Use of imaging systems for patient modeling - PET and SPECT

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Nuclear Medicine Imaging in RT

- The goal is to accurately delineate and biologically characterize an individual tumor, select an appropriate course of therapy, and to predict the response at the earliest possible time
- Image information can be categorized as:
  - Anatomical
  - Biological
    - » Metabolic
    - » Functional
    - » Physiological
    - » Genotypic
    - » Phenotypic

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The potential of Nuclear Medicine Imaging in RT

- Detection – Possibly better and earlier detection
  - Current imaging of disease is based on anatomic or physiologic changes that are a late manifestation of molecular changes that underlie the disease
- Staging - Improved staging and patient selection
  - Improved staging can define a more appropriate course of therapy

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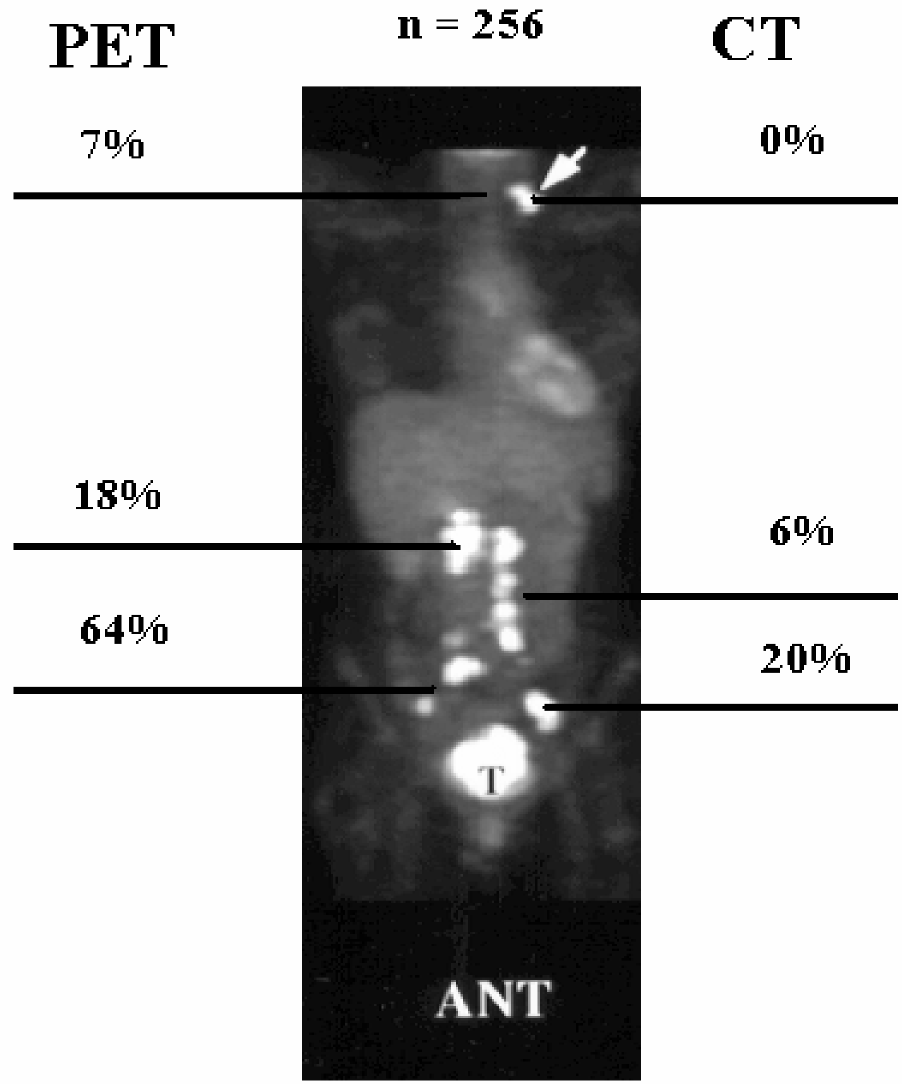

Grigsby et al, JCO, 2001

Lymph Node Status

n = 256

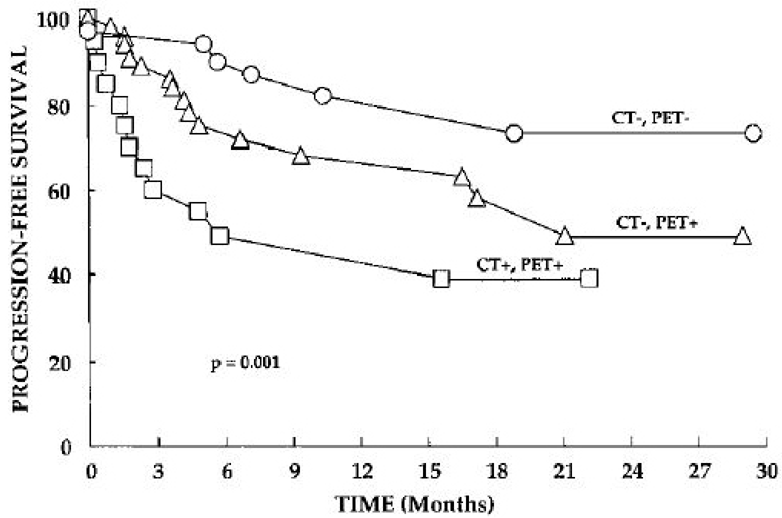

Fig 1. Kaplan-Meier progression-free survival estimates based on pelvic lymph node status (*P* = .001) (n = 101).

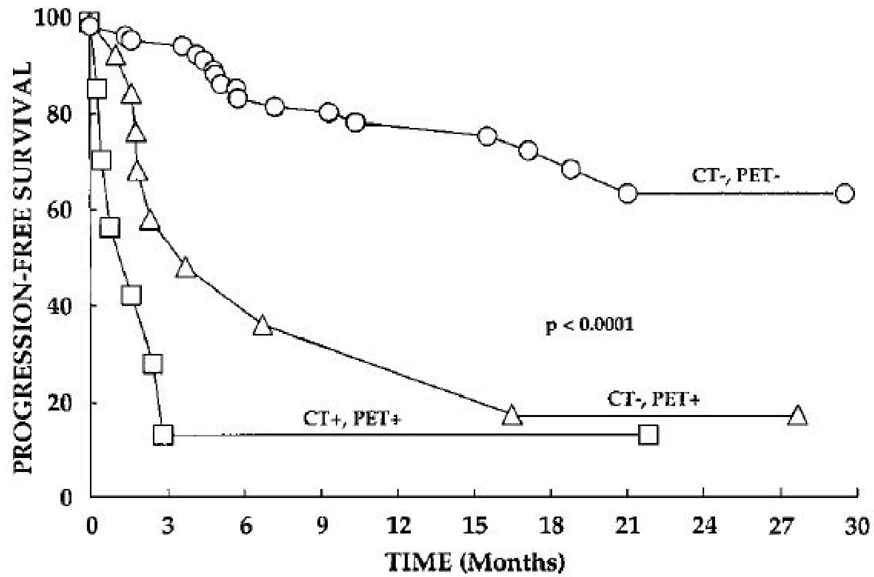

Fig 2. Kaplan-Meier progression-free survival estimates based on para-aortic lymph node status (*P* = .0001) (n = 101).

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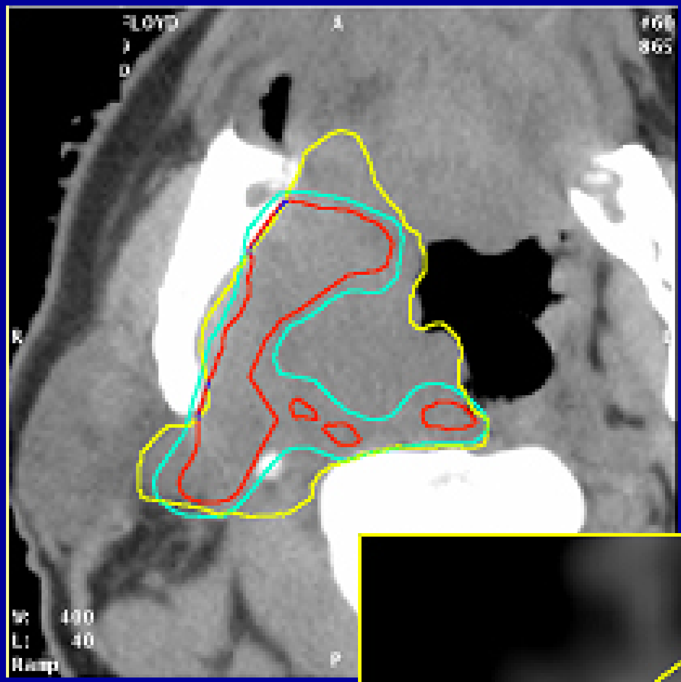
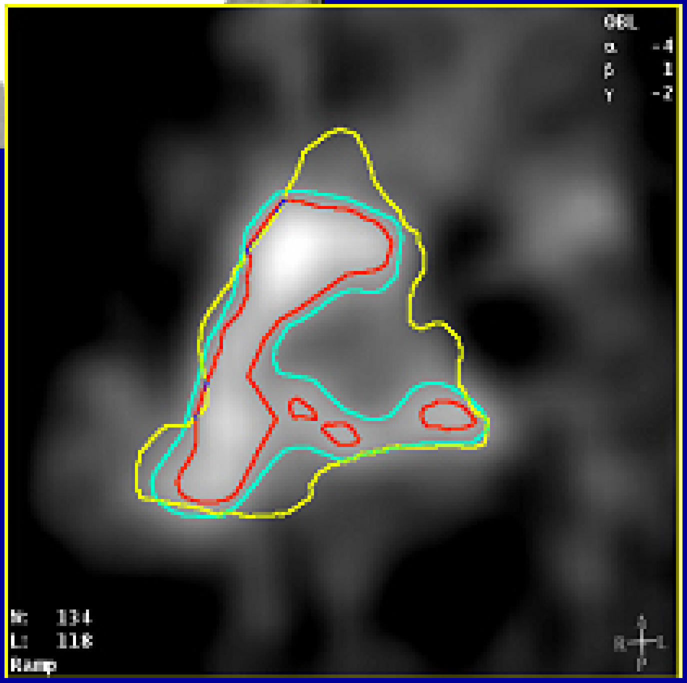
P.W. Grigsby et al, JCO, 2001

The potential of imaging in RT

- **Target definition**
  - Improved target identification can significantly alter current treatment volumes
  - The true extent of the disease may extend beyond anatomically defined volumes
  - Anatomically defined volumes may contain regions of increased importance - Biological target volume (BTV)





Ling *et al* IJROBP 47:551-560, (2000)

Cu(II)-diacetyl-bis (N^4-methylthiosemicarbazone) (^{60}Cu-ATSM) PET - used to detect regions of tumor hypoxia

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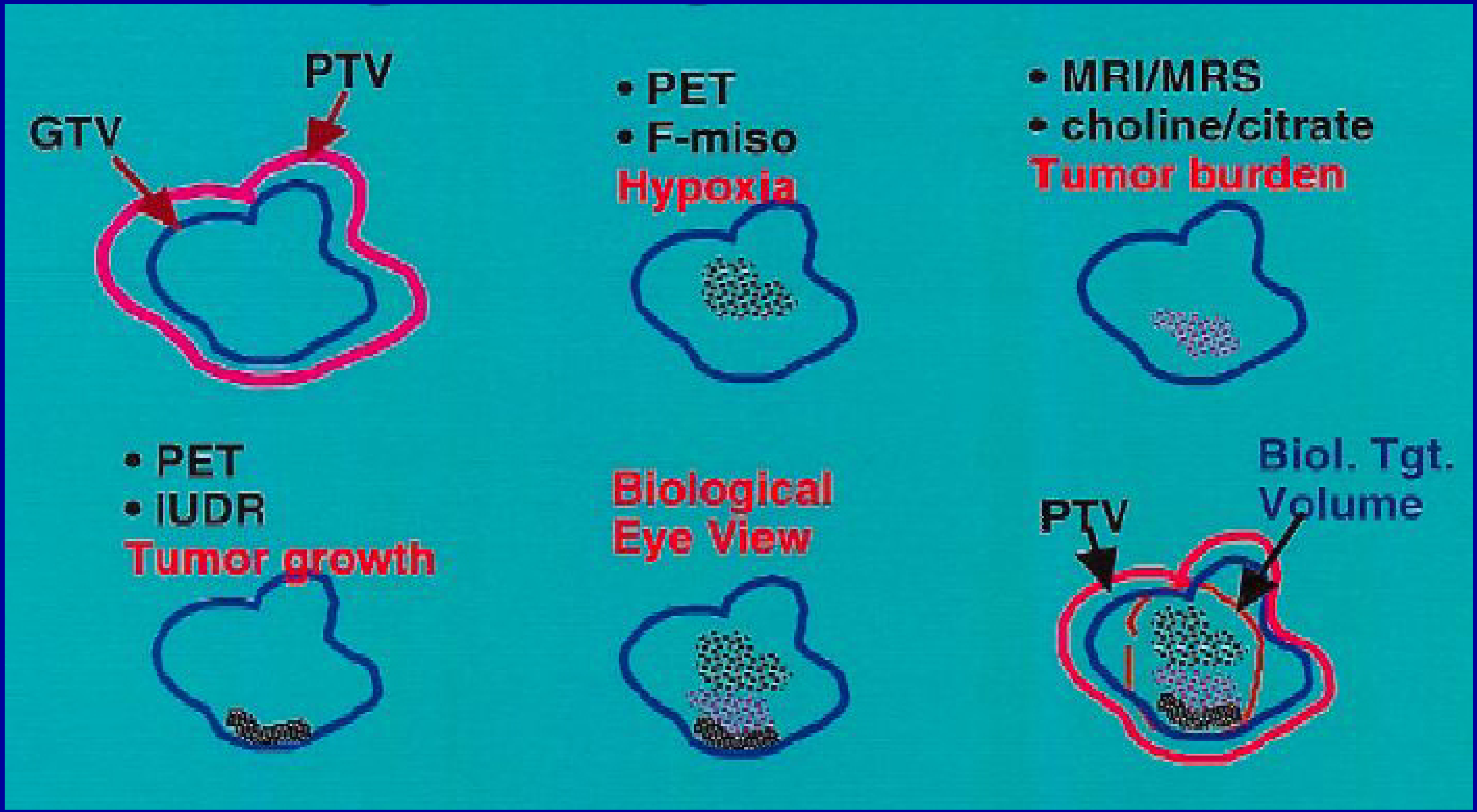
The potential of multimodality-imaging in RT

- **Target definition – Biological target volume**



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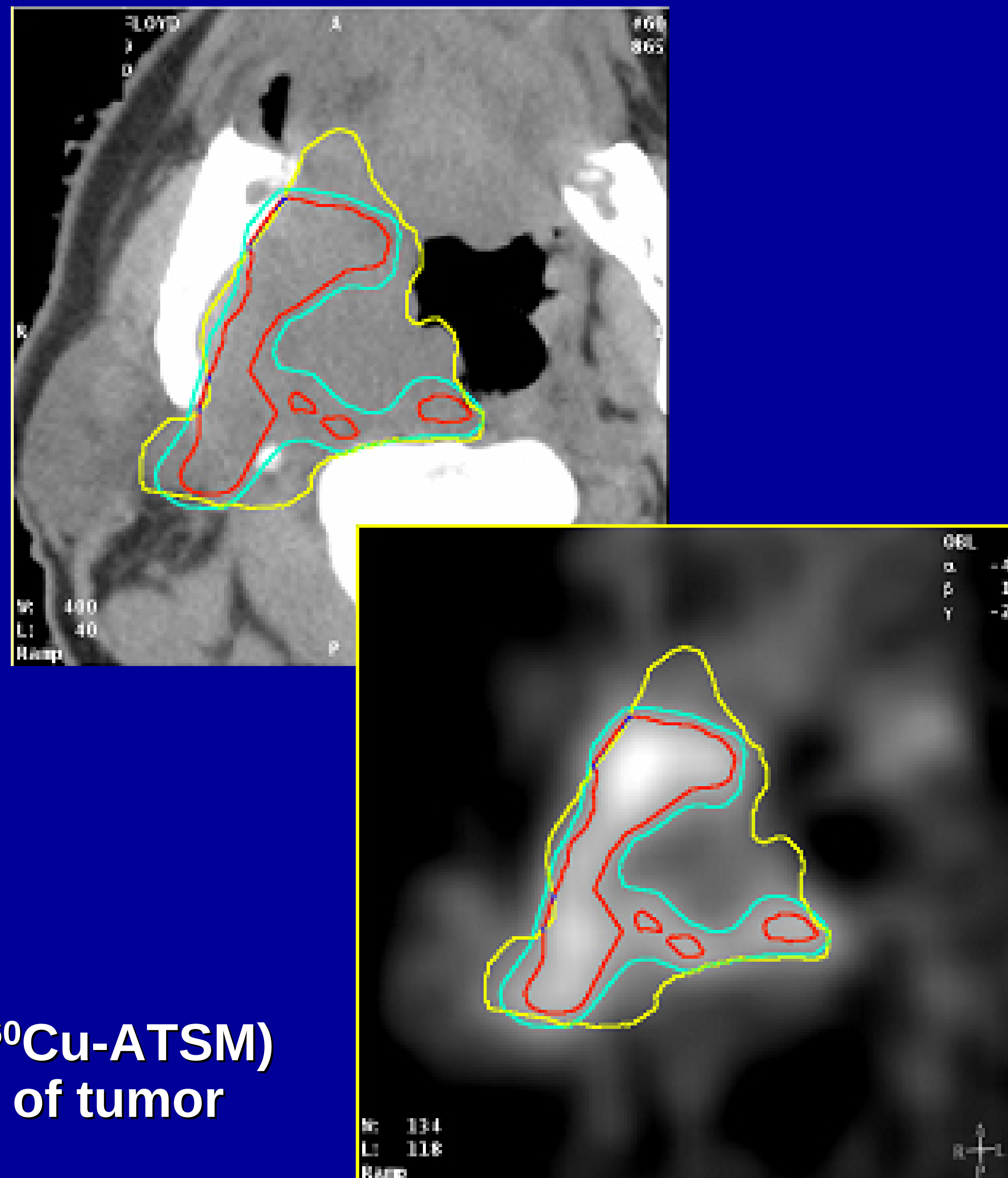
Ling et al IJROBP 47:551-560, (2000)

The potential of multimodality-imaging in RT

- **Dose distribution**
  - Treatment plans can be designed to deliver escalated doses to BTV
  - With IMRT the concept of “dose painting” can be implemented
  - The question becomes how much paint should be used



Cu(II)-diacetyl-bis (N^4-methylthiosemicarbazone) (^{60}Cu-ATSM) PET - used to detect regions of tumor hypoxia

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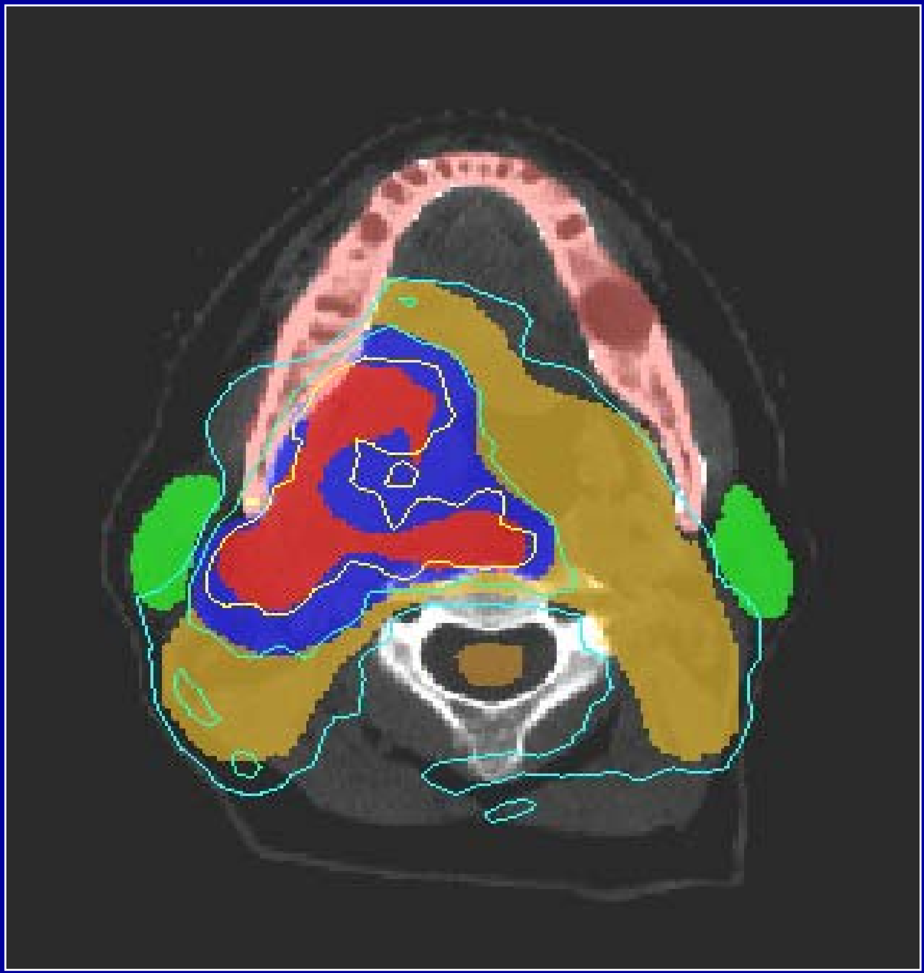
Altered/Escalated Dose Distributions

^{60}Cu-ATSM (Hypoxia) - Guided IMRT

- **80 Gy in 35 fractions to the hypoxic tumor sub-volume as judged by Cu-ATSM PET (red)**
- **GTV (blue) simultaneously receives 70 Gy in 35 fractions**
- **Clinical target volume (yellow) receives 60 Gy**
- **More than half of the parotid glands (green) are spared to less than 30 Gy.**



Chao et al. IJROBP 49:1171-1182, (2001).

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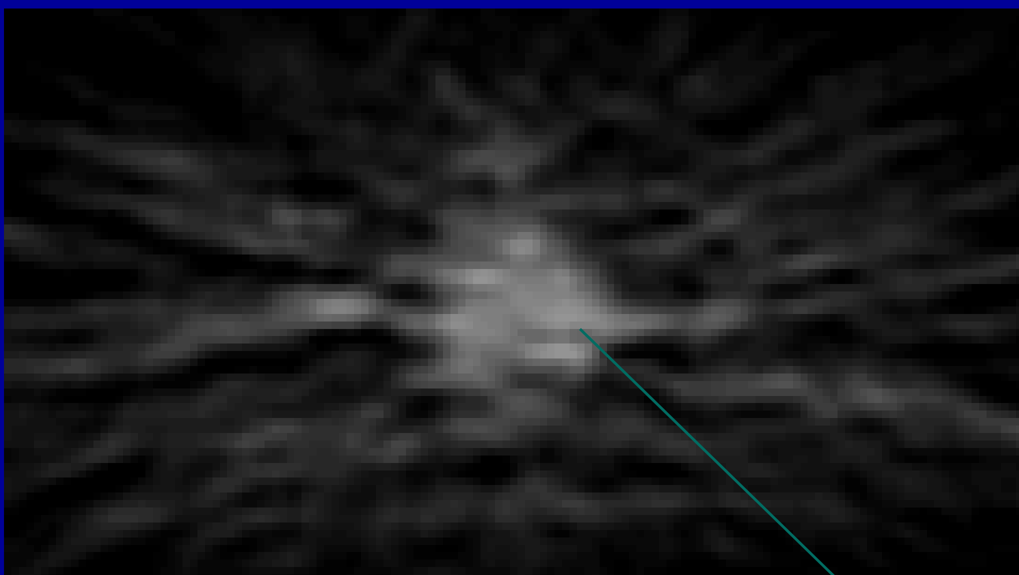
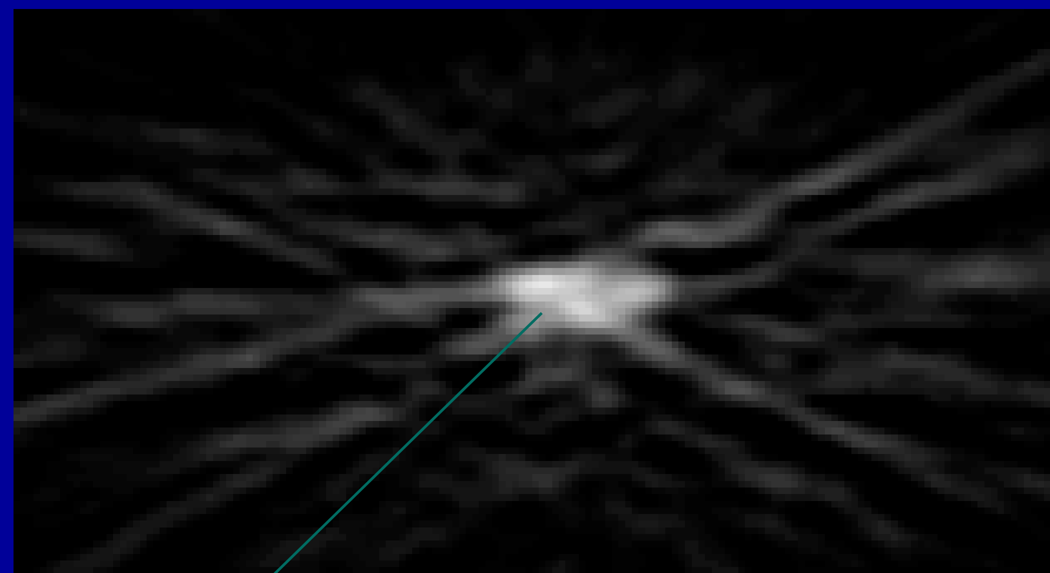
^{60}Cu-ATSM-PET

Normoxic **Hypoxic**





Cervical Cancer

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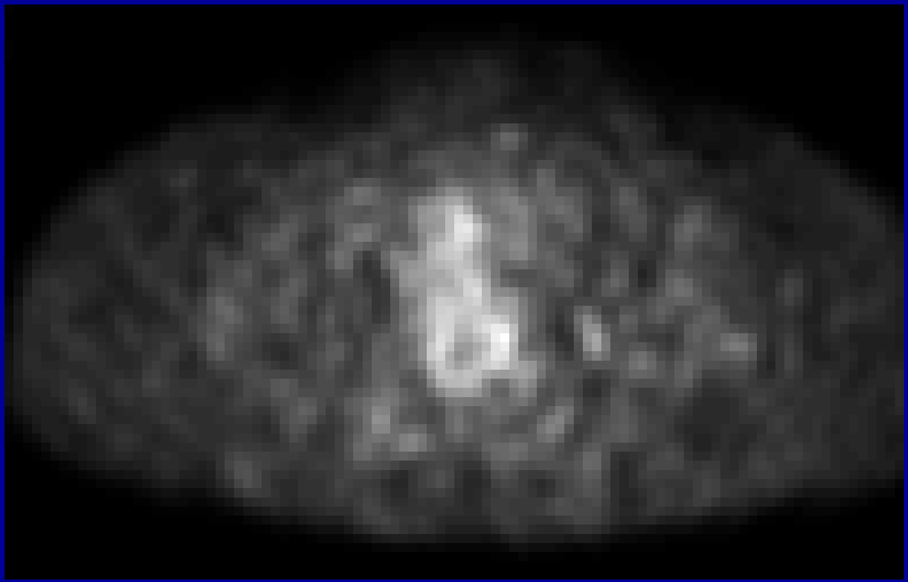
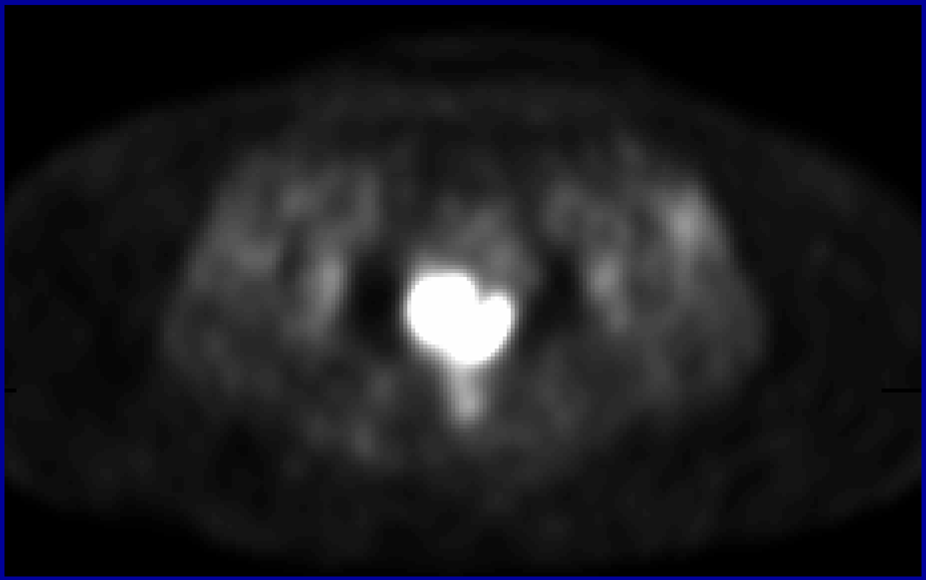
Dehdashti et al, IJROBP 55:1233-1238, (2003)

^{60}Cu-ATSM-PET

FDG-PET

Pre-therapy





T/M = 2.3

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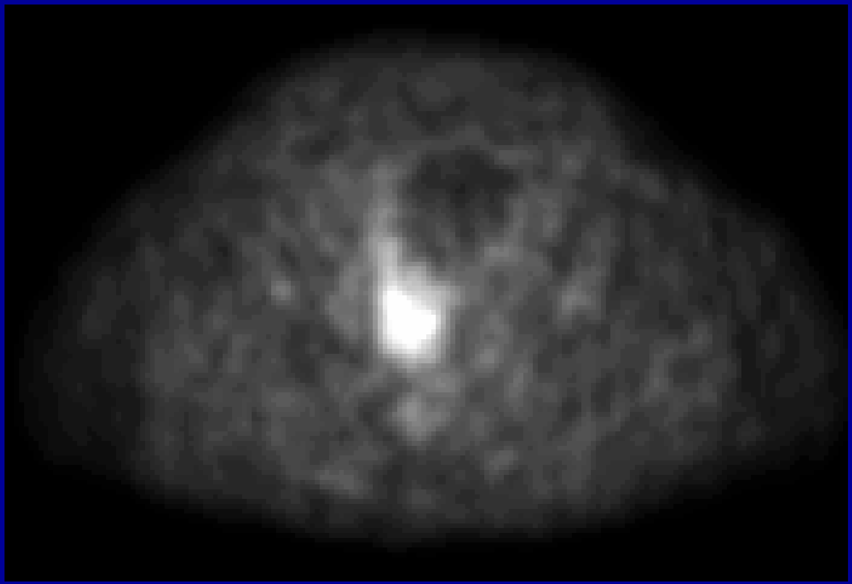
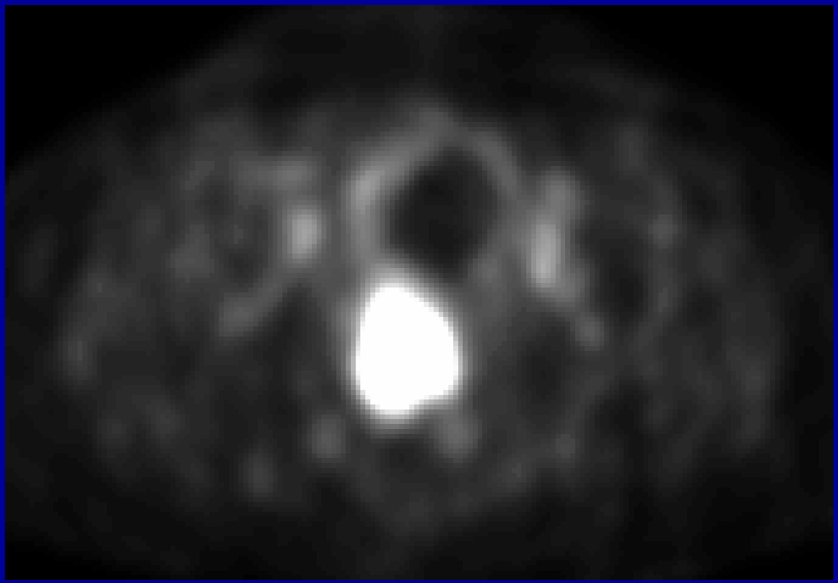
Dehdashti et al, IJROBP 55:1233-1238, (2003)

^{60}Cu-ATSM-PET

FDG-PET

Pre-therapy





T/M = 5.1

Dehdashti et al, IJROBP 55:1233-1238, (2003)

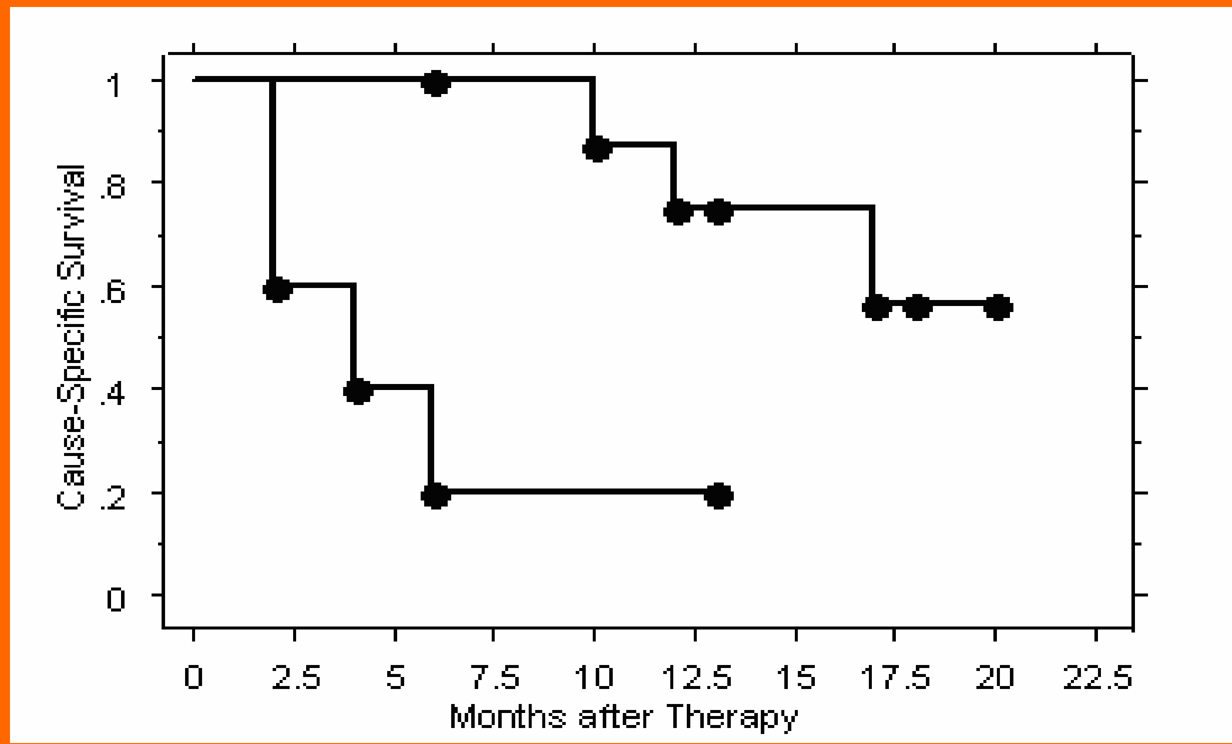
Results

- 6/15 pt's tumors were characterized as hypoxic
- All pts with hypoxic tumors developed recurrent disease (p=0.0005)
- 8/9 pts disease free

  (follow-up 6.1-13.9 months)
- All 6/6 pts with hypoxia had pelvic LN vs. 3/9 without hypoxic tumors

  (p =0.03)

ATSM T/M ratio >3.5



p = 0.0078

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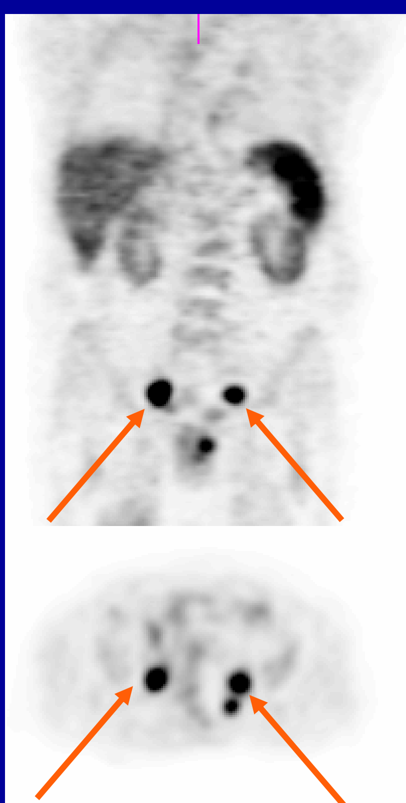
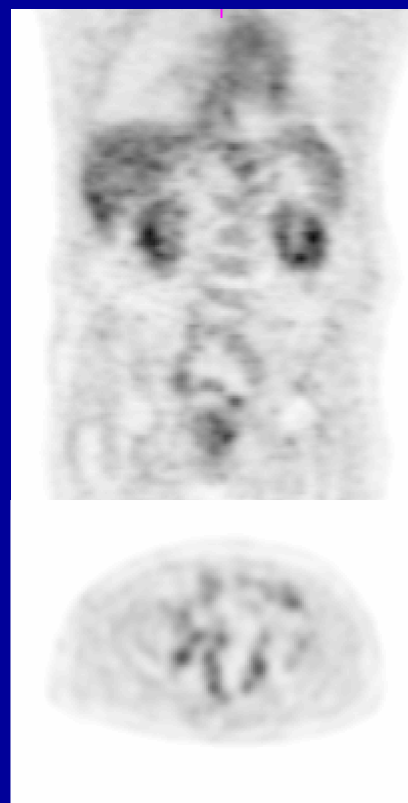
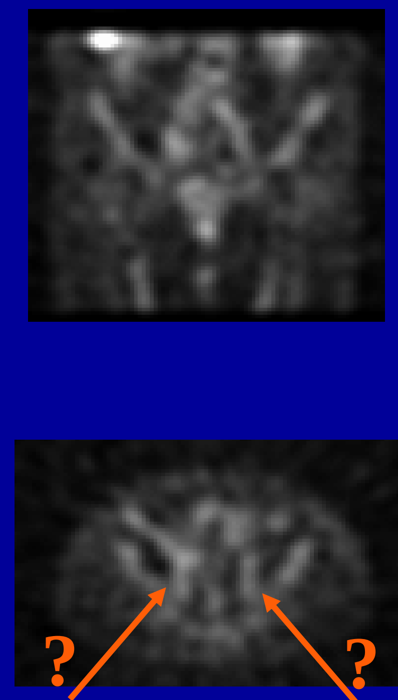
PET imaging for RT



C-11 acetate



F-18 FDG



Prostascint

CT

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Oyama *et al.* J Nuc Med 44, 549-555, 2003

The potential of multimodality-imaging in RT

- **Treatment planning- continued**
  - **Tumor biology (phenotype) and therapy selection –**
    - » **Intermodality and intramodality changes**
    - » **Radiation or chemotherapy sensitivity**
    - » **Incorporate biological response models to maximize the therapeutic ratio**
    - » **Indicator for more aggressive therapy in certain patients**
  - **New treatment techniques**
    - » **Revised target volumes and desired dose distributions will require reevaluation of current treatment techniques**

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FDG-PET Guided IMRT
Dose escalation to PALN

- **Rationale**
  - The survival of cervical cancer patients with para-aortic lymph node (PALN) metastasis is poor
  - Results of RTOG-7920 suggest 45 Gy para-aortic lymph node irradiation (PALNI) is associated with better survival - *Rotman et al JAMA 274:387-393 (1995)*
  - PALN dose is limited by bladder, rectum, colon, kidney, small intestine, and spinal cord radiation tolerances
- **Objective**
  - Dose escalation to PALN while maintaining or even reducing dose to the surrounding critical organs using IMRT
  - Use of PET to delineate target volume

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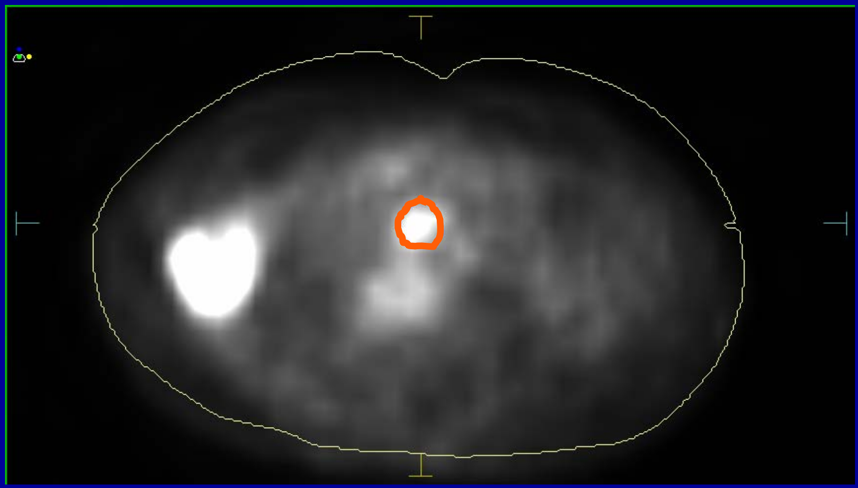
Mutic et al, Int J Radiat Oncol Biol Phys 55:1 28-35 (2003)

Process

- **PET and CT scans are acquired in treatment position with PET/CT scanner**
- **Positive PALN are identified on PET and contours are related to CT**
- **Treatment plans are created to escalate dose to positive PALN**



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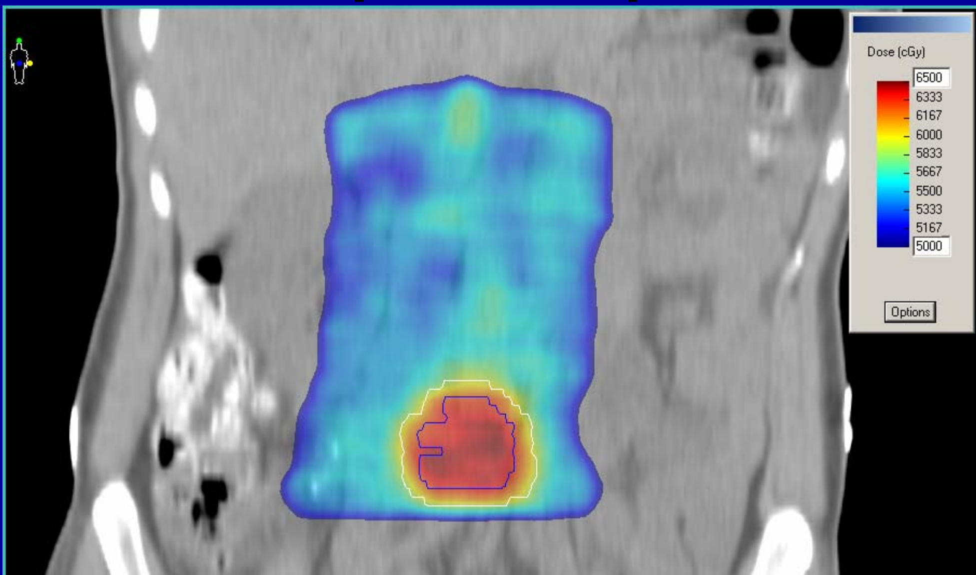
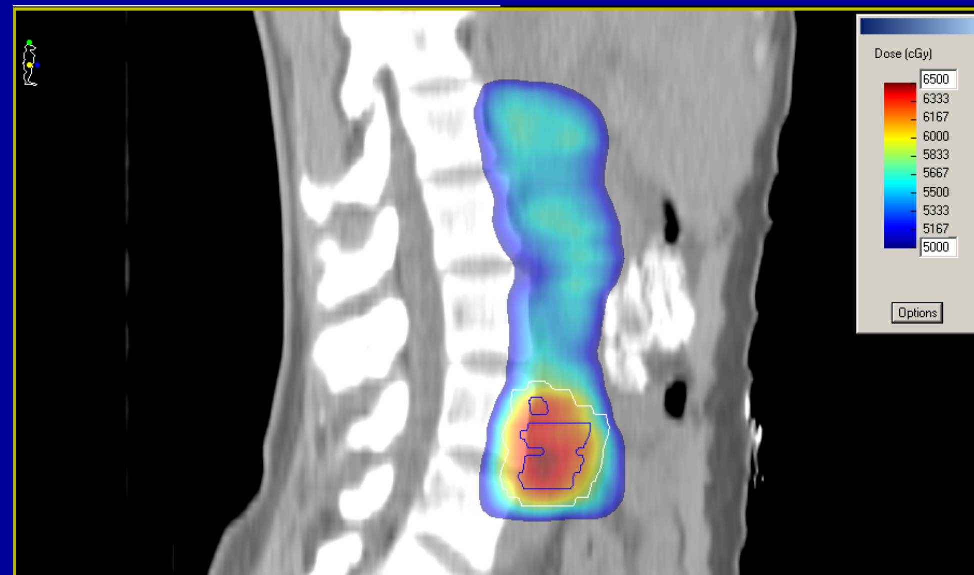
Dose Distribution

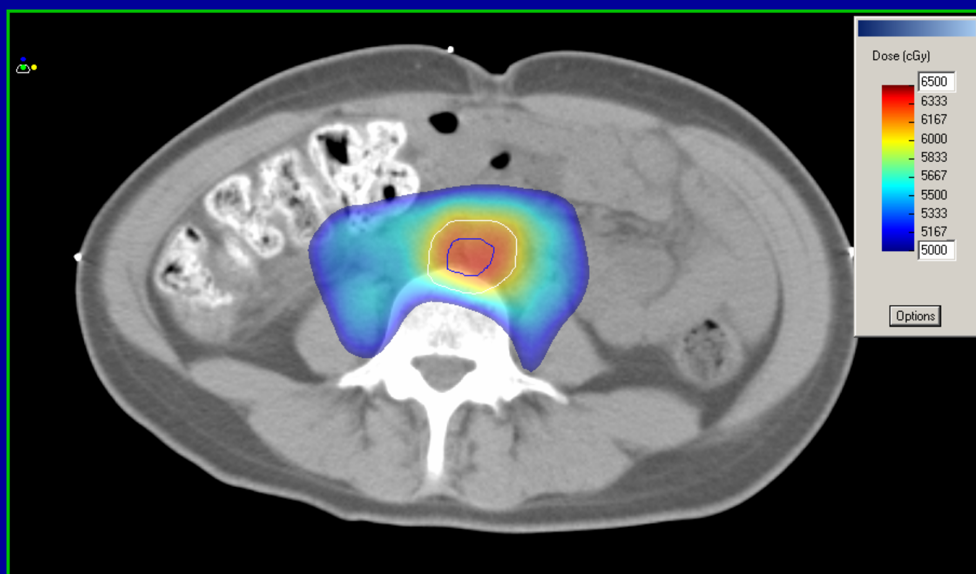
First protocol patient - treatment start date 11-3-2003

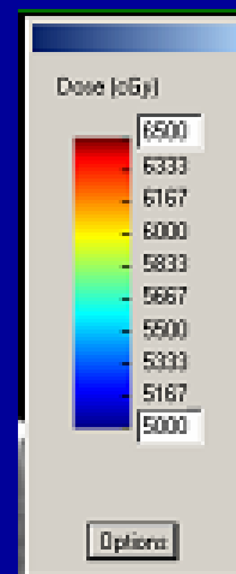




50 Gy to PALN bed

60 Gy to positive PALN





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Altered/Escalated Dose Distributions
PET Guided GYN Brachytherapy Implants

- Tandem and colpostat applicator inserted in the OR
  - Applicator design and mode of delivery (HDR or LDR) not important
- Foley catheter placed in the urinary bladder
- Patient taken to the PET scanner where 555 MBq (15 mCi) ^{18}F-FDG (^{18}F-fluorodeoxyglucose) is intravenously administered
- Three small tubes containing ^{18}F-FDG inserted into the applicator
- Whole pelvis scan obtained and images transferred to the treatment planning system (XiO, CMS, St. Louis, MO)
- 3D treatment plan created with target and normal structure DVHs

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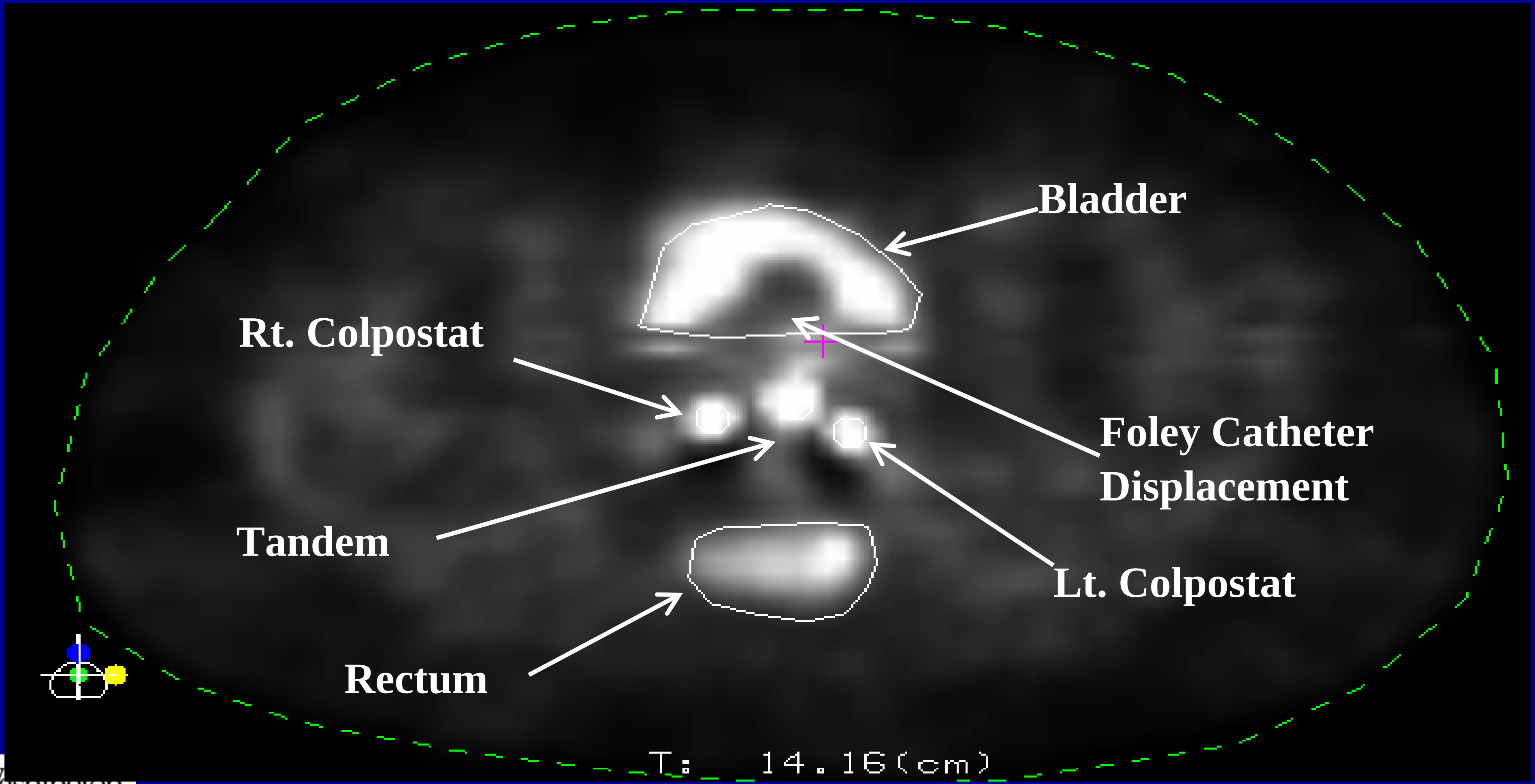
Anatomy

PET Guided GYN Brachytherapy Implants



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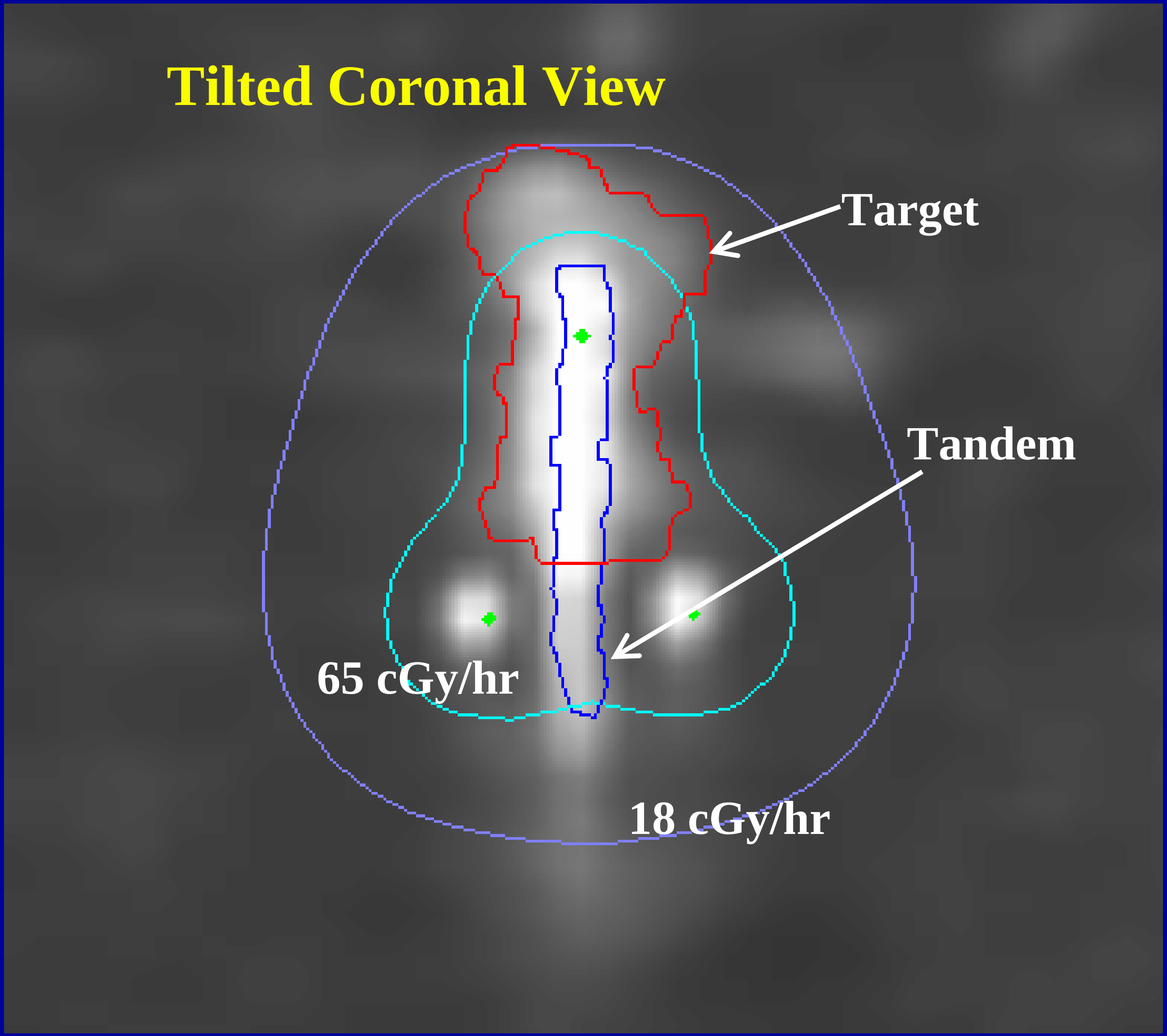
Treatment planning

PET Guided GYN Brachytherapy Implants

- Applicators, critical structures and tumor contoured
- Software places sources at predefined positions with respect to applicator tips
- Source strengths and treatments times optimized
- Alternatively, deliver conventional dose distributions



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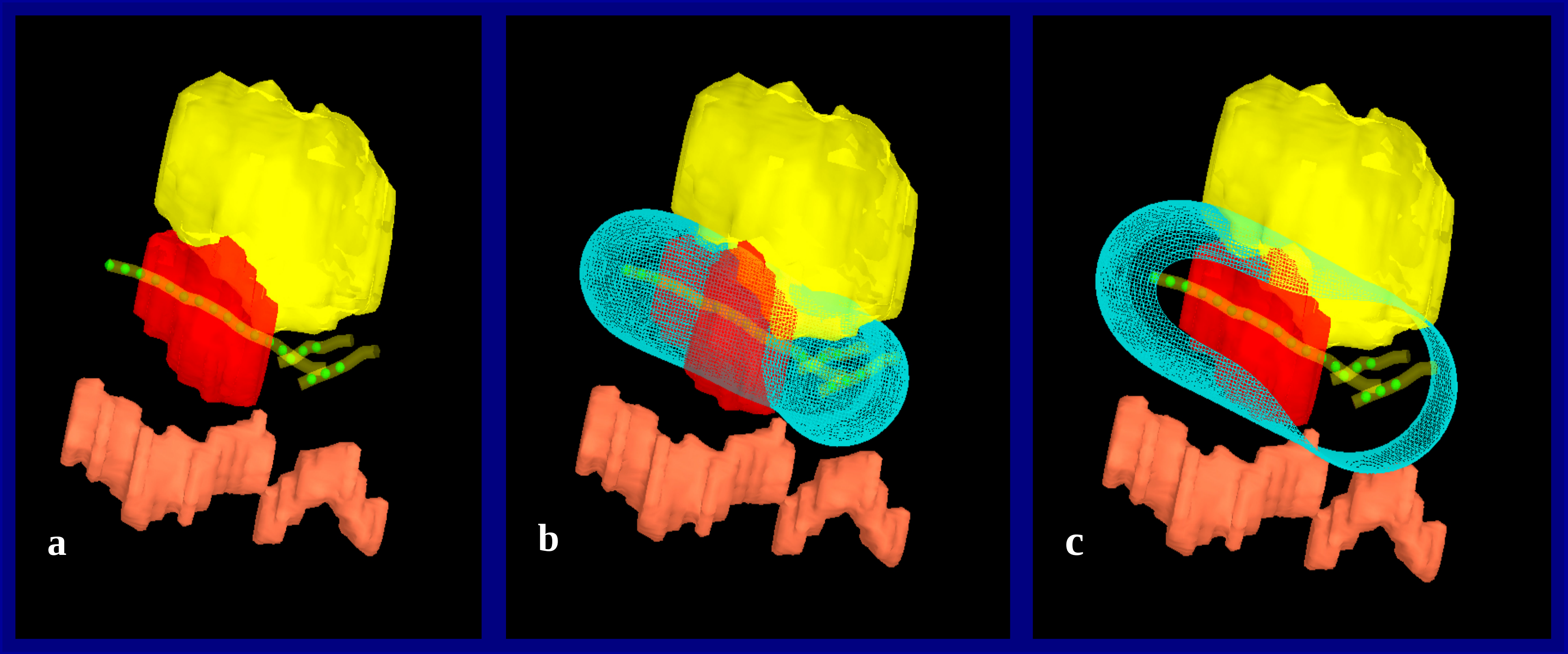
Conventional Dose Distributions

PET Guided GYN Brachytherapy Implants



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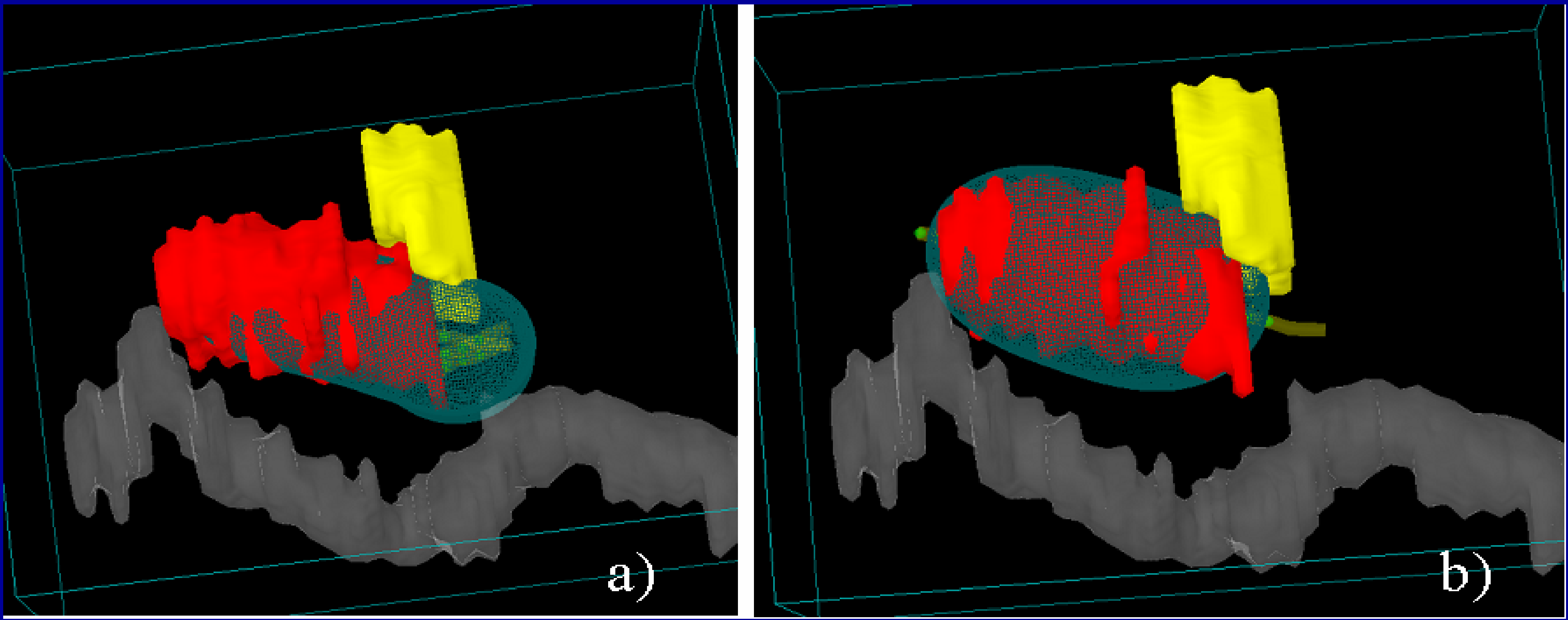
Optimized Dose Distributions
PET Guided GYN Brachytherapy Implants



- Same Integrated Reference Air Kerma (IRAK) strength used for both plans
- Dwell positions rearranged to conform dose distribution

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The potential of multimodality-imaging in RT

- **Normal Tissue Sparing**
  - Functional properties of normal structures are used for guidance in organ organ sparing
  - Highly functioning portions of critical structures are given priority
  - Potentially can simplify delivery and improve tumor dose distribution

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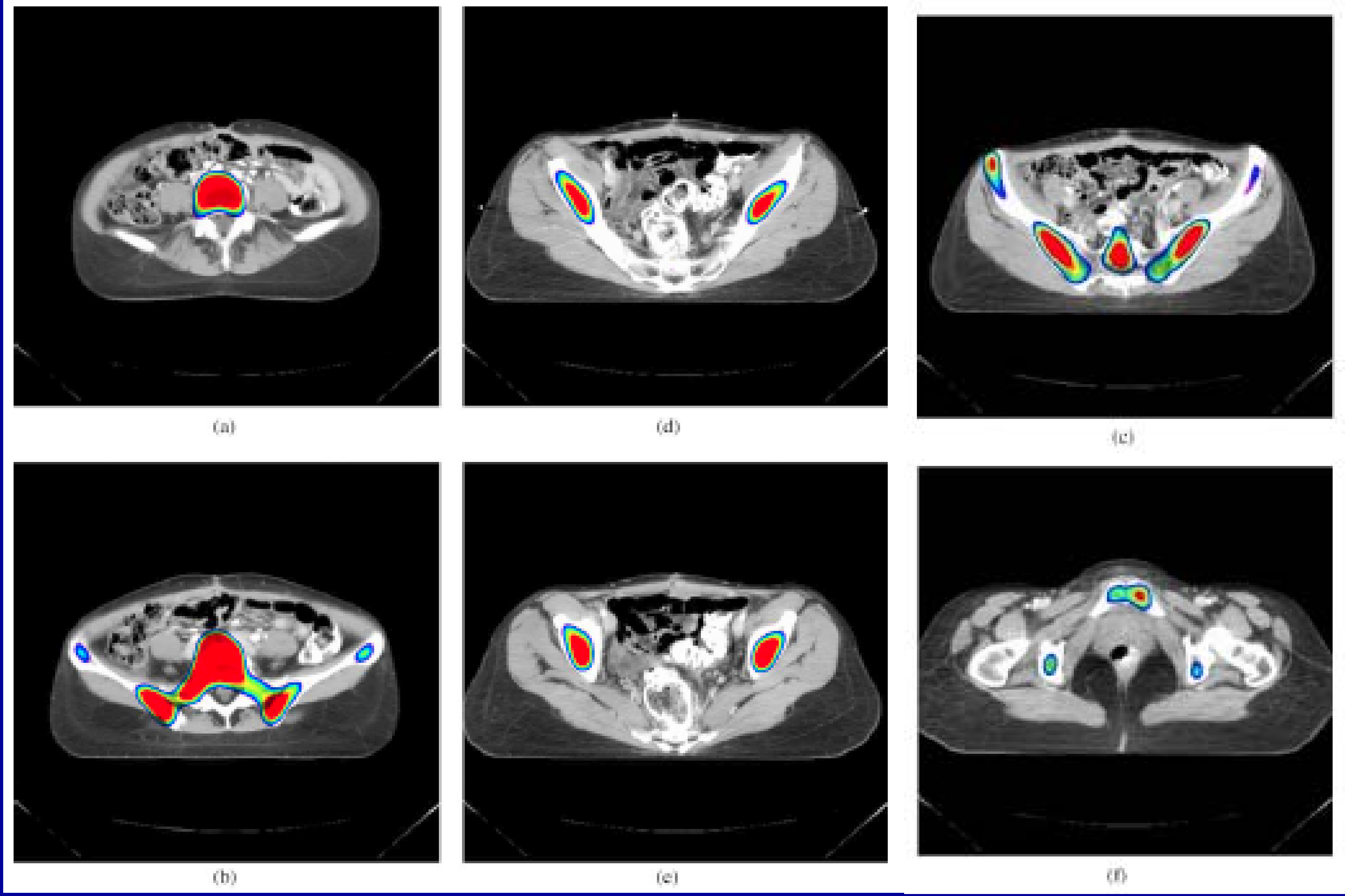
SPECT Guided Bone Marrow Sparing

Tc-99m sulfur colloid



Roeske et al, Radiotherapy and Oncology 77 (2005) 11-17.

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SPECT Guided Bone Marrow Sparing

Blue lines identify active bone marrow

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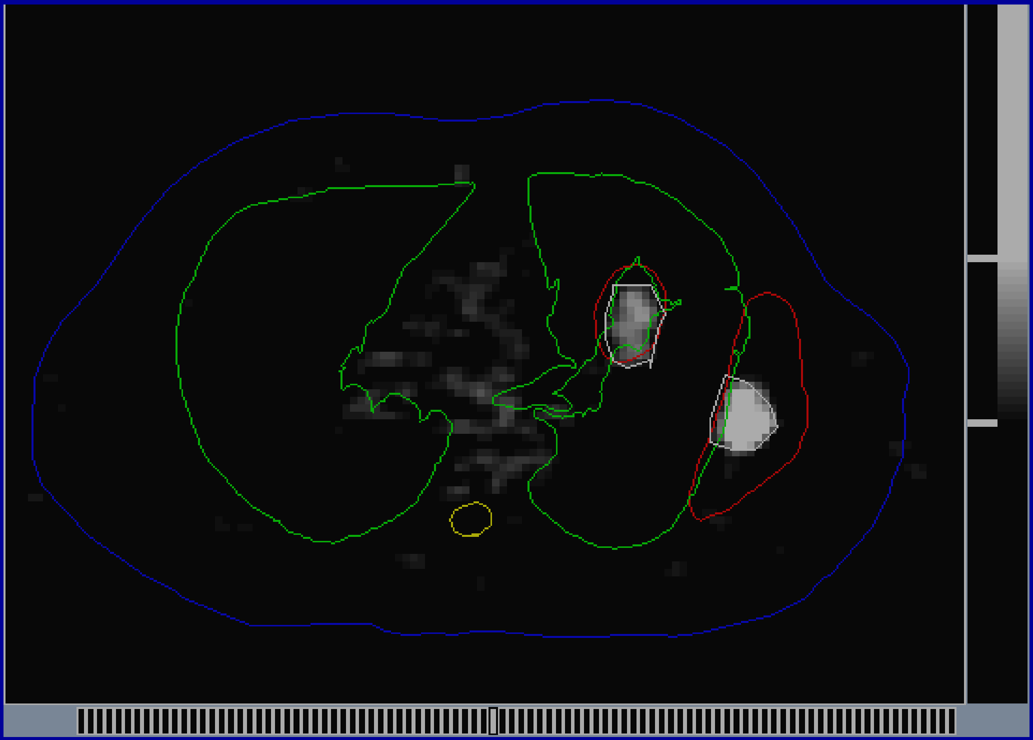
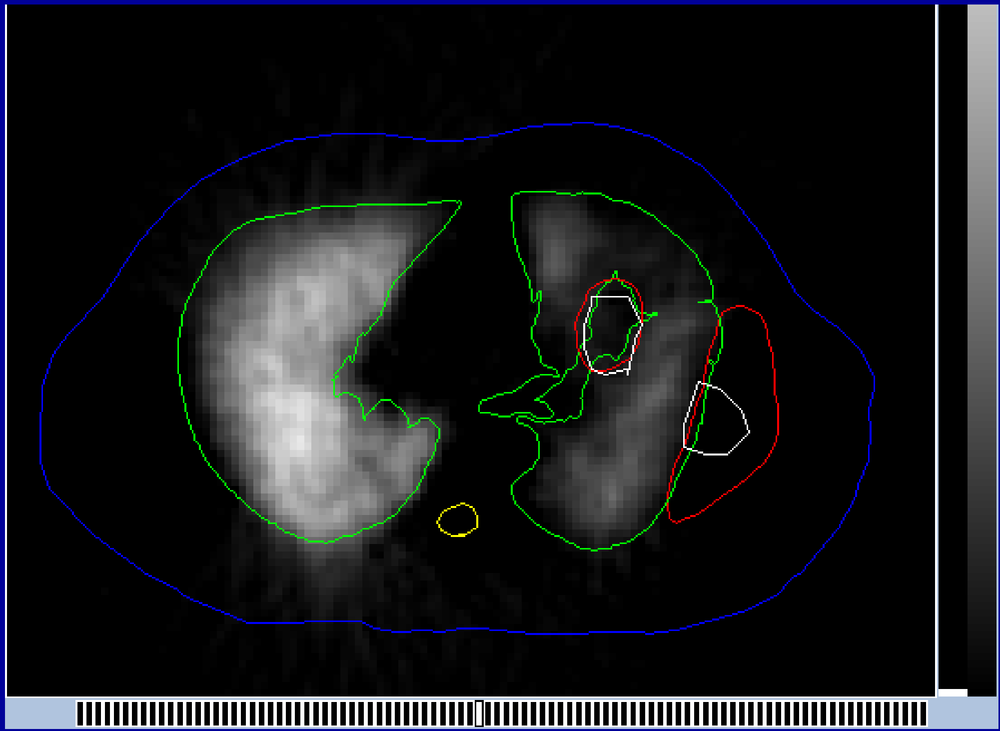
Roeske *et al, Radiotherapy and Oncology 77 (2005) 11-17.*

PET, SPECT and CT Imaging during Radiation Treatment Planning



FDG PET grayscale



MAA SPECT grayscale

Courtesy: MT Munley, MUSC

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Dose-Function Histogram (DFH)

- Similar to the dose-volume histogram (DVH), but displaying the percent relative function of a structure versus dose.
- Uses the value of each voxel element:
  - Targets: F-18 FDG PET (metabolism)
    F-18 Misonidazole PET (hypoxia)
  - Normal: Tc-99m MAA SPECT (lung perfusion)

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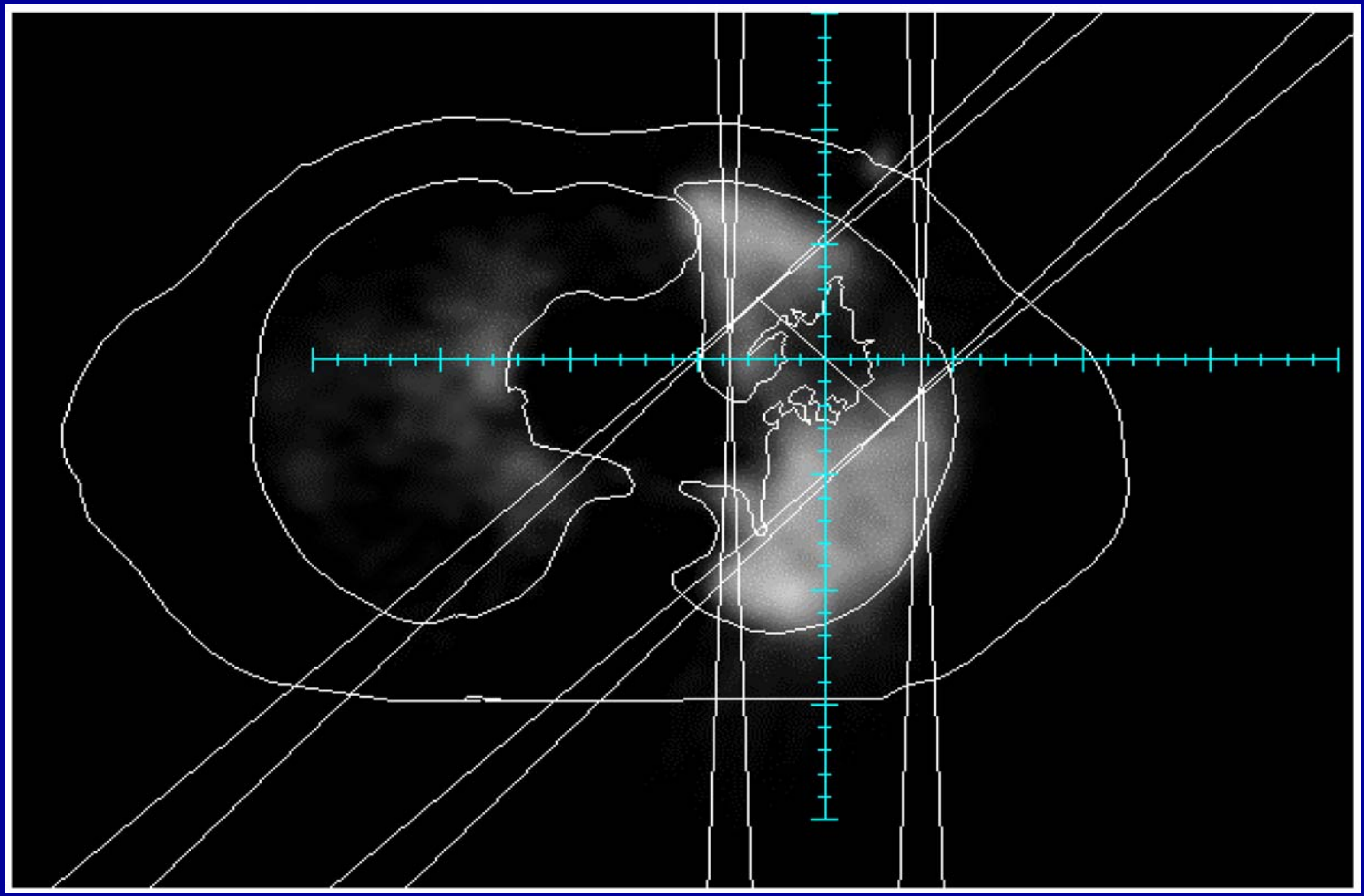
Courtesy: MT Munley, MUSC

Beam Orientation as a Function of Lung Function



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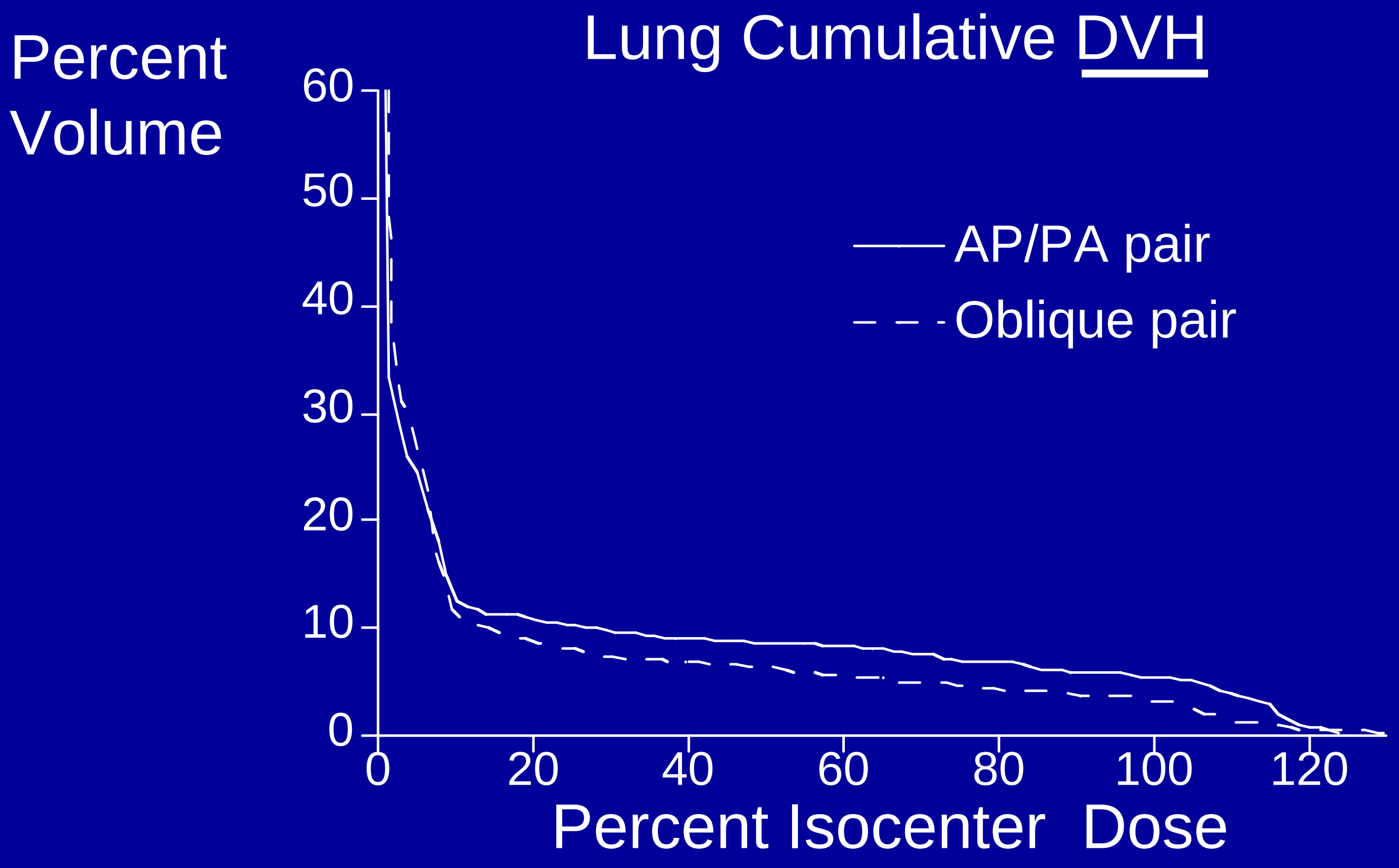
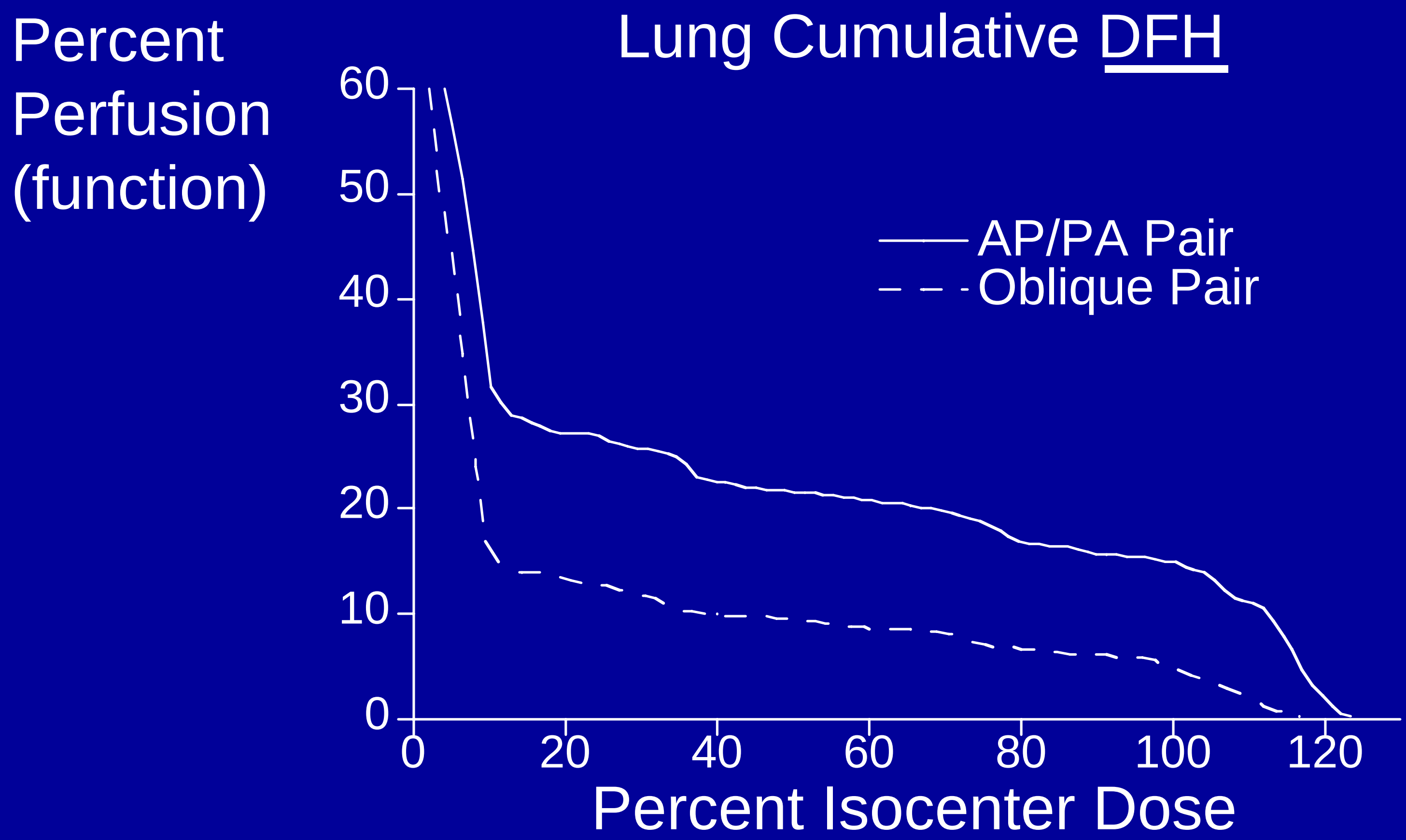
Courtesy: MT Munley, MUSC   ***Marks et al, Med Phys 26 (1999), 196-199.***

Comparison of Beam Orientations using the DVH



Marks et al, Med Phys 26 (1999), 196-199.

Comparison of Beam Orientations using the DFH



Courtesy: MT Munley, MUSC

Marks et al, Med Phys 26 (1999), 196-199.

The potential of PET-imaging in RT

- **Evaluation** - Therapy response and follow-up
  - Tumor control
    - » Image at a molecular level
    - » Evaluate response shortly after initiation of therapy
    - » Possibly modify the planned course of therapy based on the initial response
  - Normal tissue function

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FDG-PET
IIb Cx Only—Pre & Post RT

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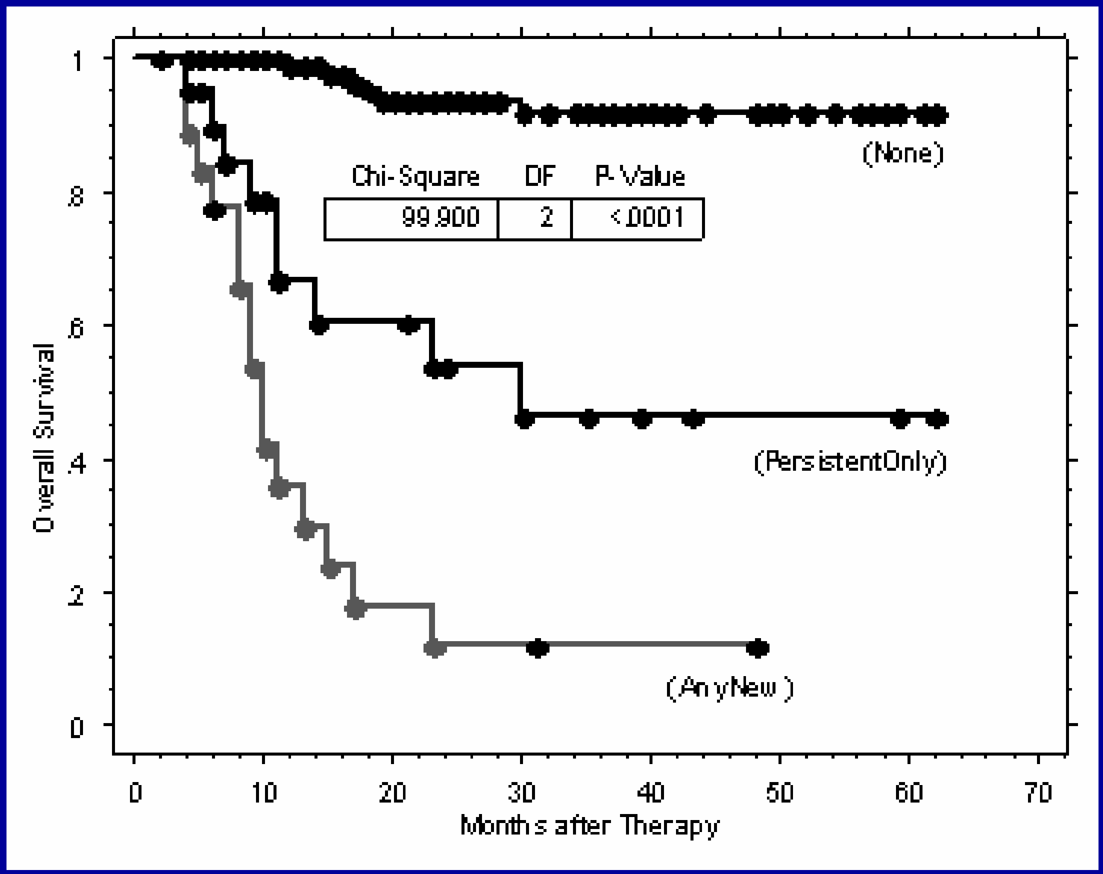
P.W. Grigsby et al

Follow-up FDG-PET

Overall Survival



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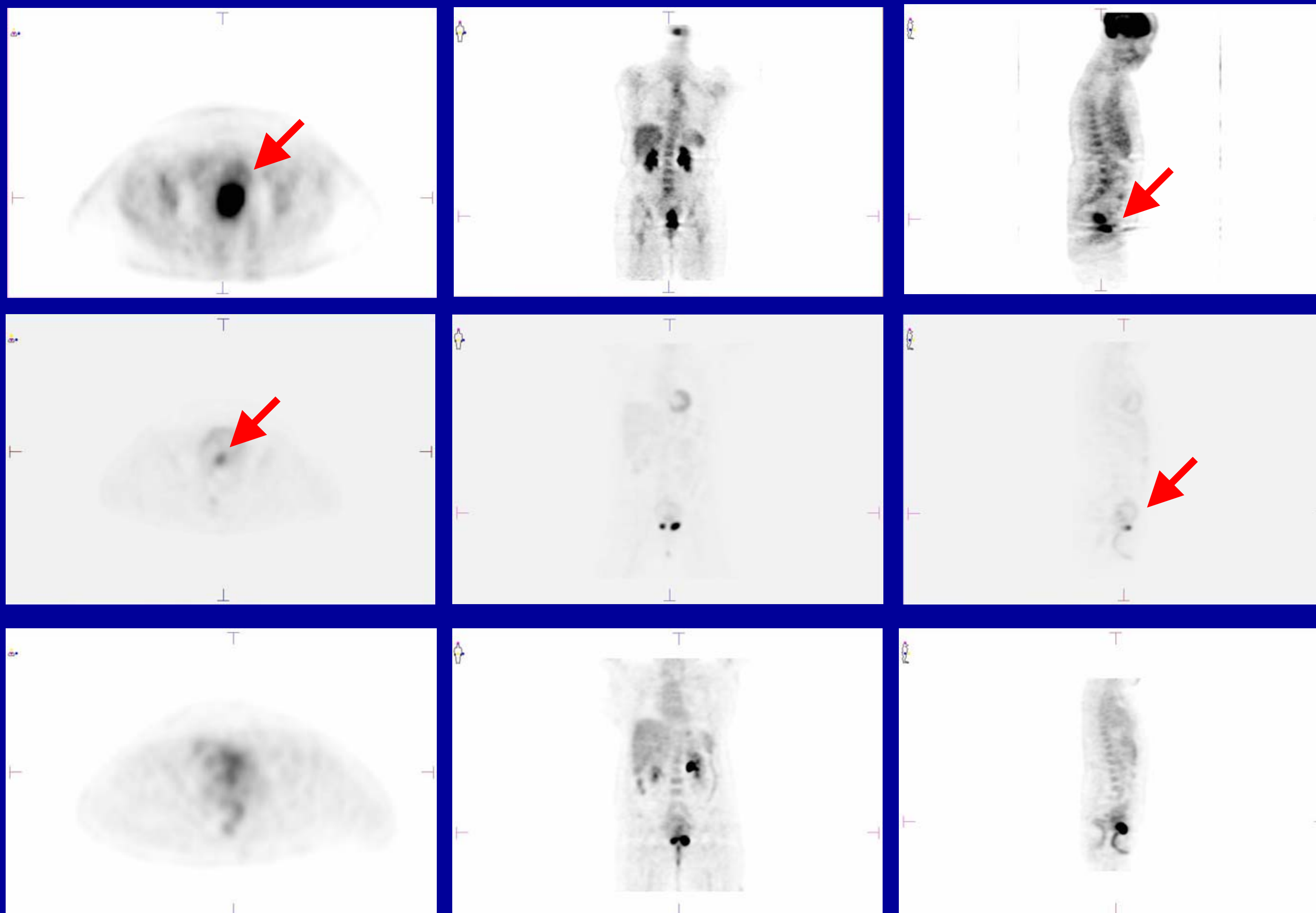
P.W. Grigsby et al

Pre Treatment

First Implant

Third Implant



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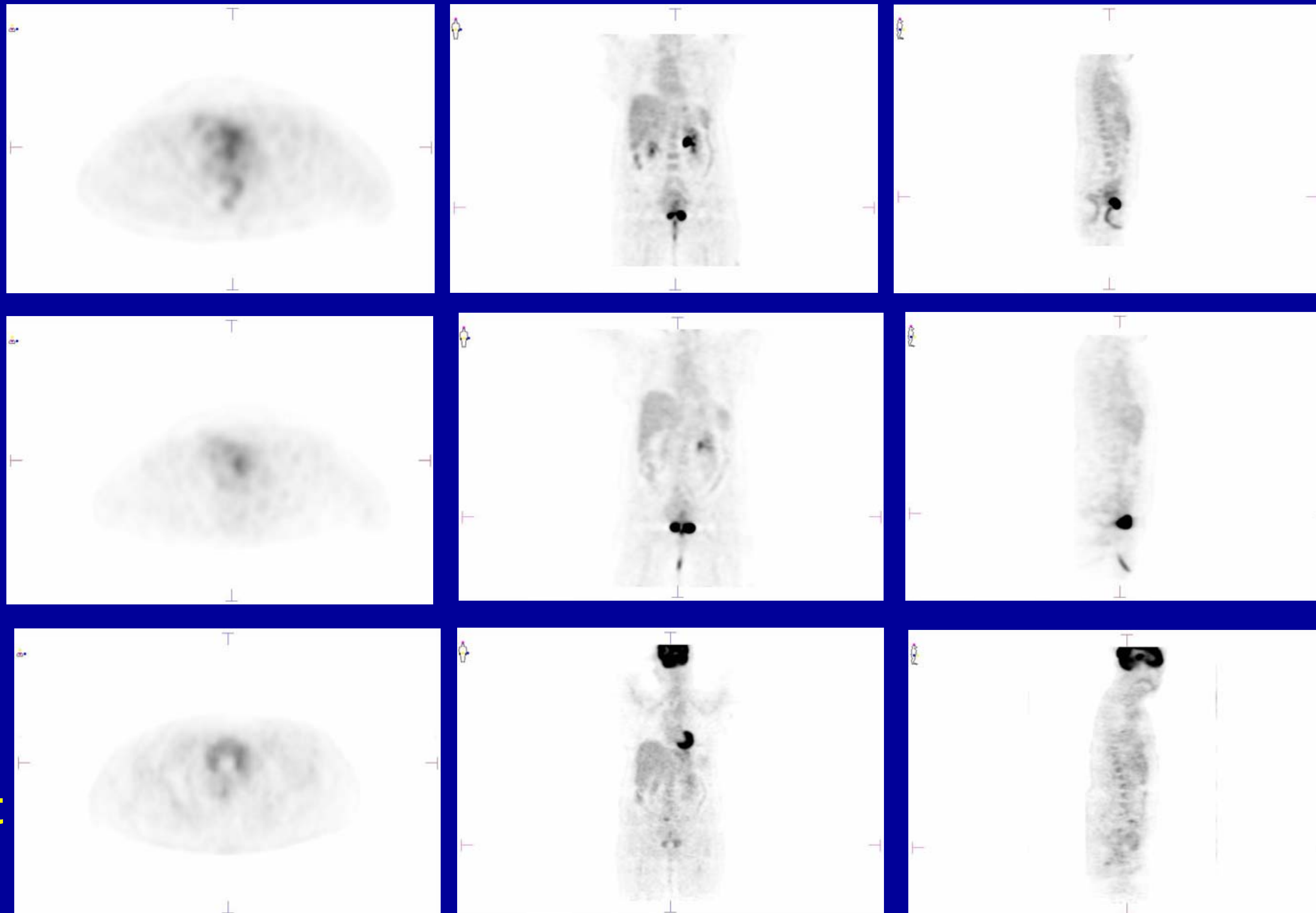
Lin et al, IJROBP 63 (2005) 1494-1501

Third Implant

Fifth Implant

Post Treatment



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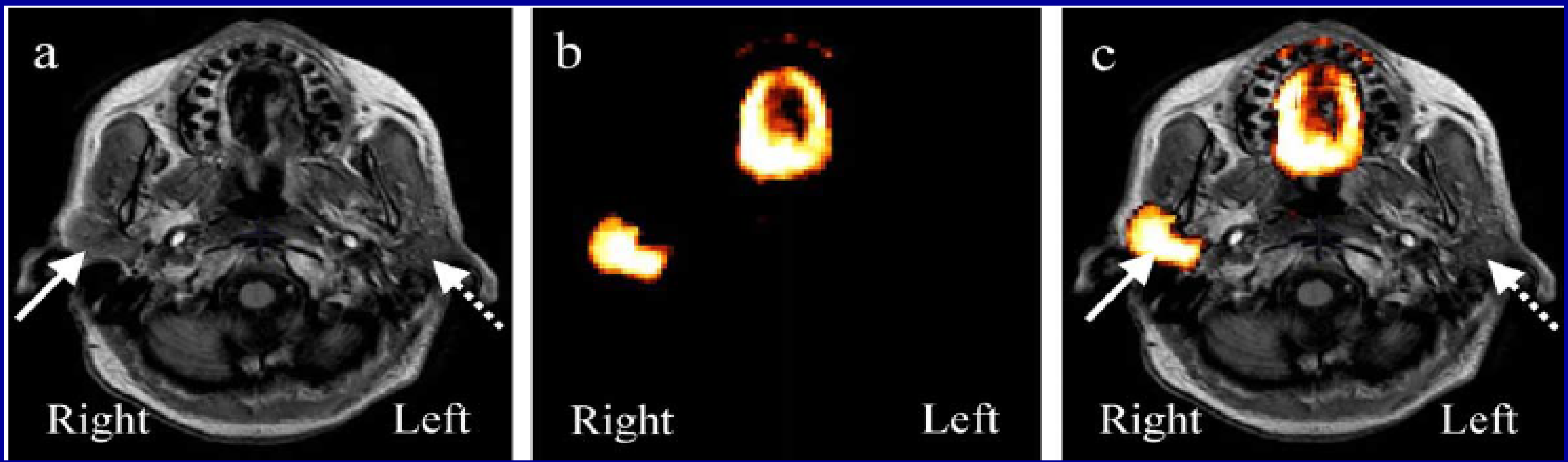
Lin et al, IJROBP 63 (2005) 1494-1501

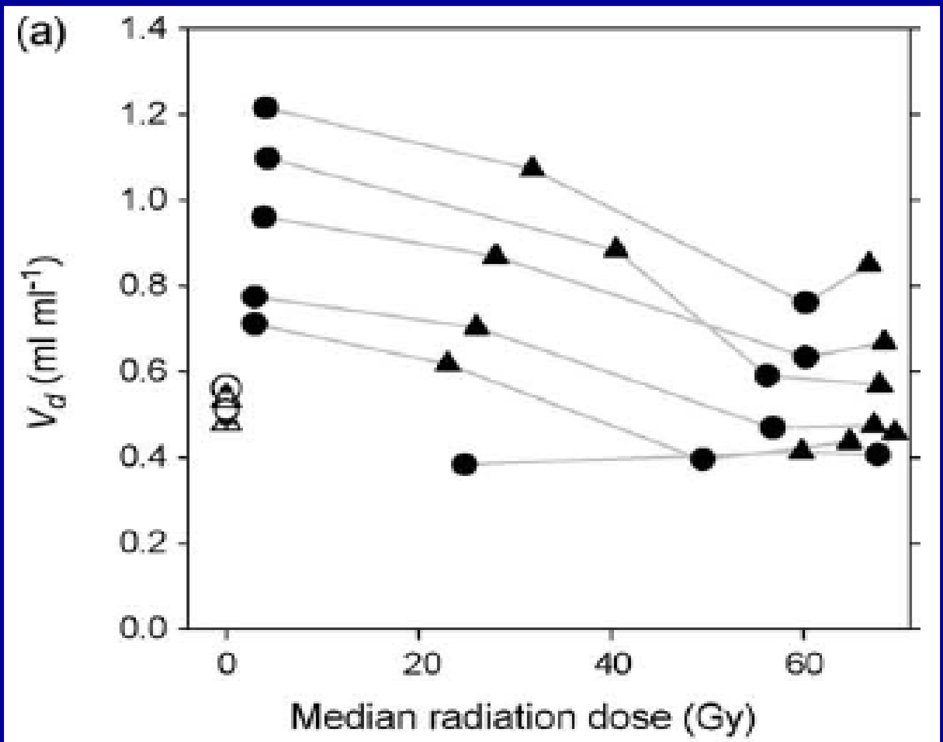
11C-methionine PET measuring regional salivary gland function

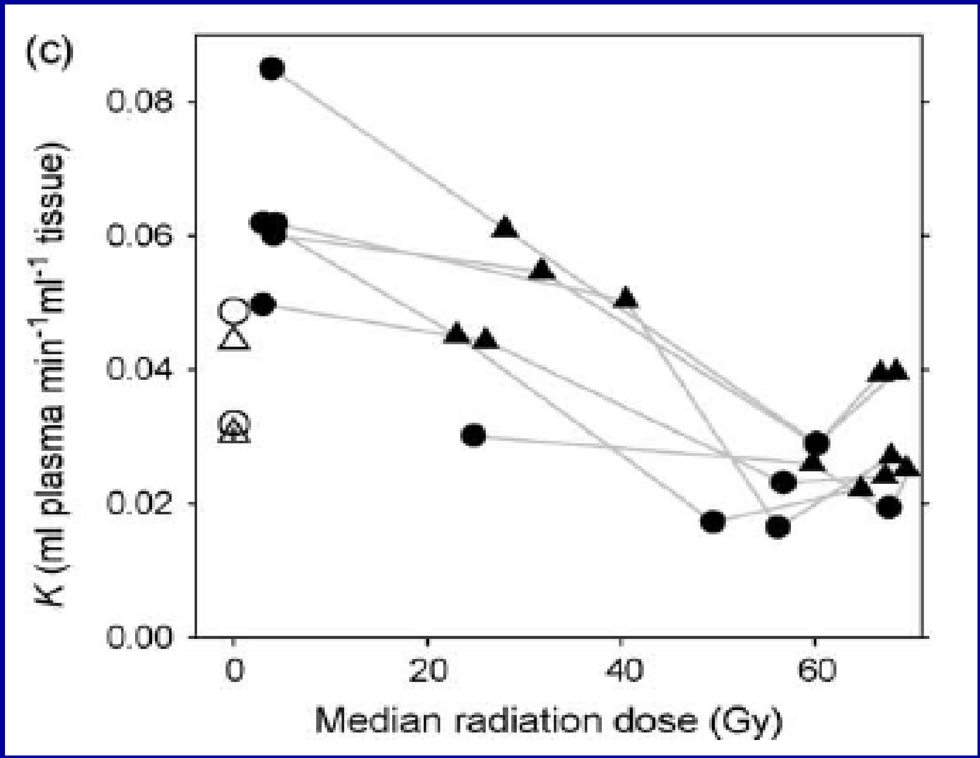


Right-mean dose 30Gy Left-mean dose 57 Gy

Buus et al, Radiotherapy and Oncology 73:289-296, (2004).

11C-methionine PET
measuring regional salivary gland function





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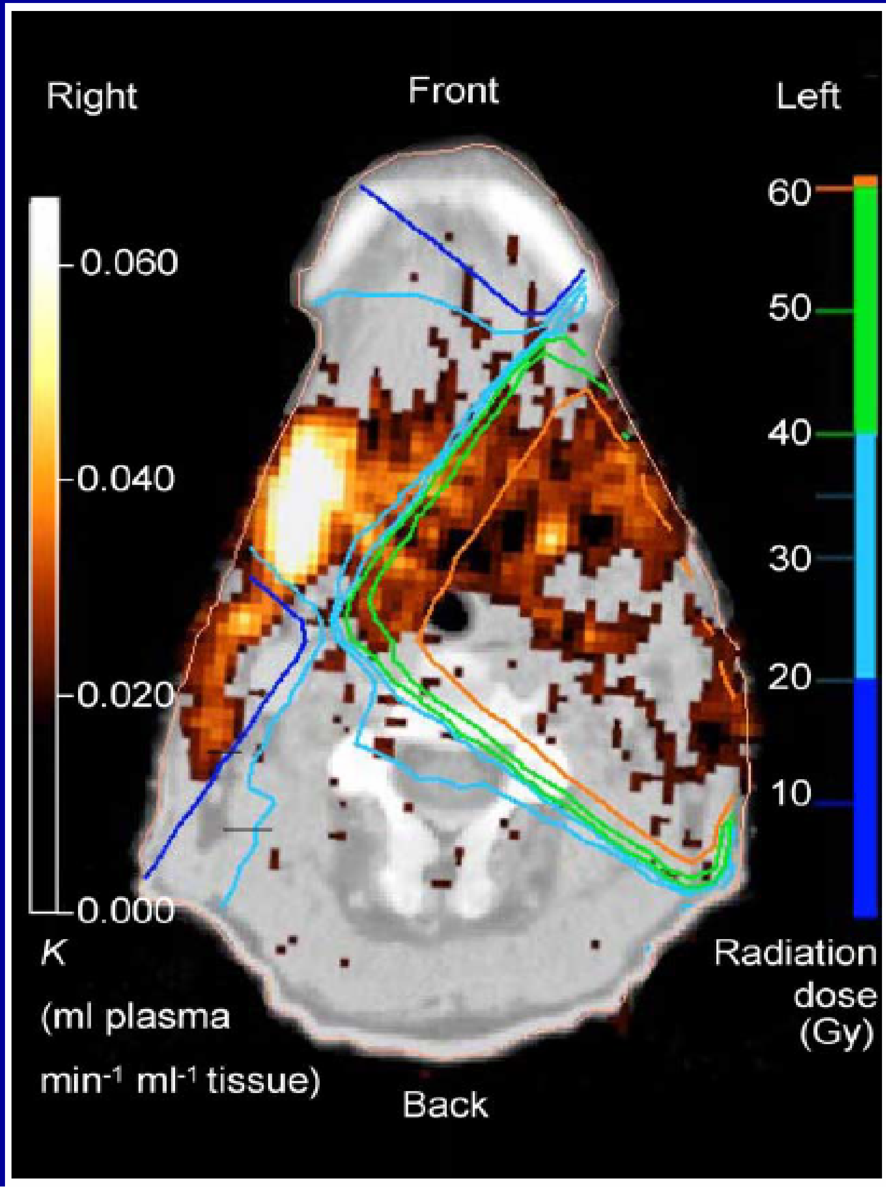
- **a) Volume of distribution of 11C-methionine**
- **b) K, the net metabolic clearance of 11C-methionine**

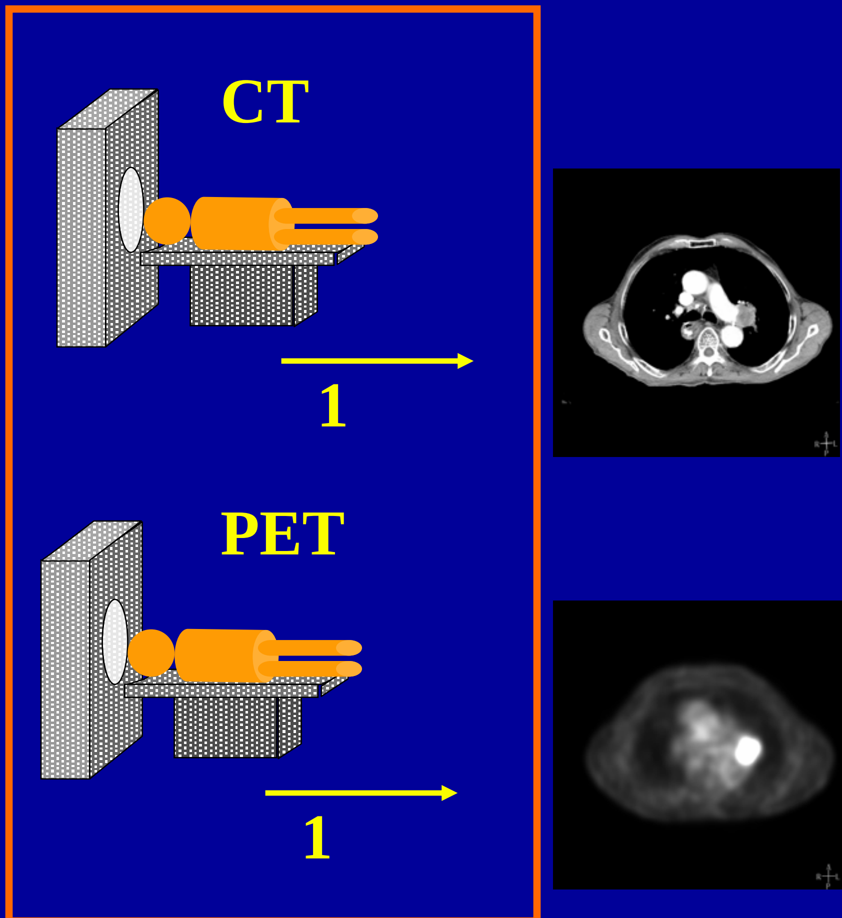
Buus et al, Radiotherapy and Oncology 73:289-296, (2004).

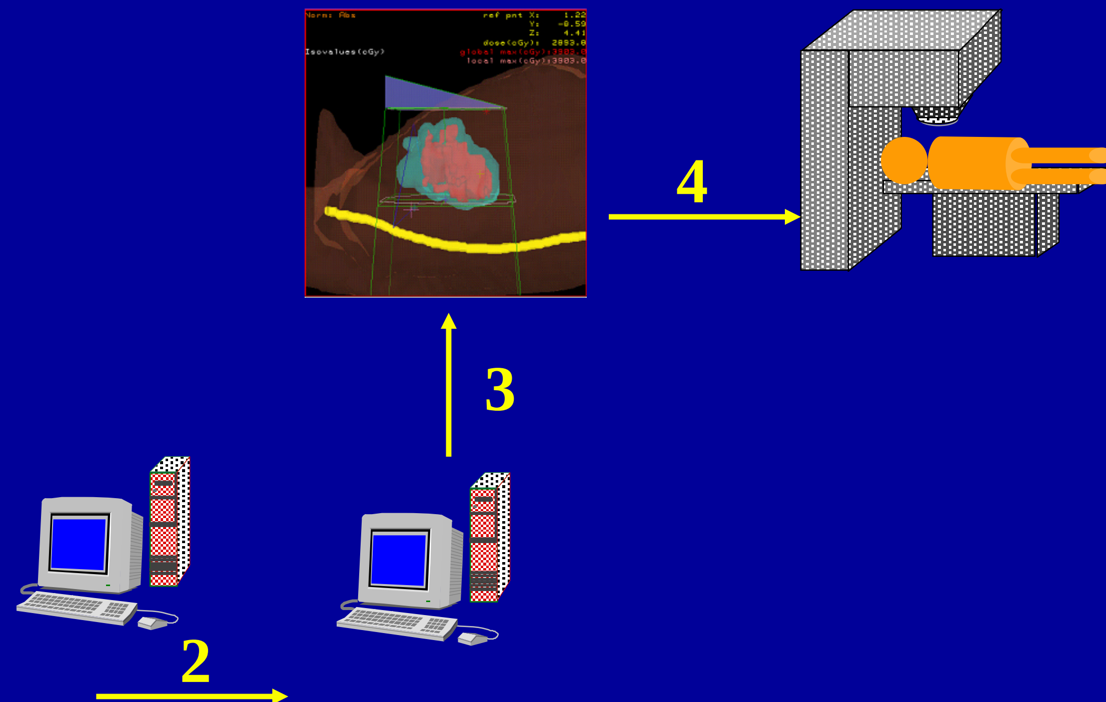
11C-methionine PET
measuring regional salivary gland function



Buus et al, Radiotherapy and Oncology 73:289-296, (2004).

RT Treatment Planning with PET/SPECT





These can be separate units or a combined CT/PET or CT/SPECT machine

- Setup reproducibility the primary concern
- Poor setup reproducibility may require deformable image registration

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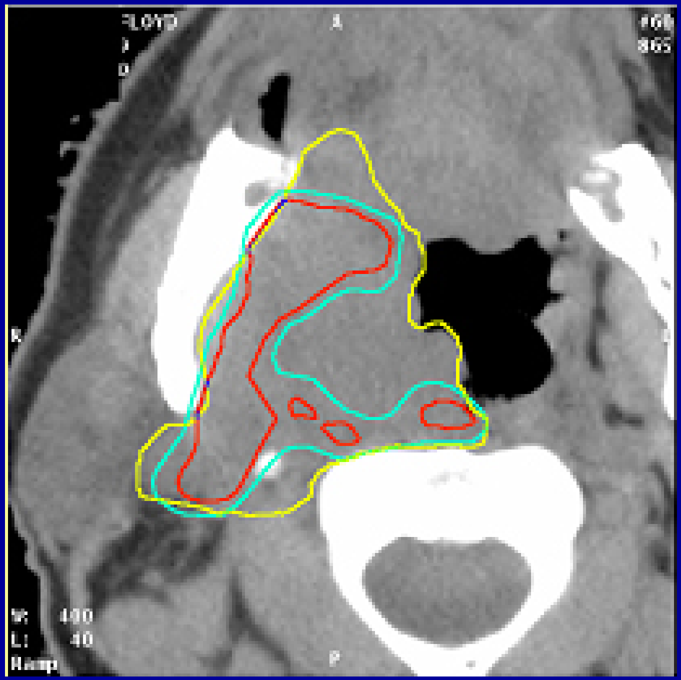
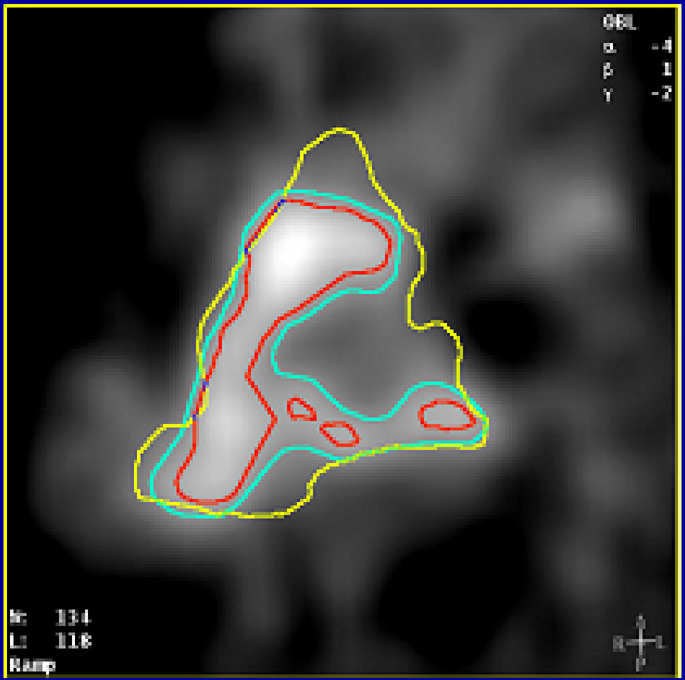
Fusion/Image Registration

- Lack of anatomical definition makes a registration with CT image a necessity
- Due to the same lack of anatomical definition, CT and PET or SPECT study registration is somewhat challenging
- Combined scanners can simplify the process





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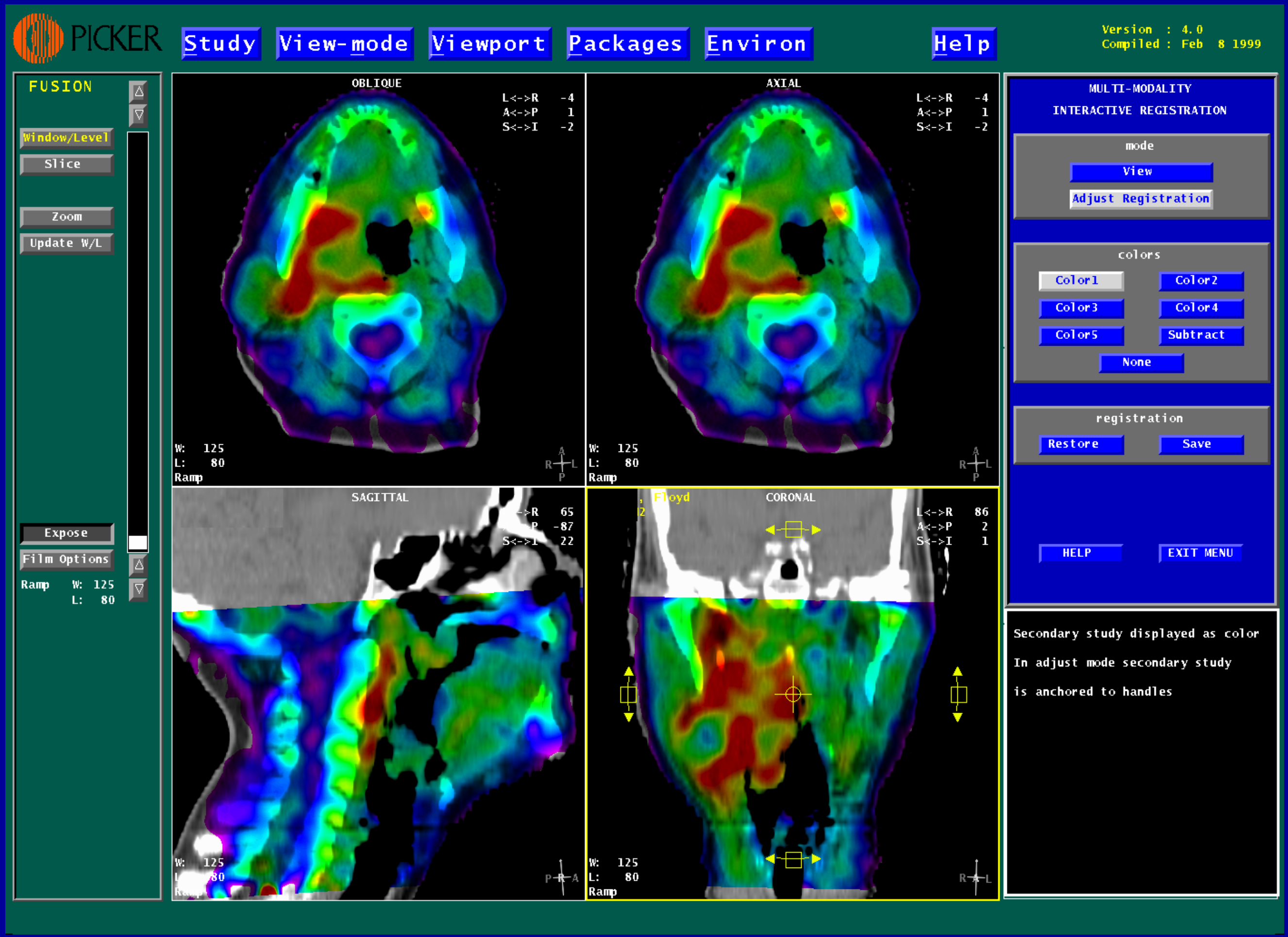
Multimodality Image Registration

- Registration Techniques:
  - Surface-based Registration
    - » Internal
    - » External
  - Image-based Registration
  - Point-based Registration
  - Automatic and semiautomatic computer assisted methods



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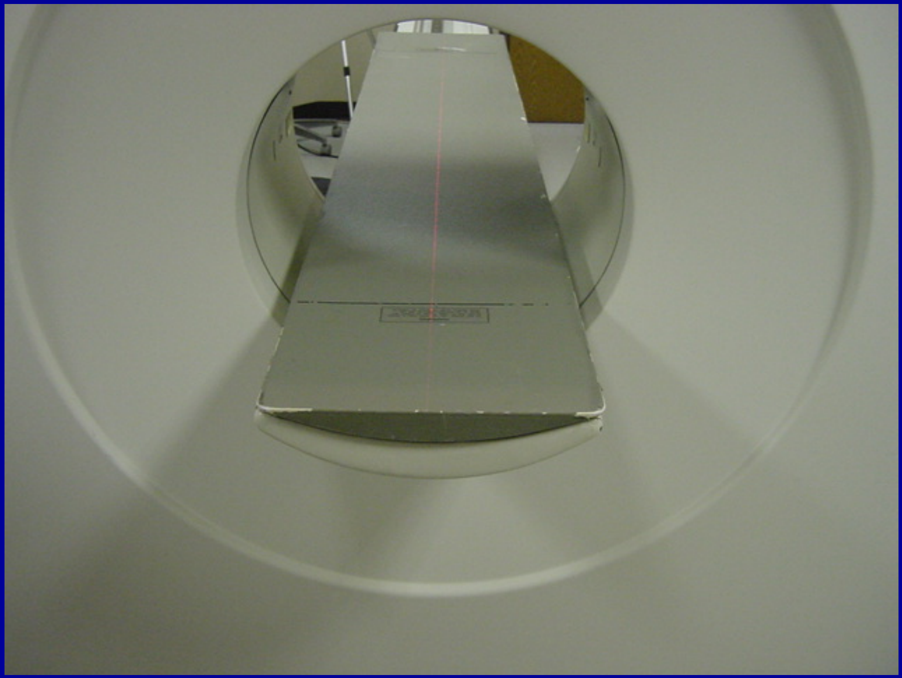
Patient positioning and immobilization



Flat Tabletop

Immobilization Device

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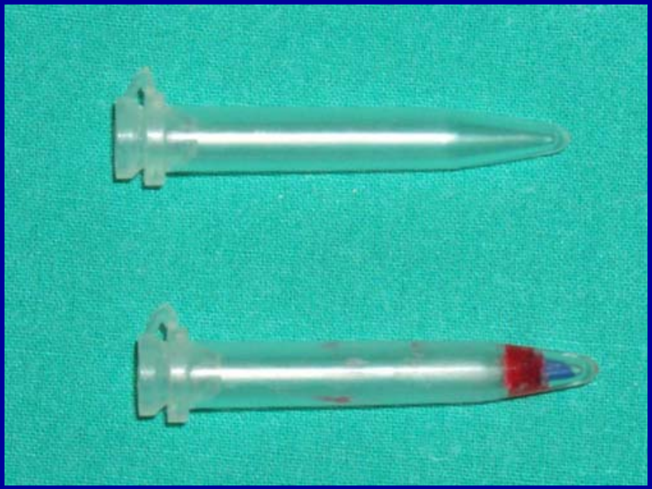
Fiducial Markers

- 0.5 cm diameter, 3.5 cm long, 0.25 ml, plastic, disposable microcentrifuge tubes
- VWRbrand Disposable Microcentrifuge Tubes, VWR Scientific Products, West Chester, PA
- CT, MR, and PET compatible
  - CT - Aluminum
  - MR - 4 mM $CuNO_3$
  - PET - ^{18}F-deoxyglucose
  - SPECT - 1 µCi of Tc-99M SC



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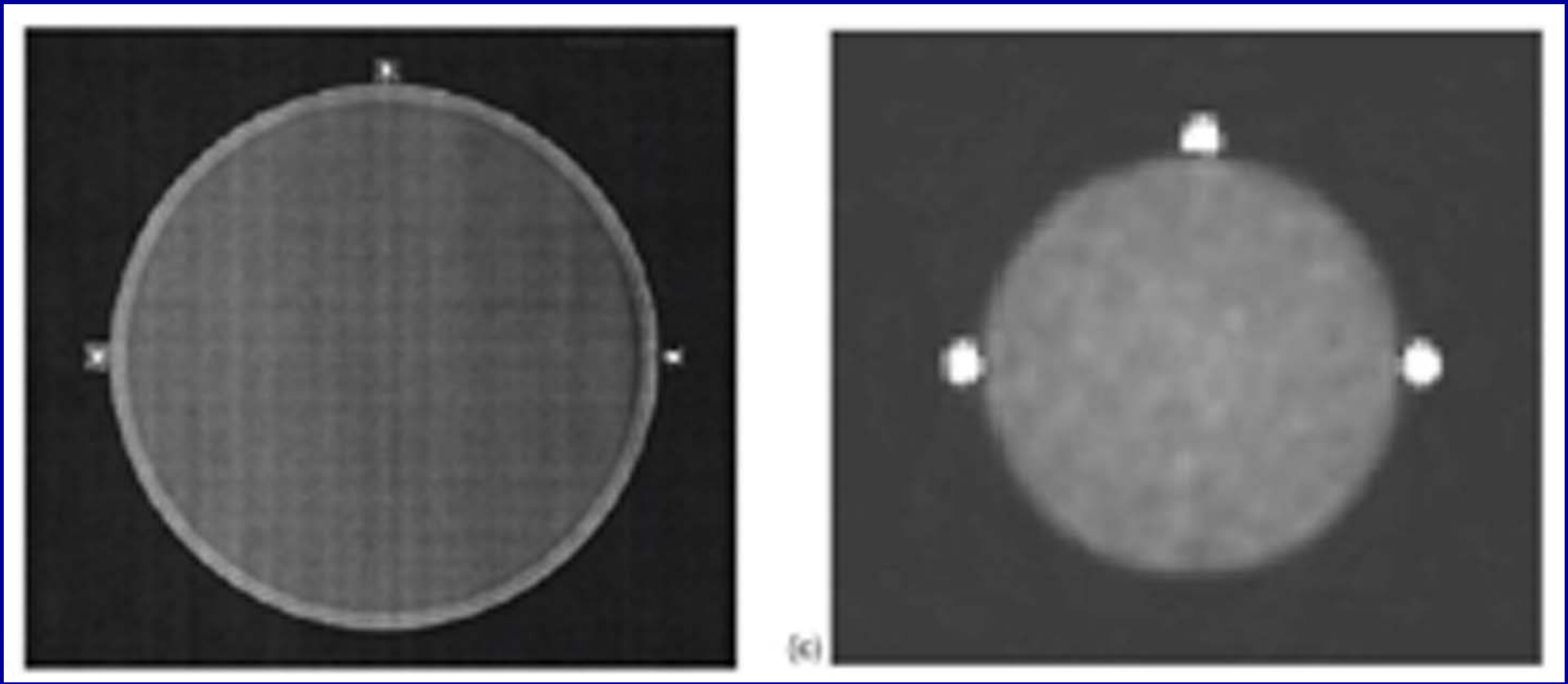
Fiducial Markers

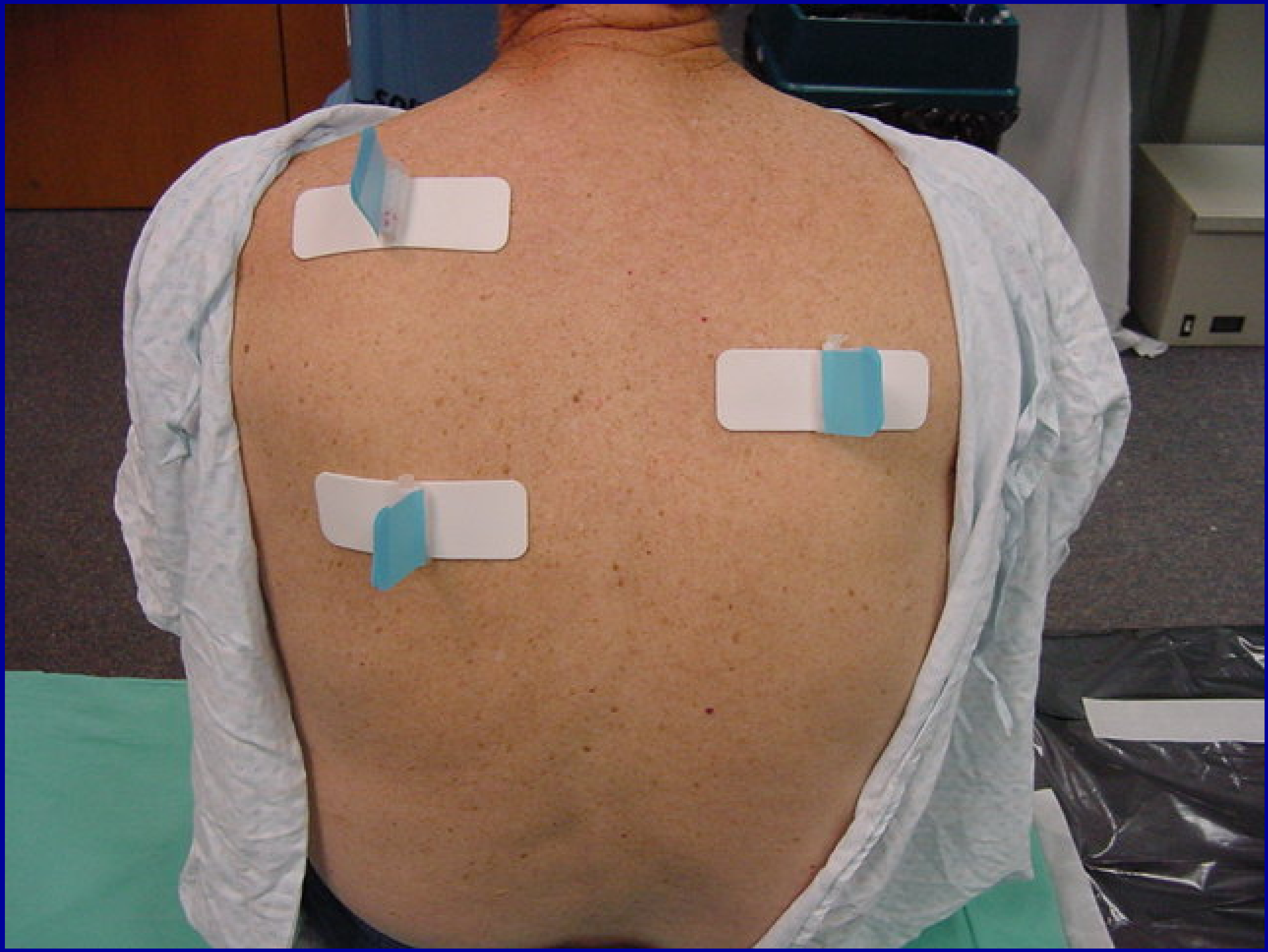
- CT/PET compatible metallic copper markers
- Cu-64



Robinson et al, Med Phys 31 (2004) 2520-2526

Fiducial Markers

- **For face mask patients, markers are attached to the mask**
- **For body mould patients, markers are attached to the skin**



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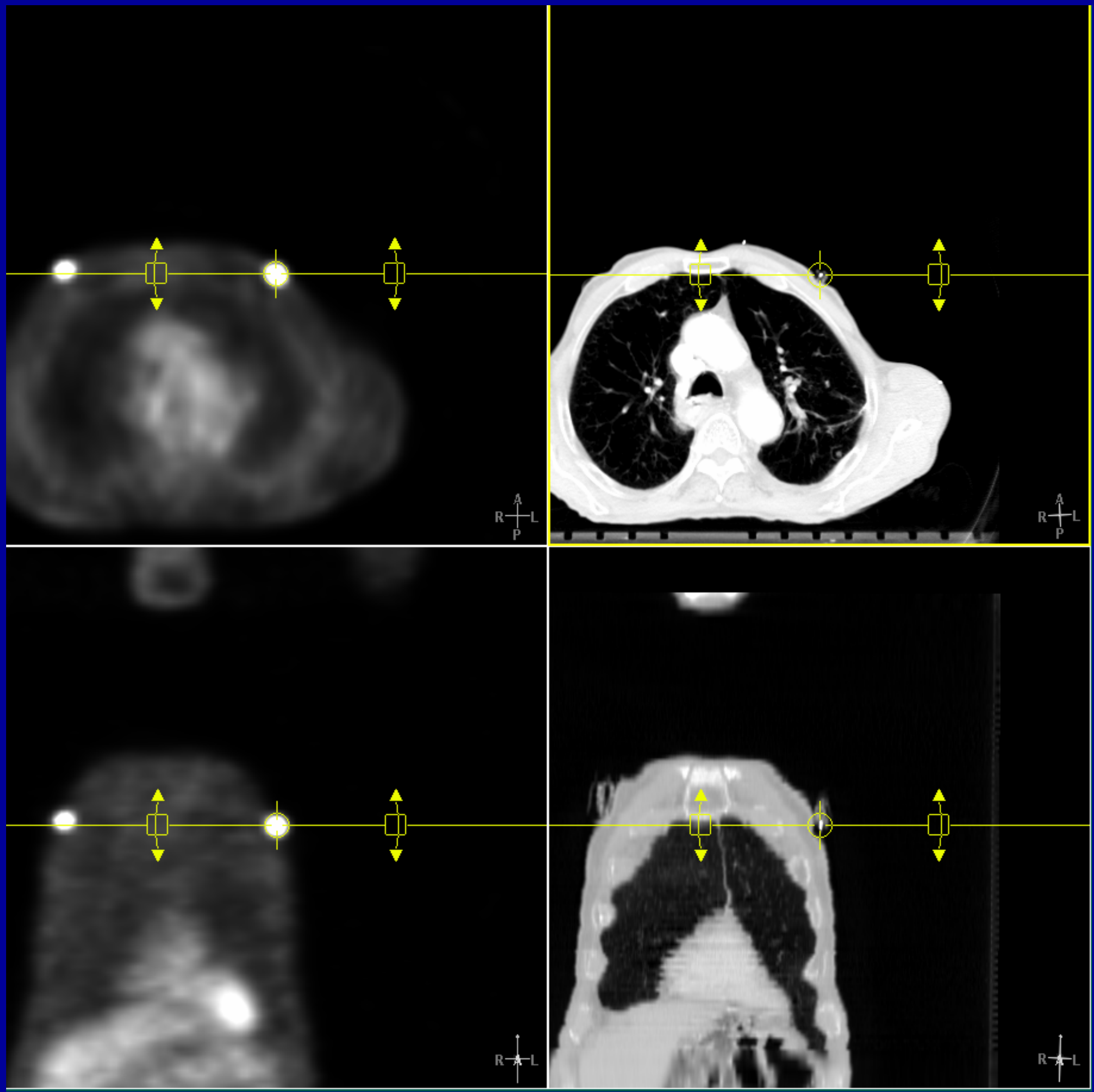
Fiducial Markers



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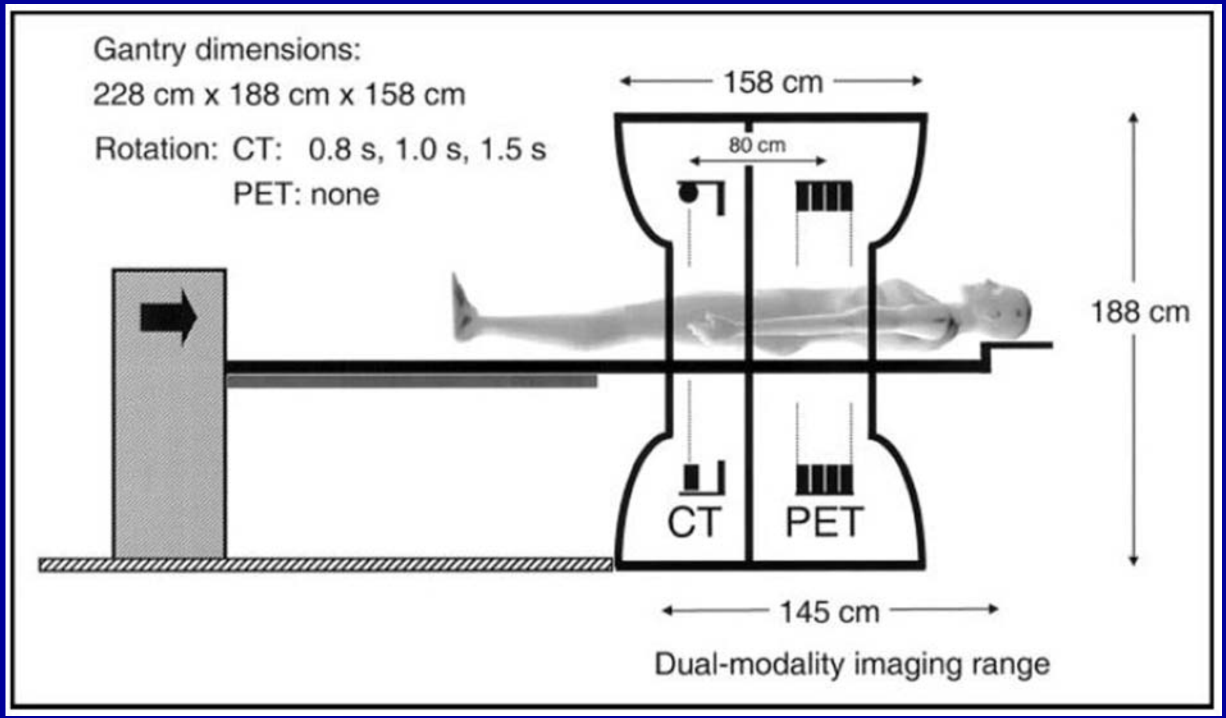
PET/CT scanner combined unit

- **Multislice CT scanner mated to a PET scanner**
- **Possibly three scans acquired during procedure**
  - **Attenuation correction CT**
  - **PET**
  - **Treatment planning CT, with contrast if necessary**



PET/CT Scanner

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SPECT/CT Scanner

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PET/CT scanner combined unit
Patient Motion

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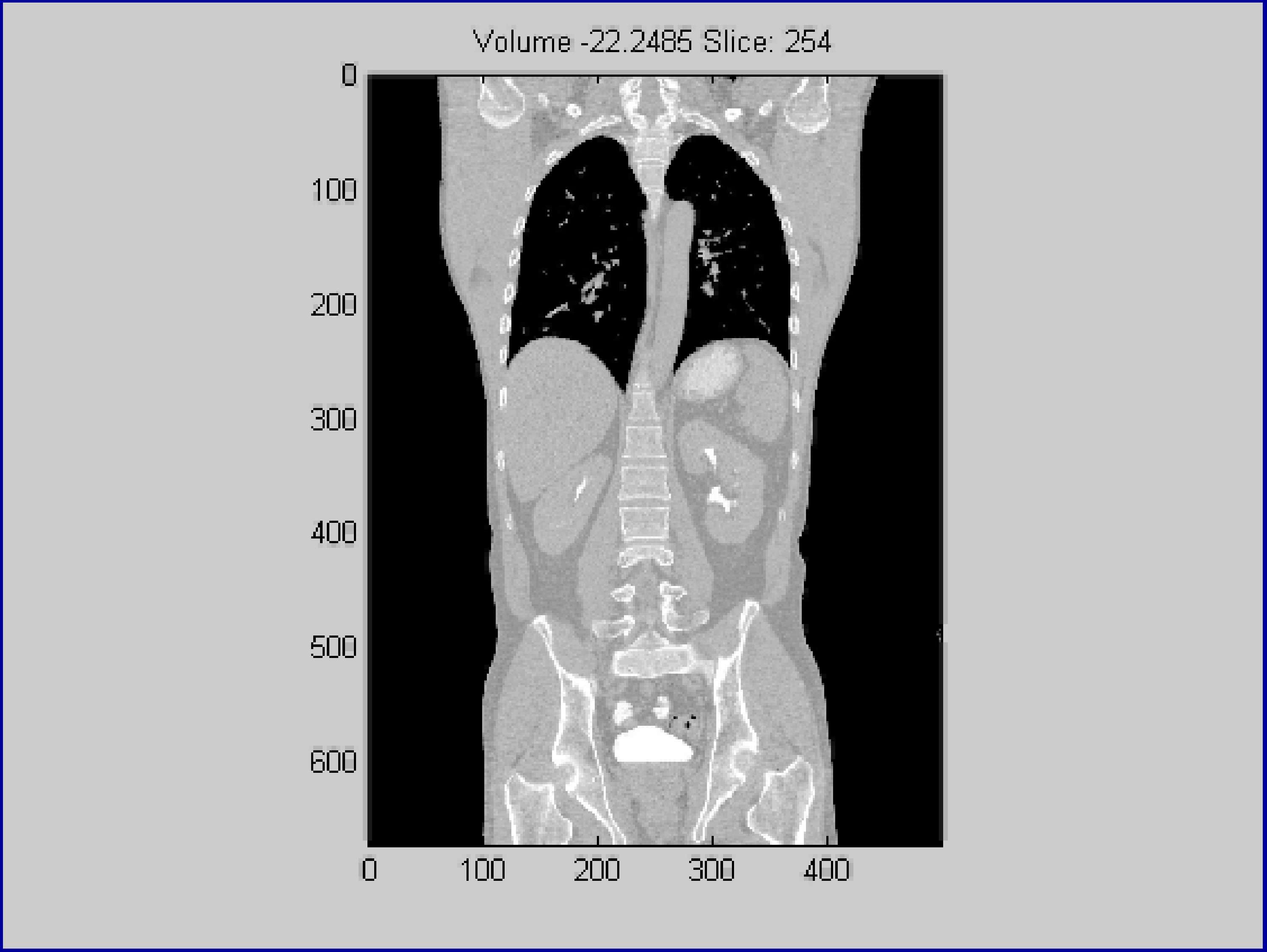
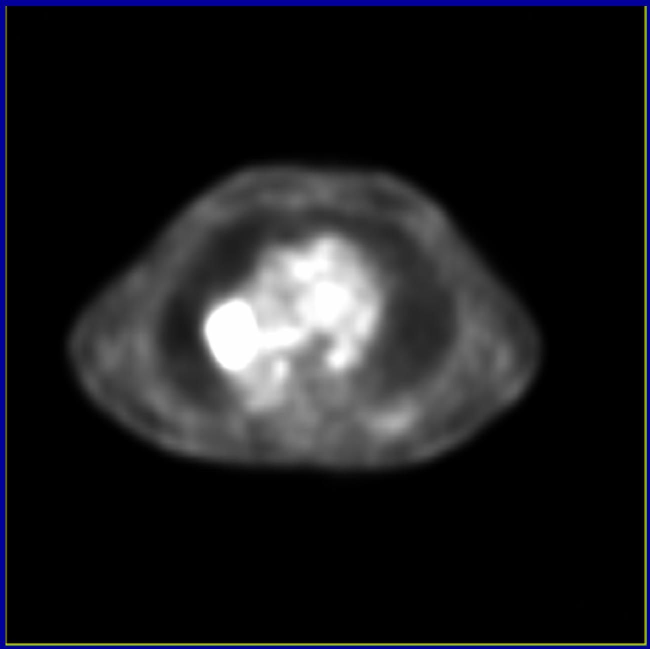
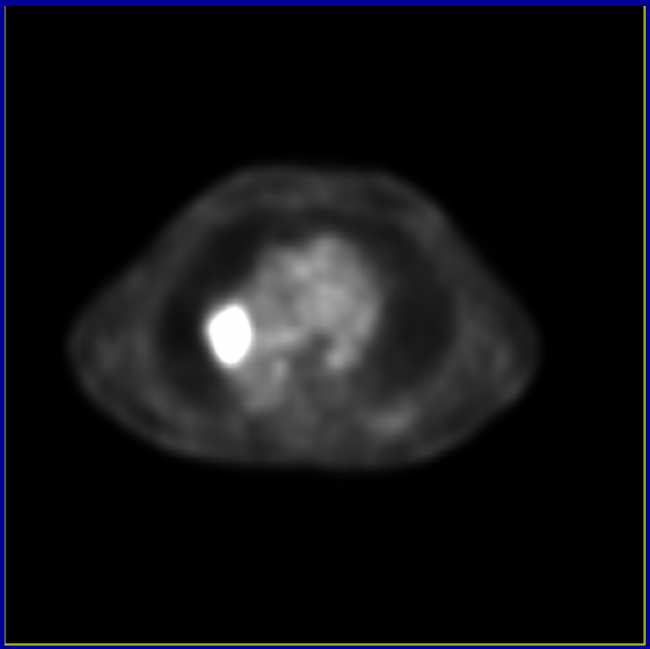
Patient Motion



RT Treatment Planning with PET
TARGET DEFINITION





- Depending on image window and level setting, target volume can easily change by 50%

- SUV not a part of DICOM data
- SUV utility unclear

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Conclusions

- The role of nuclear medicine imaging in radiation therapy and its impact needs further evaluation
- For several treatment sites it has already been shown that PET studies have a strong potential to improve staging, outcome prognosis, therapy selection, treatment planning, and follow-up
- Understanding PET and SPECT limitations is imperative for implementation in the treatment planning process
- The combined PET/CT and SPECT/CT scanner will simplify the treatment planning process

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