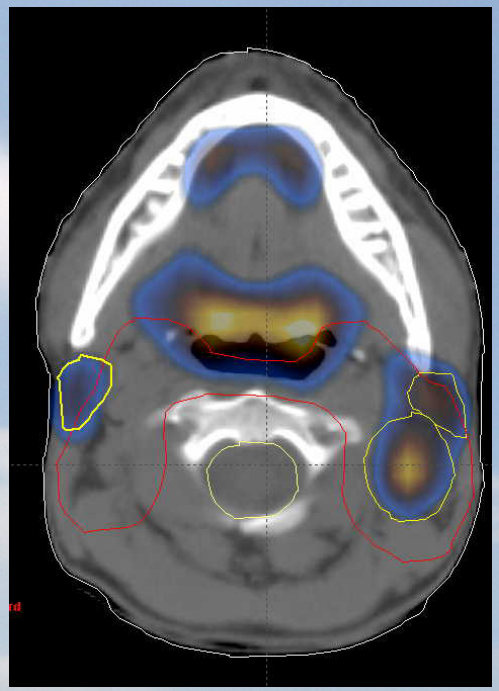
• high dose irradiation of healthy tissues → *increase of radio-induced damage probabilty*



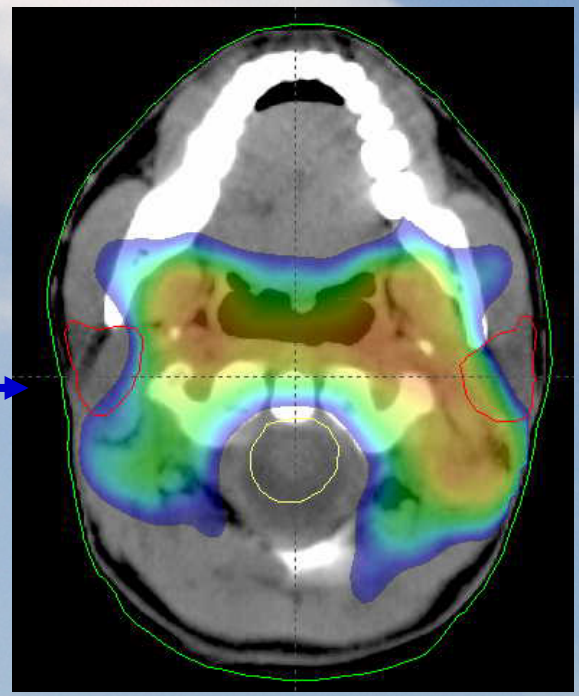
PET/CT in RTP: aim



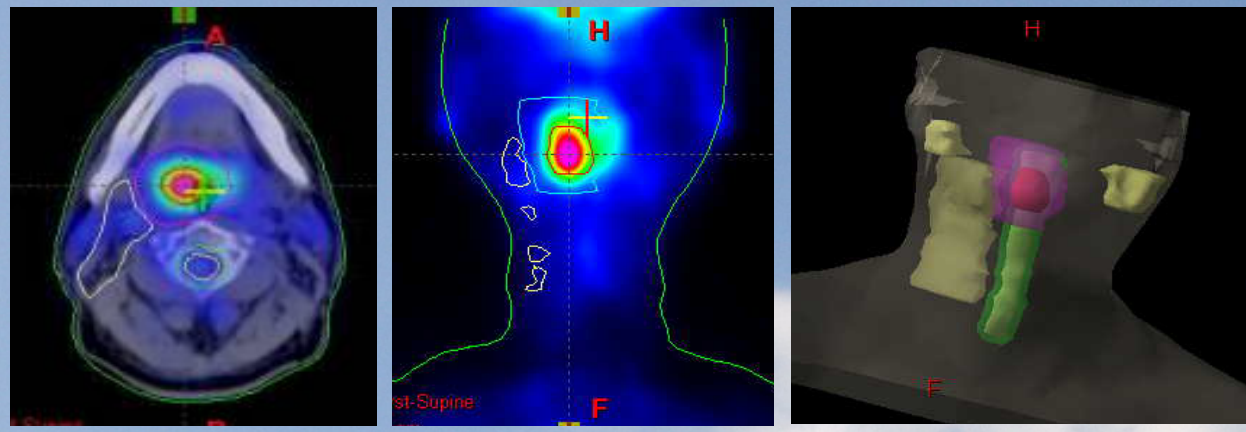
1. Proper inclusion of the disease in the high dose volume



2. Safer OARs sparing



What the radiation oncologist needs



The radiation oncologist expects from the functional imaging important aids to evolve towards a

biological dose conformation

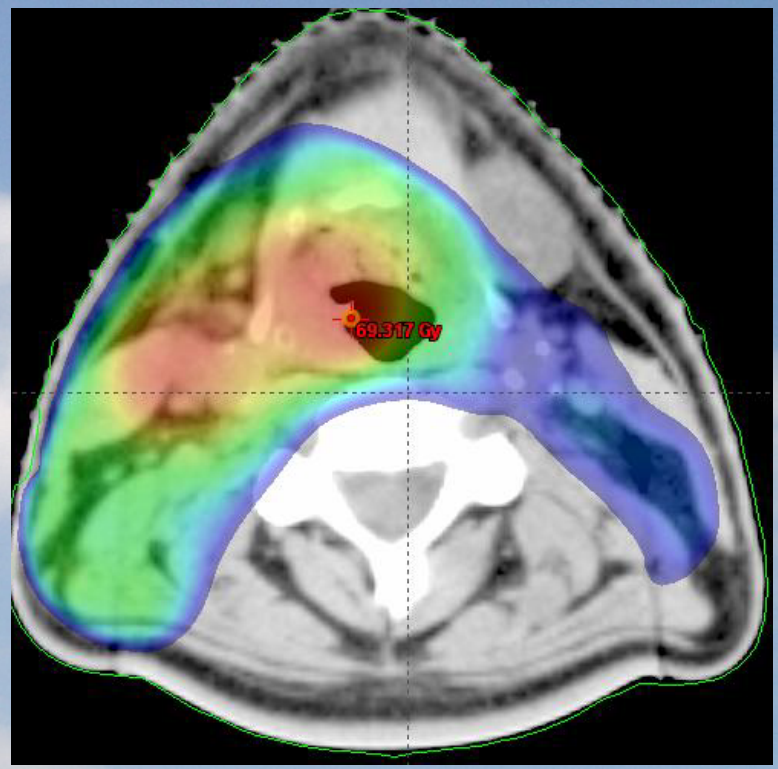
(BTV –Biological Target Volume)

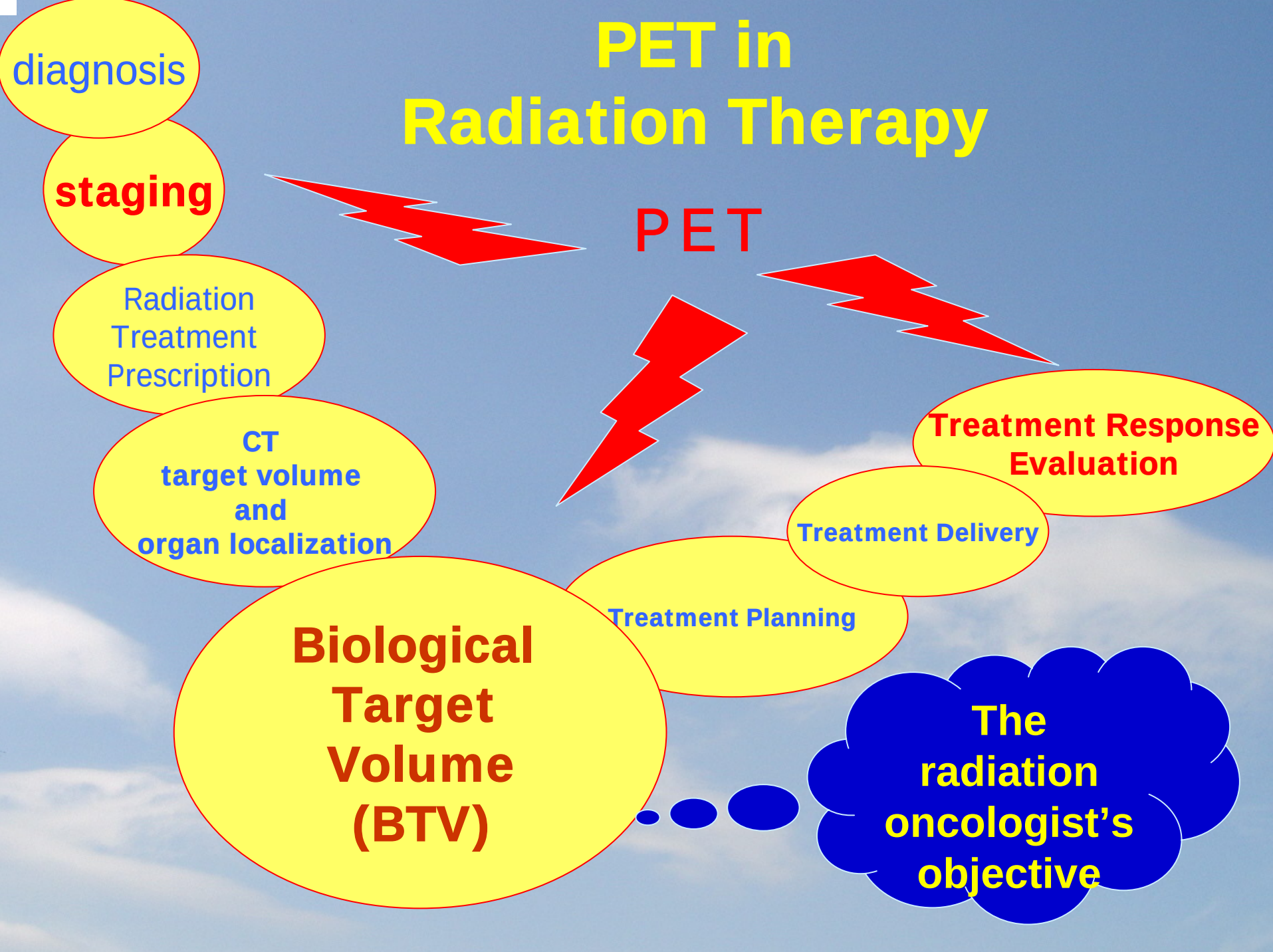
Intensity Modulated Radiation Therapy

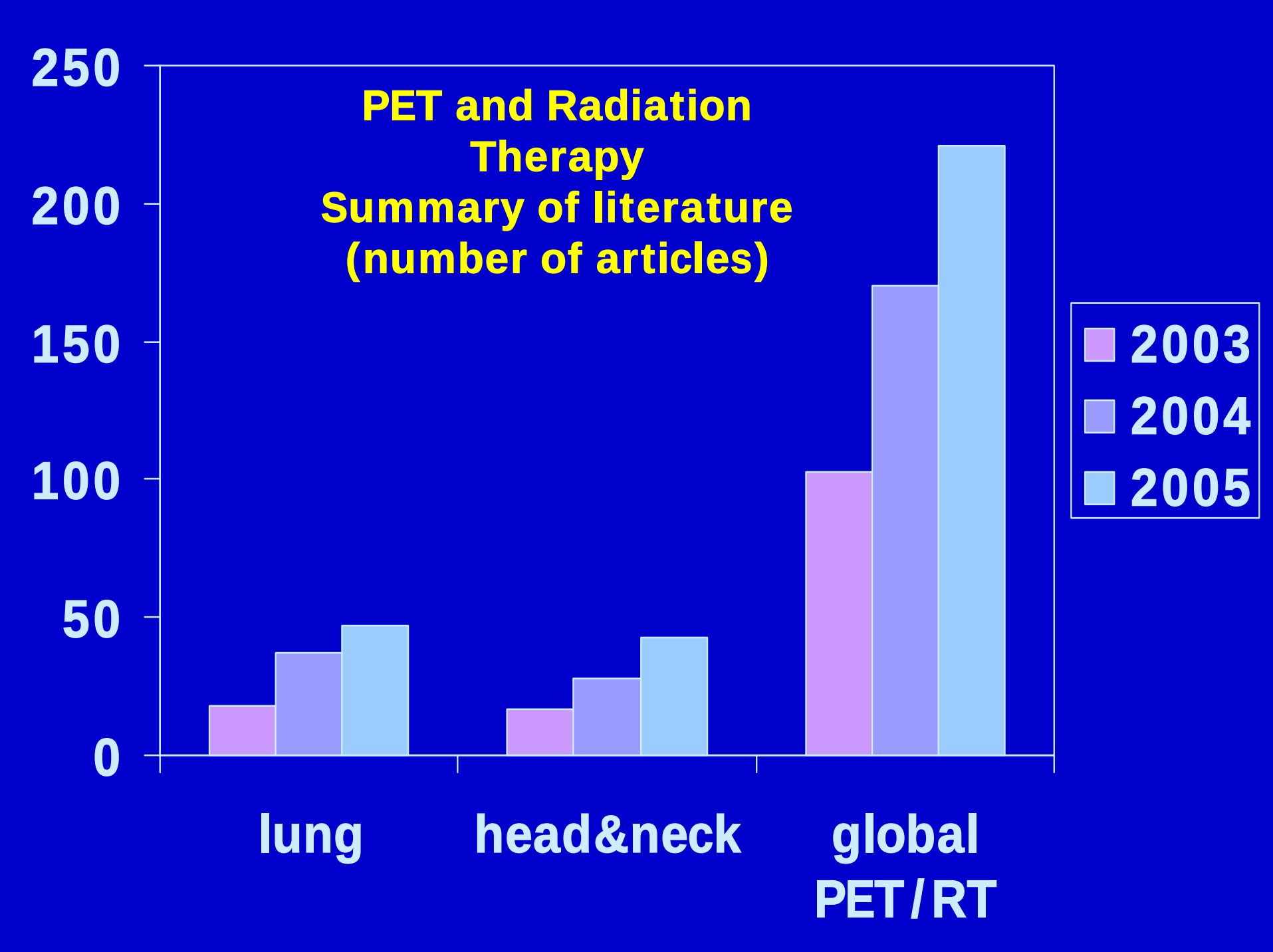
DOSE PAINTING

✓ **Production of controlled inhomogeneous dose distribution**

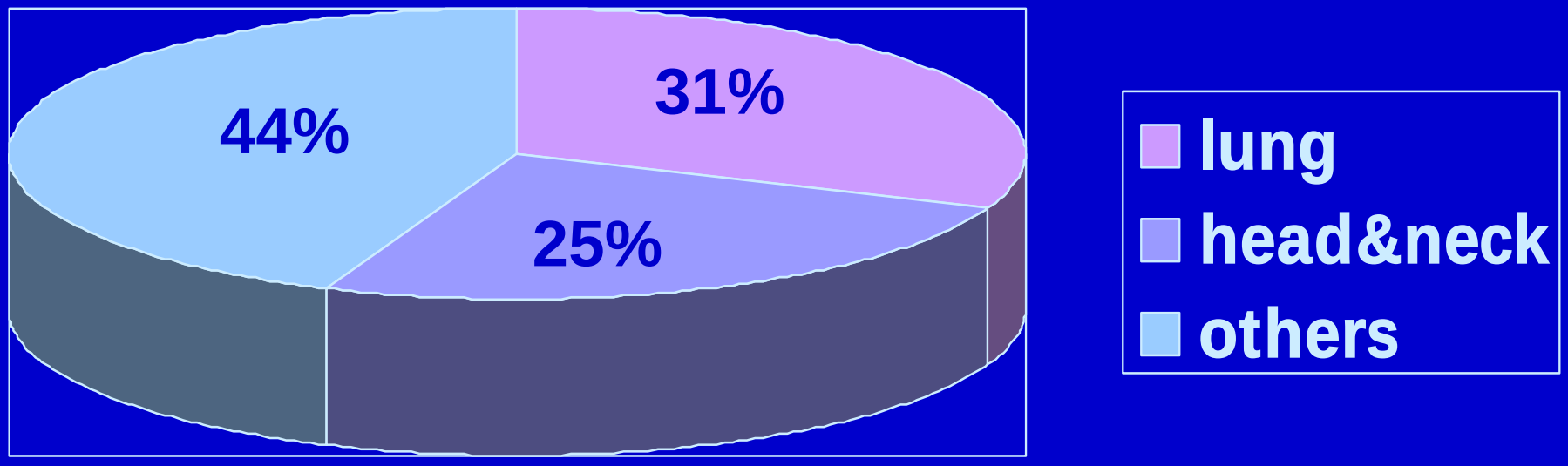
✓ **Simultaneous irradiation of multiple targets with different dose/fraction**




PET in
Radiation Therapy
diagnosis
staging
PET
Radiation
Treatment
Prescription
CT
target volume
and
organ localization
Treatment Response
Evaluation
Treatment Delivery
Treatment Planning
Biological
Target
Volume
(BTV)
The
radiation
oncologist's
objective


PET and Radiation Therapy
Summary of literature
(number of articles)
250
200
150
100
50
0
2003
2004
2005
lung
head&neck
global
PET/RT

PET for Radiation Therapy Planning Experience of Reggio Emilia



ARCISPEDALE
SANTA MARIA NUOVA
AZIENDA OSPEDALIERA
REGGIO EMILIA
Regione Emilia-Romagna

U.O. di Medicina Nucleare - Centro PET
U.O. di Radioterapia Oncologica
U.O. di Fisica Sanitaria

Washington
University in St.Louis
SCHOOL OF MEDICINE

BJC International Healthcare Service

International Meeting

Metabolic PET Imaging for a New Radiotherapy

Reggio Emilia, Italy
October 14-15 2003

Under the auspices of

AIMN - Associazione Italiana di Medicina Nucleare
AIFM - Associazione Italiana di Fisica in Medicina
AIRO - Associazione Italiana di Radioterapia Oncologica

Associazione Italiana di Medicina Nucleare
ed Imaging Molecolare

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Washington
University in St.Louis
SCHOOL OF MEDICINE
BJC International Healthcare Services

2nd International Meeting

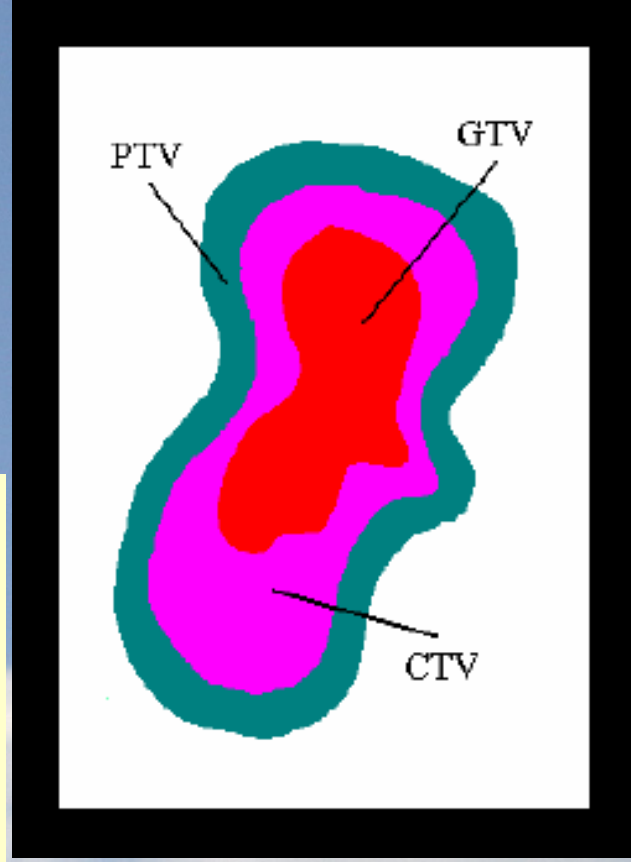
Metabolic PET imaging for a new Radiotherapy

October 4-5,2005

Hotel Mercure Astoria - V.le L. Nobili, 2 - Reggio Emilia - Italy

The radiotherapist's language

TARGET VOLUME



- **Gross Tumor Volume (GTV)**
  Volume of visible disease requiring **higher dose**

- **Clinical Target Volume (CTV)**
  Volume of suspected microscopic disease requiring **prophylactic lower dose**

- **Planning Target Volume (PTV)**
  CTV+margins to account for geometrical variation (e.g. set-up errors and internal motion)

- **Biological Target Volume (BTV)**
  Volume as defined by molecular imaging (e.g. FDG-PET)

PET and Radiotherapy

FDG-PET Problems

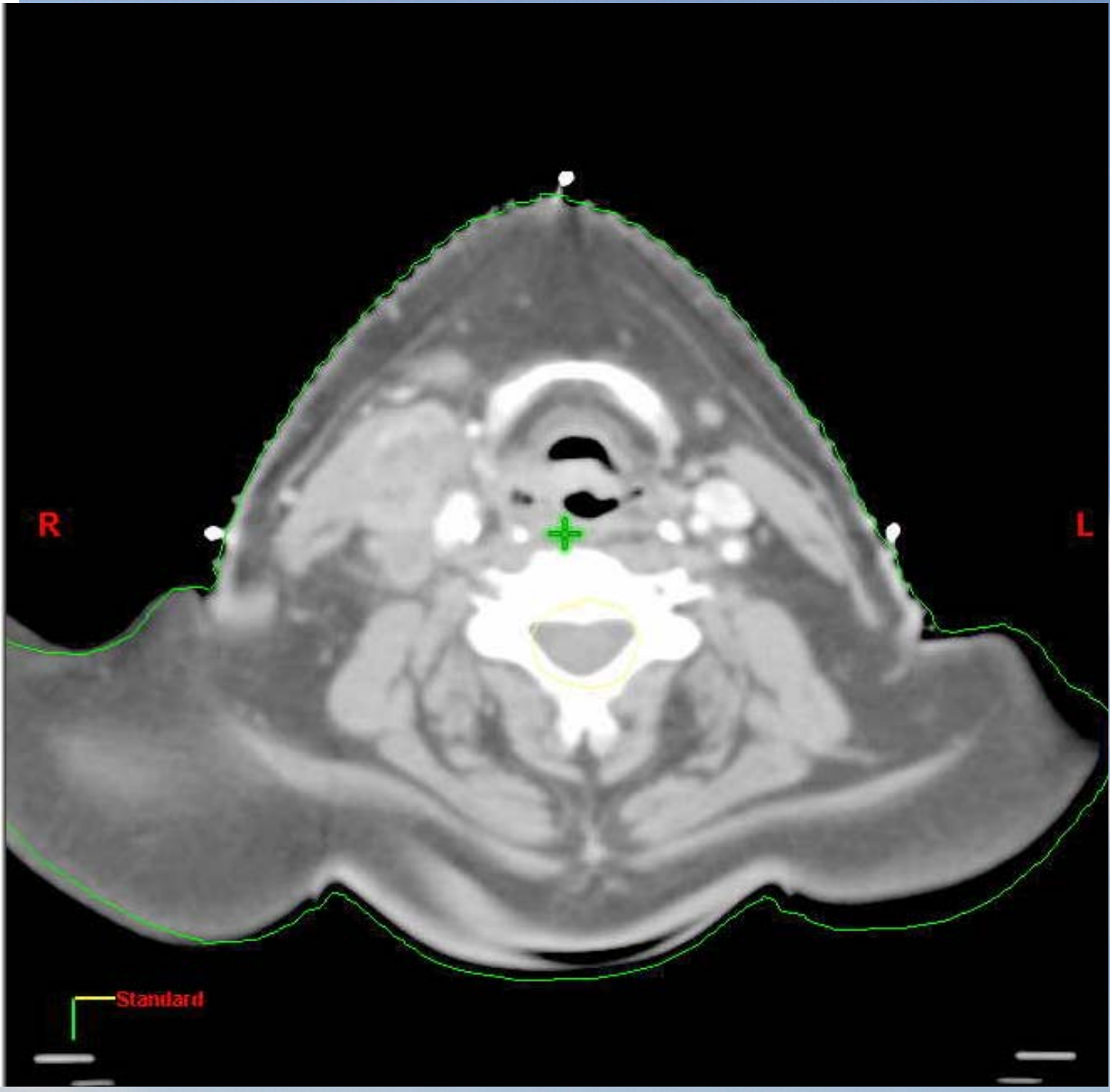
- **Lack of anatomic detail**
- **Several and variable foci of physiologic FDG uptake**
- **Lower spatial resolution than CT and MRI**

PET and Radiotherapy

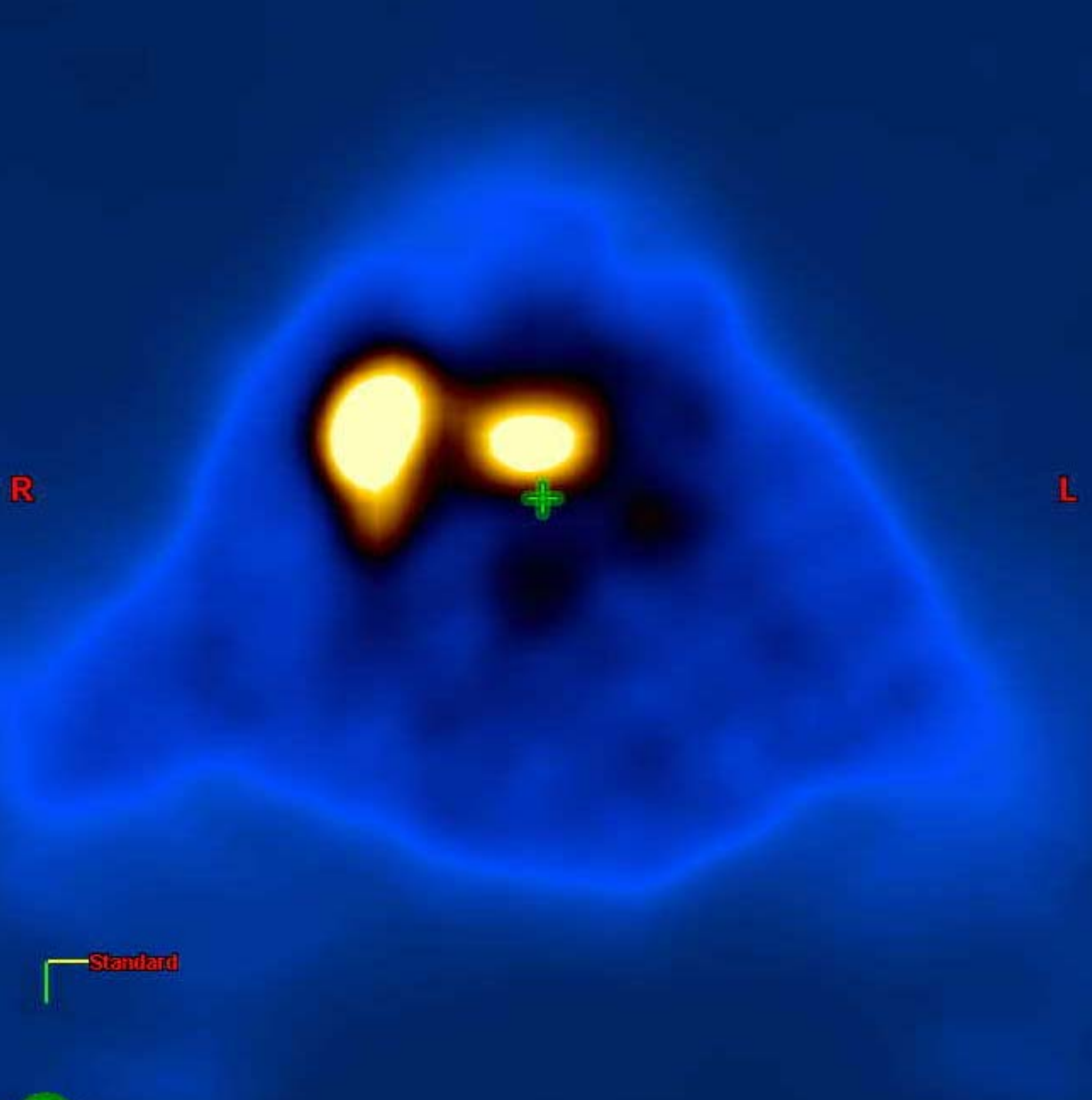
FDG-PET Problems

Solution

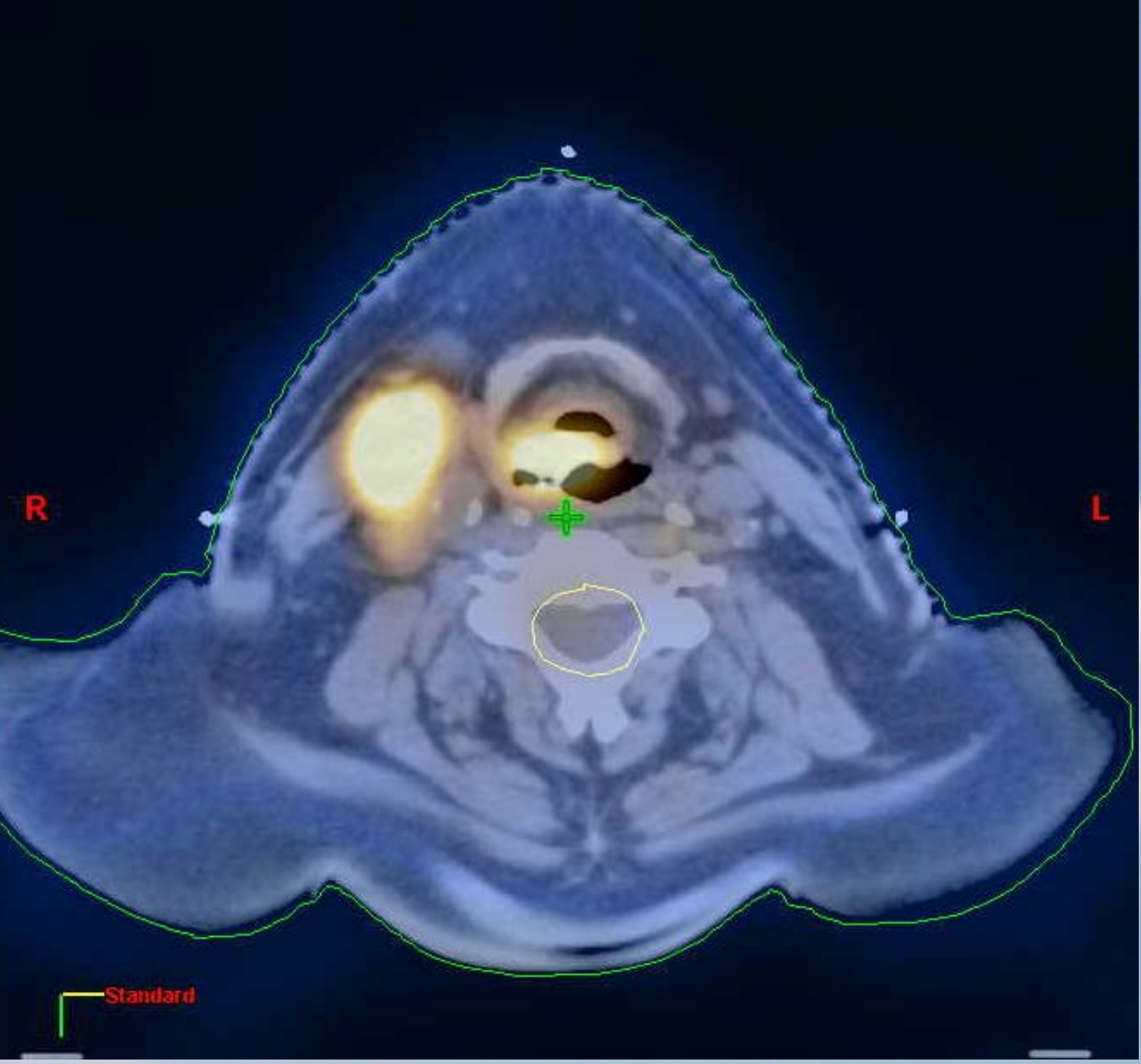
PET / CT ?



CT



PET

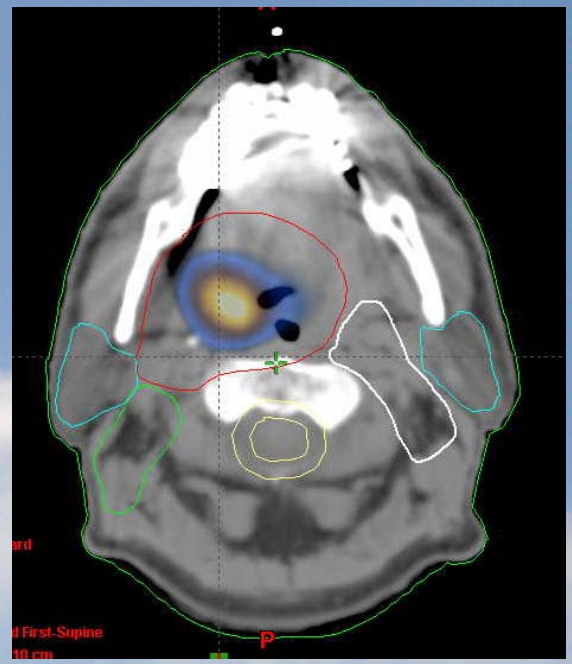


Images Fusion

CT + PET

Head & Neck Cancer
PET/CT Image Fusion

68 patients (155 lesions)



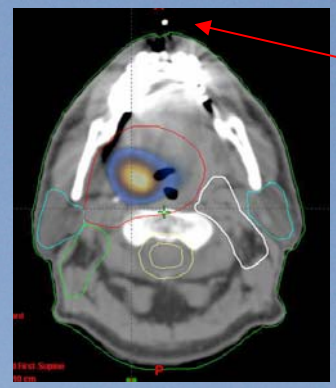
Accuracy

PET	PET/CT
90%	96%

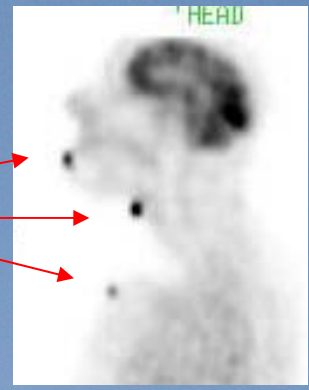
Schöder H et al Radiology, 2004

Patient positioning reproducibility: PET

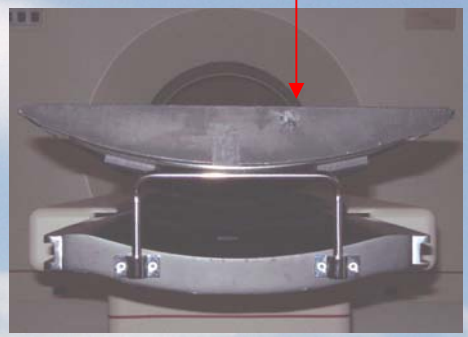
CT simulation and
PET imaging in the same day



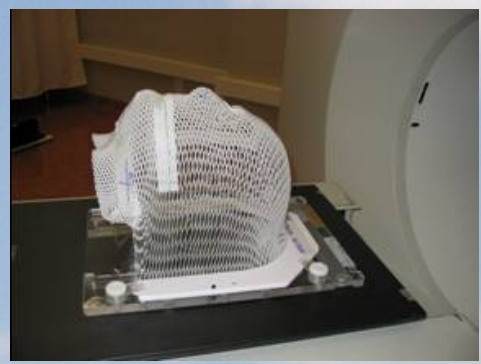
fiducial markers



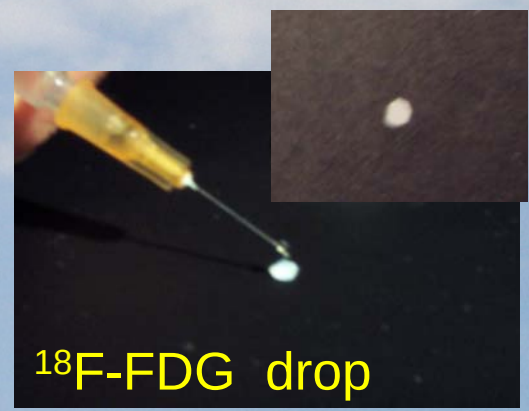
Flat bed



Immobilization mask



Blotting paper

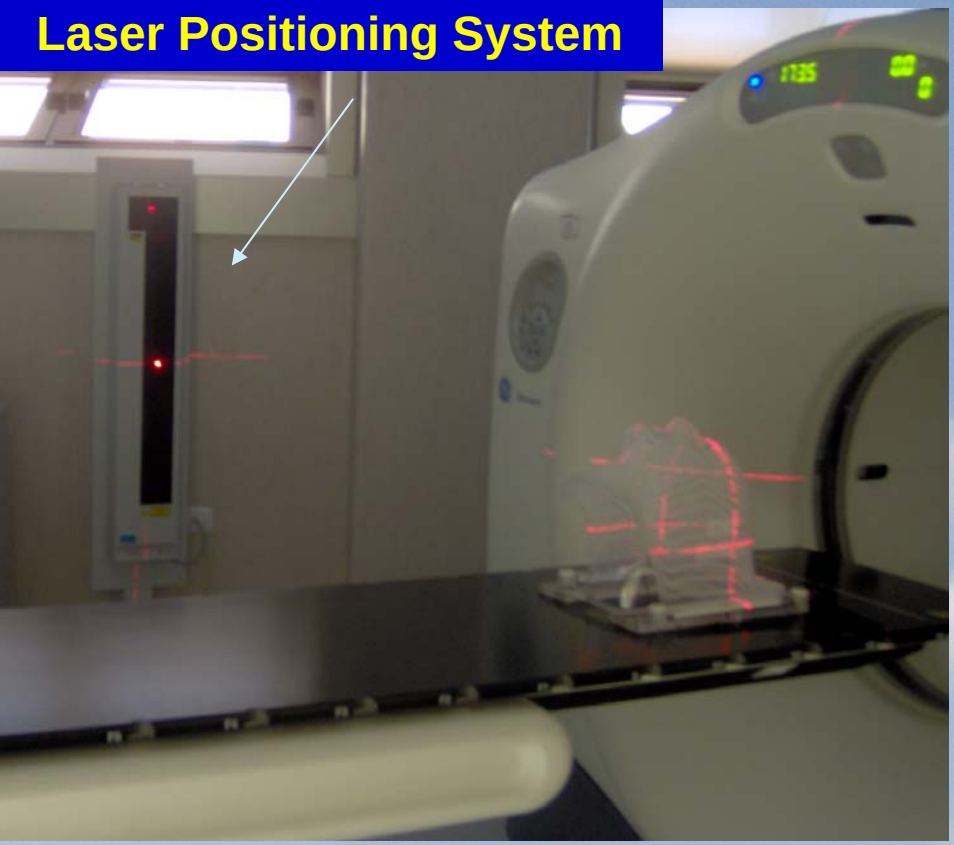


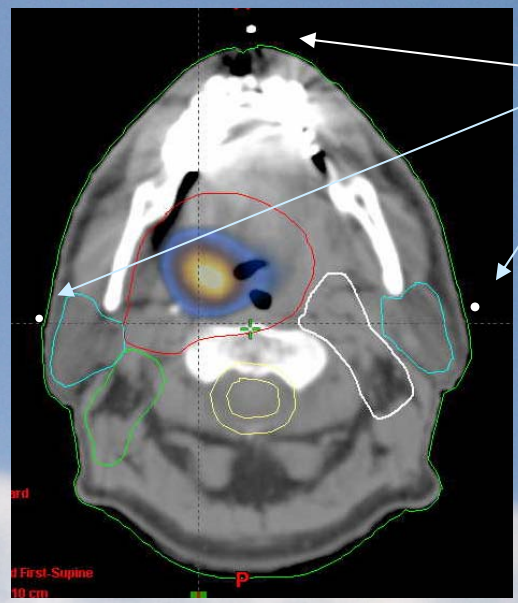
About 20-25%of sub-optimal repositions

Patient positioning reproducibility: PET/CT

CT simulation and
PET imaging in the same day

Laser Positioning System





Lead markers

Immediate verification of the correct reposition during the CT acquisition by the lead markers used for CT simulation

But PET/CT allows the best reposition with the possibility of CT simulation on PET/CT in the same session

PET in Radiation Oncology
Main Applications

- Lung Cancer (NSCLC)
- Head & Neck Cancer
- Cervical Cancer

Perspectives

- Pancreas Cancer
- Prostate Cancer
- ..... and many others

Lung Cancer

FDG-PET – Lung cancer (NSCLC)
Impact on the Radiation Therapy Planning

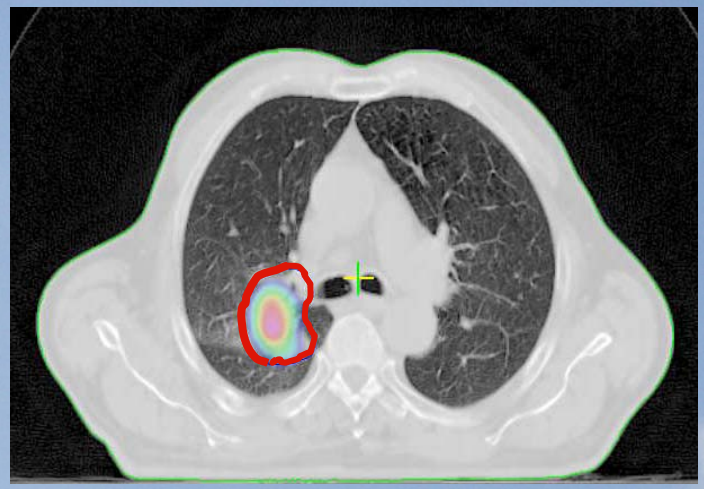
Review of literature: 1998-2005

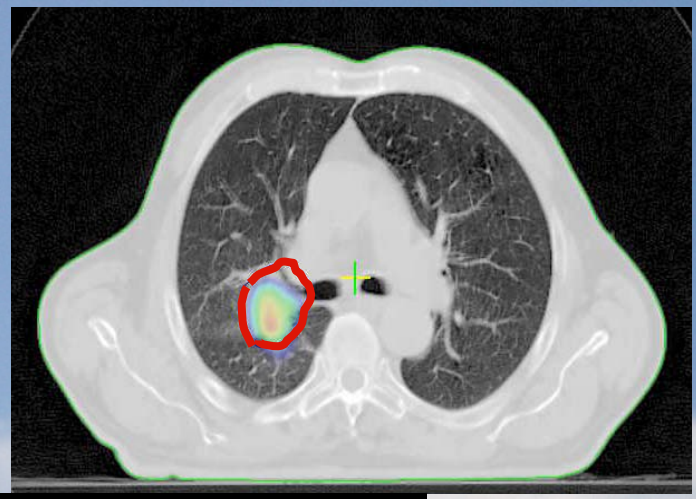
- 459 Patients
- Changes in the Radiation Treatment Volume

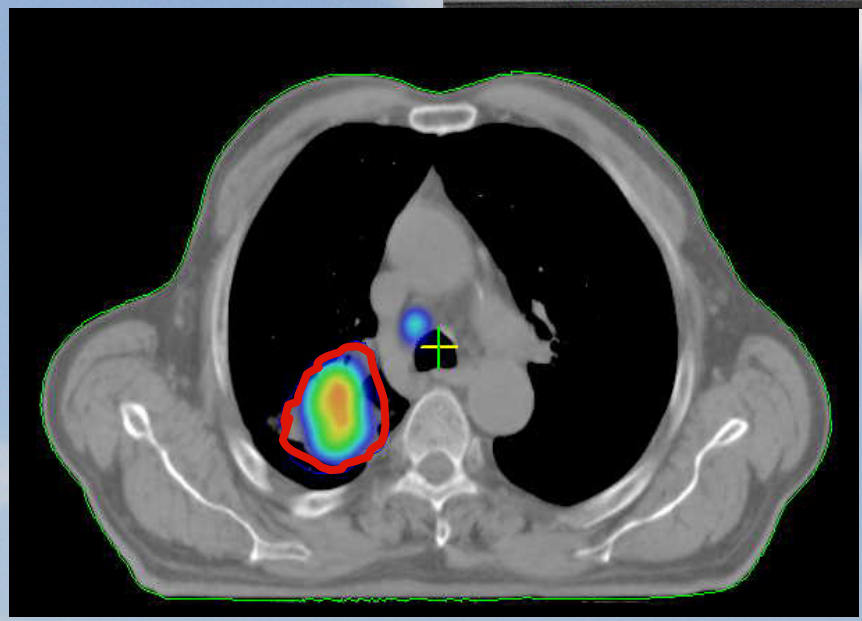
54% of cases

- 33% ⬆ GTV
- 21% ⬇ GTV

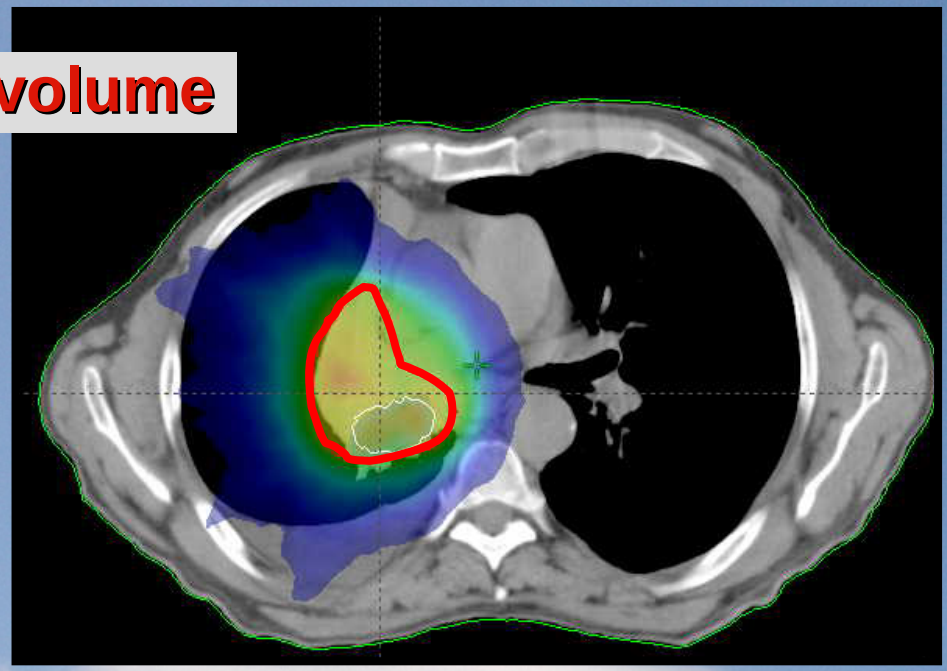
↑ GTV



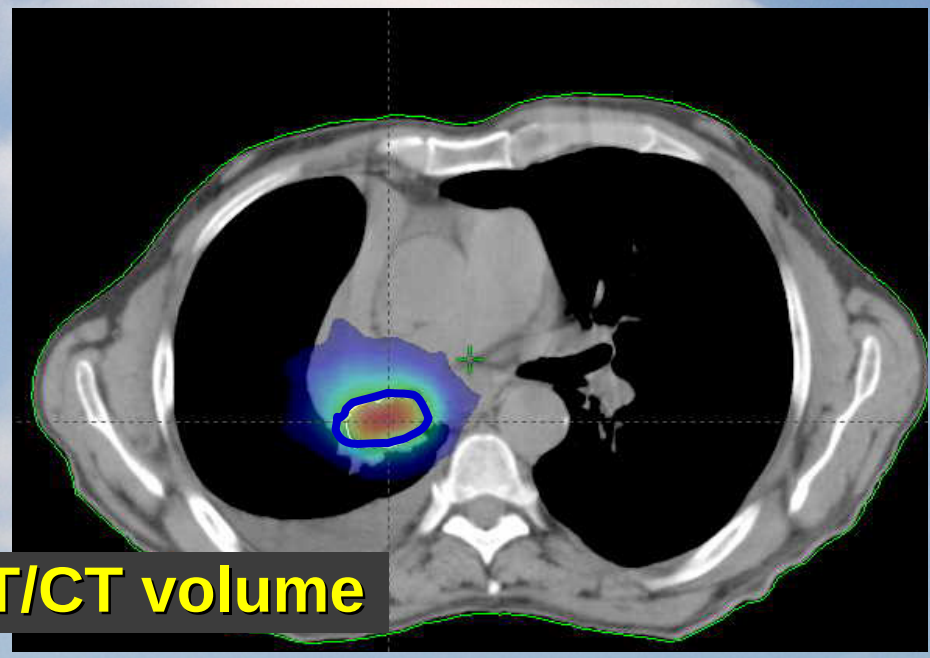




CT volume



GTV



PET/CT volume

Head & Neck Cancer

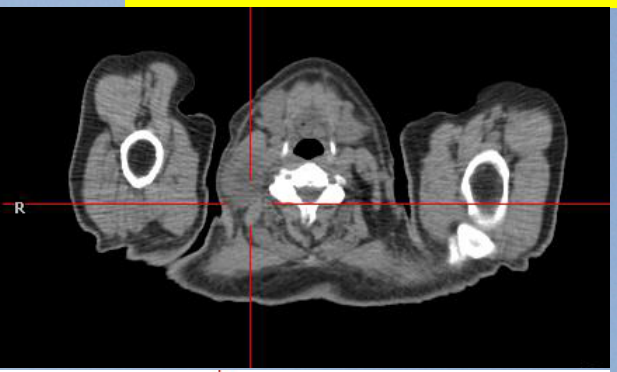
Head & Neck Cancer
PET and Radiotherapy ?

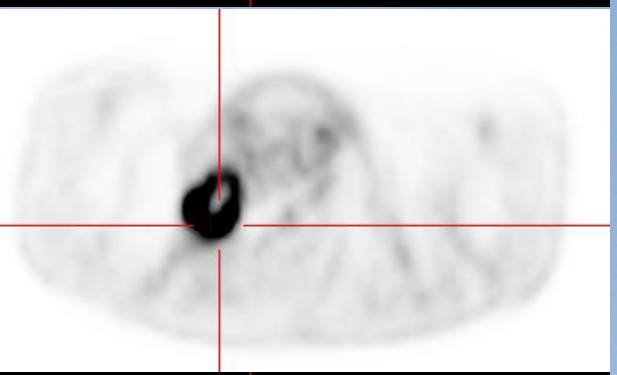
Why ?

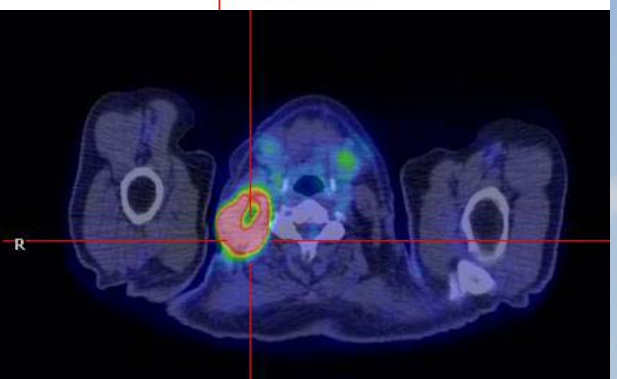
- 3 % of all cancers
- Radiation Therapy is part of the treatment in the majority of cases
- Local control is the big challenge
(recurrence >50 % of the treated pts)

Selection of the patients to treat

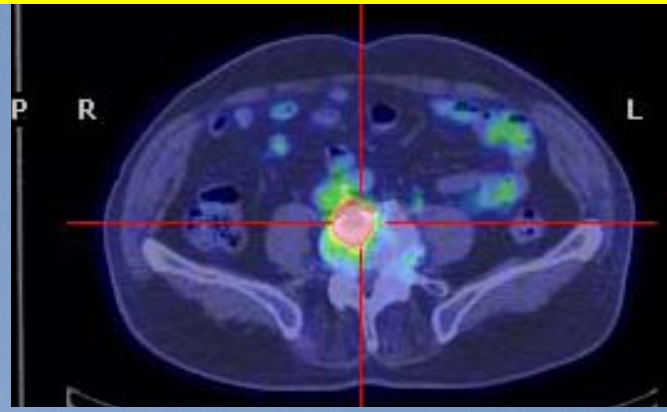
CT: Cancer of the base of the tongue with right latero-cervical metastasis

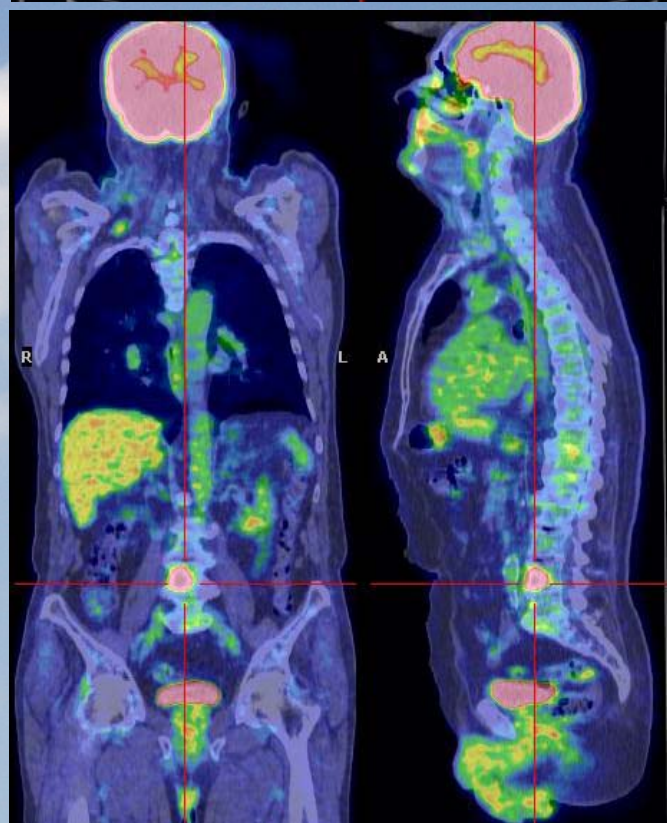






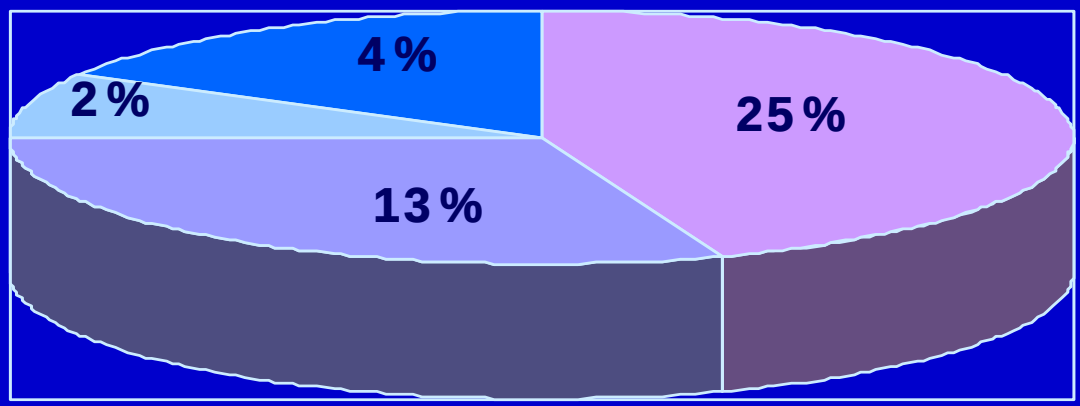
PET/CT for RT planning but… lumbar spine metastasis





FDG-PET for H&N-IMRT

Reggio Emilia Hospital (from 2/03 to 4/06)



52 patients

Changes in 23/52 (44%)

Versari-Iotti, 2006

Clinical outcome: preliminary results

patients with FU ≥ 6 months (29)

n	*status*
21	Disease free
1	Distant metastases
5	Local failure * (high dose volume)
1	Dead
1	Lost at FU

* 1 pt with distant metastases

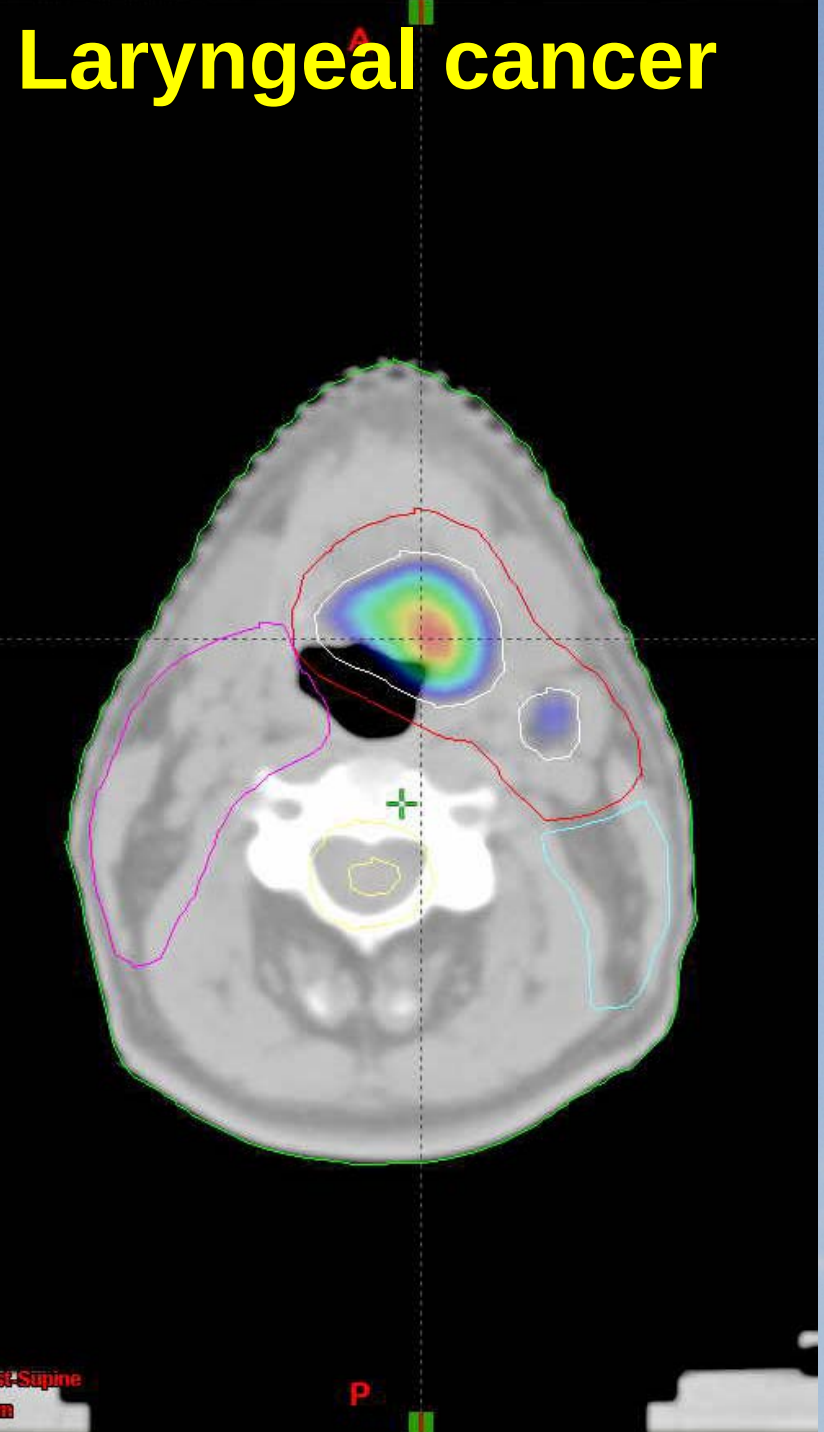
- No patient had failure in regions excluded from the high dose because of PET negativity.
- No patient had parotid glands toxicity more than grade 2 (ROTG scale).

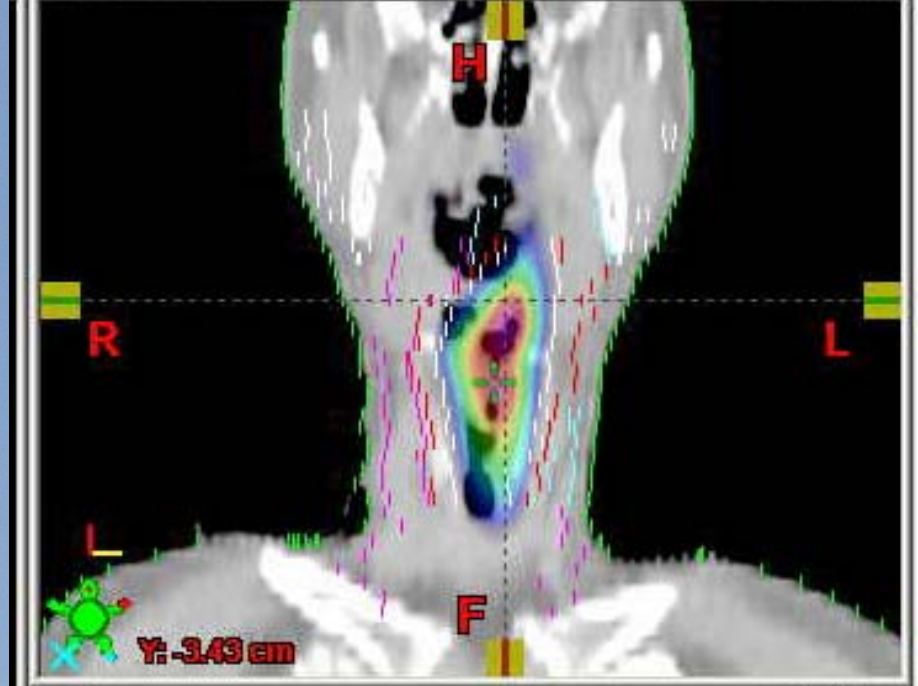
Head & Neck Cancer
Impact of PET/CT in radiotherapy treatment planning

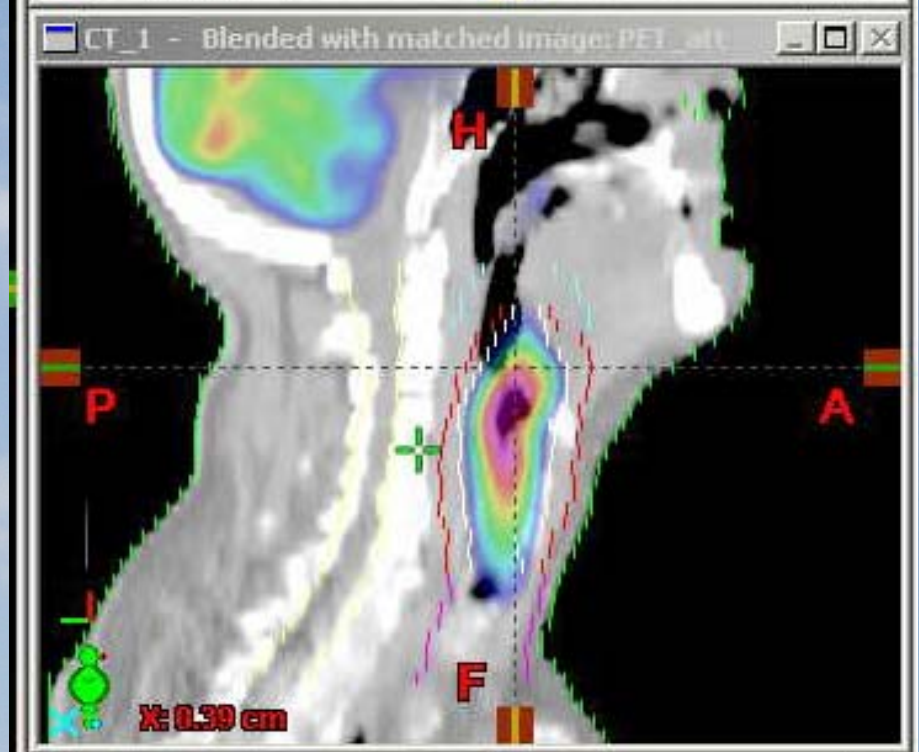
		Changes		
		Stage	Treatment Volume	Treatment Dose
Patients	36	13 (36%)	5 (14%)	4 (11%)

Koshy M et al Head Neck, 2005

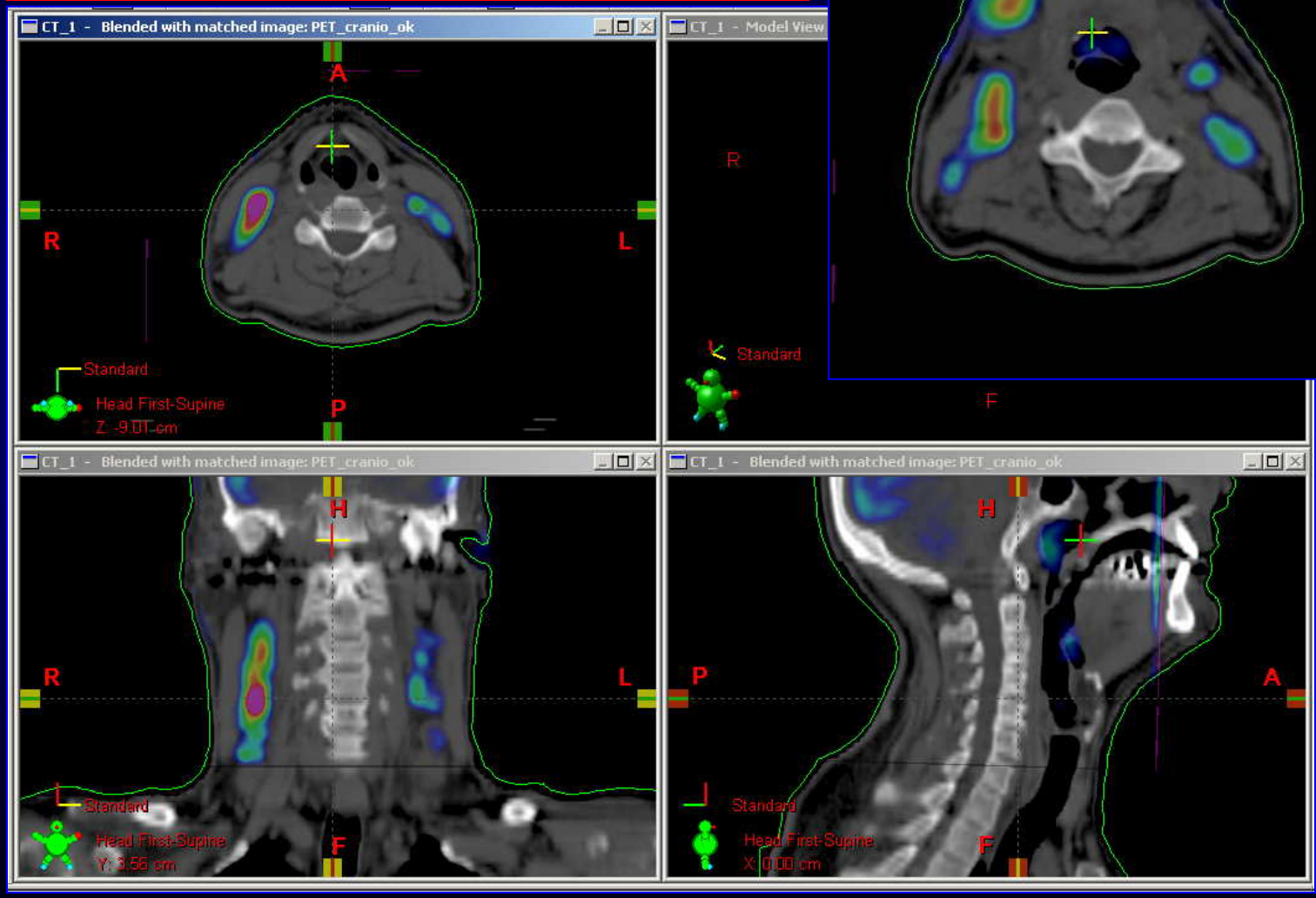
Laryngeal cancer



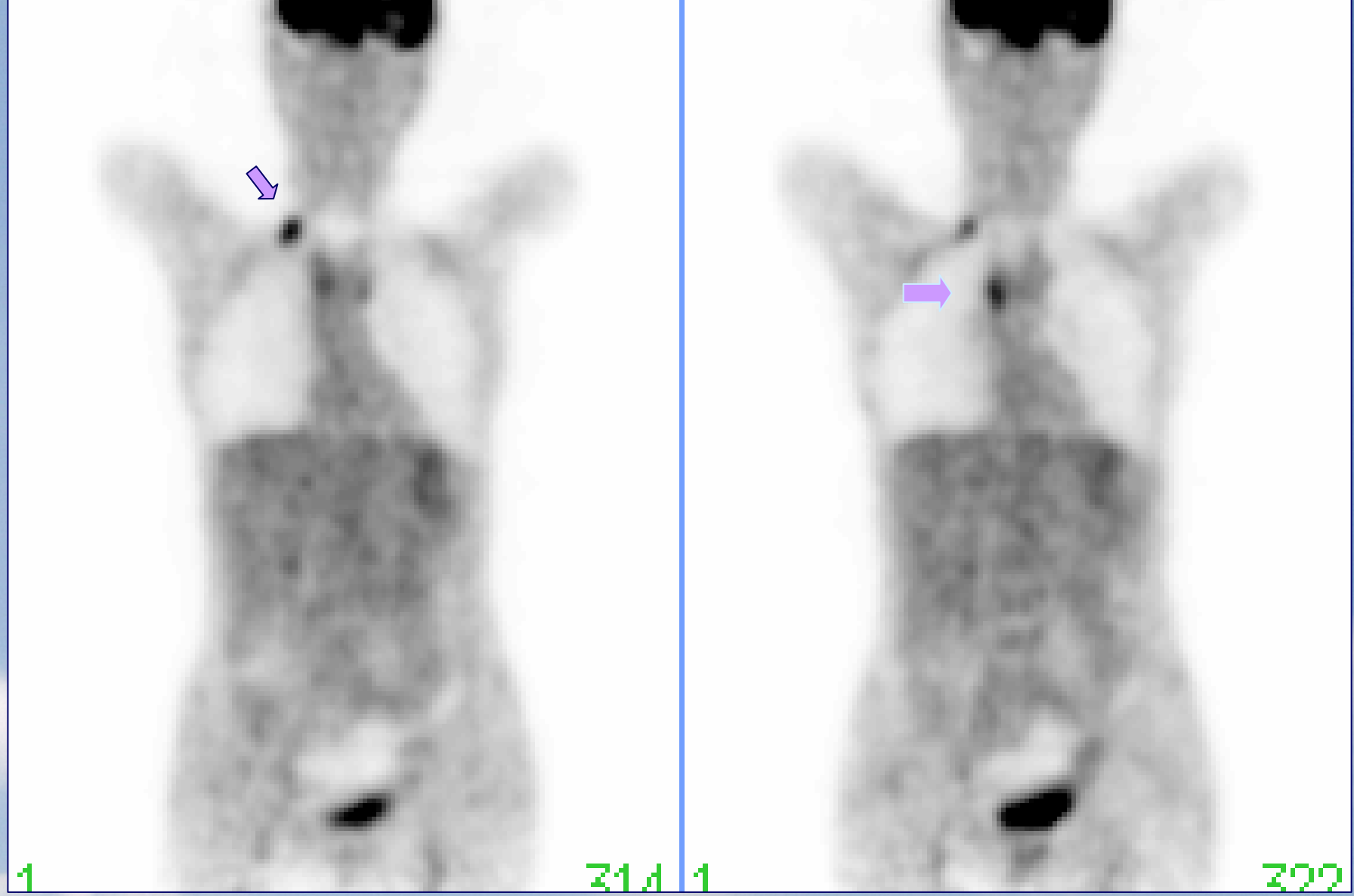




Nasopharyngs Carcinoma



Cervical Cancer



L.L., 65 anni - Ca Cervice uterina: follow up
Metastasi sopraclaveare dx e mediastinica

Cervical cancer

FDG-PET and Radiotherapy planning

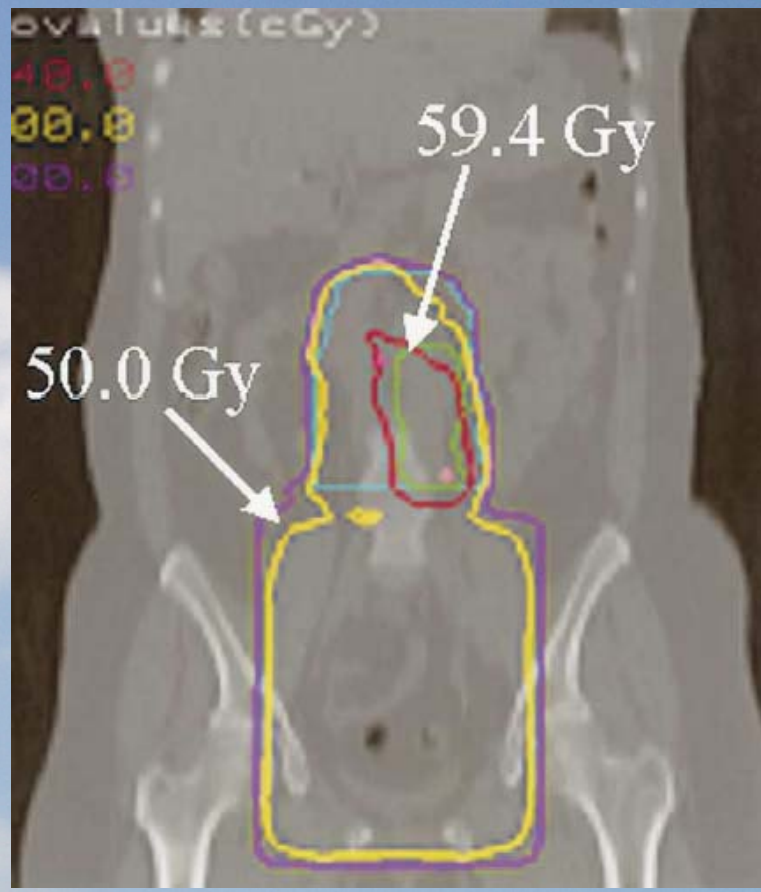
PET-guided IMRT

allows

a dose-escalation treatment

in patients with

positive paraaortic lymph nodes



Mutic S et al, Int J Radiation Oncology Biol Phys, 2003

Perspectives

Pancreatic cancer

Pancreatic Cancer
PET and Radiotherapy ?

Why ?

2005 - Cancer Mortality in USA: estimated values

Site	Deaths	5-year survival
Lung	163.510	15%
Colon	56.910	61%
Breast	40.870	86%
Prostate	30.350	96%
Pancreas	31.800	4%

Jemal et al Cancer J Clin 2005

… further progress in the treatment of pancreatic cancer can only be achieved by an interdisciplinary management of this disease

Heinrich S et al Schweiz Rundsch Med Prax. 2005

Pancreatic Carcinoma
Summary of the FDG-PET Literature
(1999-June 2000; 419 articles and abstracts)

Diagnosis

- Sensitivity: **94%** (n=293)
- Specificity: **90%** (n=281)
- Change in management: **50%** (n=26)

Staging

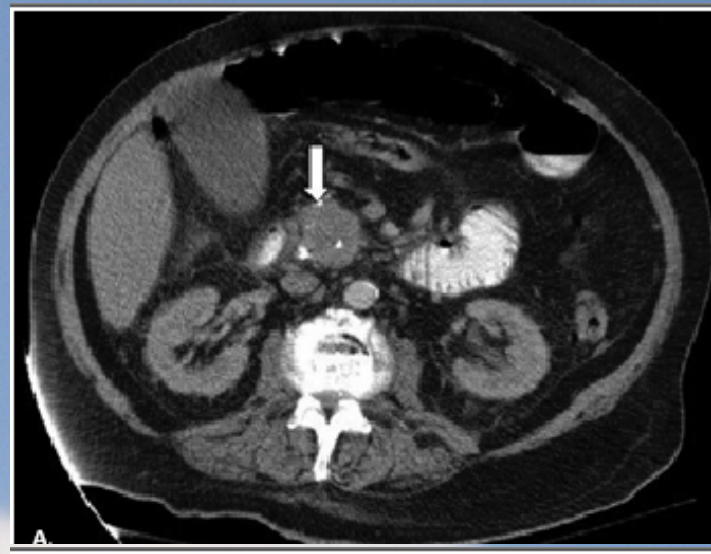
- Sensitivity: **70%** (n=182)
- Specificity: **93%** (n=182)
- Change in management: **53%** (n=33)

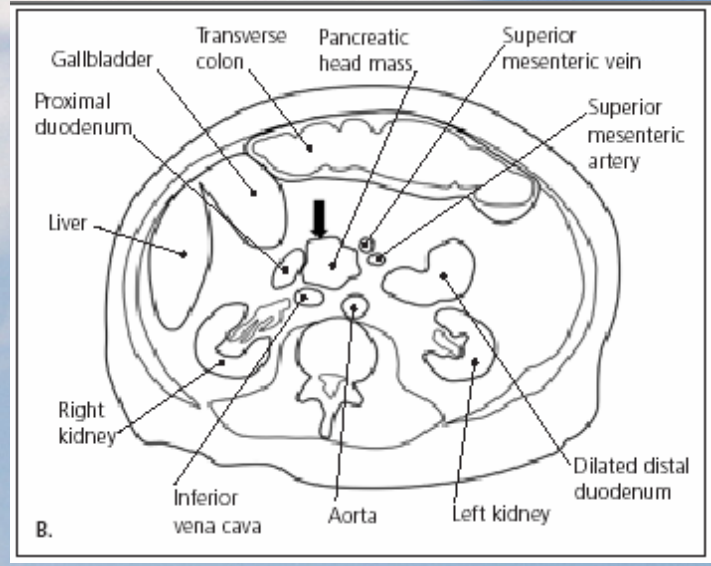
Monitoring therapy

- Change in management: **16%** (n=19)

Gambhir SS et al J Nucl Med 2001

Radiation Therapy in Pancreatic cancer



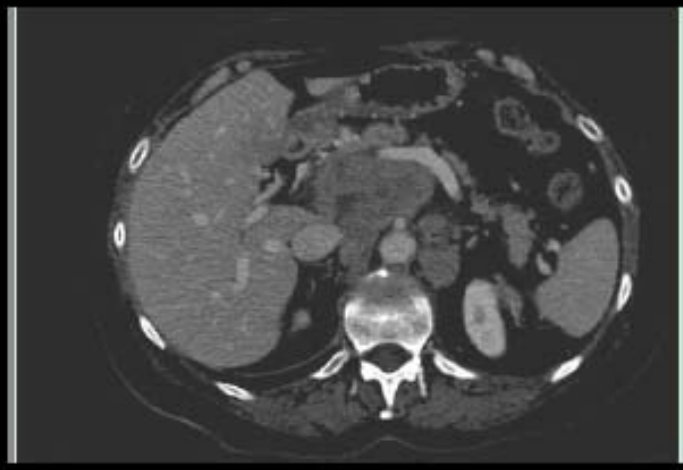


Problems

- Movement of organs and lesions
- Difficulty in target defining by CT
- Close organs at risk

R Freelove, AD Walling,
Am Fam Physicians 2006

Pancreas

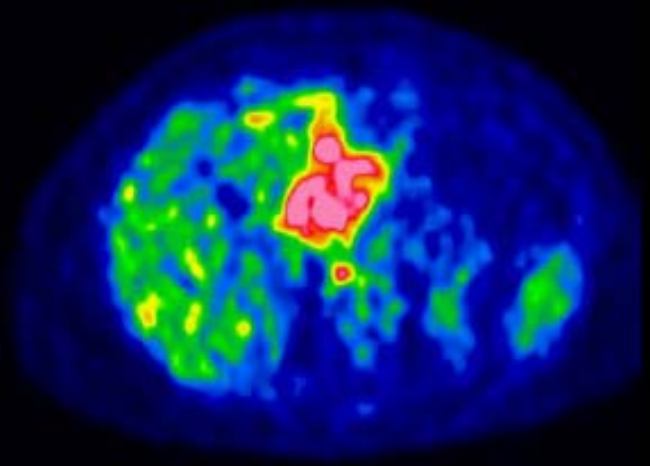


contrast enhanced CT

(arterial phase)

contrast enhanced CT

(venous phase)

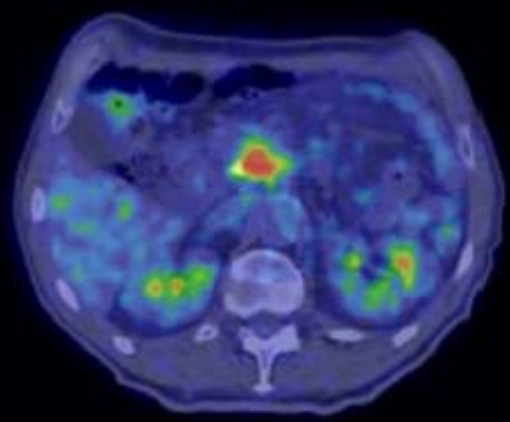


PET

CT (basal)

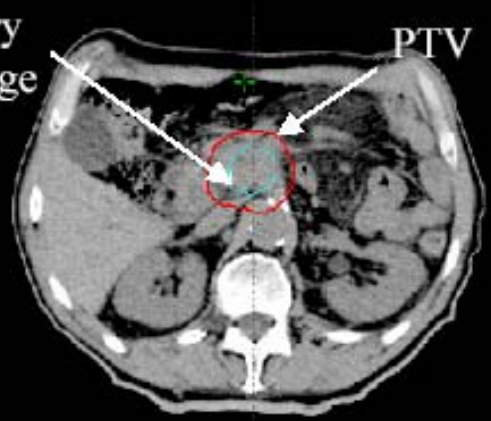
By courtesy
of N. Di Muzio
HSR - Milan

PANCREAS

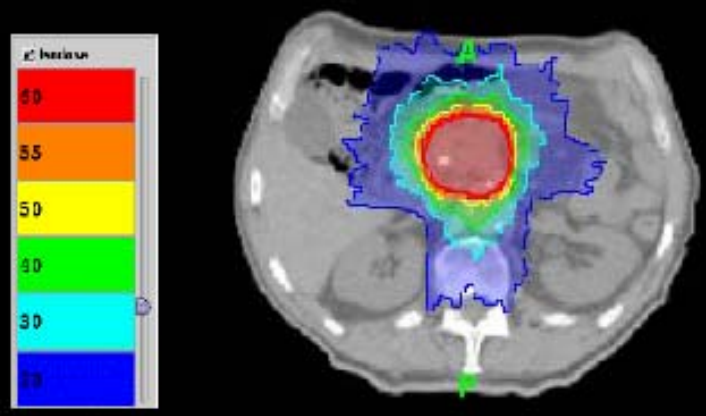


PET/CT

- pancreas adenocarcinoma T4N0
- 5 FU c.i.
- Radical Tomotherapy : 60 Gy , 2 Gy/f on PTV



PTVs and OARs



Tomotherapy plan

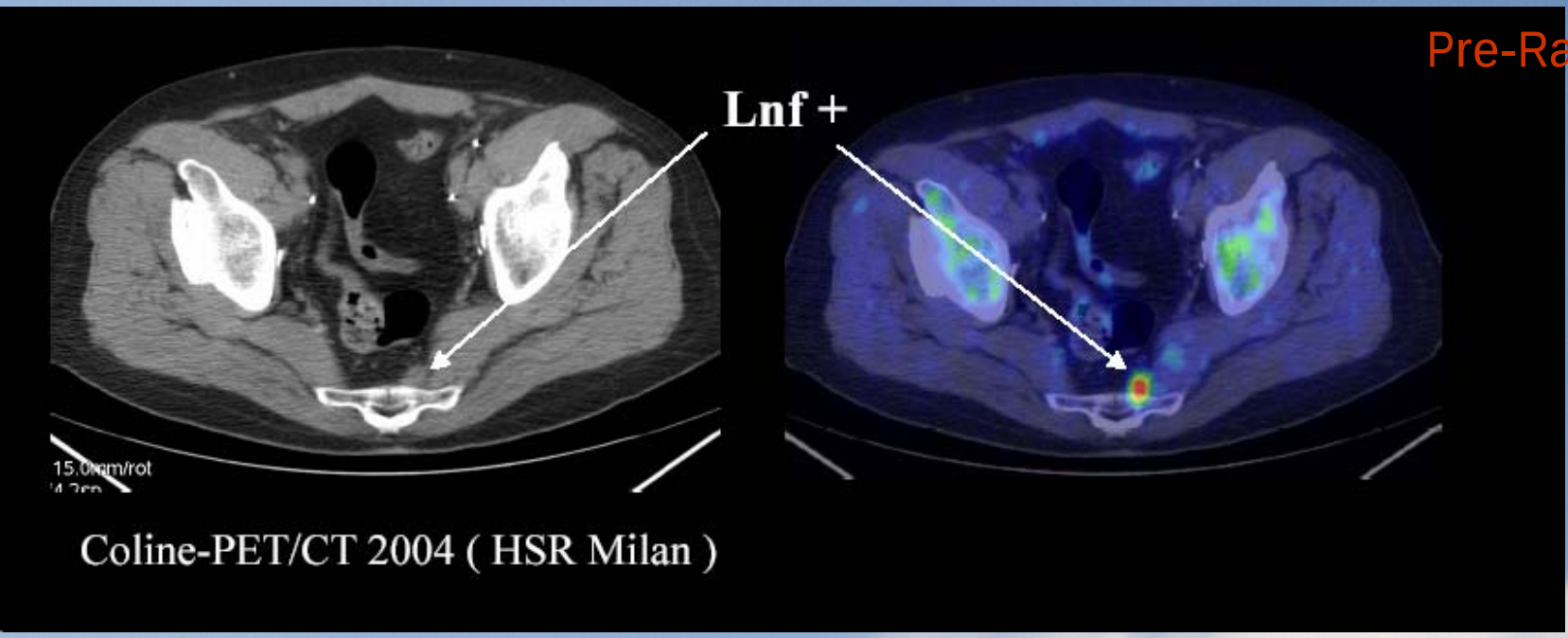
By courtesy of N. Di Muzio
HSR - Milan

Perspectives

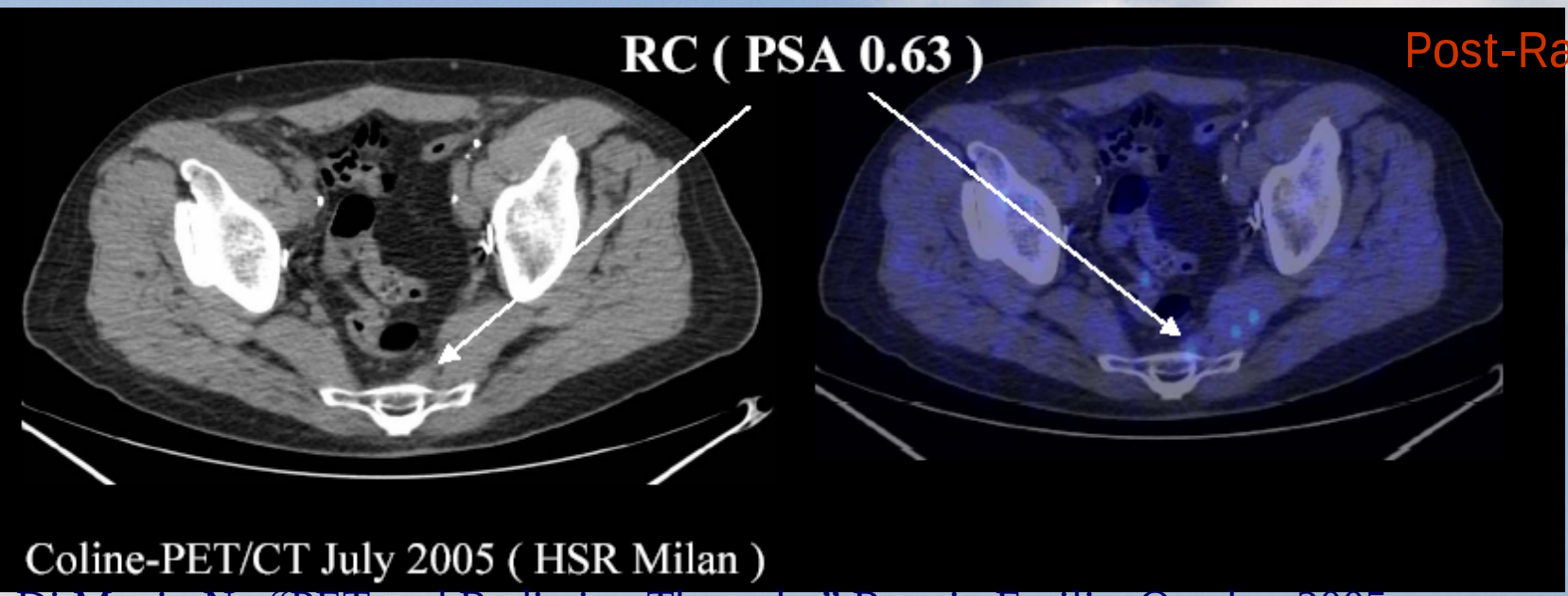
Prostate Carcinoma

Recurrence of prostate cancer

Pre-Radiotherapy



Post-Radiotherapy



Di Muzio N. "PET and Radiation Theraphy" Reggio Emilia October 2005

FDG-PET
Evaluation of the response to Radiation Therapy

Morphologic Response =

- Mass reduction

but

- Rarely the mass disappears
- Often residual tissue
  - scar
  - tumor

?

FDG-PET – Evaluation of the response to Radiotherapy

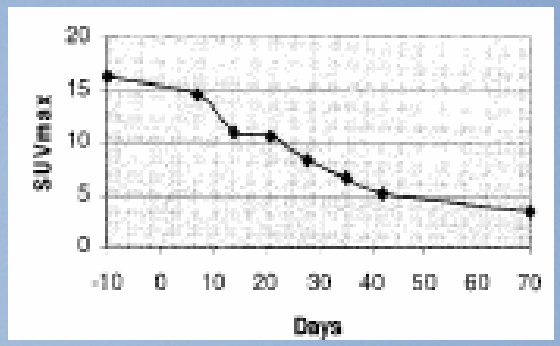
Authors	Neoplasm	Sens %	Spec %	PPV %	NPV %
Jerusalem G et al EJC - 2003	Lymphoma			100	83
Kelly RF et al – Chest - 2004	Lung			89	92
Conessa C et al Ann Otol Rhinol Laryngol, 2004	Head & Neck	100	81	46	100
Scarfone C et al – JNM - 2004	Head & Neck	84	95		

FDG-PET – Evaluation of the response to Radiotherapy

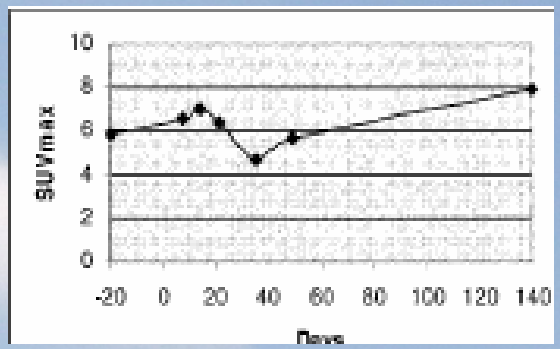
When?

- Most Authors agree that **3 months** after Radiotherapy is a correct timing

FDG-PET and NSCLC: Evaluation during Radiation Therapy



Disease remission



Disease progression

Interesting objectives

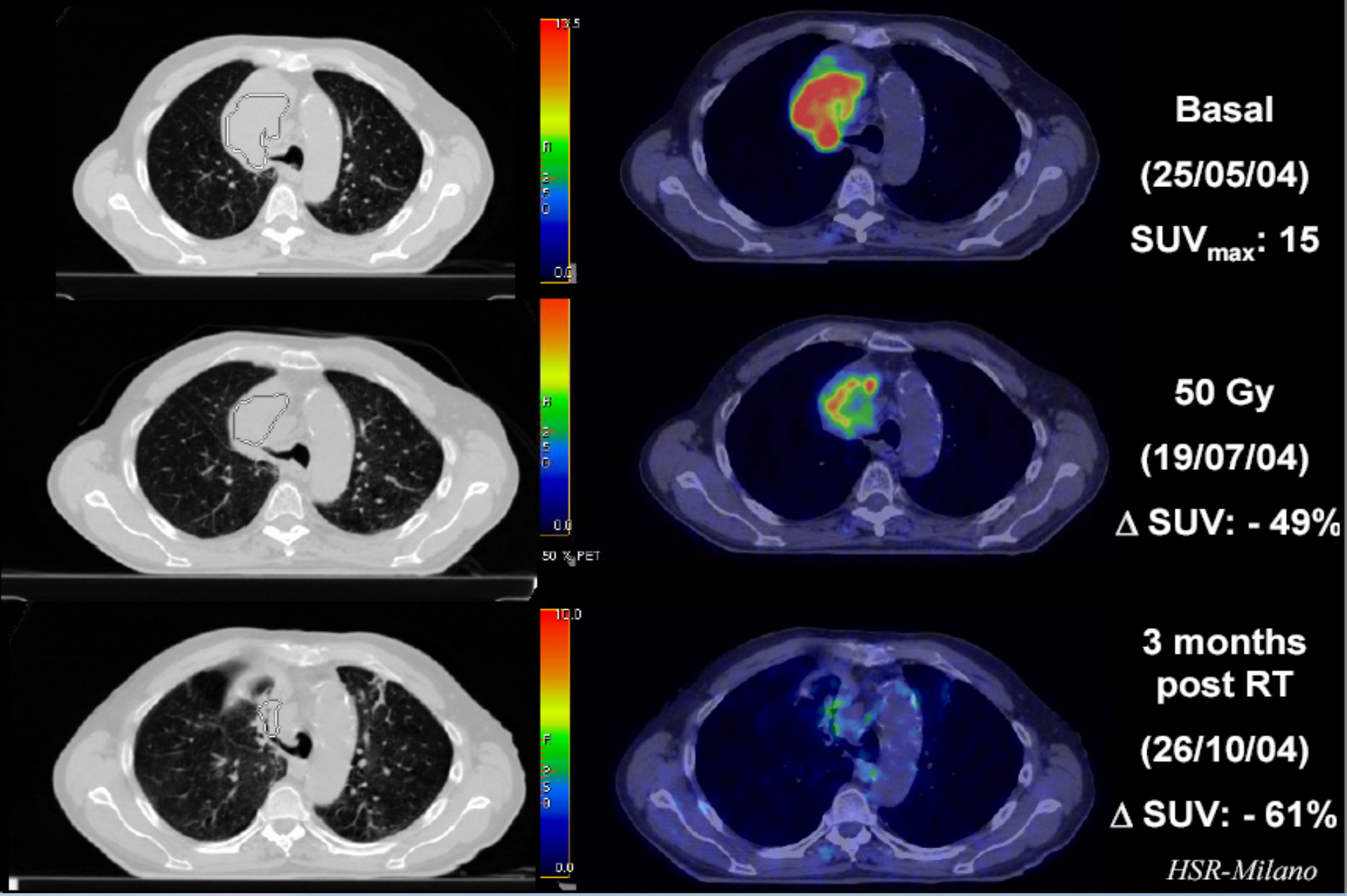
- **Define early response**
  (PET changes may predict RT response)

Erdi YE et al Eur J Nucl Med 2000

- **Adaptive Radiation Therapy**

(define new target volumes and doses according to the changes during treatment)

PET/CT evaluation during RT (lung cancer)



By courtesy of N. Di Muzio HSR - Milan

PET and Radiotherapy
Open Problems

- **Tumor Hypoxia**

- **Respiratory Movement**

Tumor Hypoxia

Tumor hypoxia is considered a predictor of poor prognosis

- Increased likelihood of local recurrence and metastases
- Resistance to radiation therapy

Tumor hypoxia
PET radiopharmaceuticals

- ^{18}F-fluoromisonidazole (^{18}F-MISO)
- ^{64}Cu-diacetyl-bis(N(4)-methylthiosemicarbazone (^{64}Cu-ATSM)
- ^{18}F-Fluoroazomycin Arabinoside (^{18}F-FAZA)

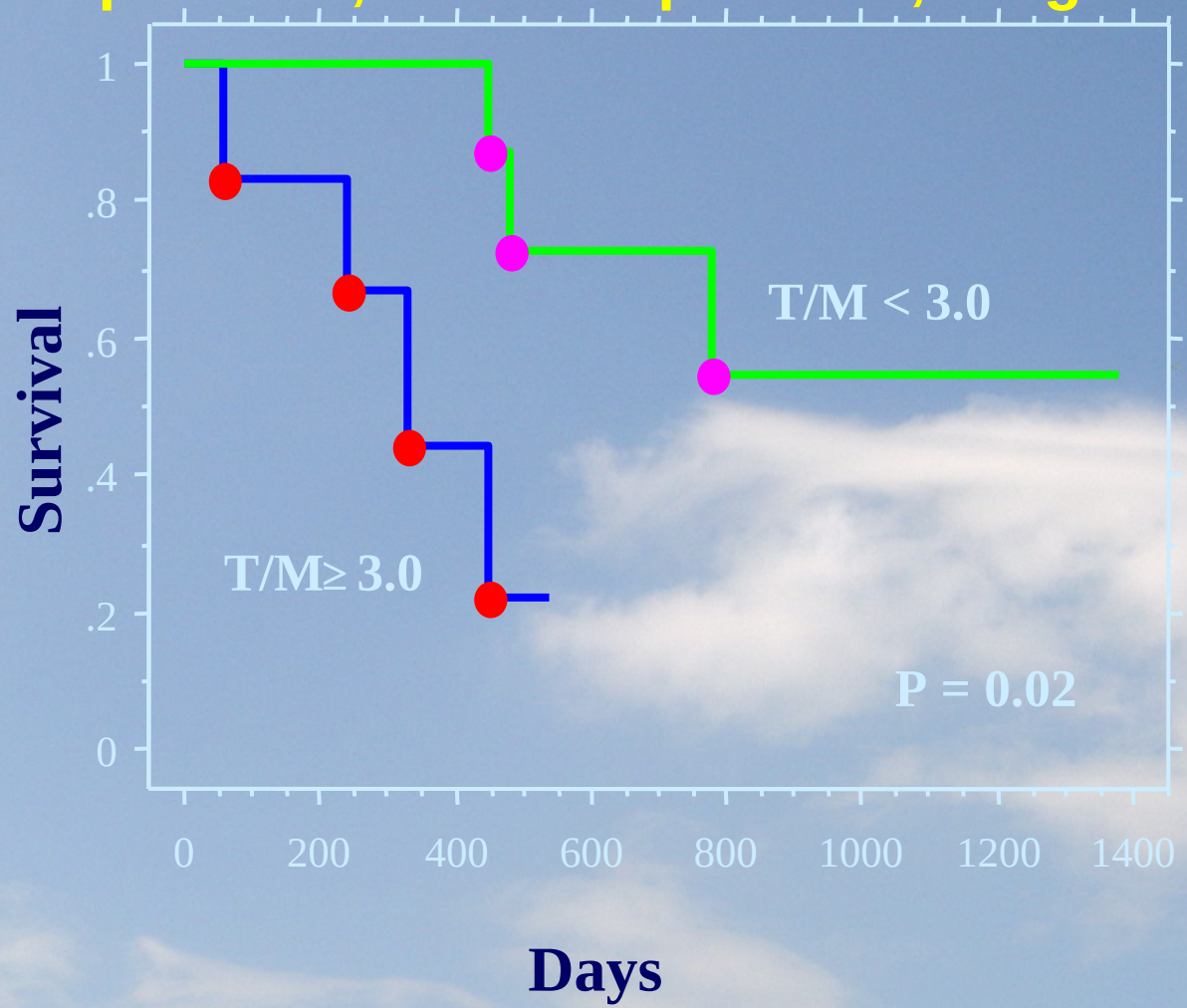
Mechanism of uptake

- ischemic tissue: bioreduction and deposition
- well-oxigenated tissue: rapid removal

NSCLC

Survival according to ^{60}Cu-ATSM uptake

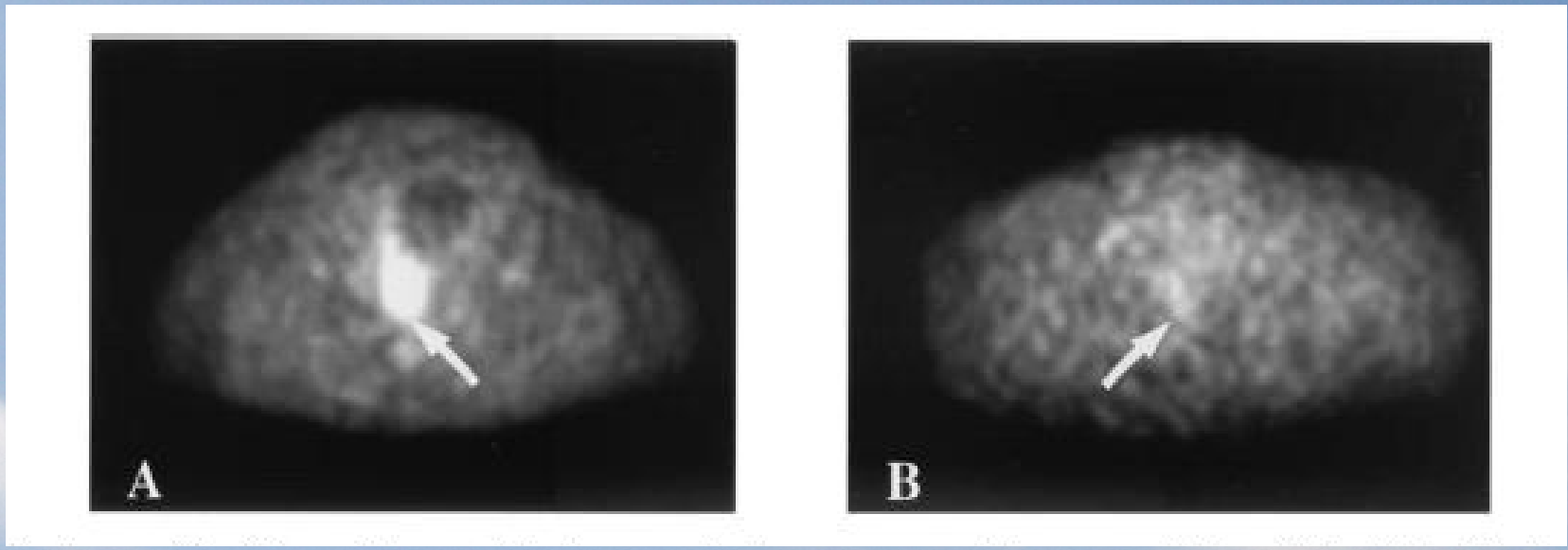
(8 Responders, 6 Nonresponders, Stage IA - IV)



Dehdashti et al., Eur J Nucl Med Mol Imag 2003; 30:844-850

PET and cervical cancer
Tumor Hypoxia

^{60}Cu-ATSM-PET

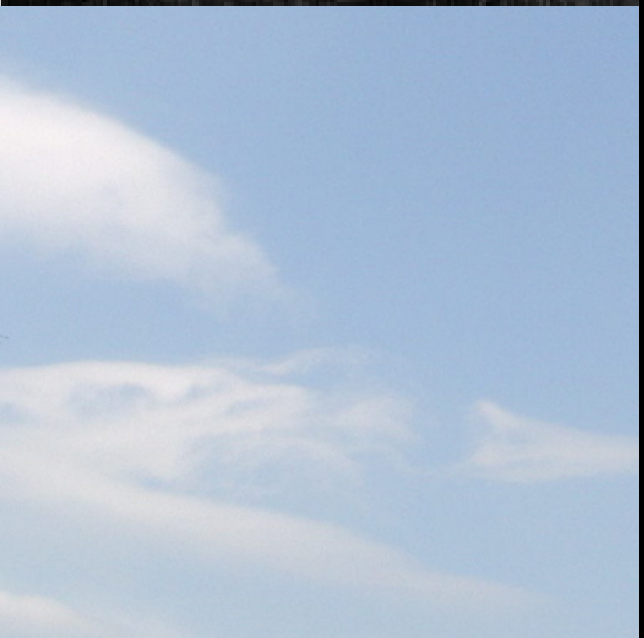


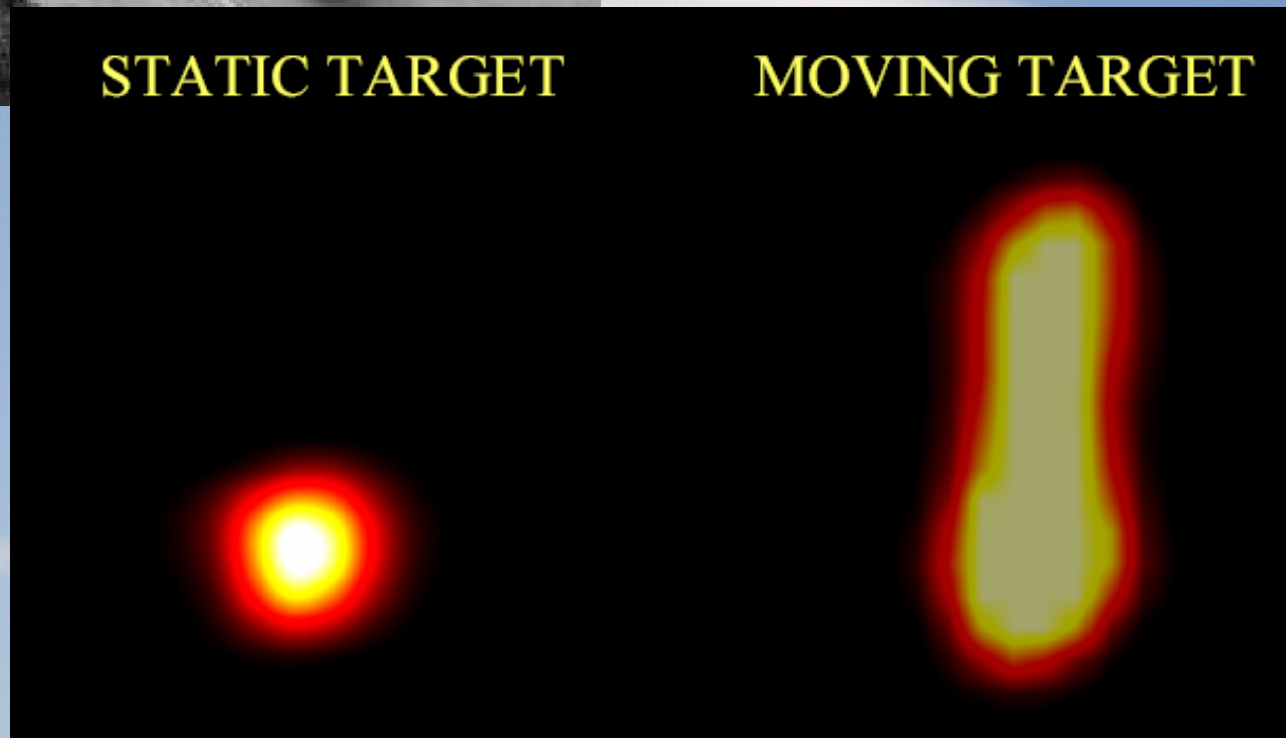
High uptake
Recurrence at 6 months

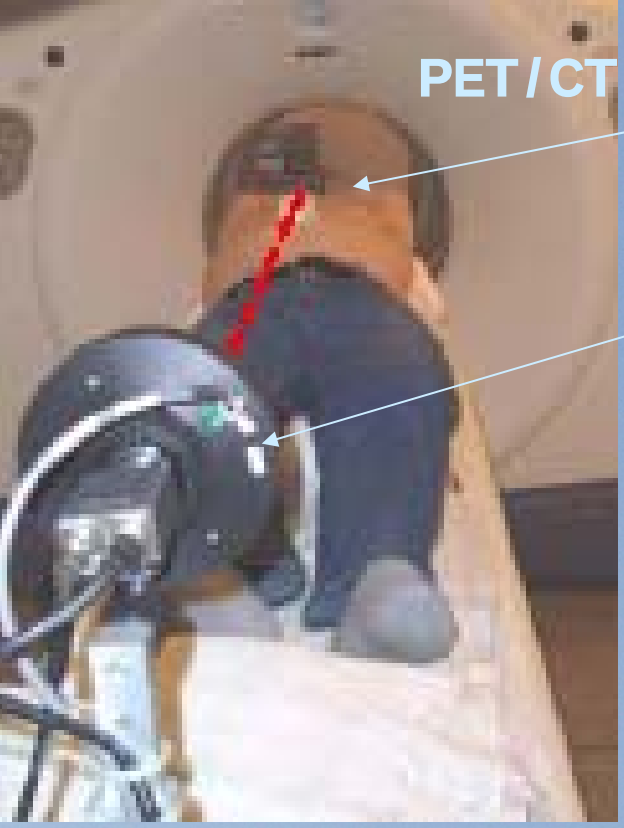
Low uptake
Free of disease at 23 months

Dehdashti F et al., Int J Radiation Oncology Biol Phys, 2003

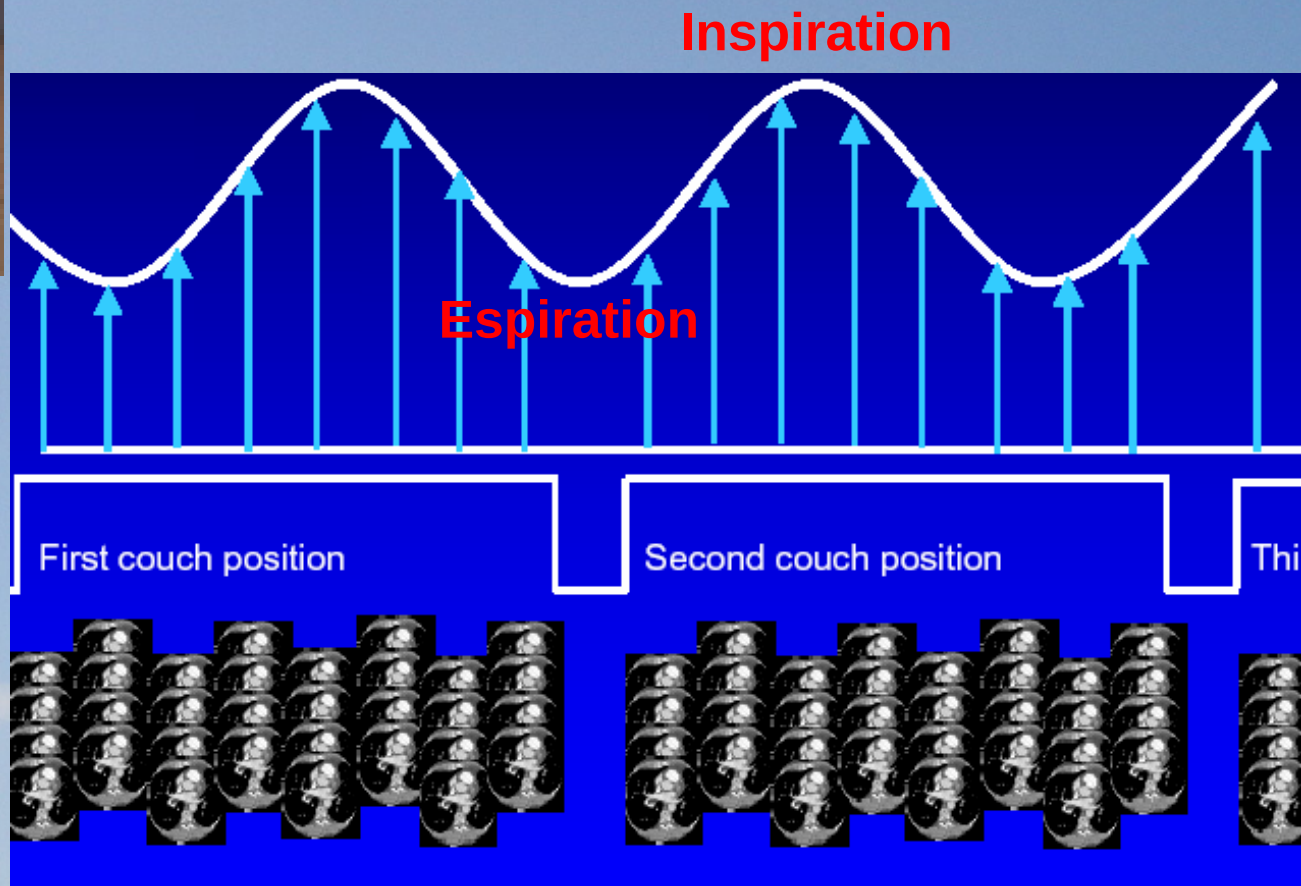
Respiratory Movement





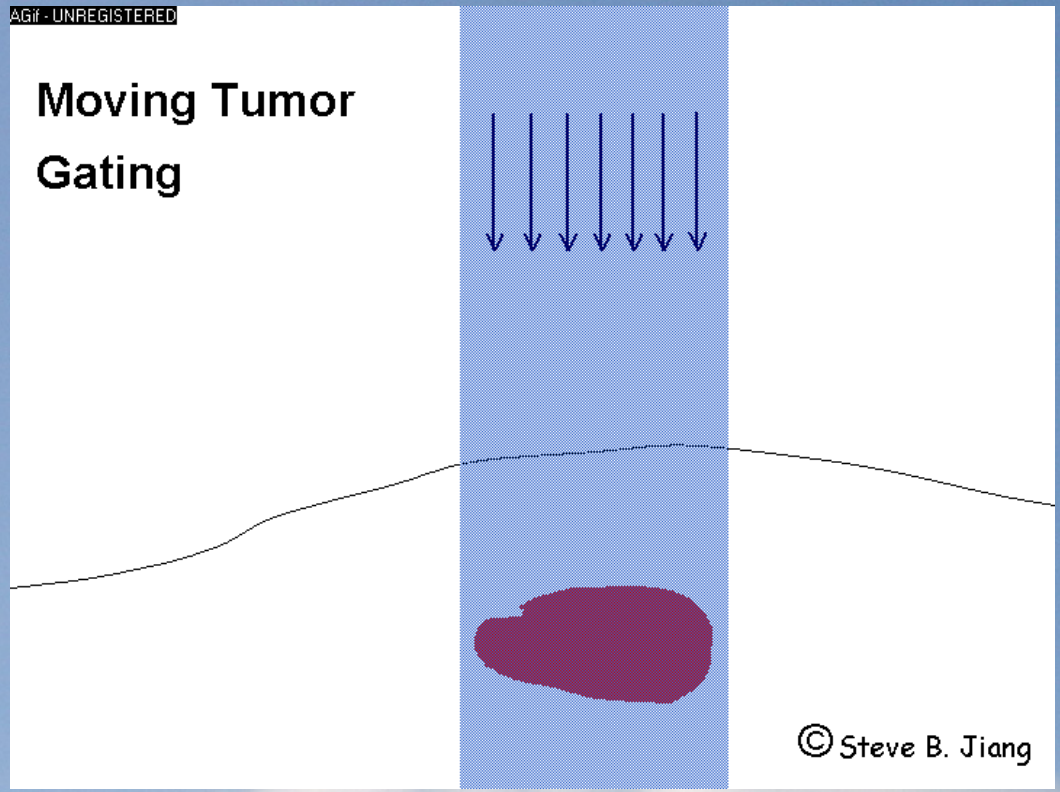


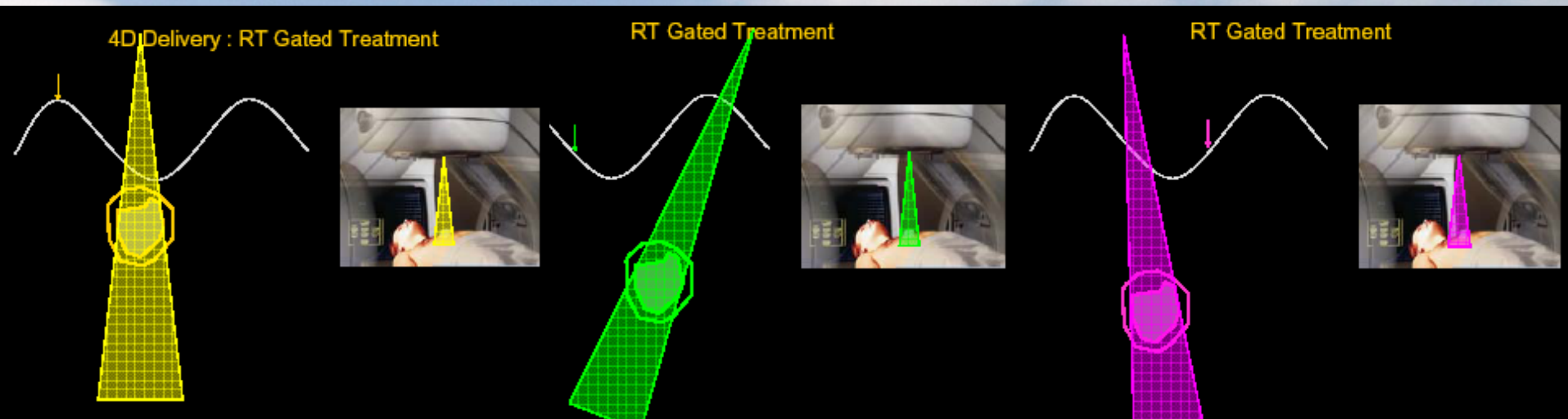
4D-PET / CT Respiratory Gating



Pan et al Med Phys 2004

Radiotherapy Gated Treatment





FDG-PET
Impact on Radiation Treatment Planning
Summary

Review of literature: 1998-2005

- 628 Patients (lung, head&neck, limphoma, haesophagus)

- Changes in Radiation Treatment Volume

59% of cases

- 31% ↑ GTV
- 28% ↓ GTV

FDG-PET/CT: Lung cancer
Impact on Radiation Treatment Planning

19 Patients

- Changes in Radiation Treatment Volume
  52% of cases
- Interobserver GTV variability

  Concordance (difference from mean of GTVs<10%)

  - **CT: 37%**
  - **PET/CT: 84%**

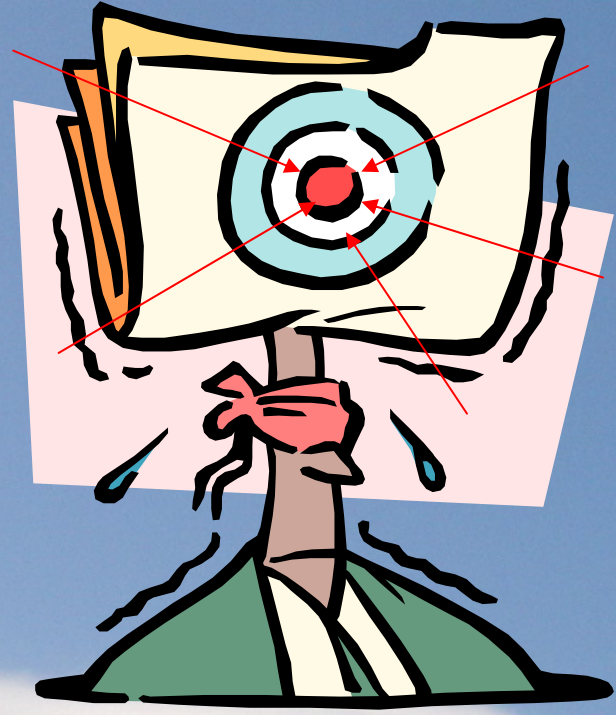
Ashamalla H et al Int J Radiat Oncol Biol Phys 2005

Don’t forget!!!!!!

Interdisciplinary Discussion

An interdisciplinary discussion of the cases, particularly in head and neck cancer, is indispensable

PET / CT and Radiation Therapy Conclusions



PET/CT imaging helps

- **To select more correctly the patients** for radiation therapy
- **To identify the right target**, avoiding irradiation of non neoplastic areas and, at the same time, preventing the omission of active tumor tissue from the radiation field
- **To evolve towards a biological dose conformation**
  (BTV –Biological Target Volume)

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SCHOOL OF MEDICINE

BJC International Healthcare Service

3rd

AIMN - Associazione Italiana di Medicina Nucleare
AIFM - Associazione Italiana di Fisica in Medicina
AIRO - Associazione Italiana di Radioterapia Oncologica

Thank you for your attention and… see you at