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In Memoriam
Acad. Prof. Matey Mateev

Target Definition and Target Tracking in Radiation Therapy – Resolved and Unresolved Problems

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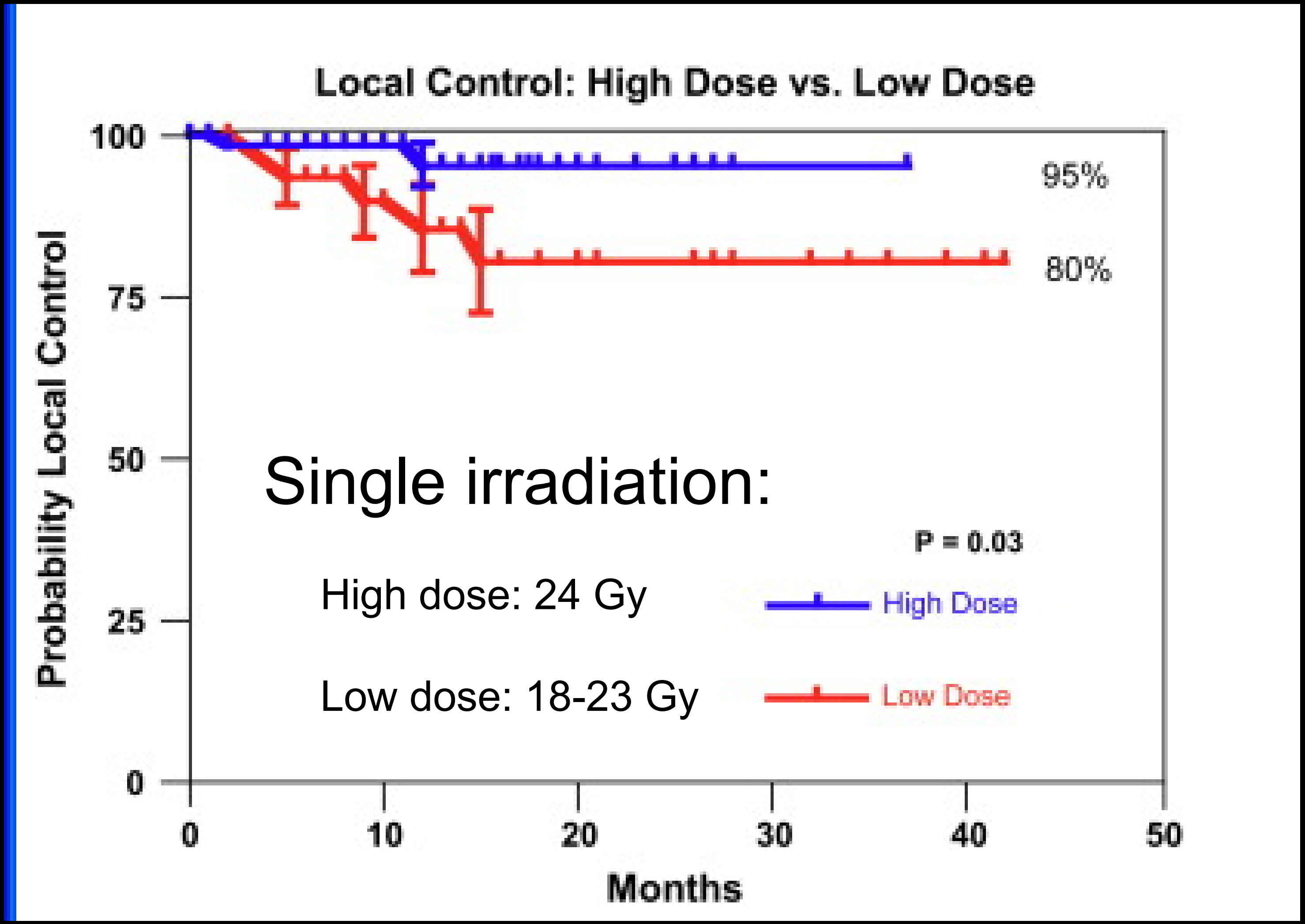
Introduction: A significant dose response has been observed in high dose single-fraction treatments

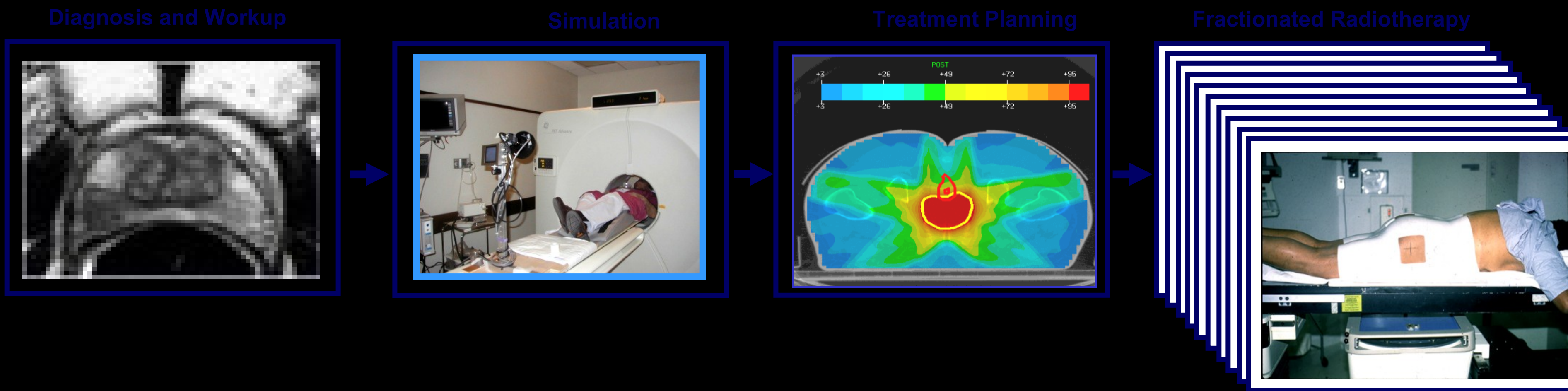
Radiographic Local Control



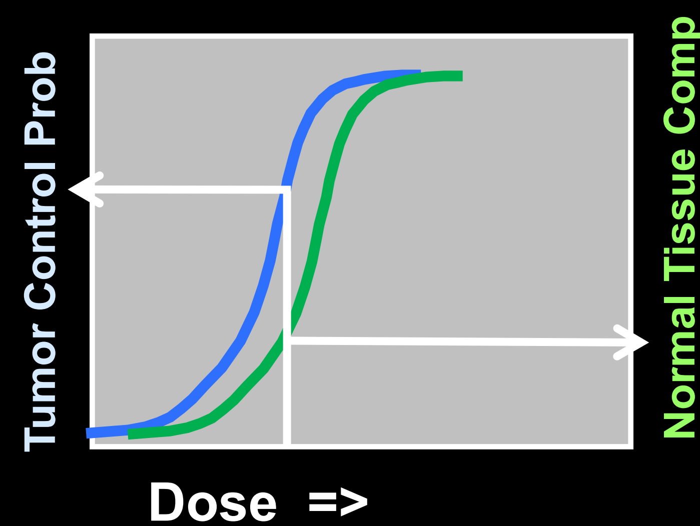
Courtesy M. Lovelock

Yamada et al IJROBP 71(2) 2008 p 484-90

How fast should the dose be delivered, or in how many fractions: 1, 3, … 36 ?

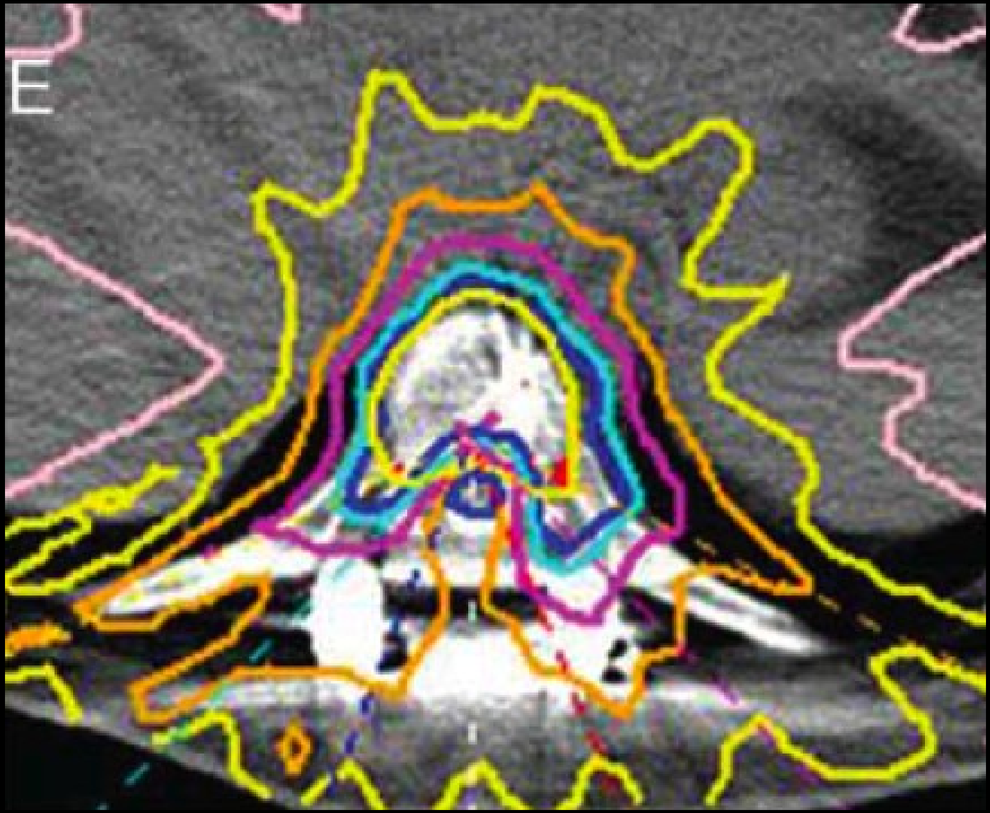


- At the low dose range normal tissues repair radiation damage more proficiently than tumors
- Fractionated radiation enables tumor dose buildup with reduced normal tissue toxicity
- For Hypo- or Single- Fraction the Normal Tissue Complication Curve will move left
- Need to pull the two curves apart



Courtesy M. Lovelock

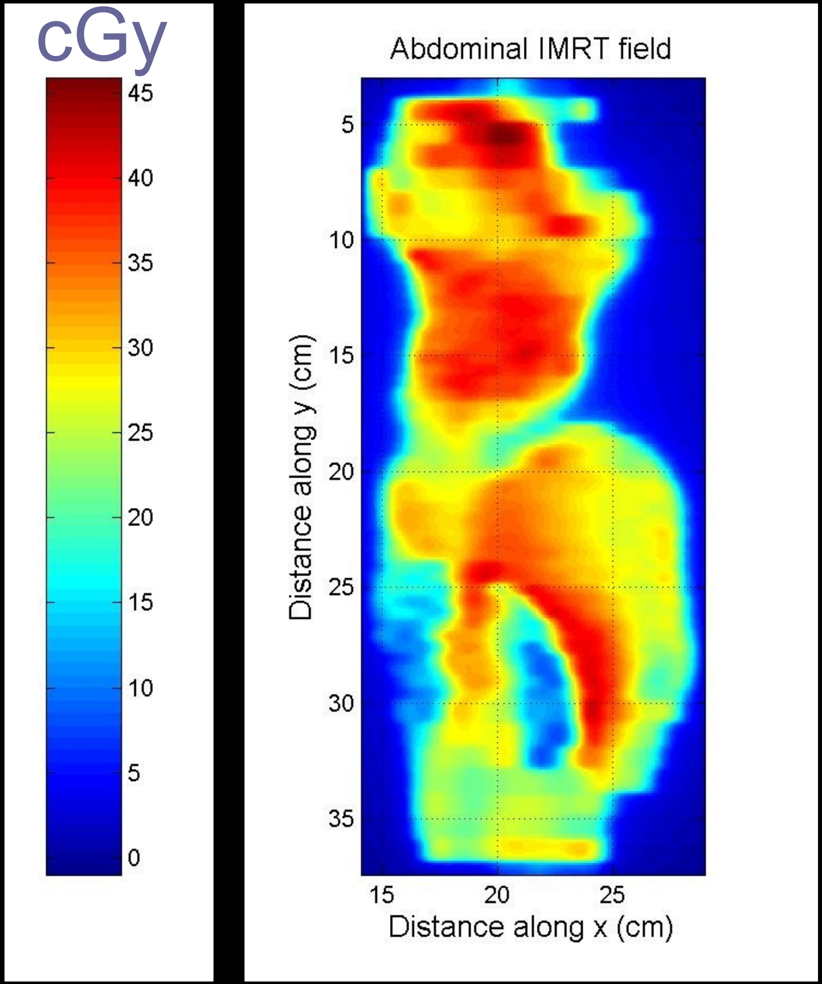
What is required to deliver such high doses in a single fraction?



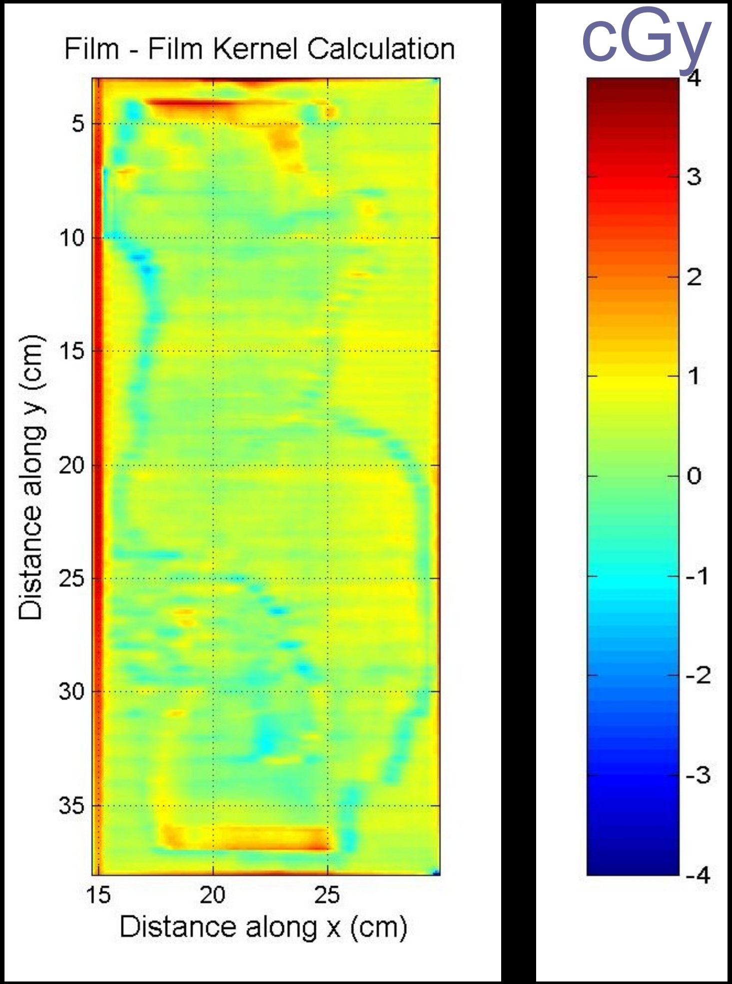
- Accurate target definition
- High treatment delivery accuracy
  - Dosimetric – under 3 %
  - Spatial
    - stationary tumors < 1 mm

Courtesy M. Lovelock

High Dose Delivery Accuracy using Intensity Modulated Radiation therapy



Film dose



Film – calculation

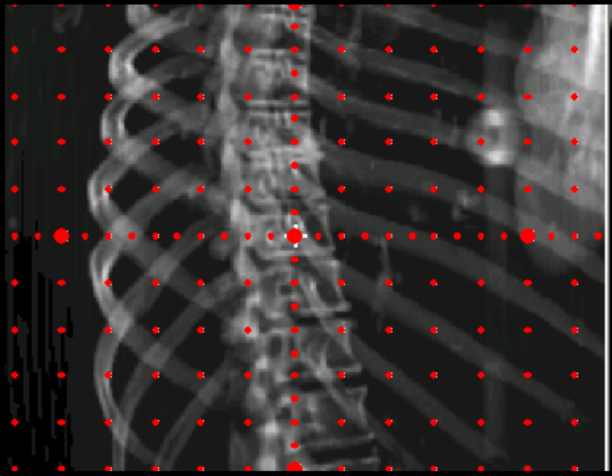
Med. Phys. 2006

Patient set-up and positioning using planar imaging

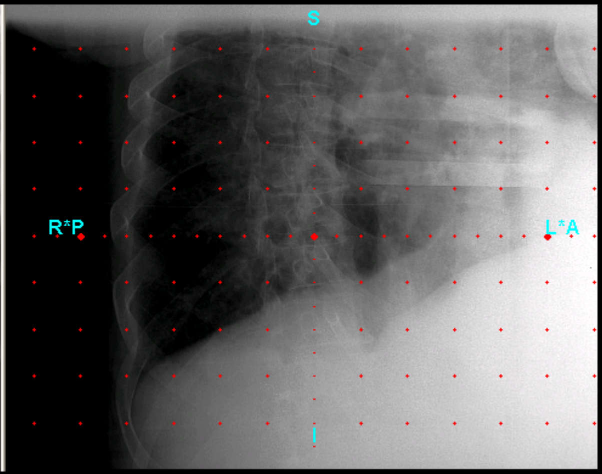
Electronic portal imaging, kV radiographs

- effective at correcting setup error (positioning of skeletal anatomy)
- Poor visualization of soft tissue
- Projection of anatomy onto a planar image: difficult to discriminate different structures

Varian kV imaging system



DRR



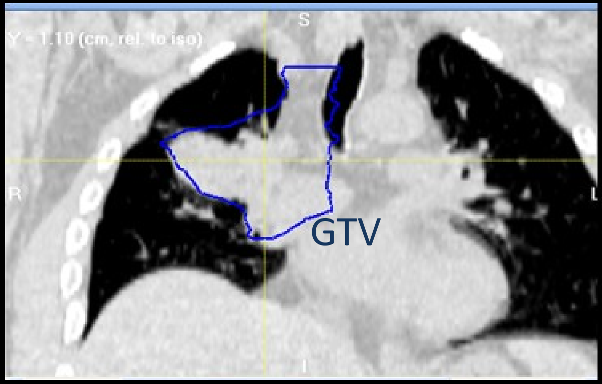
kV radiograph

Courtesy G. Mageras

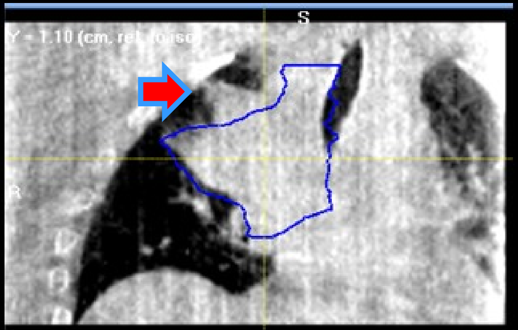
Tumor tracking between simulation and treatment

CBCT reveals tumor changes not seen in radiographs

Pt 1
Tumor growth

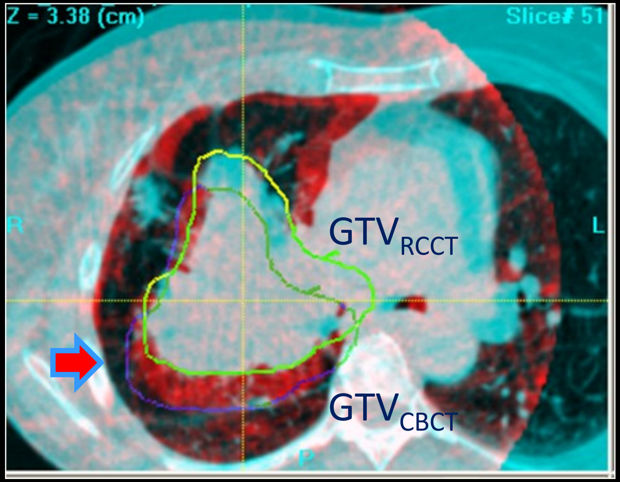


RCCT (End exp.)



Tx #1 CBCT – 19 days later

Pt 7
Shift in tumor position



Tx #1 CBCT – 12 days late

10/13/2010
(Santoro astro 2010)

Courtesy G. Mageras

Patient and target tracking during treatment

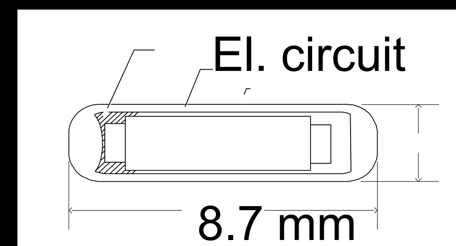
Infrared or Optical monitoring system

Marker Locations

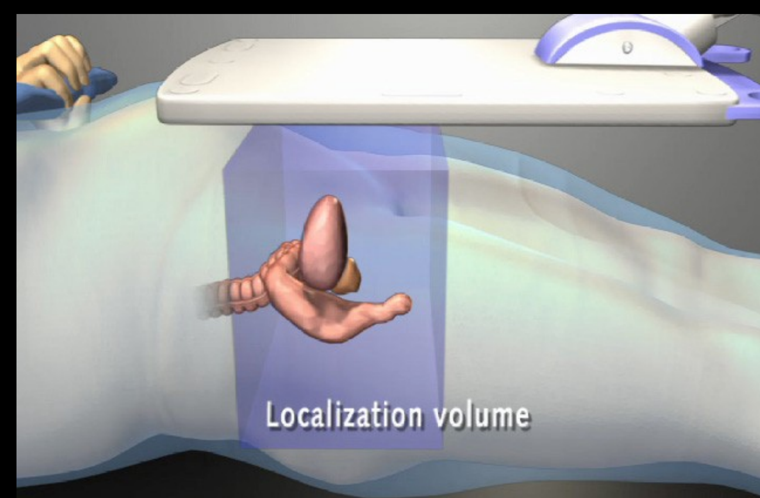
- Left chest
- Right chest
- Belly

Internal Markers Tracking

Calypso

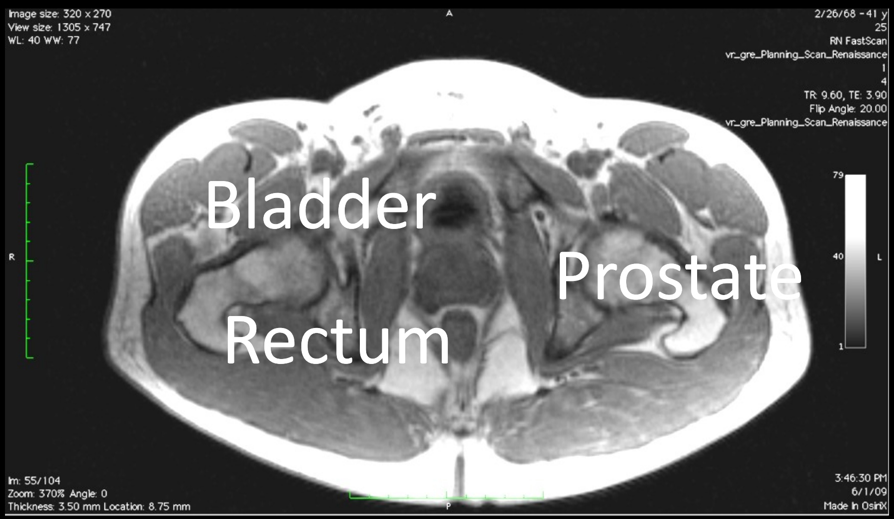


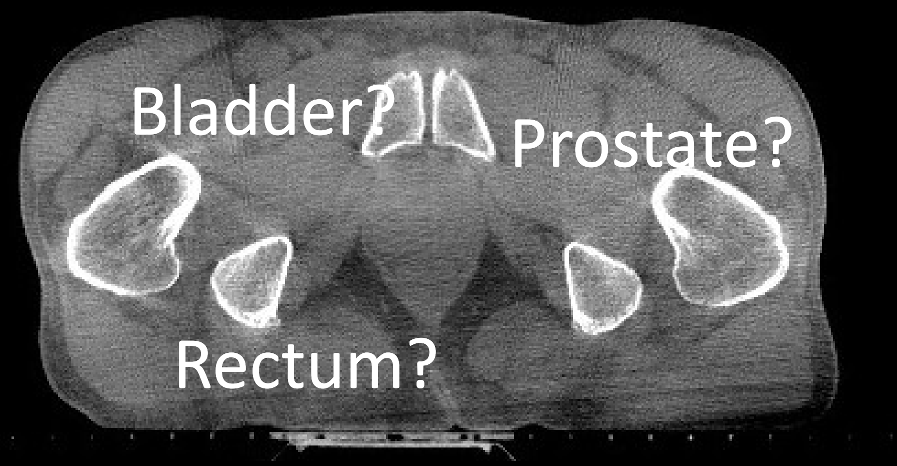
1.85 mm



Set-up and tracking

To Treat Better you need to See Better





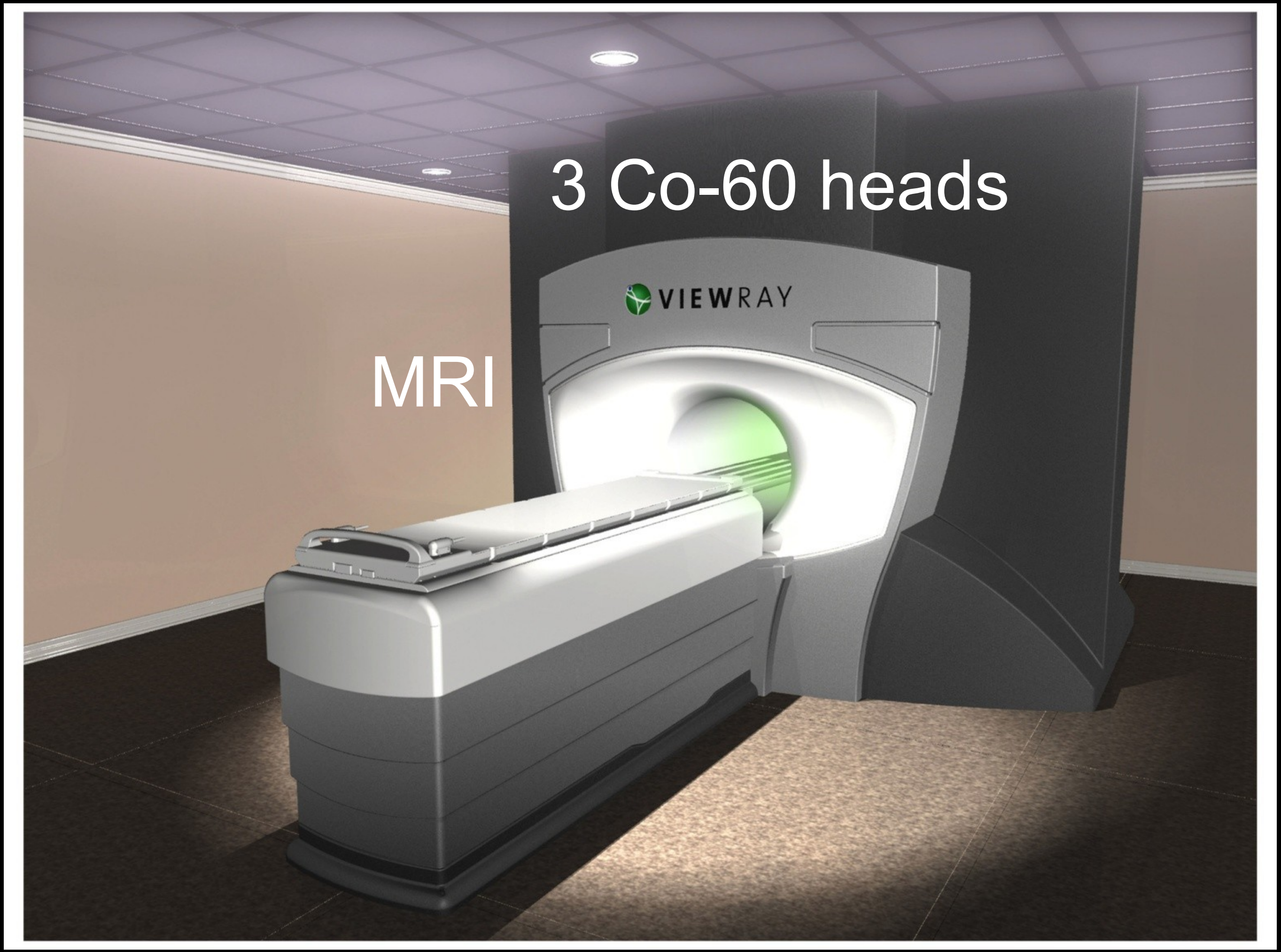
Cone Beam CT

Courtesy J Dempsey, ViewRay Inc.

The ViewRay system has not been cleared by the U.S. Food and Drug Administration (FDA) for commercial distribution in the U.S.

Set-up and tracking using MRI

The ViewRay System

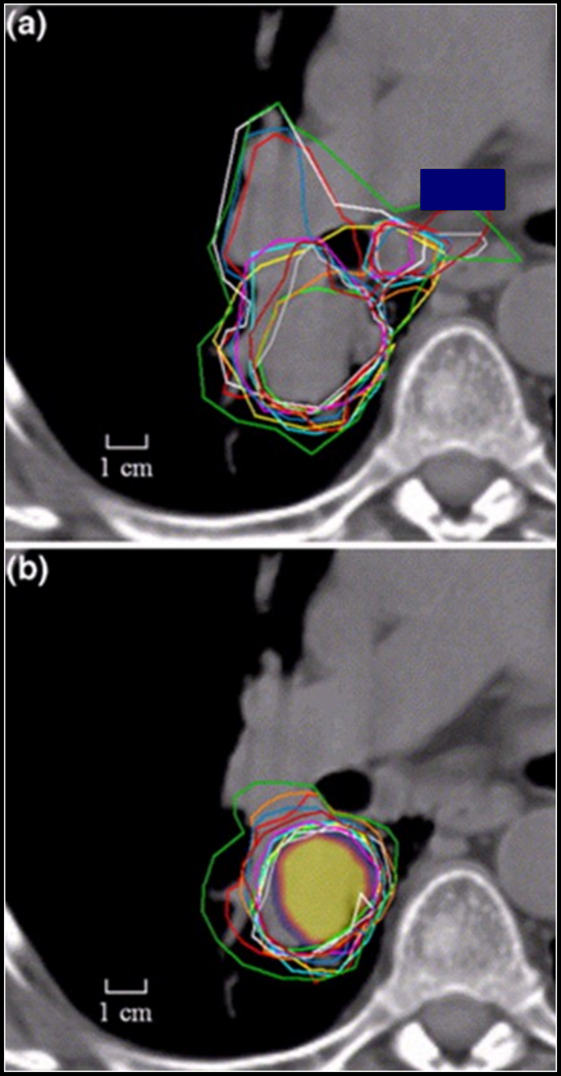


Courtesy J Dempsey, ViewRay Inc.

The ViewRay system has not been cleared by the U.S. Food and Drug Administration (FDA) for commercial distribution in the U.S.

Target Definition & Organ at Risk Delineation

- Large uncertainties based on CT alone:
  - Intra- & inter-observer variation, tumor/atelectasis, lymph nodes
- Use of FDG-PET to reduce, from 1cm SD to 0.4cm



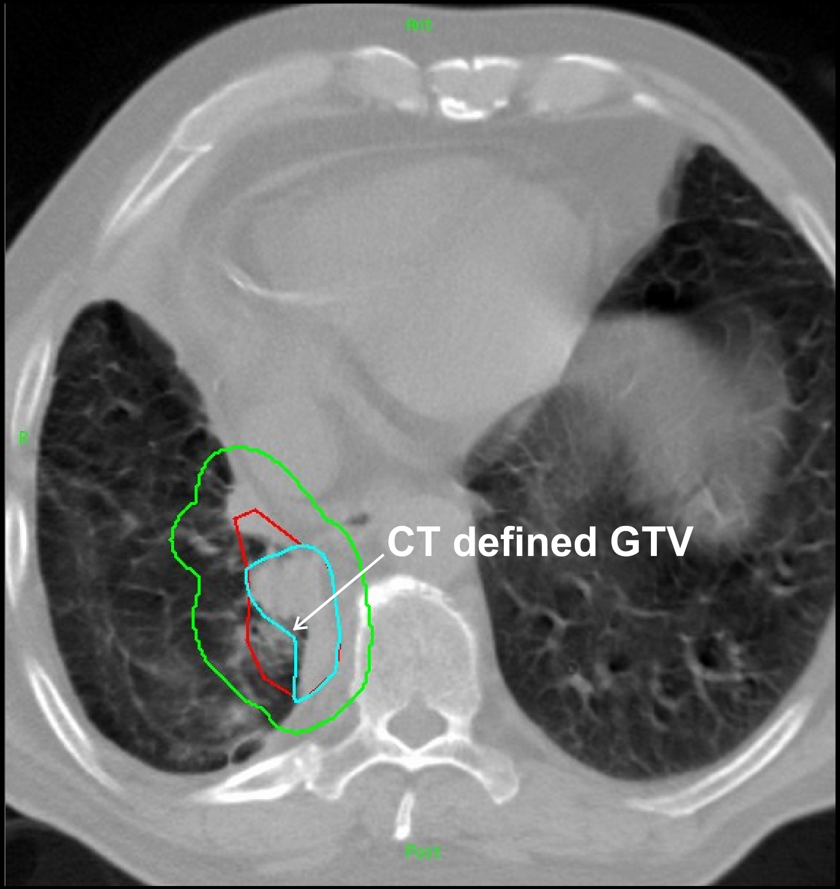
CT alone

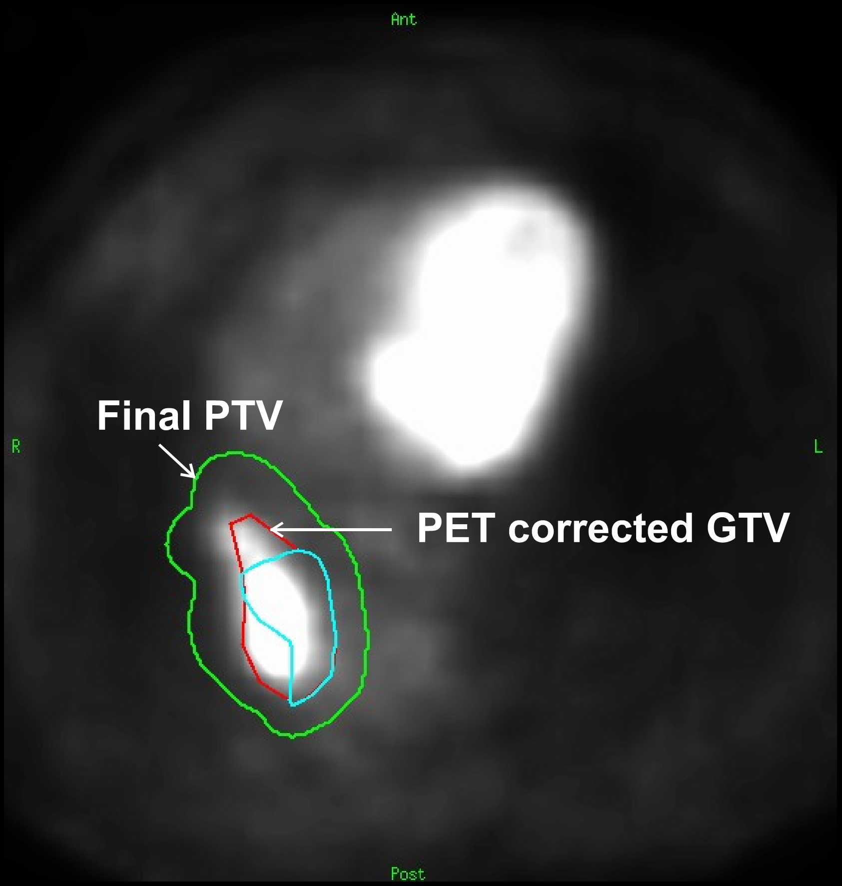
CT + PET

Courtesy G. Mageras

Steenbakkers, IJROBP ,2006

PET Modification of the GTV and Desired Accuracy

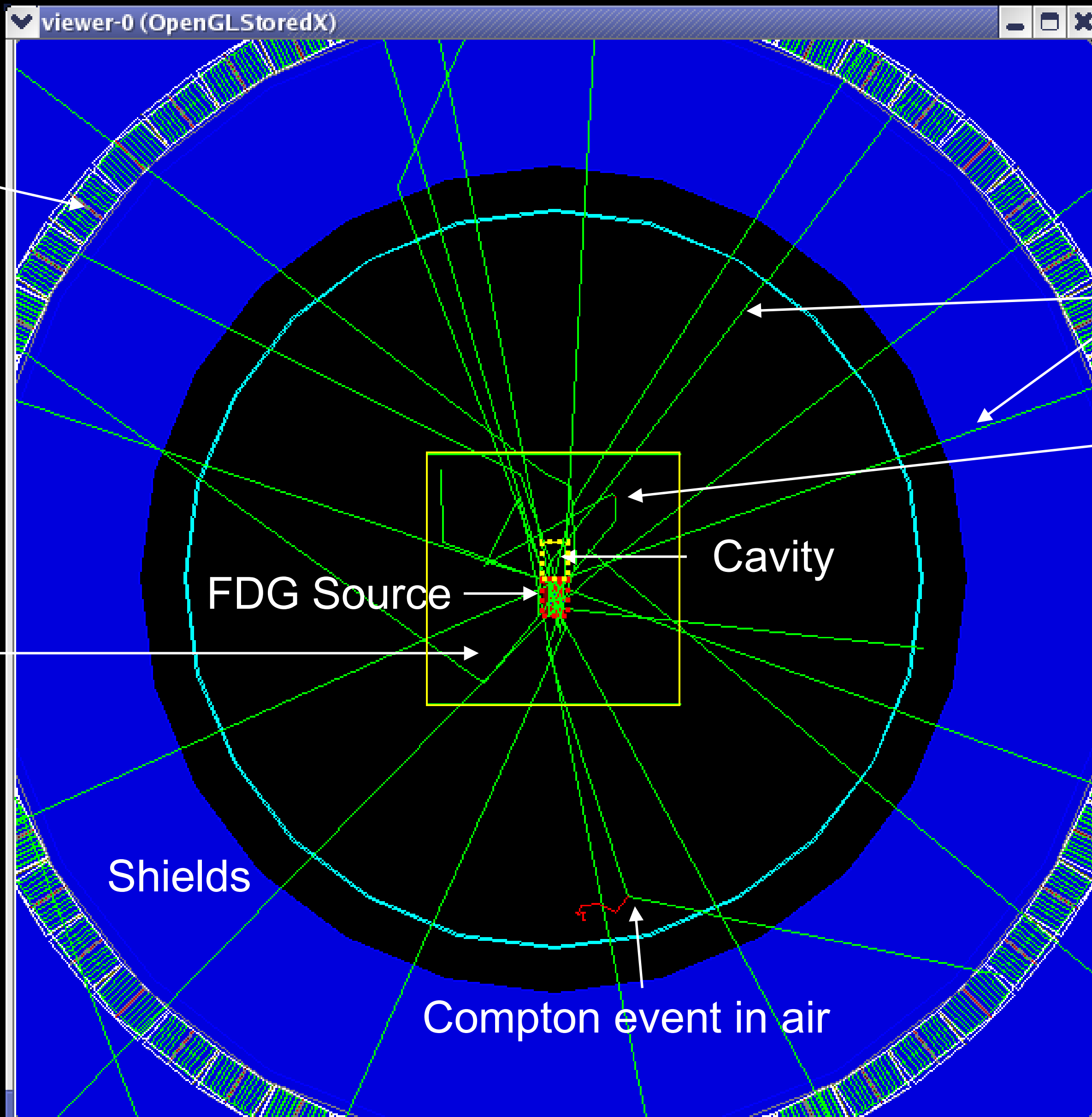




*NO ! Since PET **biological and the physical uncertainties** are not known !*

Can we trust the PET contour to ~ 1 mm accuracy ?

Monte Carlo simulation of annihilation photons propagating in a PET scanner



Simulated with the GATE Monte Carlo code

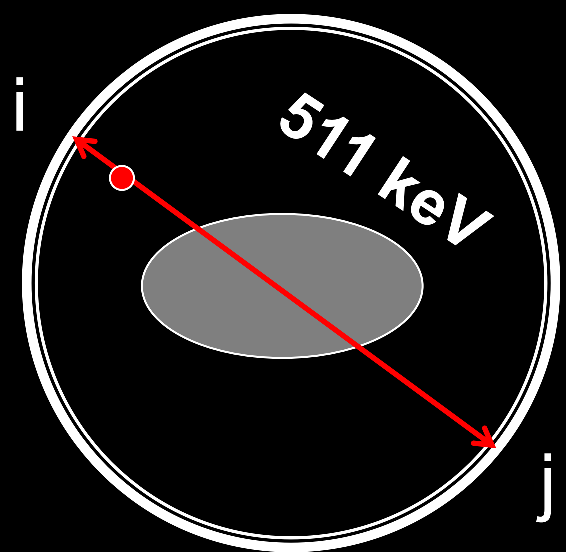
Attenuation Correction

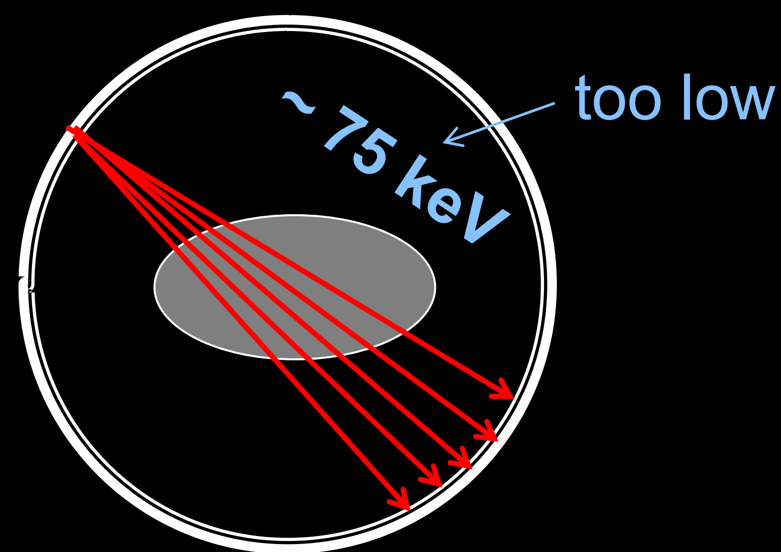
For each LOR (Line of Response) i-j:

$$A_{ij} = \ln\left\{\frac{Transmissi\quad on_{ij}^{with\_patient}}{Transmissi\quad on_{ij}^{no\_patient}}\right\}$$

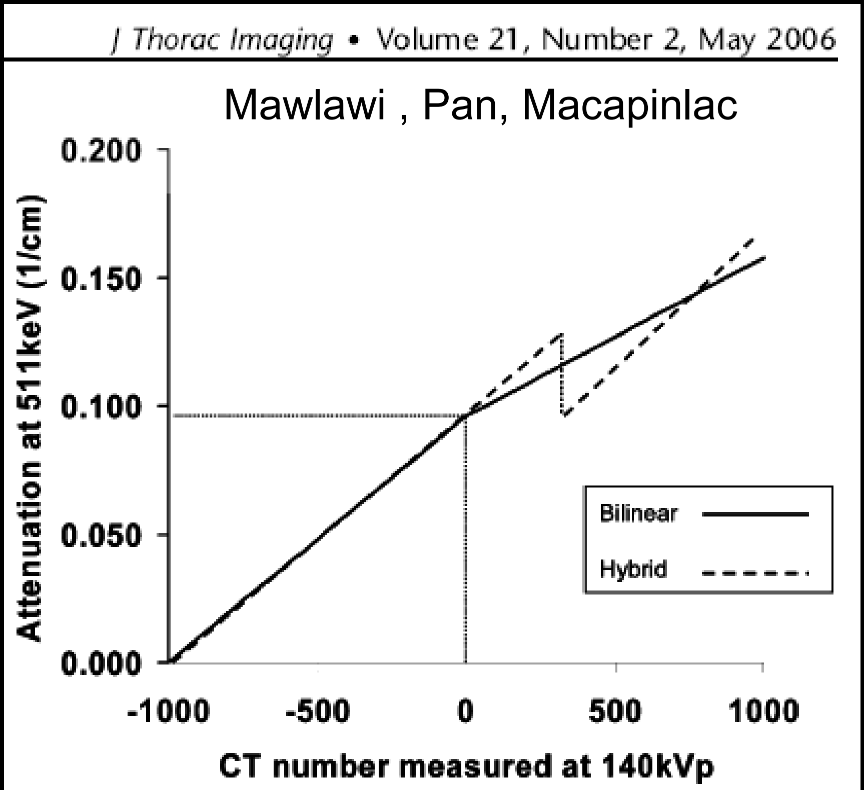
using

<u>Annihilation photons</u> or <u>CT –X-rays in PET/CT</u>





CT-based Attenuation Correction Challenge



Scaling Methods:

- Current Transforms:
  - Bi-linear, Tri-linear
  - Hybrid

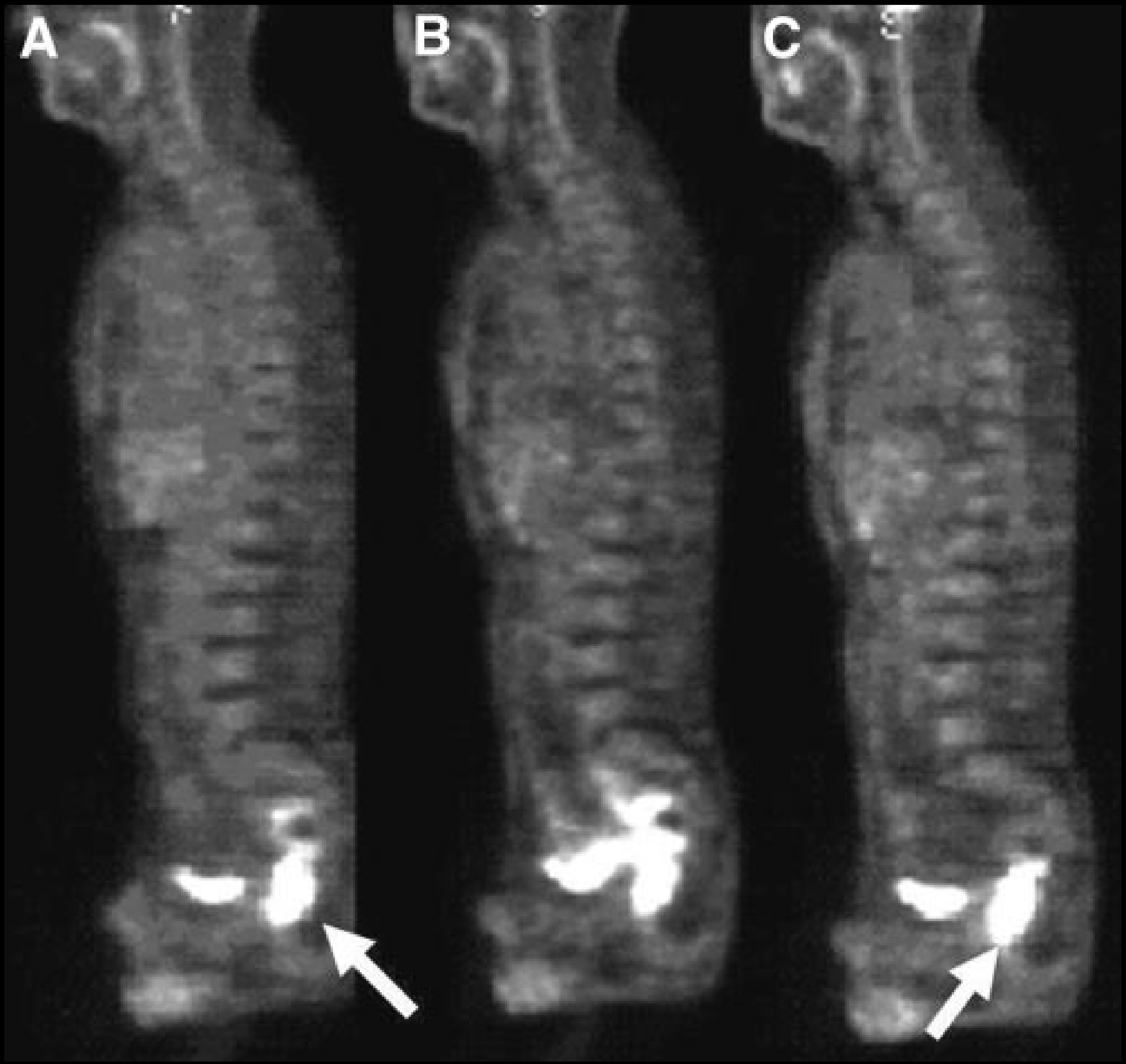
- Under investigation:
  - Dual Energy CT (Kinahan et al, 2006)
  - Energy sensitive CT

Illustration: basis for dual energy CT(Rehfeld *et al , Med. Phys.35,5,2008*)

$$\mu^{i}_{eff} = \sum_{Z,A} c_{Z,A}\left(\mu^{Compton}_{Z,A} + \mu^{Phtotoeffect}_{Z,A}\right)^{i} \approx \rho^{e}_{eff} K(E^{i}_{eff}) + a_{eff}(E^{i}_{eff})^{n}$$

where, i=1 (140kVp), 2 (80kVp), $a_{eff} \sim Z^m/A$, m= 3 to 4, n= - 3 to - 3.5

CT - based Attenuation Correction artifacts: Contrast



^{68}Ge

CT AC

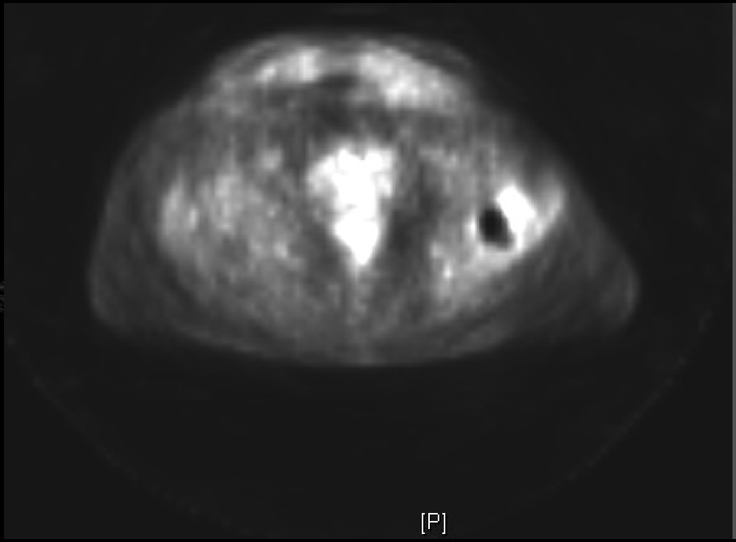
CT AC + Segmented Contrast Correction

Nehmeh *et. al., J. Nuc. Med. 44, 1940, 2003*

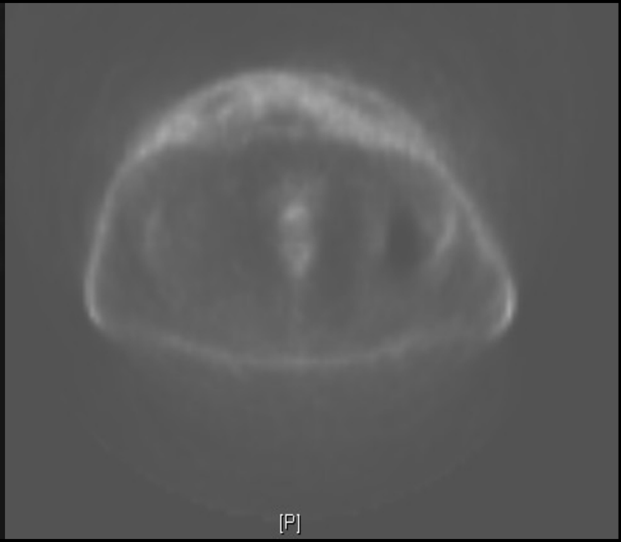
Example of CT -based Attenuation Correction Artifact: Leg prosthesis

CT

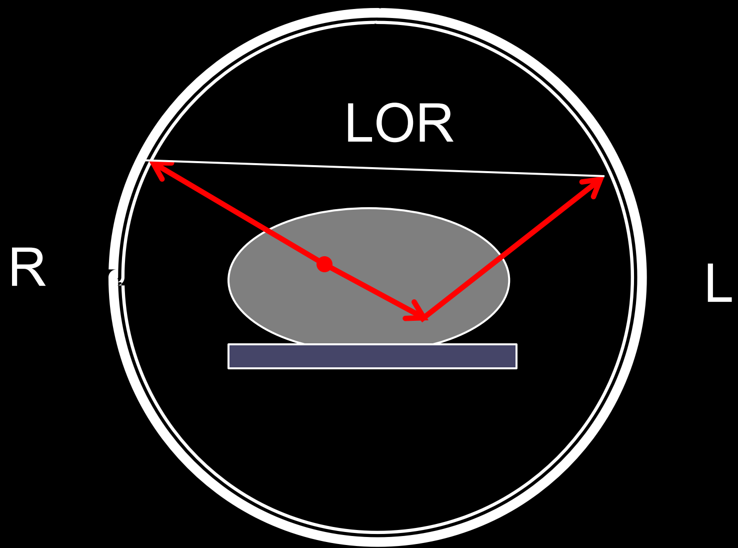
PET

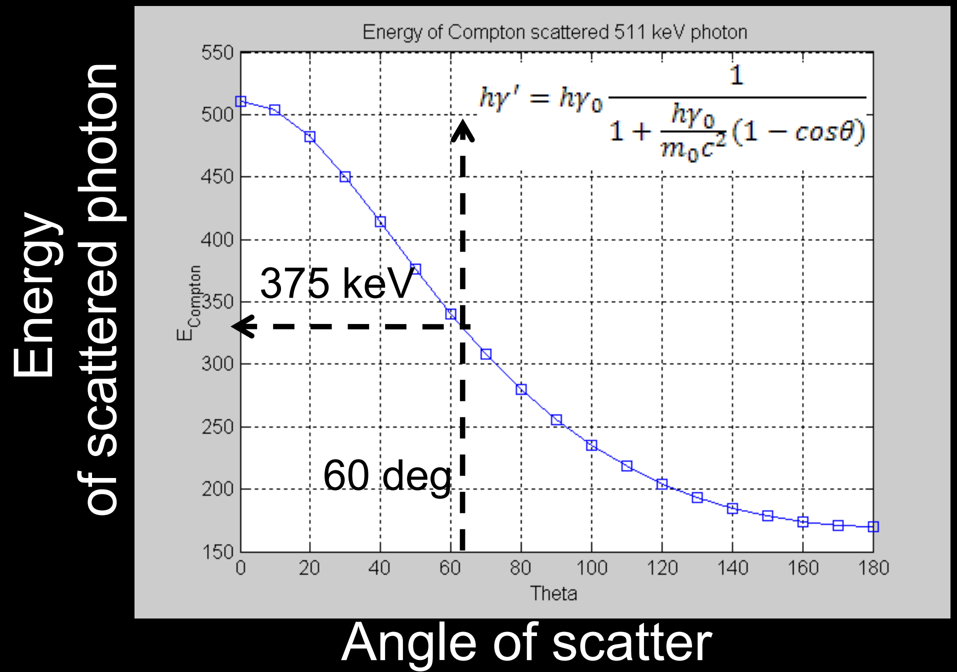


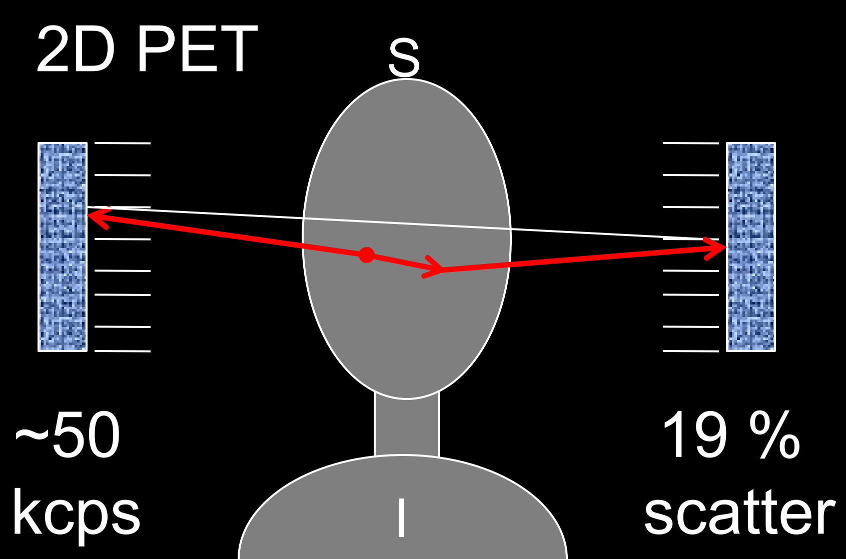
PET no AC

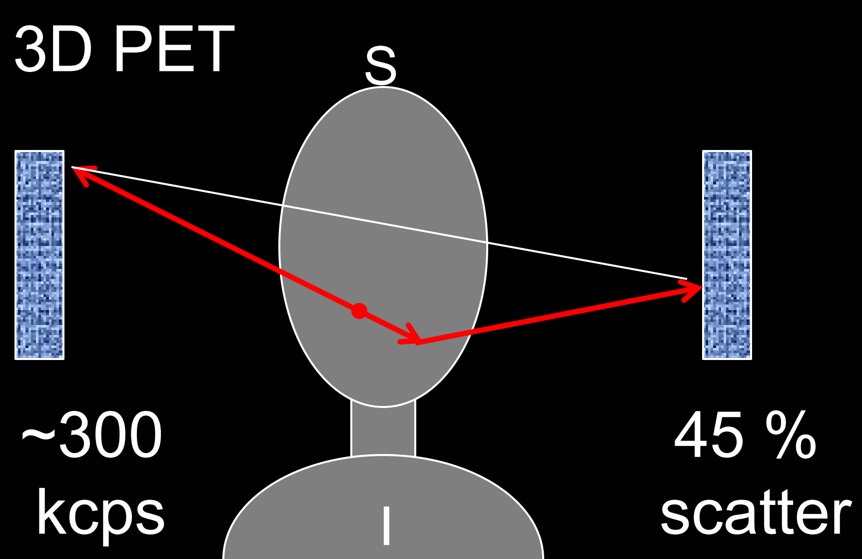


Photon scatter

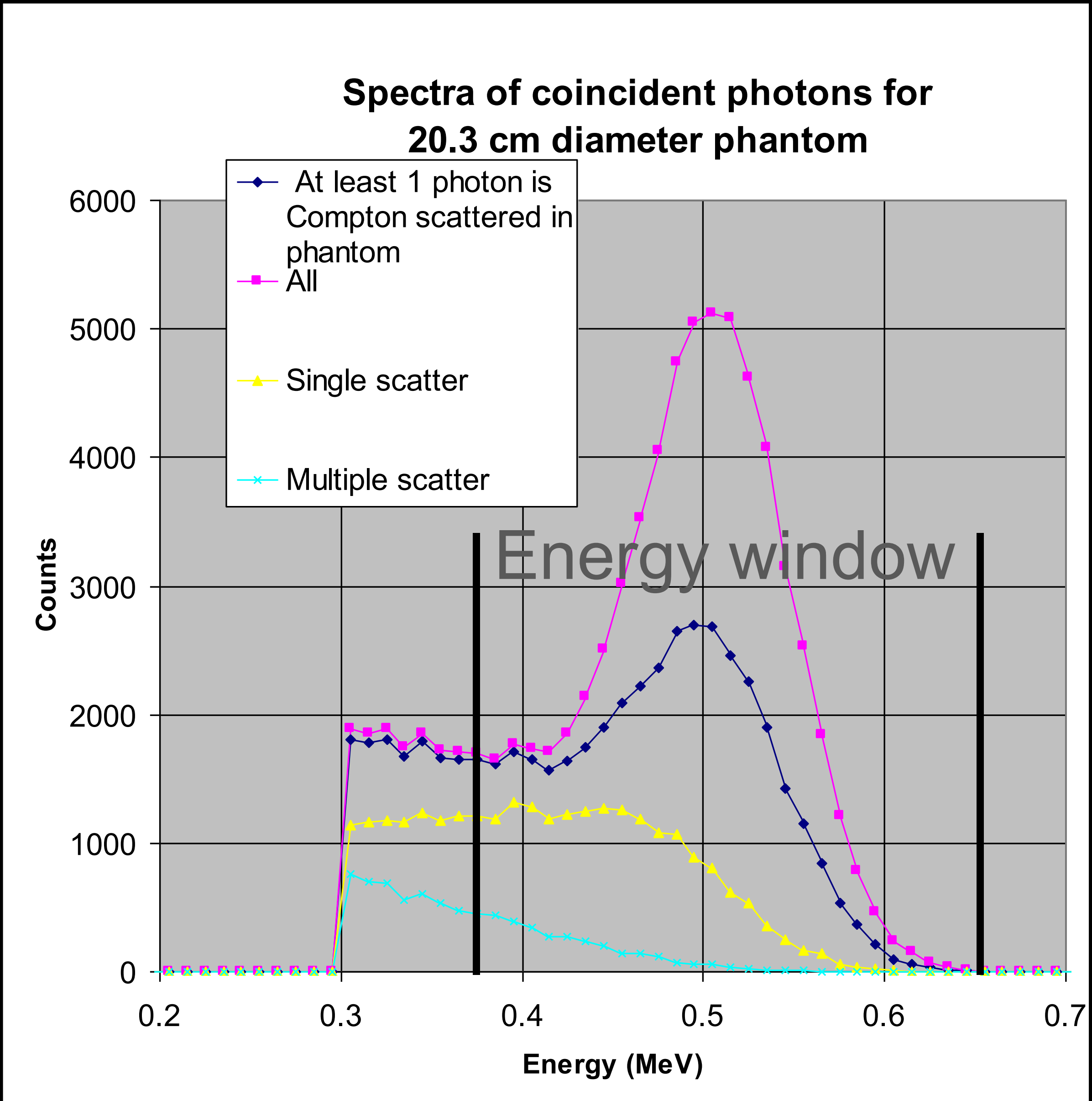








Spectra of coincident photons for 3D PET



Scatter Corrections

-uniform tail fitting

-multiple energy windows

-modeling of the single scatter

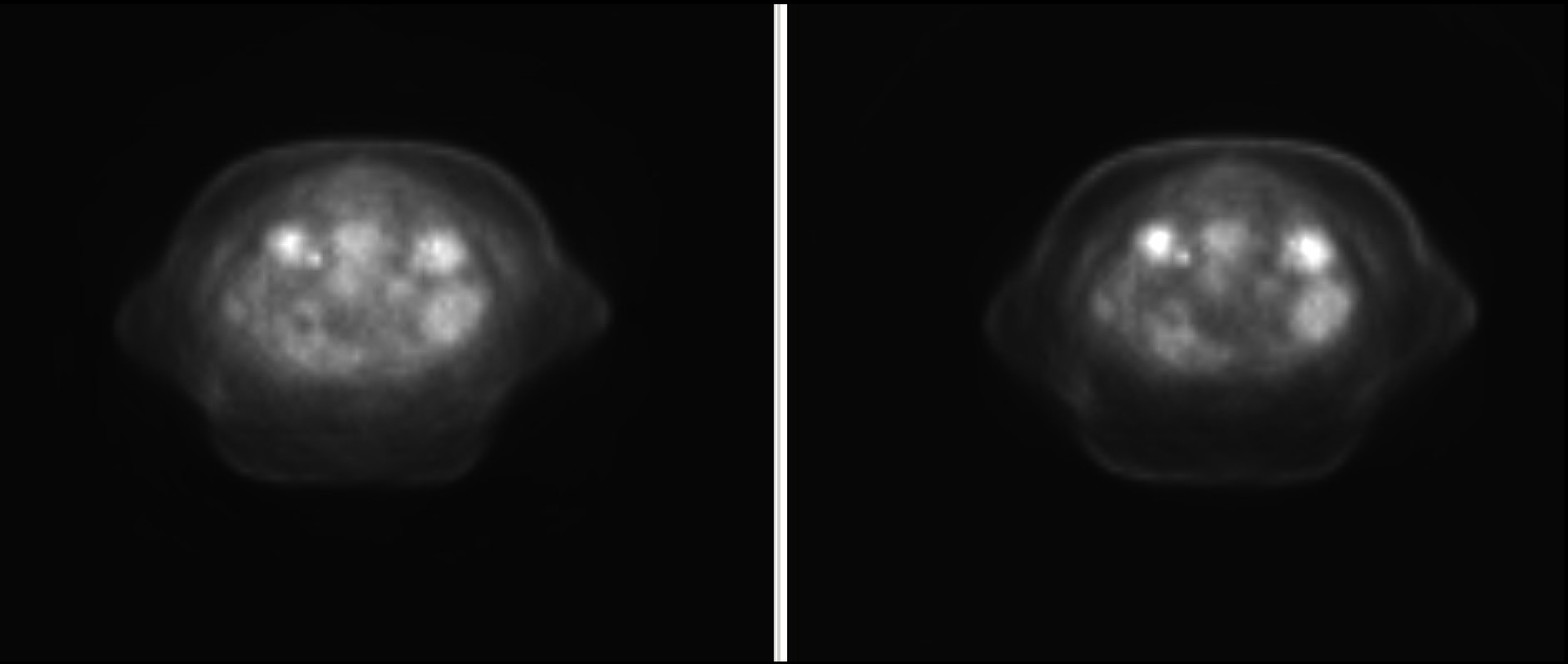
-full Monte Carlo

...

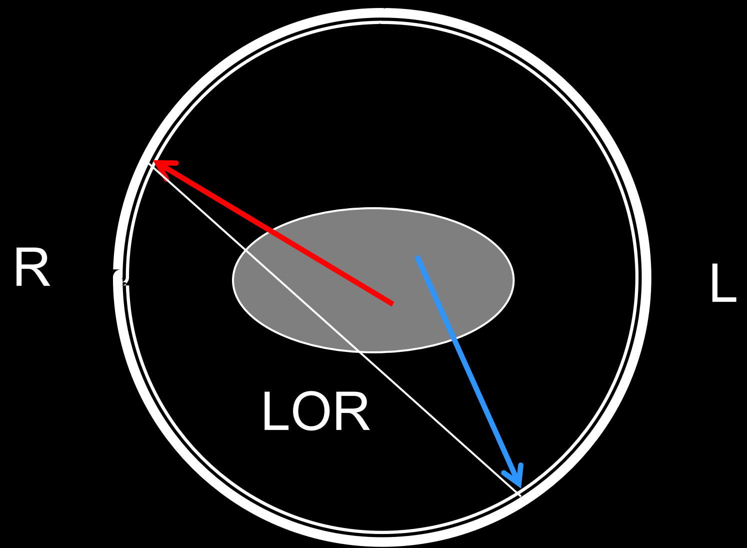
Effect of scatter correction

Without Correction

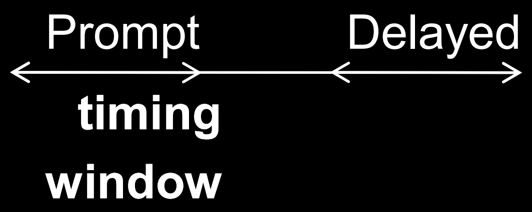
With Correction



Random coincidences and corrections for randoms



- Delayed window



- Smoothed delayed coincidences

- From Singles

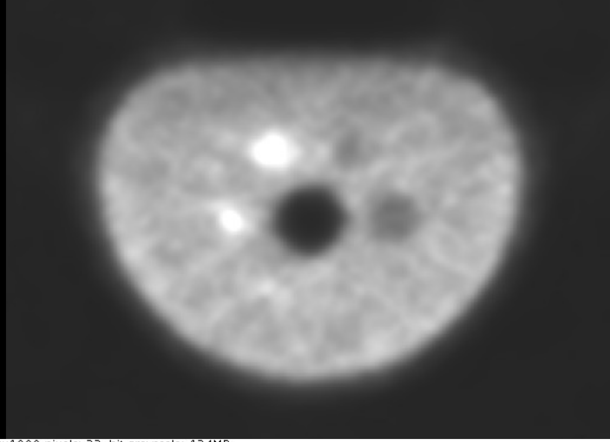
$$R_{1,2} = 2\tau \cdot S_{\text{det }1} \cdot S_{\text{det }2}$$

Timing window ~ 12 ns

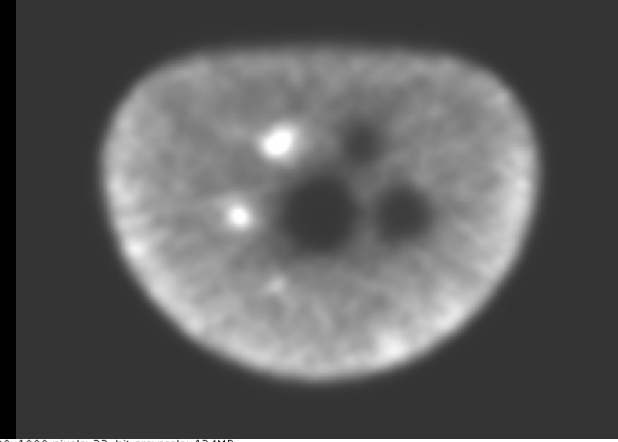
Single Event Rates

Effect of Scatter and Random Counts on the image quality: Image Quality Phantom - simulated

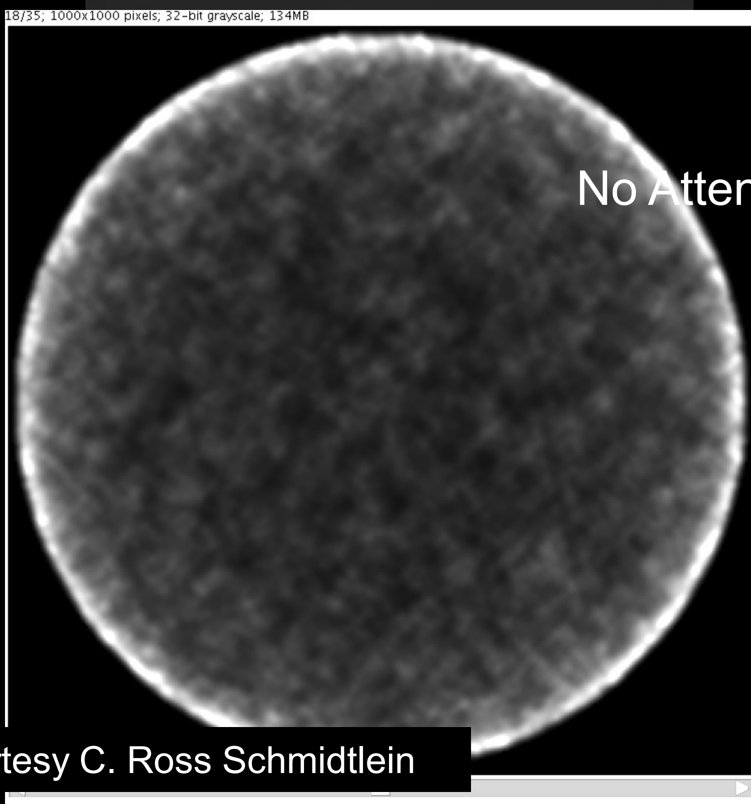
With scatter and random events



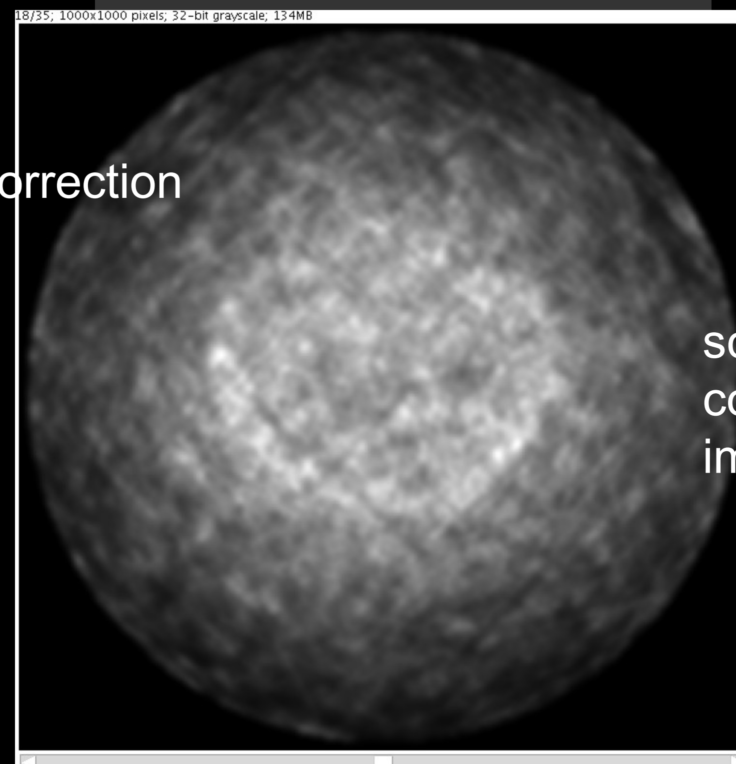
No scatter and random events



No Attenuation Correction



random counts image

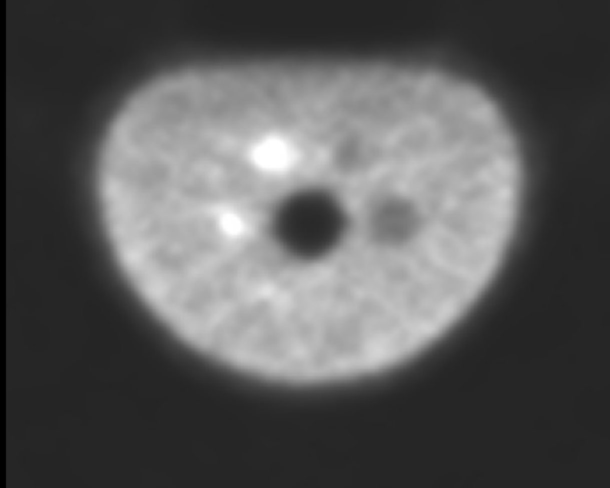


scatter counts image

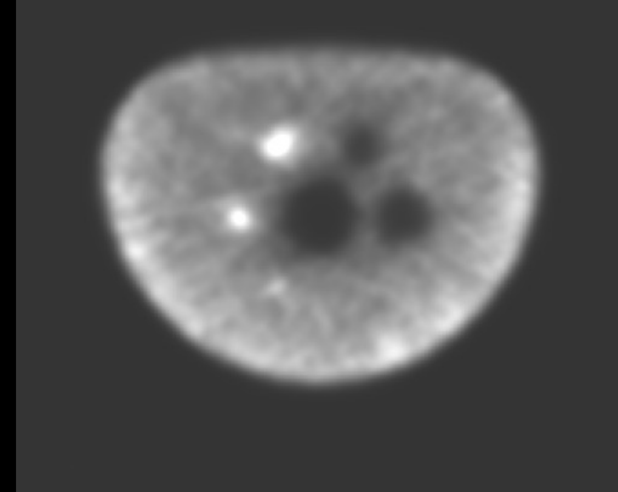
Courtesy C. Ross Schmidtlein

Effect of Scatter and Random Counts on the image quality: Image Quality Phantom - simulated

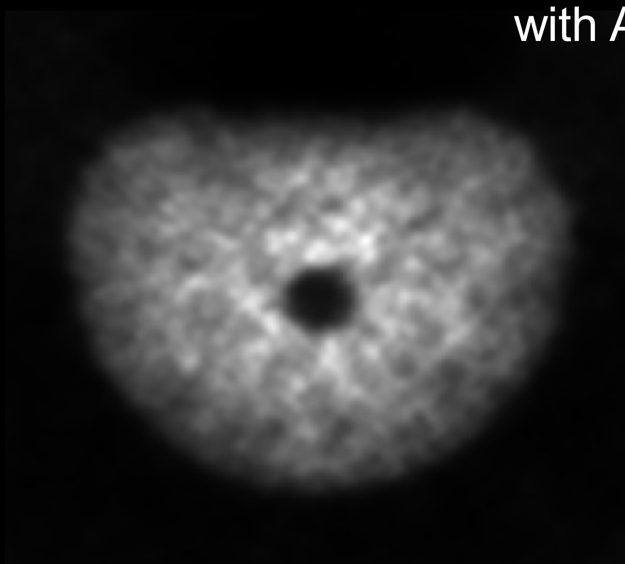
With scatter and random events



No scatter and random events



with Attenuation Correction



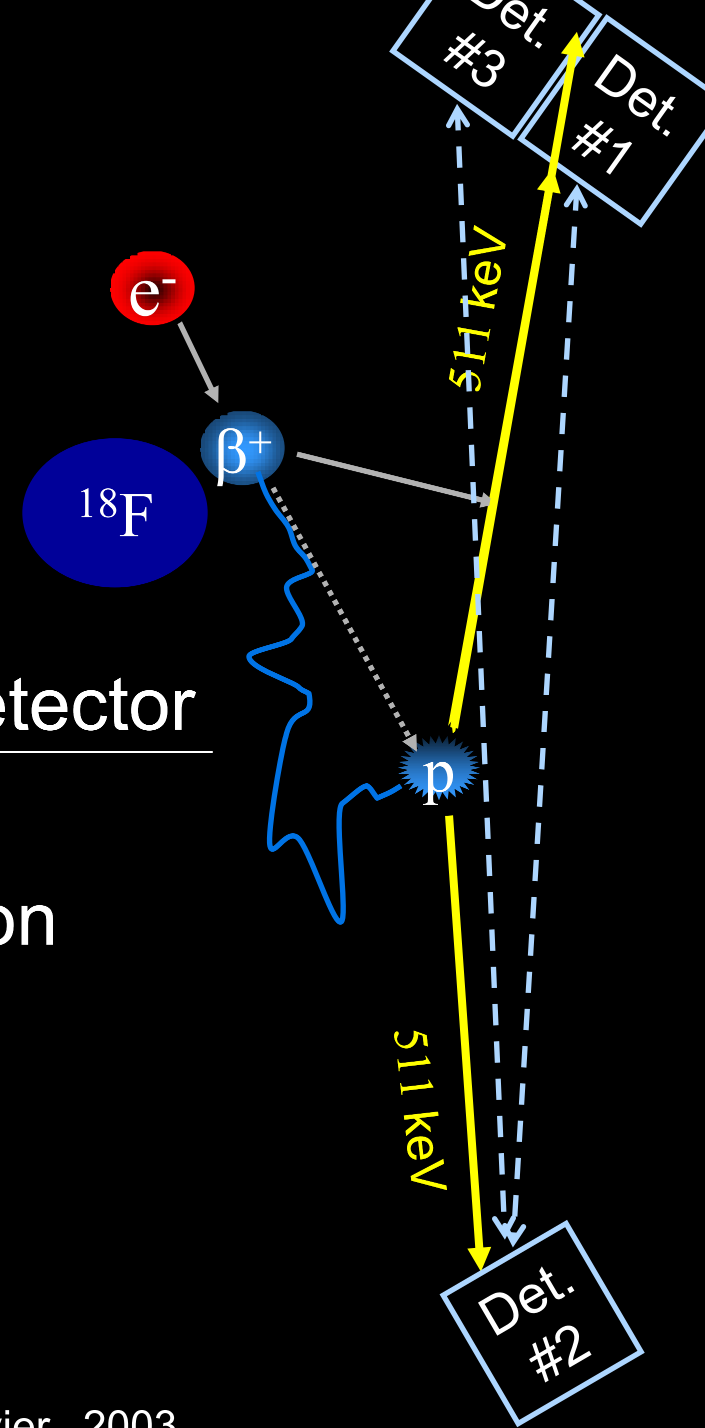
random counts image

scatter counts image

Courtesy C. Ross Schmidtlein

PET resolution components

- Positron range
- Photon non-colinearity
- Detector size and distance to detector
- Block detector effect
- Arc effect and depth of interaction
- Spatial and angular sampling
- Reconstruction



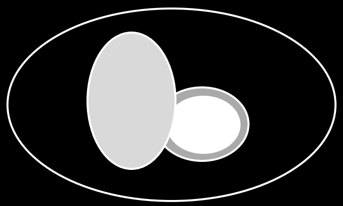
Levin & Hoffman , PMB, 1999;

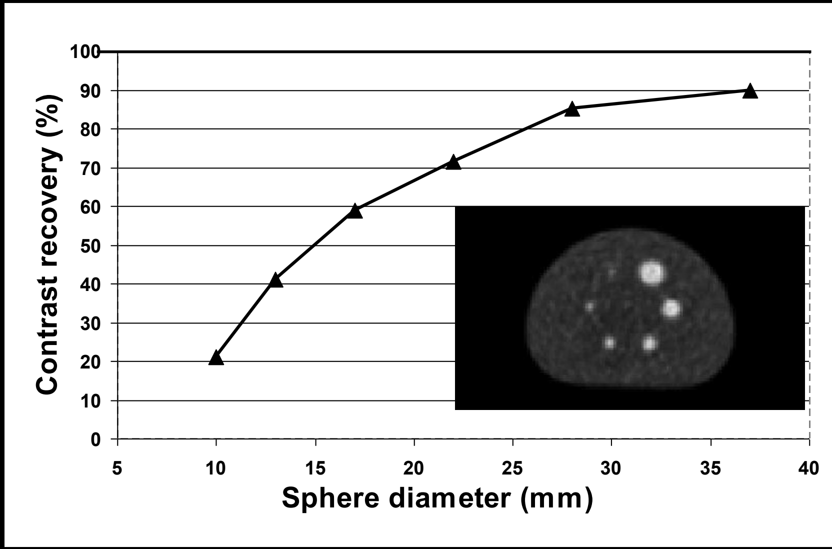
Cherry, Sorenson, Phelps, Physics in Nuclear Medicine, Third Edition, Sounders –Elsevier, 2003

Resolution Correction methods:
Classification of Soret *et al. JNM, 48, 2007*

A. At a Regional level

1. Recovery coefficients (Piper *et al*, SU-FF-I-92)
2. Geometric transfer matrix (Rousset *et al,* 1998)





B. At a Voxel level

1. Partition based:Convolution of every sub-structure with the PSF and then using the difference for correction (Meltzer *et al.* 1996, Teo *et al,* 2007)

2. Multi-resolution approach: Merge Wavelet Transformations of PET and MR images (Boussion *et al.* 2006)

3. The PSF is incorporated in the reconstruction process (Alleviat *et al.* 2006, Rizzo *et al, 2007,…)*

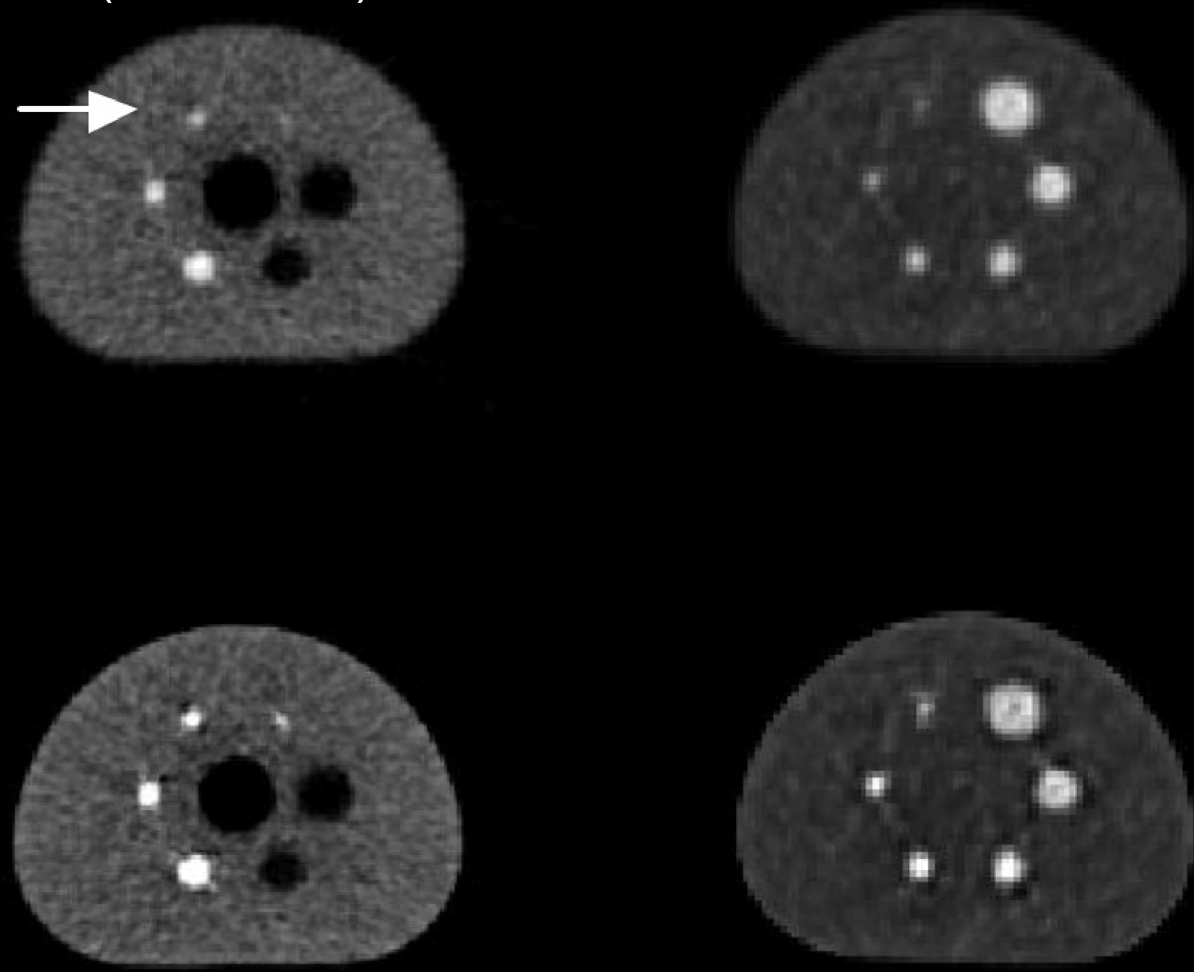
4. Iterative deconvolution (Boussion *et al*, 2007, Kirov *et al* 2008)

Partial volume effect correction

PET scan 1 (simulation) | PET scan 2

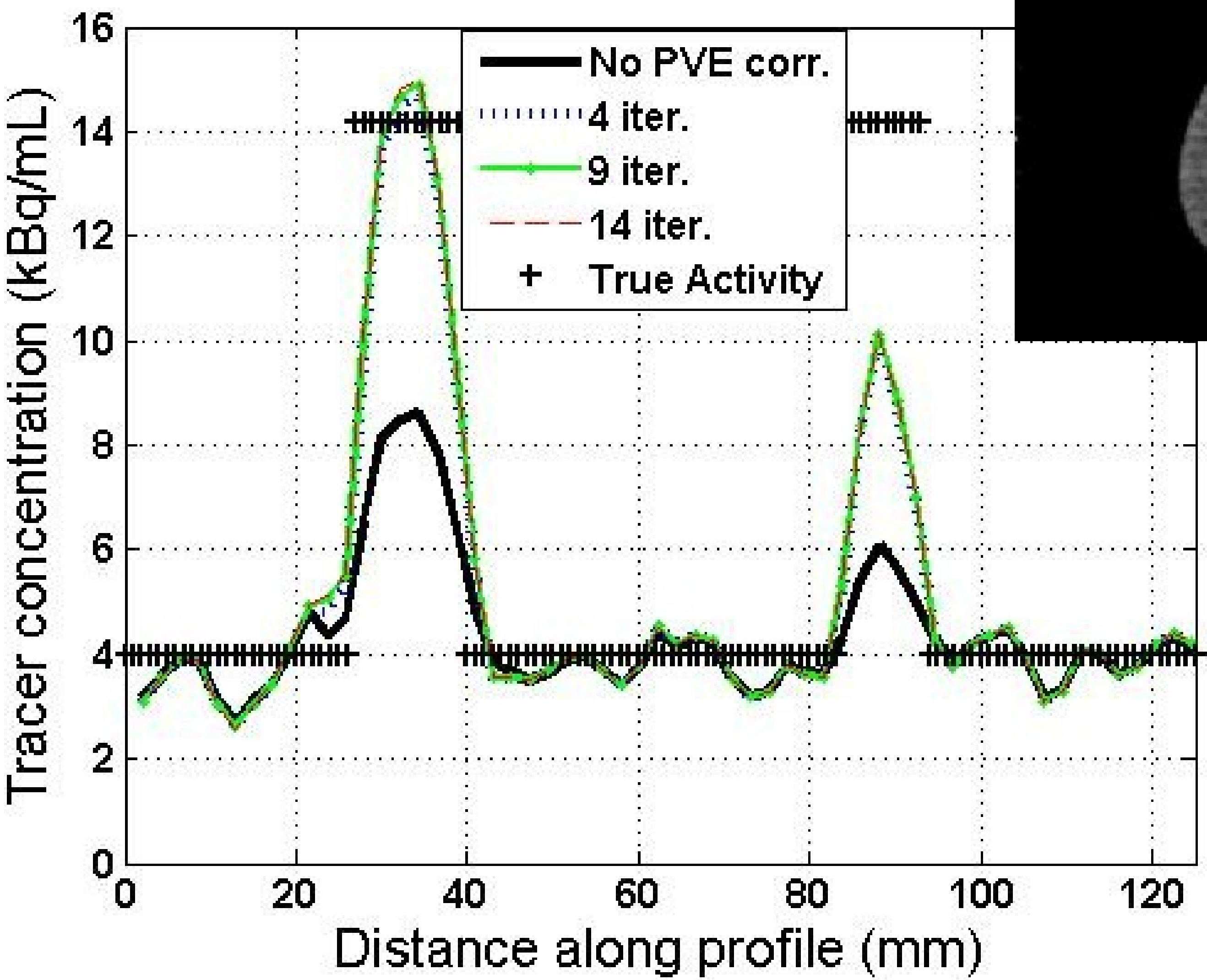
Before

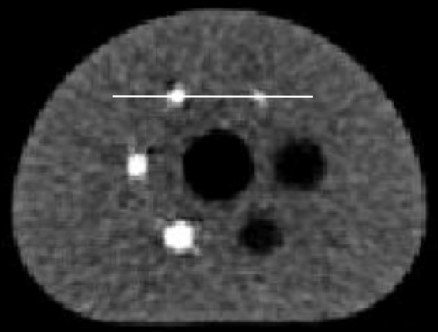
After the PVE correction



Phys. Med. Biol. 53, 2008, p. 2577

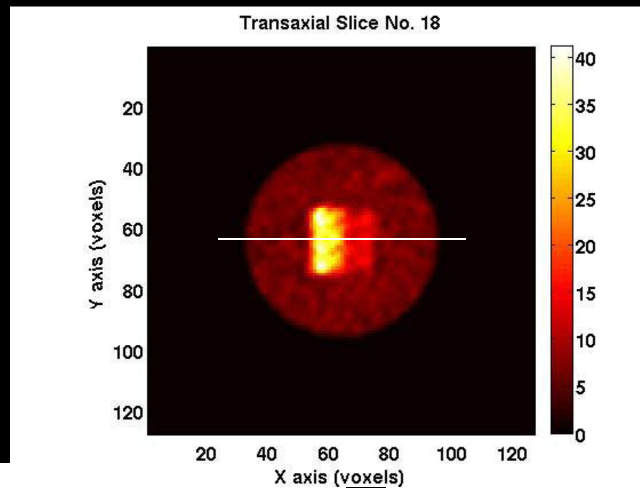
Partial Volume Effect Correction



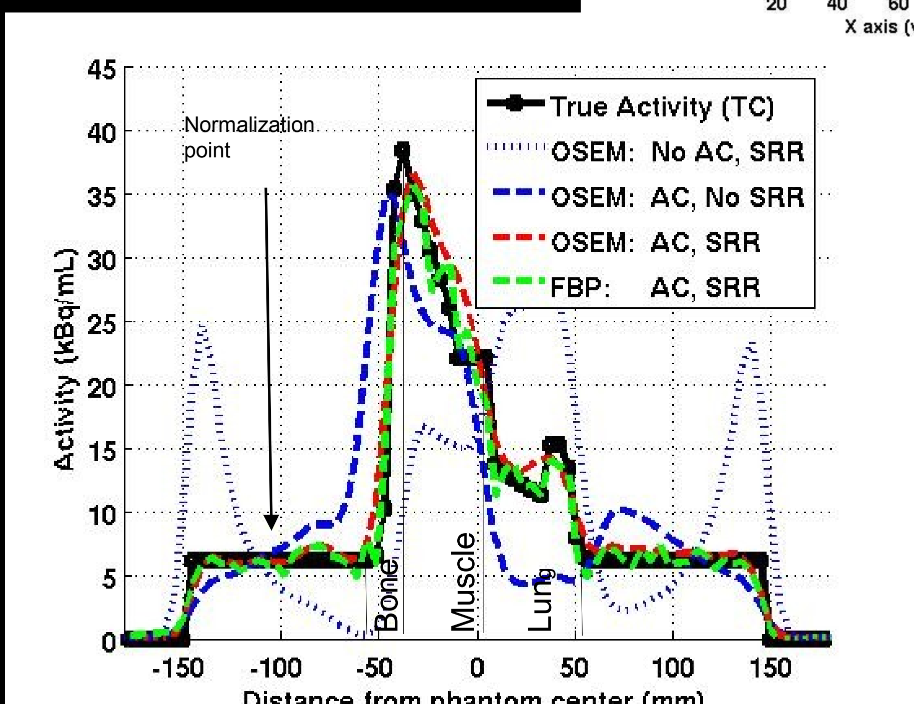


Phys. Med. Biol. 53, 2008, p. 2577

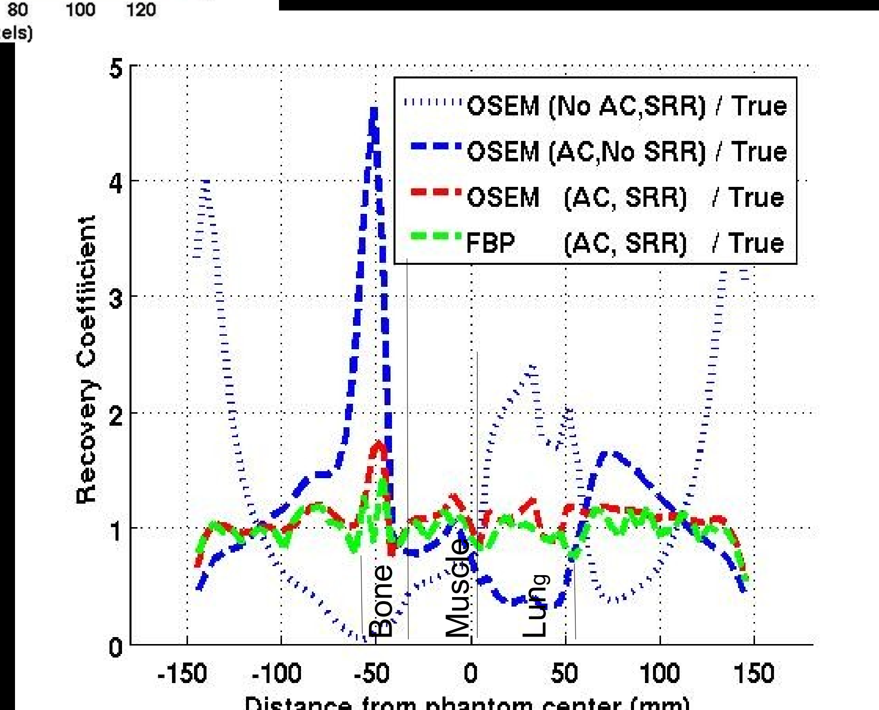
12 cm non-uniform activity and non-uniform attenuation cube inserted in a 30 cm diameter water cylinder



Activity profiles

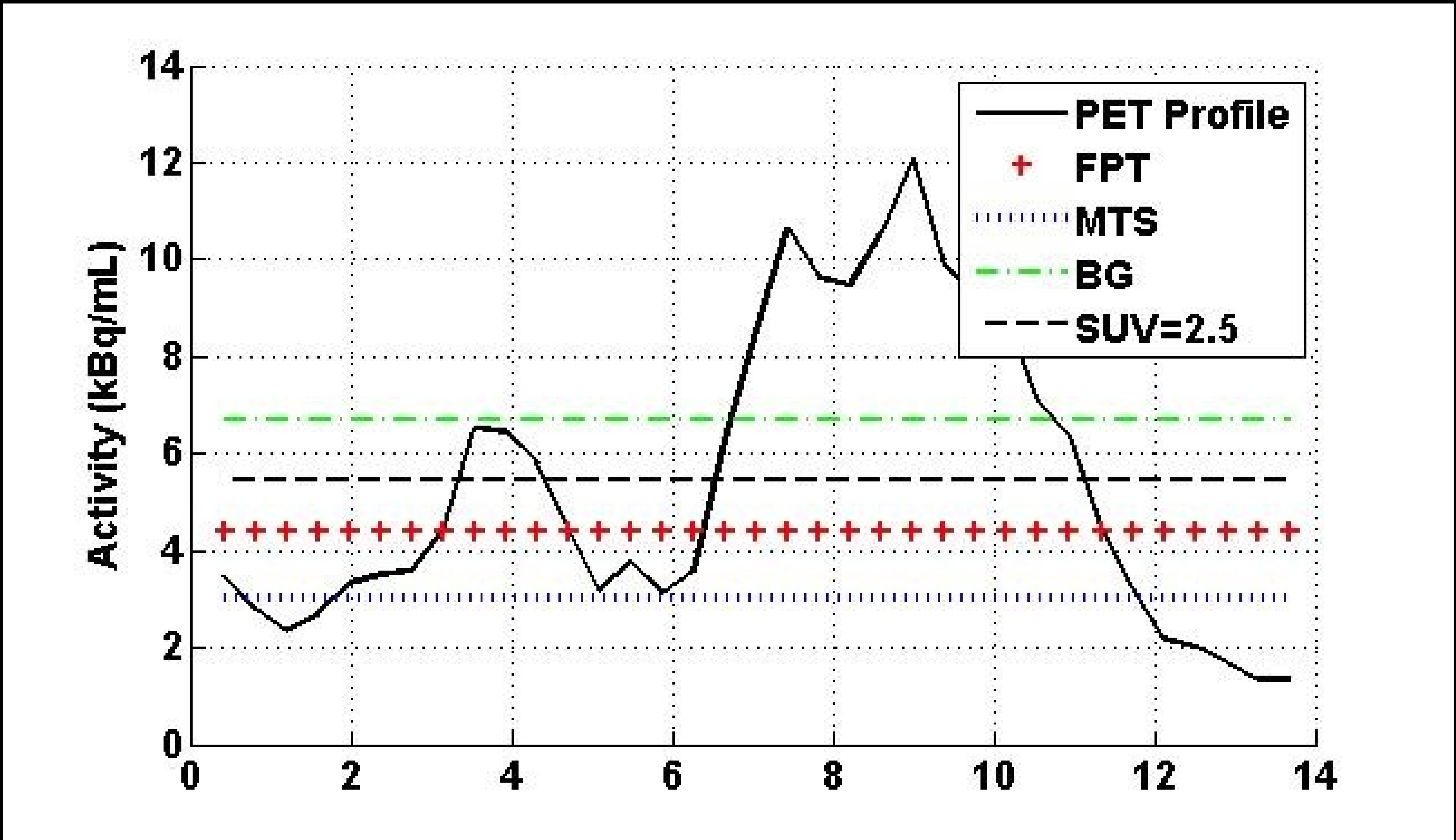


Recovery coefficients



2007 IEEE Nuclear Science Symposium Med. Imaging Conference Record , M13-5, 2838-2841

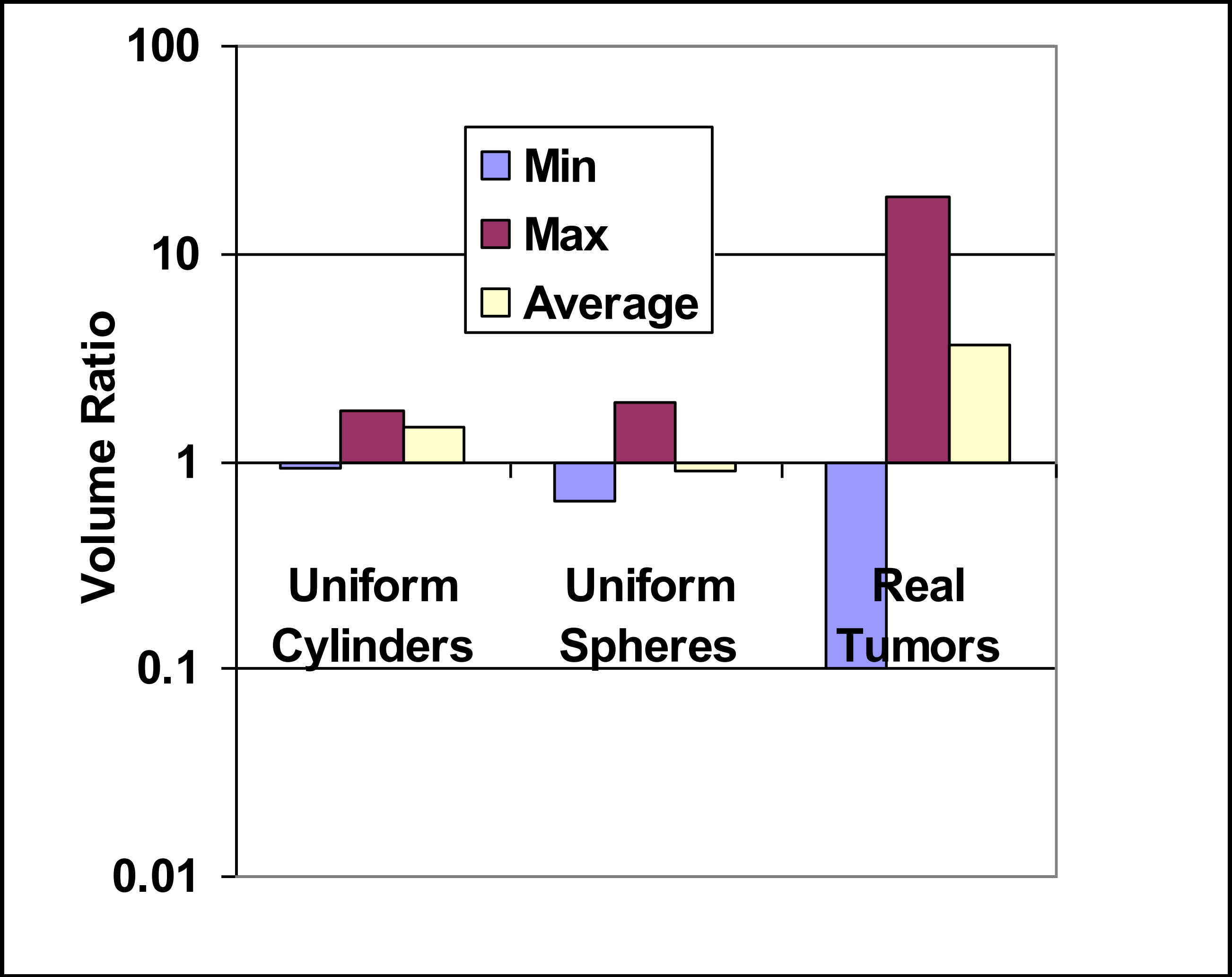
Threshold levels from different fixed threshold methods on top of the activity profile of a lesion



AAPM 2006, Med. Phys. **33**, p 2039,

Challenges for PET based tumor segmentation

Ratios of volumes segmented with the same four protocols

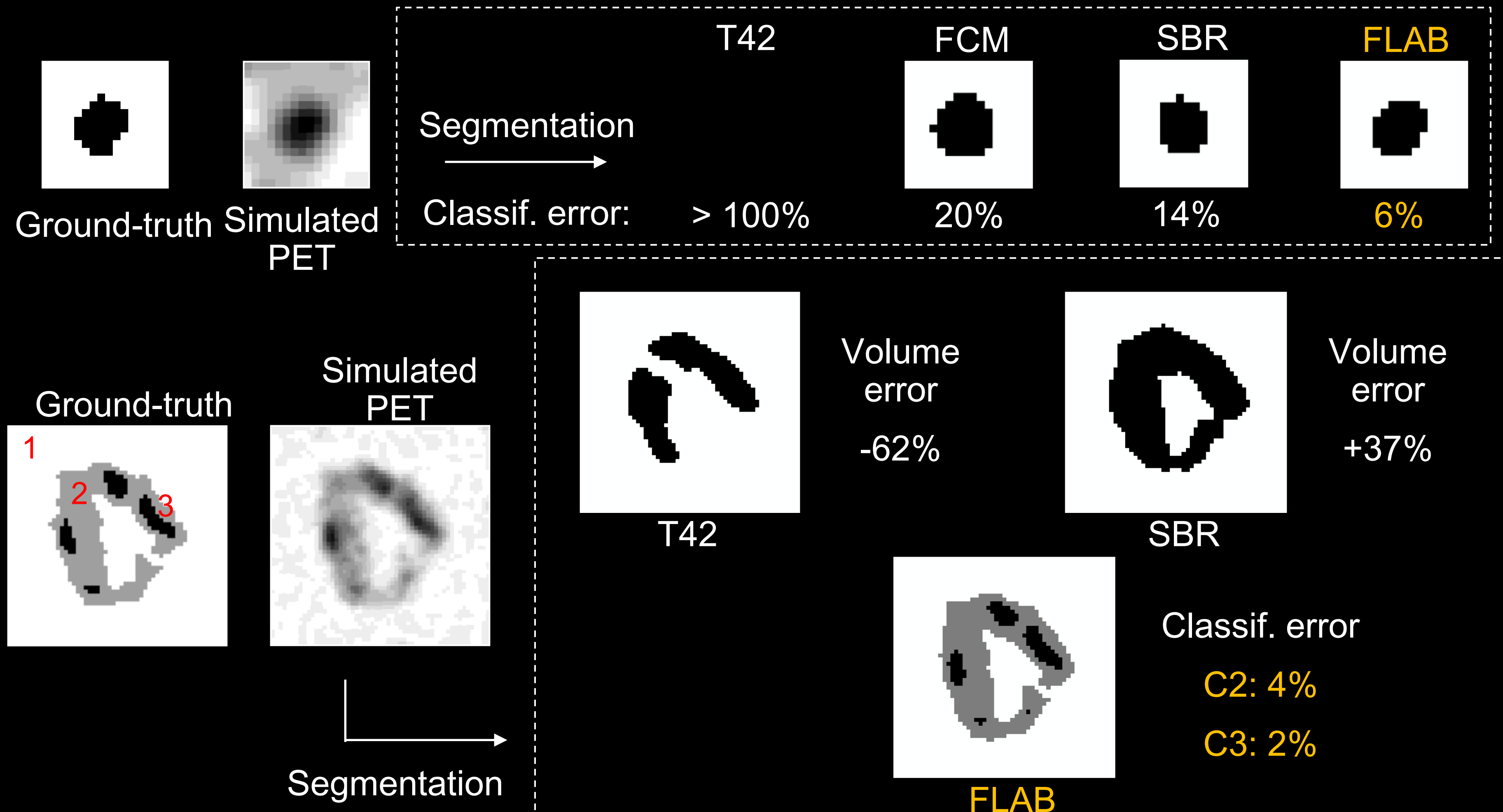


AAPM 2006, Med. Phys. **33**, p 2039,

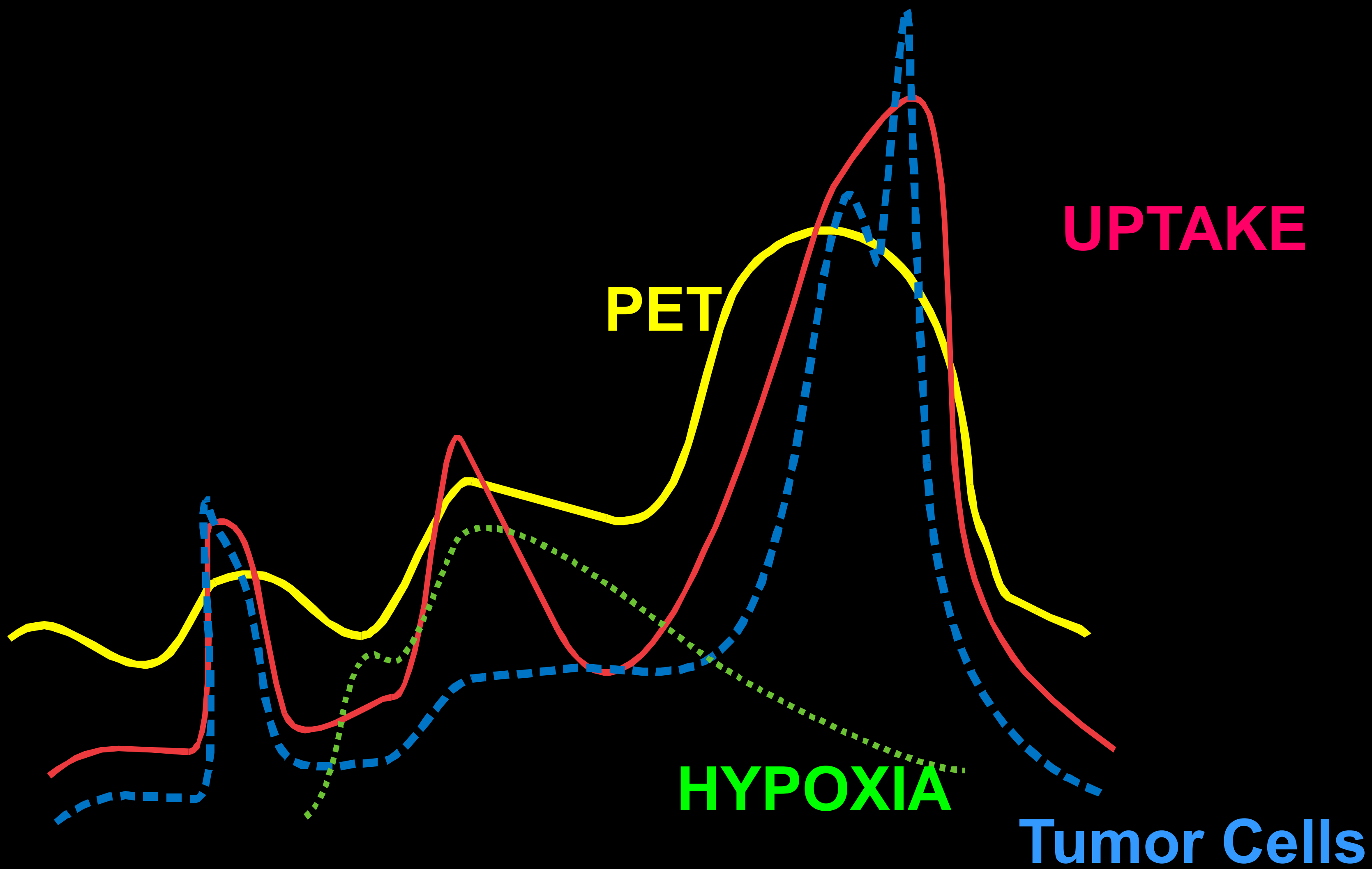
M. Hatt et al, “A fuzzy locally adaptive Bayesian segmentation approach for volume determination in PET” *IEEE Transactions on Medical Imaging*, 2008, and 2007 IEEE NSS/MIC Conference Record, 3939-3945

Courtesy Dimitris Visvikis (INSERM U650, Image proc. lab, Brest)

simulated tumors



The problem: What would be PET assisted dose painting ?
(artists view)



Summary:
Problems in Radiation Therapy

Un- Resolved | Resolved

Accurate dose delivery

Patient and tumor tracking

Target definition

PET,

MRI,

SPECT ?

Are we doing the right thing with the tumor ?

People

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Nehmeh S, Ph.D.

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Mageras, G.S.

Lovelock, M

Memorial Sloan - Kettering Cancer Center

Joe Piao, Cleveland Clinic Foundation

Chris Danford, **Duke Medical School**

Krasimir Mitev Ph.D. , Georgi Gerganov, Jordan Madzhunkov : Sofia University