3D-RD Imaging-Based Dosimetry

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Patient-Specific Dosimetry

- Patient's Anatomy
  - CT/MRI
- Patient's Activity Distribution
  - SPECT/PET
- Spatial distribution of absorbed dose
  - non-uniform activity distribution
  - absorbed dose "images"
  - dose volume-histograms

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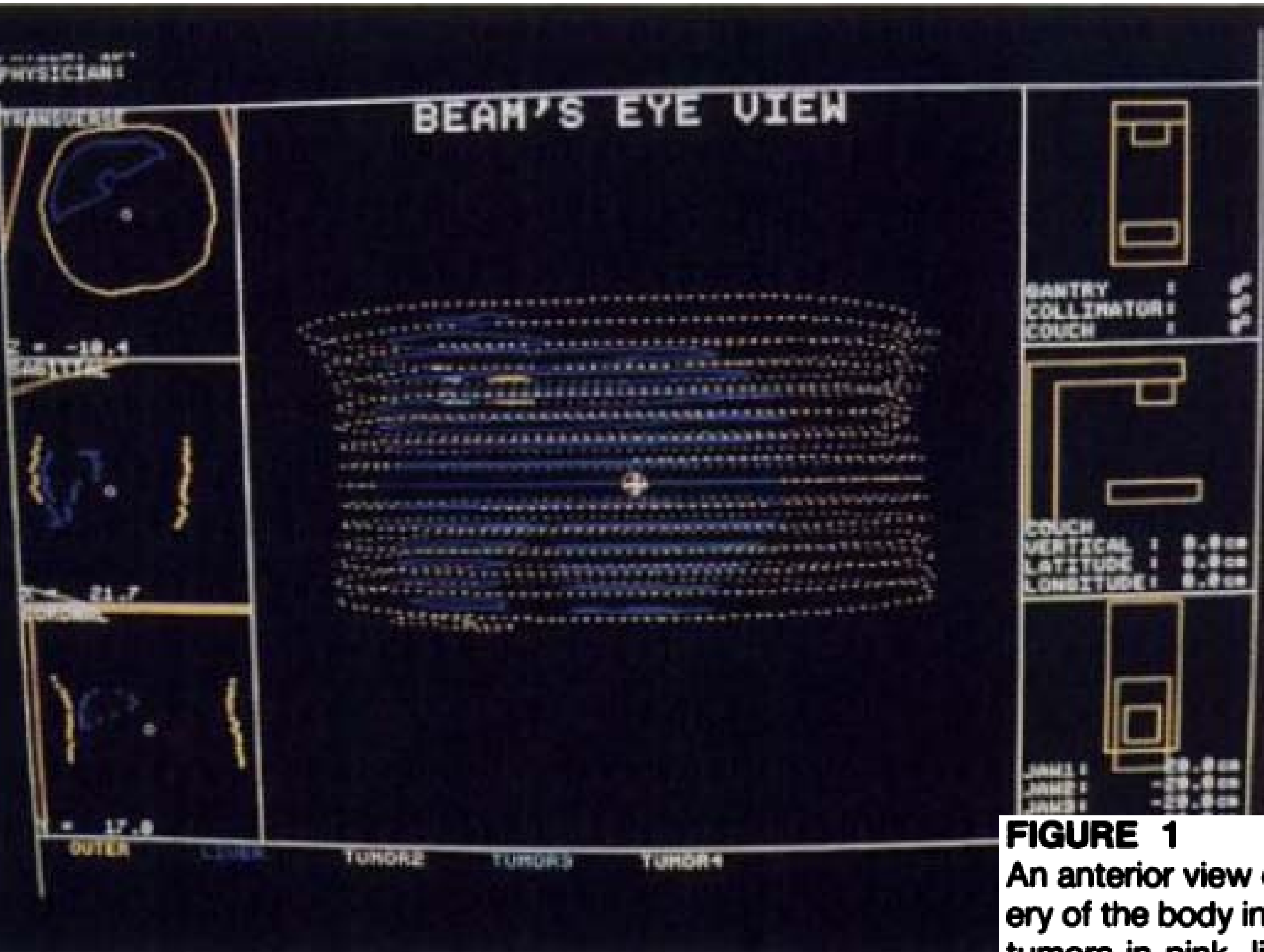


FIGURE 1

An anterior view of a wire frame diagram depicting the periphery of the body in yellow, the liver in dark blue, and three small tumors in pink, light blue, and orange, Each set of contours represents contours drawn from the anatomy of the patient as shown on a consecutive series of CT images. To the left of the wire frame diagram are shown a transverse, sagittal, and coronal slice (each taken through the mid-plane, at the level of the cross-hair, of the respective view). To the right of the wire frame diagram a view of the gantry and couch is depicted from the front, from the side and from above in the top, middle and bottom panel, respectively.

Sgouros, *et al.*, JNM '90

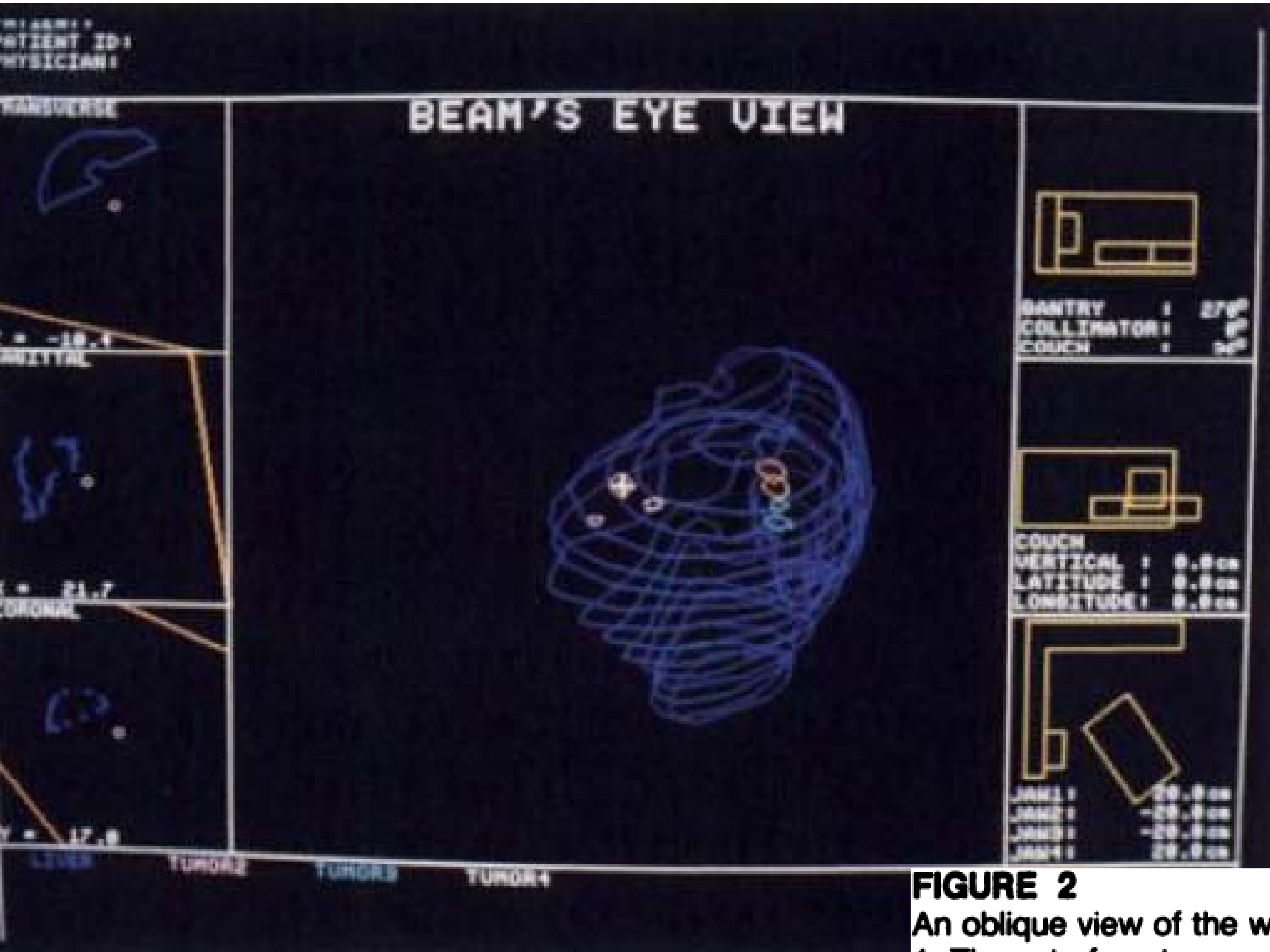
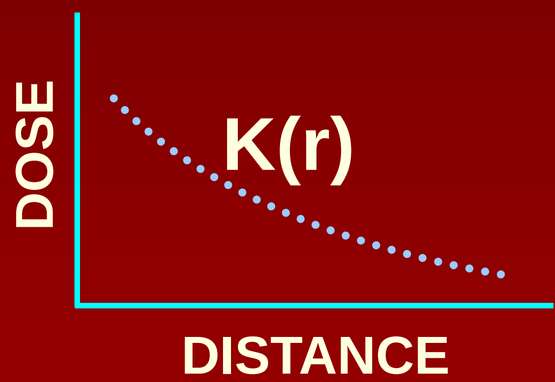


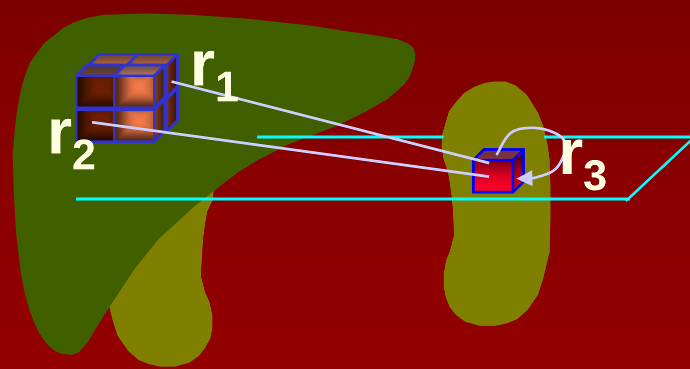
FIGURE 2
An oblique view of the wire frame diagram depicted in Figure 1. The set of contours representing the periphery of the body have been "turned off" to better display the liver and the intrahepatic tumors. To the right of the wire frame diagram the gantry and couch orientations used to obtain this view are depicted.

Sgouros, *et al.*, JNM '90

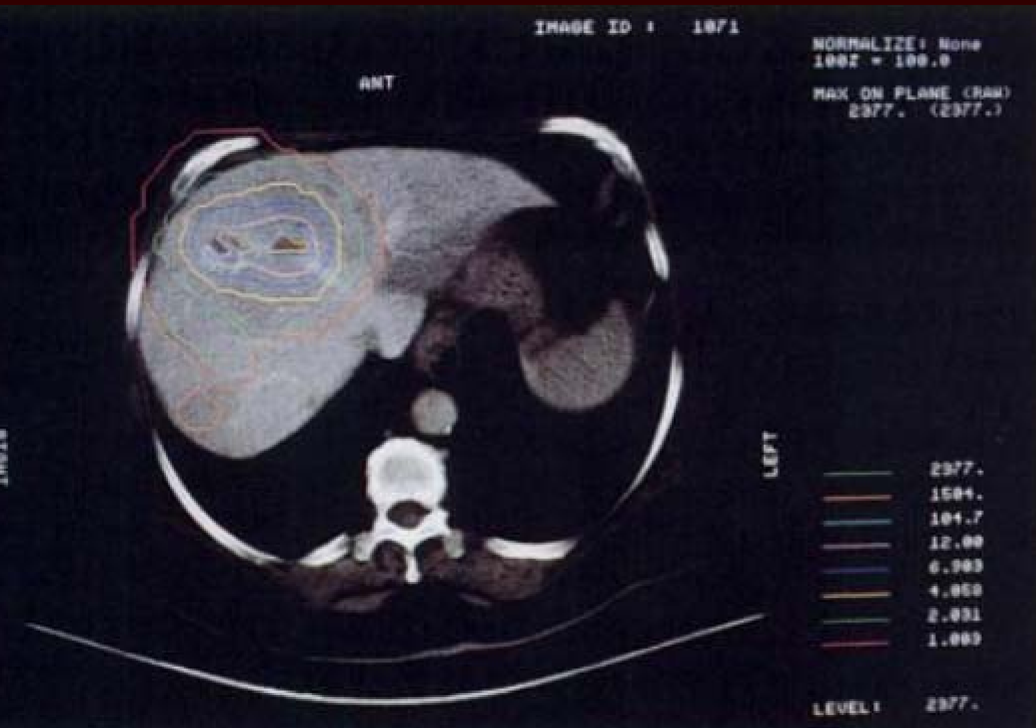
Methods

- 3D-ID used for dose calculations
  - ROI for each lesion.
  - mean, min, max, DVH
  - point-kernel method





$$\mathbf{DOSE} = \mathbf{CA_1 \times K(r_1) + CA_2 \times K(r_2) + \ldots}$$



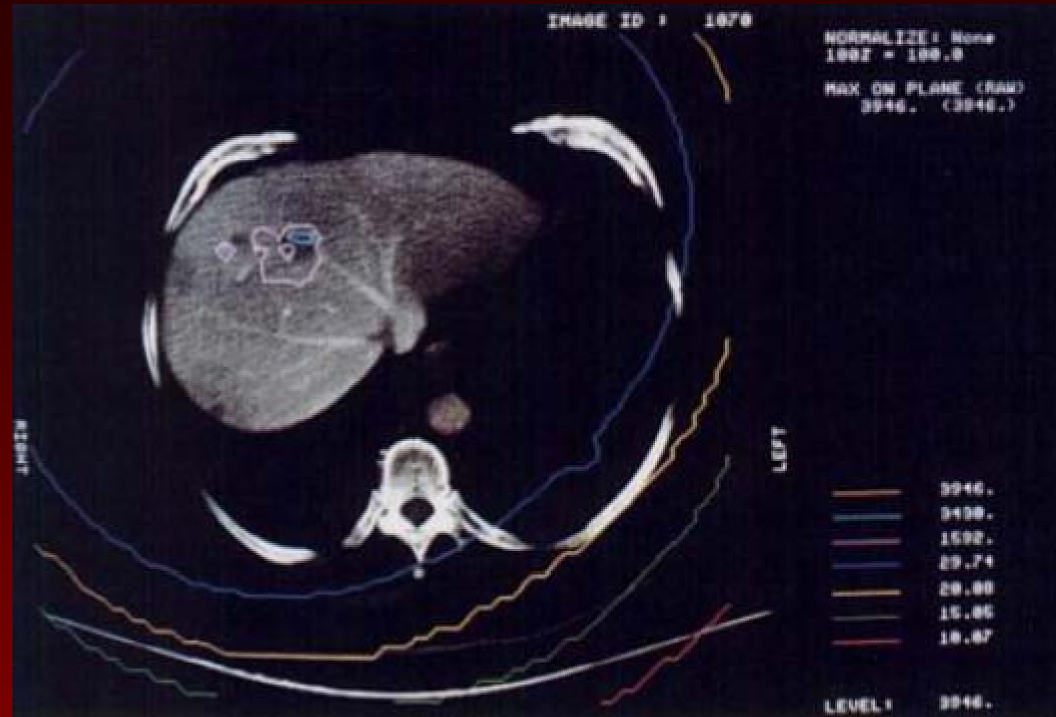


FIGURE 4
A CT image through the liver showing two small tumors in the anterior portion of the liver. The isodose contours resulting from a cumulated activity concentration of 7.4×10^5 MBq-s/ml of ^{131}I in the two visible tumors as well as in a third tumor not visible in this plane—Cf. Figures 1 and 2) have been overlaid. The dose values (in cGy) assigned to each isodose contour are shown on the lower right. The orange contour is broken into two closed circles both corresponding to a dose of ~1 cGy. The smaller circle is located above the third tumor in the posterior part of the liver and reflects an enhancement in dose due to activity in the third tumor.

FIGURE 5
A CT image showing the isodose contours resulting from an ^{131}I cumulated activity concentration of 1.1×10^6 MBq-s/ml in each of the three tumors and 3.7×10^5 MBq-s/ml in the normal liver.

Sgouros, *et al.*, JNM ‘90

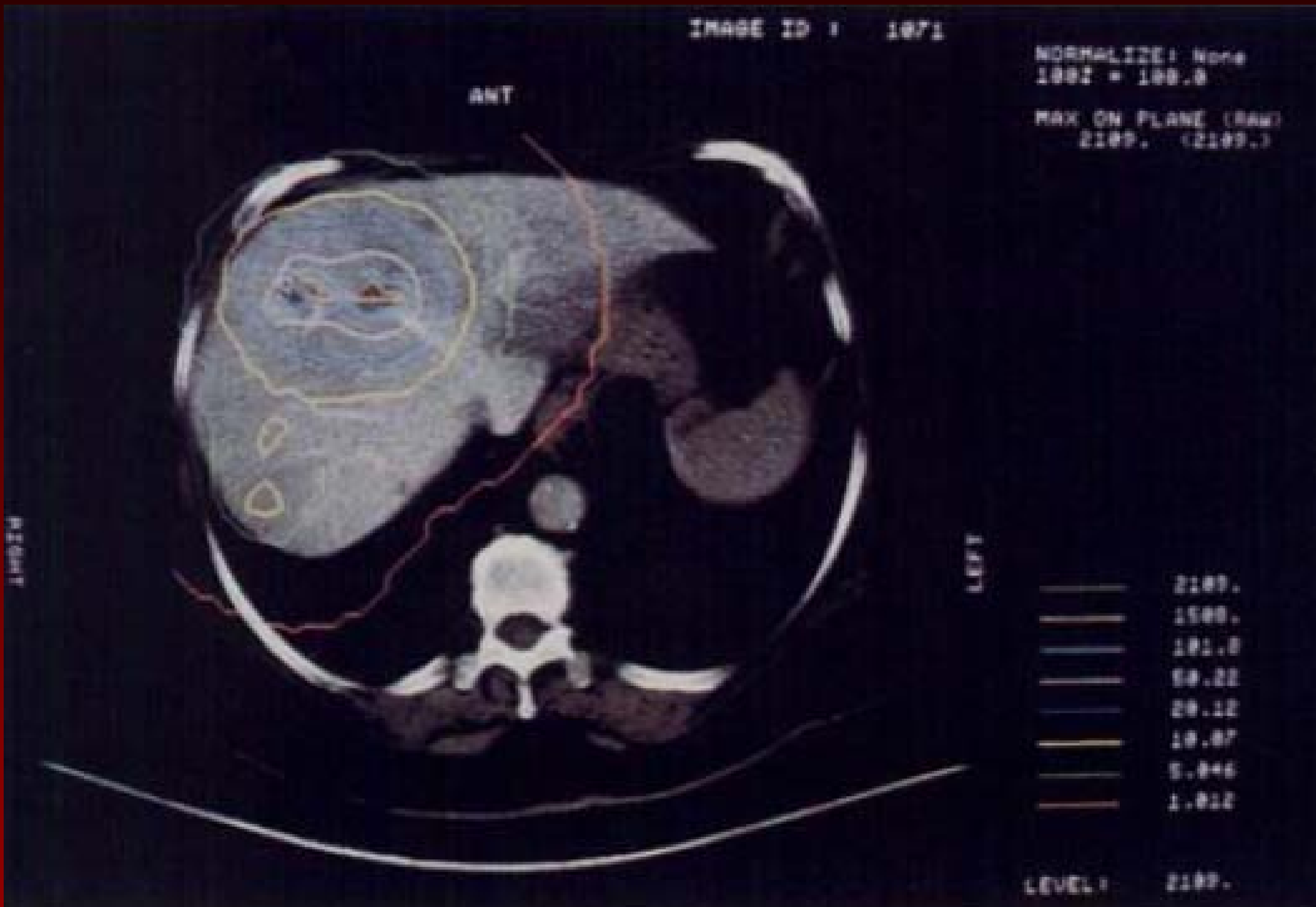
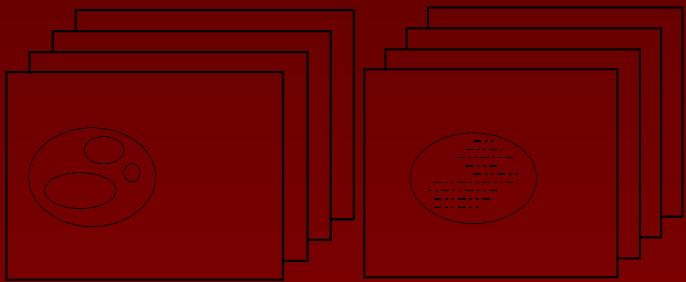


FIGURE 6
The CT image of Figure 4 is shown with the isodose contour
resulting from an ^{111}In cumulated activity concentration of 2.
$\times 10^6$ in each of the three previously described tumors.

Sgouros, *et al.*, JNM '90

3D-ID System

Input: *Registered anatomic & functional images*



(CT/MRI images,
SPECT/PET images)

Convert images from a variety of sources into a common data format.

Define regions-of -interest volumes by drawing contours.

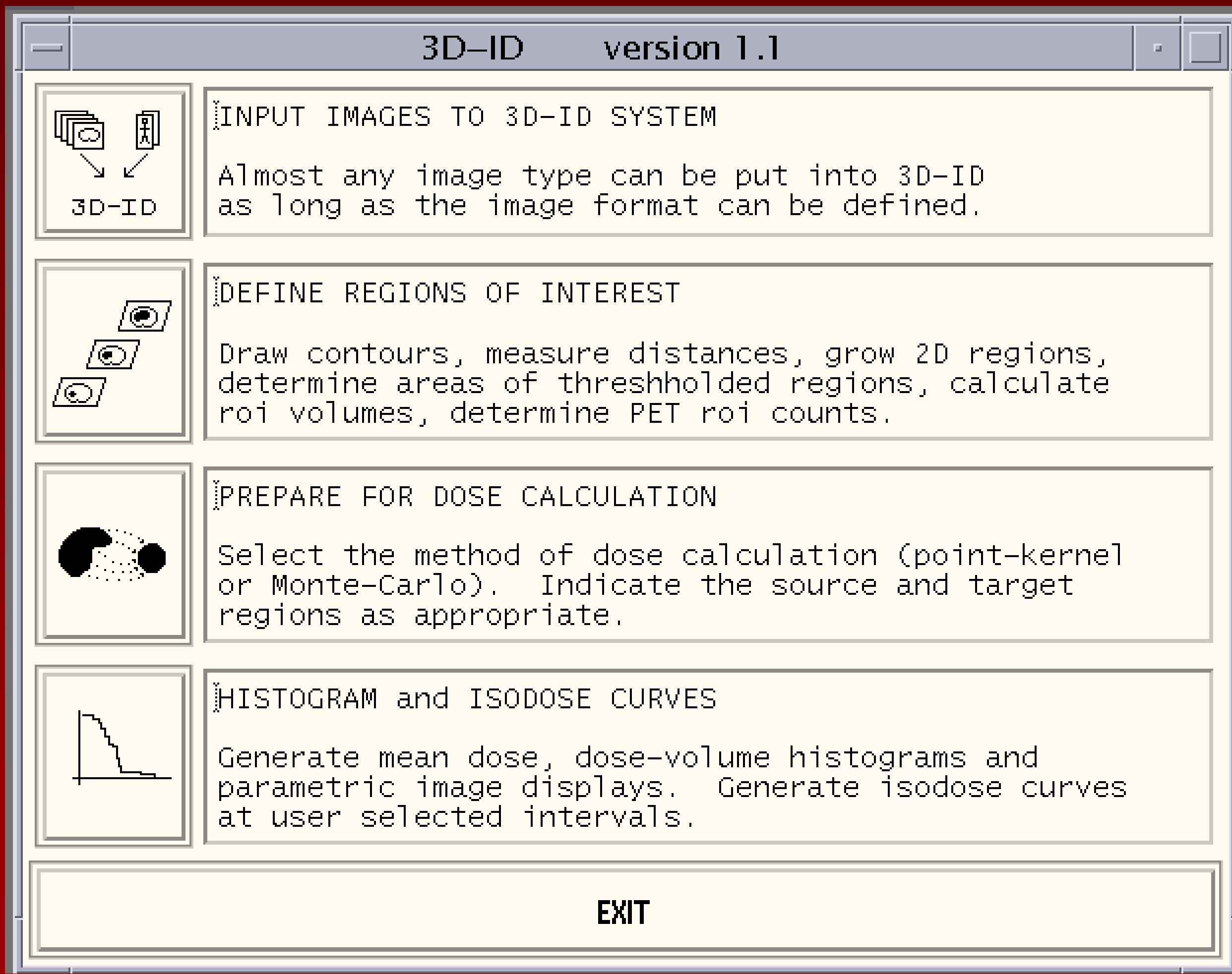
Select source and target volumes for dose calculation.

Calculate absorbed dose to target from source volume.

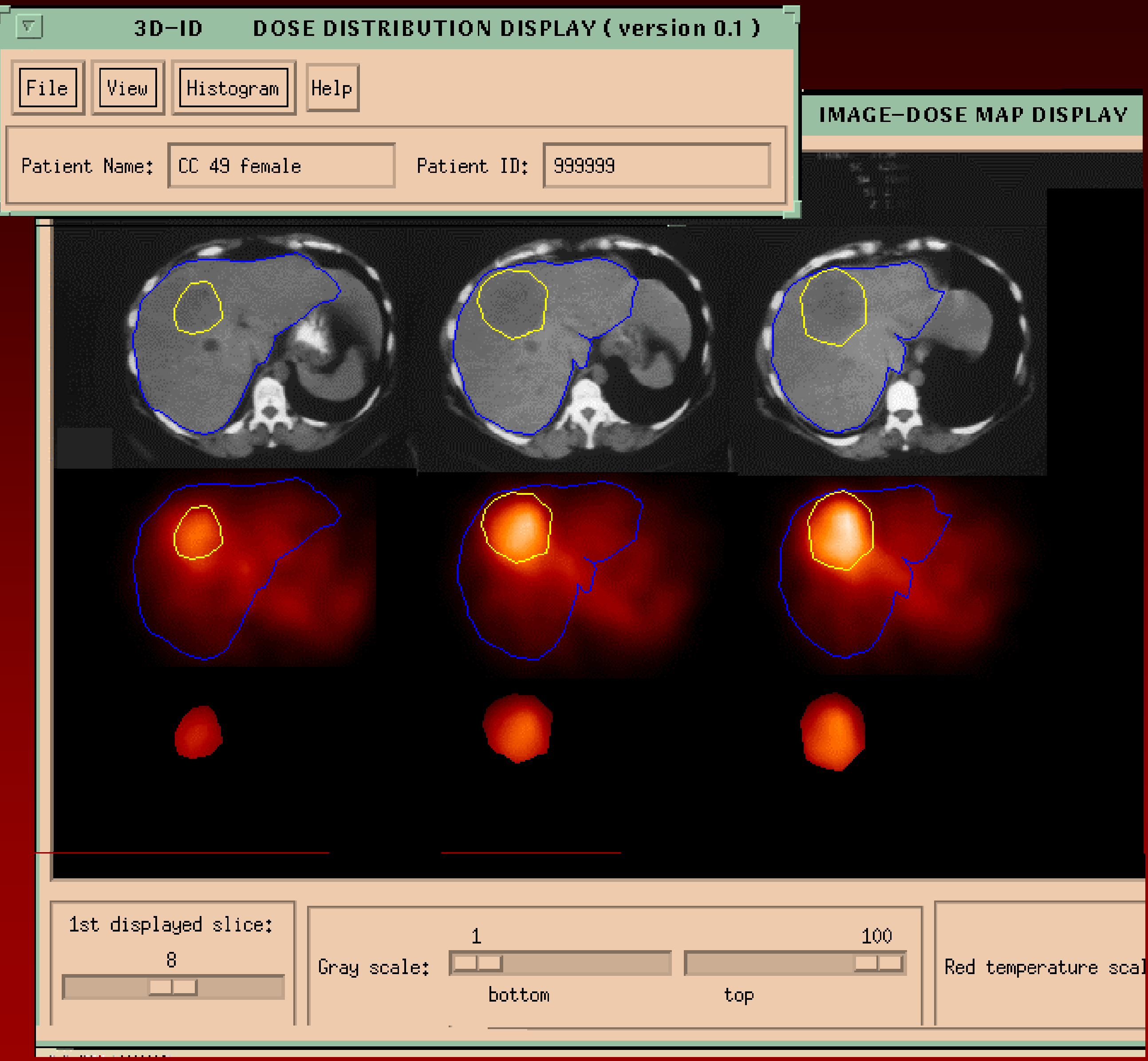
Create 3D dose distribution maps.

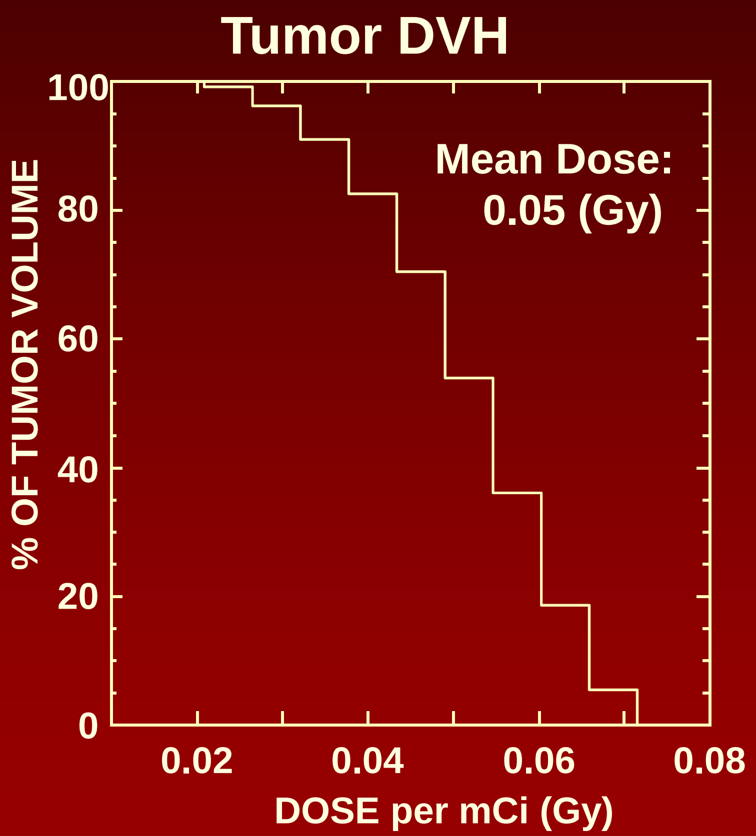
Generate mean dose, dose-volume histograms and parametric images.

3D-ID Function Access Panel



3D-ID Methodology





Kolbert, *et al.*, JNM 9

I-124 PET-based thyroid dosimetry

- Feasibility of ^{124}I-PET-based 3-D dosimetry
- Fully 3-D calculation
  - 3D kinetics based on multiple PET scans
  - not planar imaging and one SPECT
- Evaluate dose uniformity (or lack thereof)
  - DVH, min, max
  - images
- correlate with response

Sgouros, *et al.*, JNM '04

Methods

- 15 patients w/ metastatic thyroid Ca.
  - 3 - 4 ^{124}I-PET scans over 7 days (pre-therapy)
  - treated with ^{131}I
- PET scans were co-registered
  - MIAU (Multiple Image Analysis Utility) Software Package
  - transmission studies for anatomical landmarks
  - 4-d data set (x,y,z,t) for each patient
- Convert images to ^{131}I effective distribution
  - ^{124}I effective $\rightarrow$ biological $\rightarrow$ ^{131}I effective

$$A_{131}(x,y,z,t) = A_{124}(x,y,z,t) \cdot e^{\lambda_{124} \cdot t} \cdot e^{-\lambda_{131} \cdot t}$$

Sgouros, *et al.*, JNM ‘04

Clinical Implementation

- 15 patients w/ metastatic thyroid Ca.
  - 3 - 4 ^{124}I-PET scans over 7 days (pre-therapy)
  - treated with ^{131}I
- PET scans were co-registered
  - MIAU (Multiple Image Analysis Utility) Software Package
  - transmission studies for anatomical landmarks
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- Convert images to ^{131}I effective distribution
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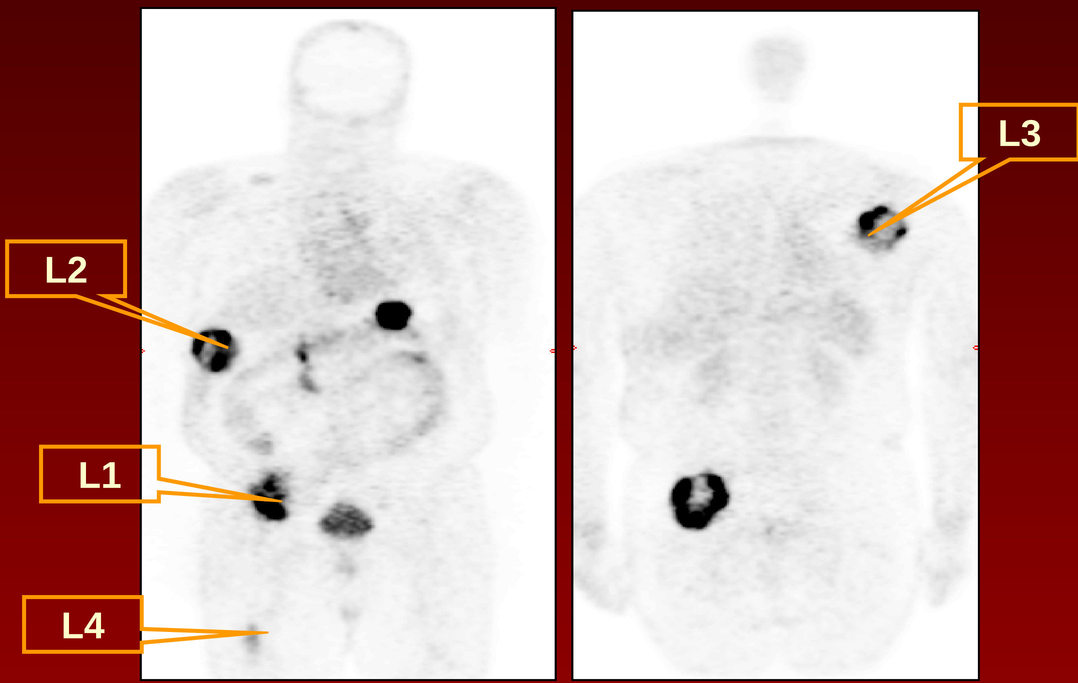
$$A_{131}(x,y,z,t) = A_{124}(x,y,z,t) \cdot e^{\lambda_{124} \cdot t} \cdot e^{-\lambda_{131} \cdot t}$$

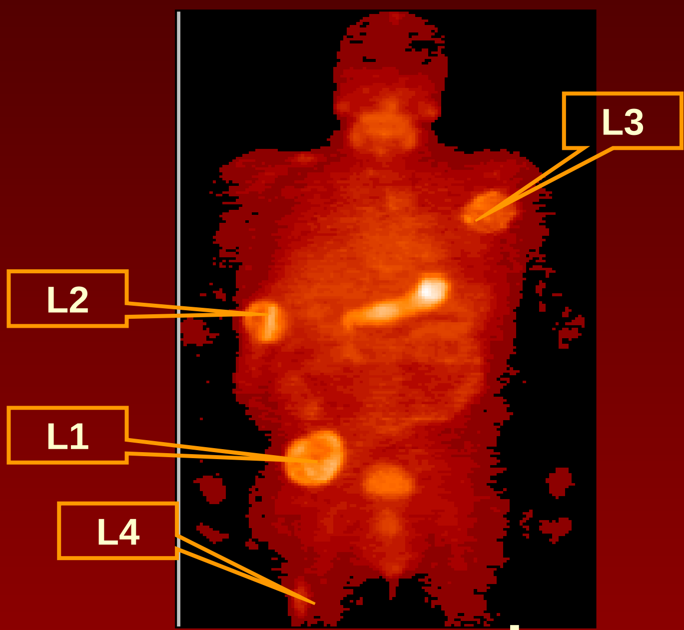
Sgouros, *et al.*, JNM '04

Lesion identification database

Pt. 13



Selected coronal slices



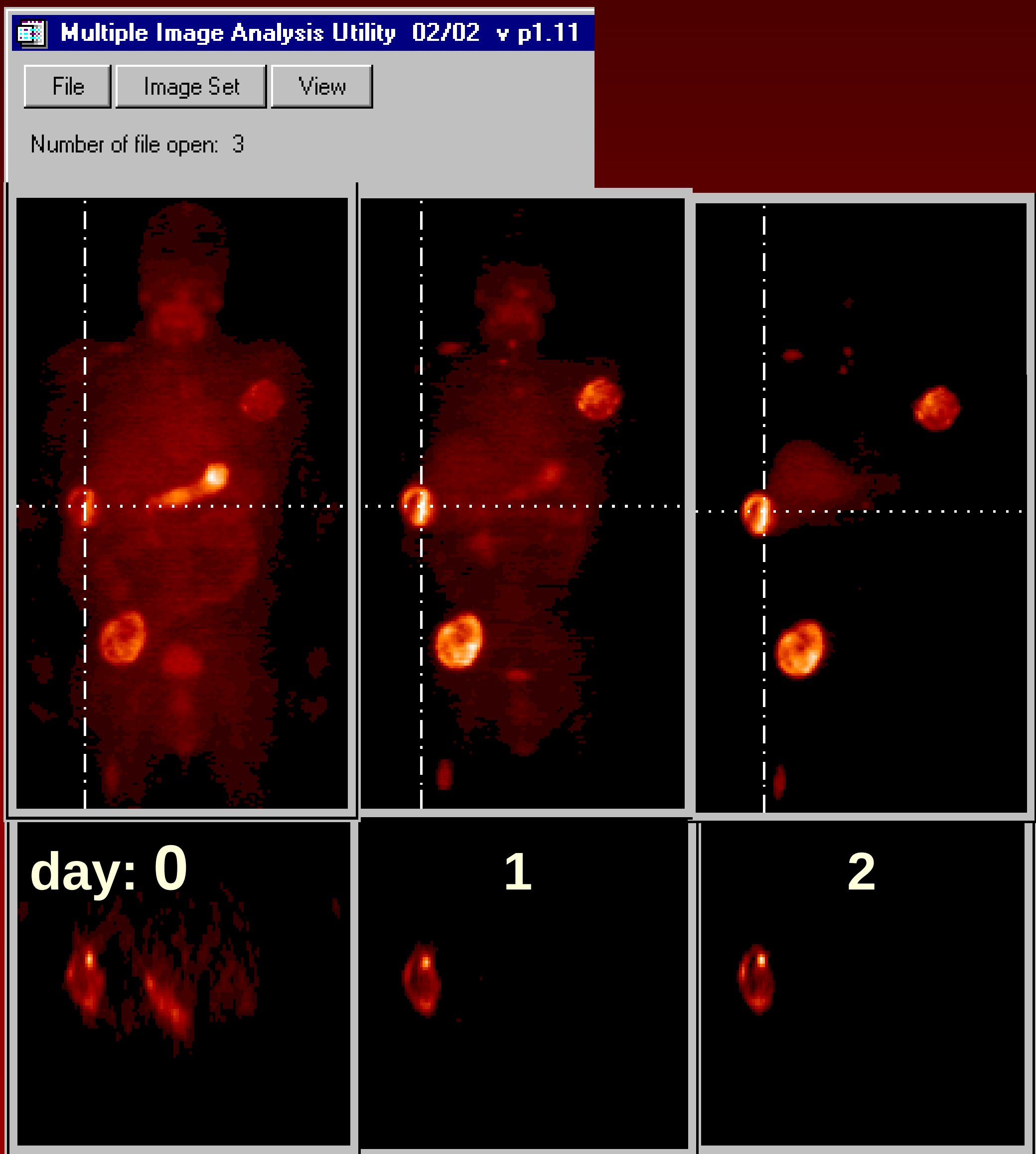
summed coronal

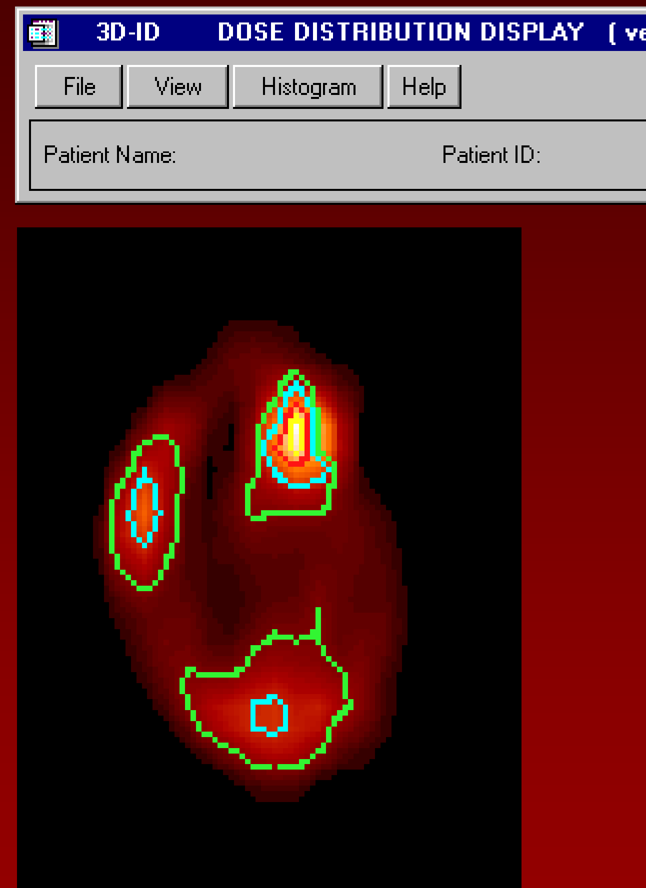
"… with tracer avid disease. There are multiple metastases visualized in the bony structures, in particular in the left scapular region, right lower lateral chest wall, right hip and proximal femur, and the right mid-femoral diaphysis. Vertebral mets are visualized in the lower thoracic region, and approximately …."

Sgouros, *et al.*, JNM '04

Results - isodose contours

Pt. 13

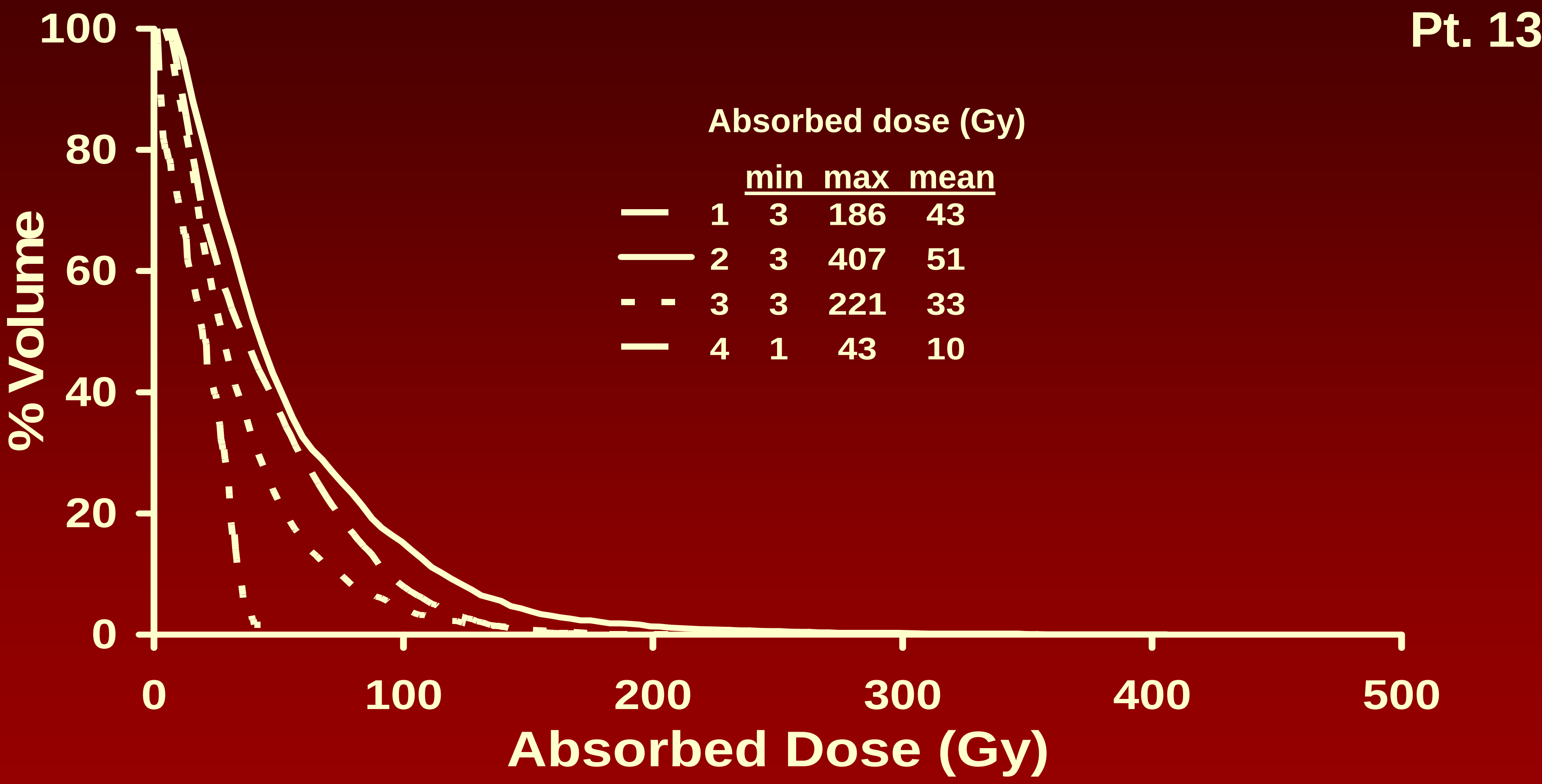




Isodose levels of 10,25,50,75%

Sgouros, *et al.*, JNM '04

Results - Dose-volume histogram



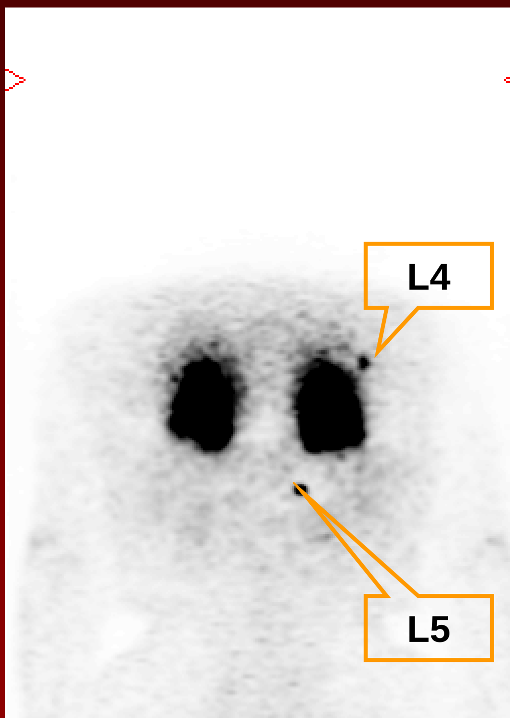
(104 mCi)

Sgouros, *et al.*, JNM '04

Lesion identification database

Pt. 16

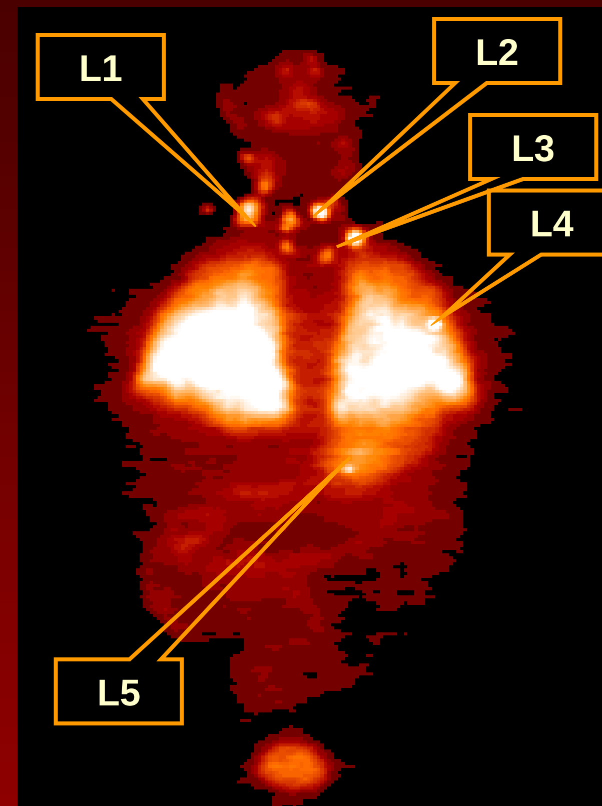
PET



coronal

sagittal

MIAU



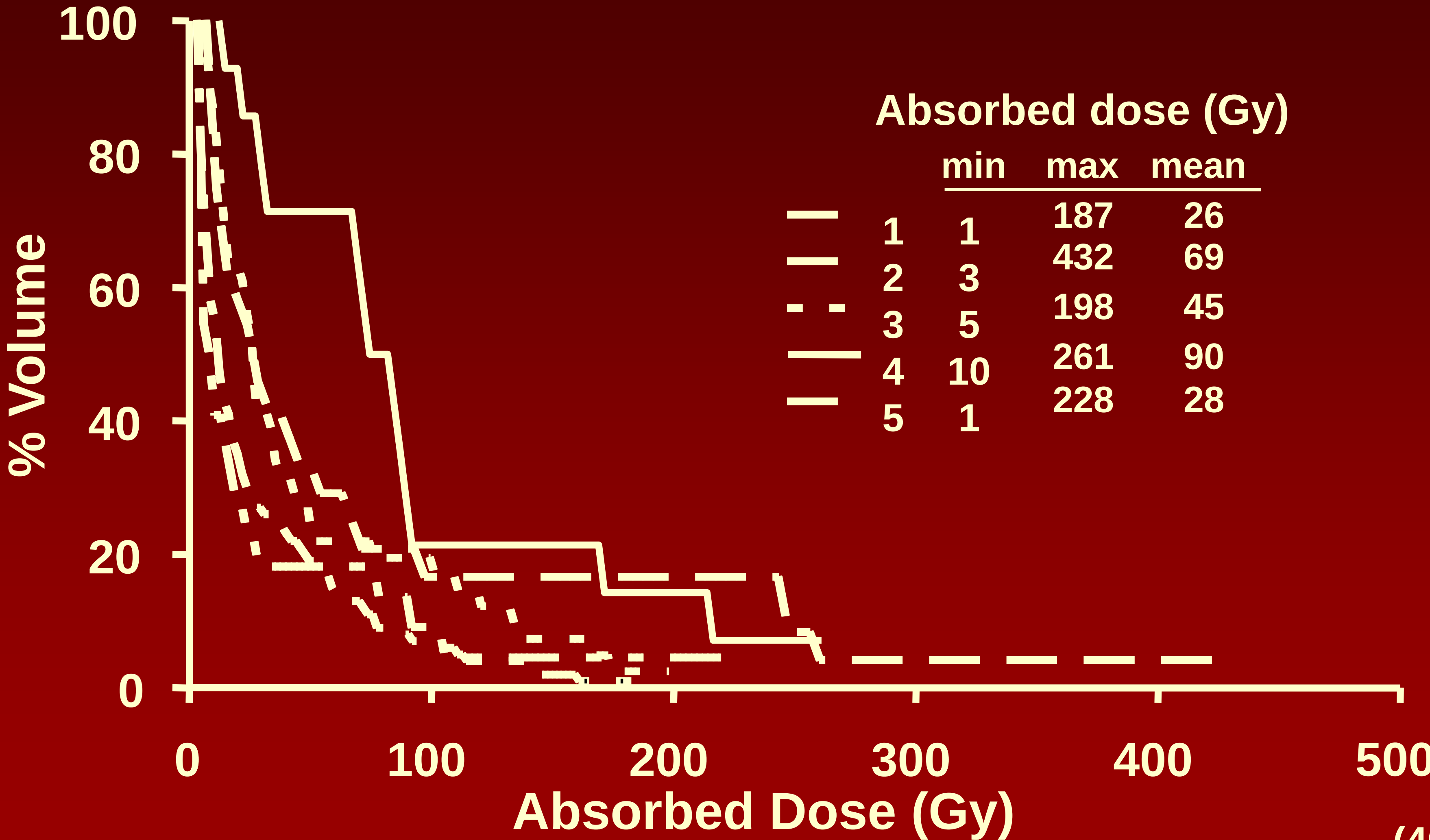
summed coronal

" … showed diffuse bilateral lung activity, as well as uptake in the neck, the superior mediastinum, as well as near the left posterior chest wall area, all consistent with …."

Sgouros, *et al.*, JNM '04

Results - Dose-volume histogram

Pt. 16



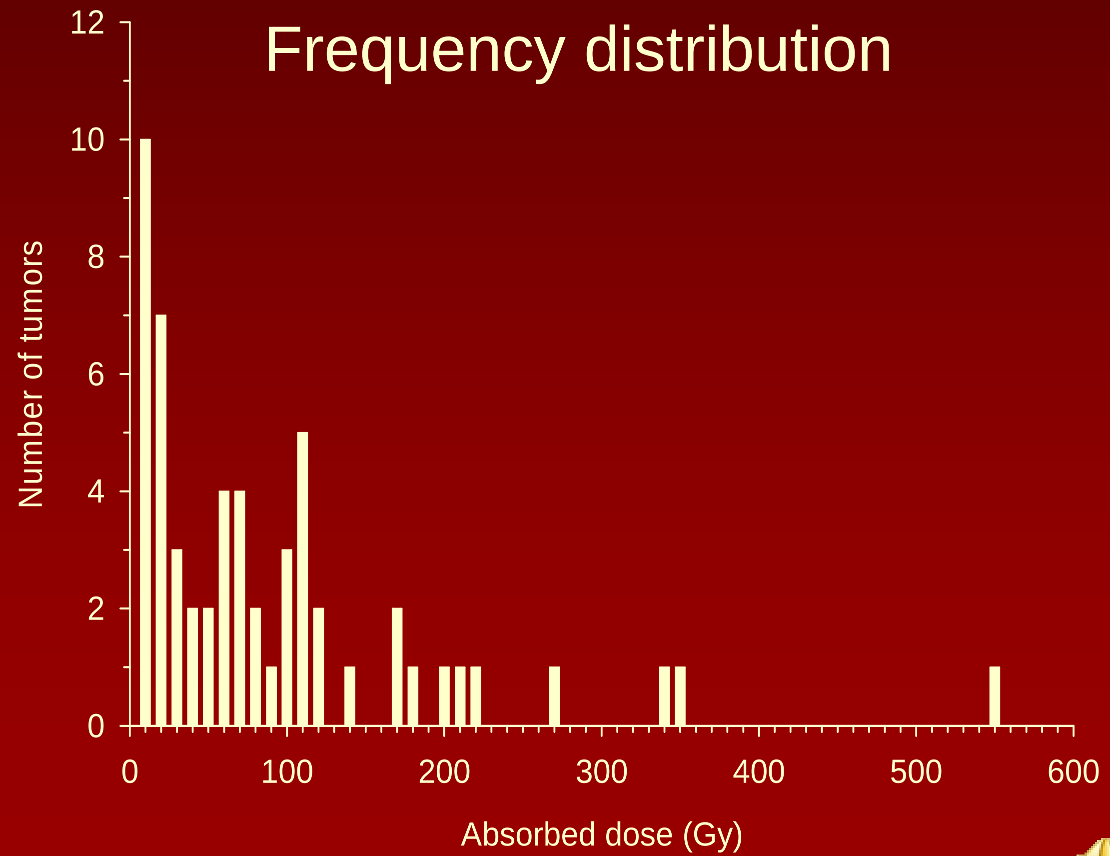
(400 mCi)

Sgouros, *et al.*, JNM ‘04

Results - Summary

Mean, min, max calculated for 56 different lesions

Absorbed Dose (Gy) (admin. activity, GBq)		
Mean	1.2 (15)	540 (11)
Min	0.3 (15)	50 (14)
Max	1.5 (15)	4000 (11)



Sgouros, *et al.*, JNM '04

3-D Radiobiological Dosimetry (3D-RD)

- 3D-ID
- Radiobiological modeling
- Dose-rate differences
- Non-uniformity in activity distribution
- Density differences

Prideaux et al. J Nucl Med '07

3-D Radiobiological Dosimetry (3D-RD)

- **Extension of 3D-Internal Dosimetry (3D-ID)** (Kolbert *et al* JNM '97)
- **Radiobiological modeling with tissue/tumor specific α, β, μ values are used to get**

Biologically Effective Dose (BED)

- **Accounts for dose rate variations**
- **Reference value relates to dose rate**

$$BED = D\left(1 + \frac{G(\infty)}{\alpha/\beta} D\right)$$

$$G(\infty) = \frac{2}{D^2}\int_0^{\infty} \dot{D}(t)dt \int_0^{t} \dot{D}(w)e^{-\mu(t-w)}dw$$

α and β are the tissue specific coefficients for radiation damage; μ is repair constant

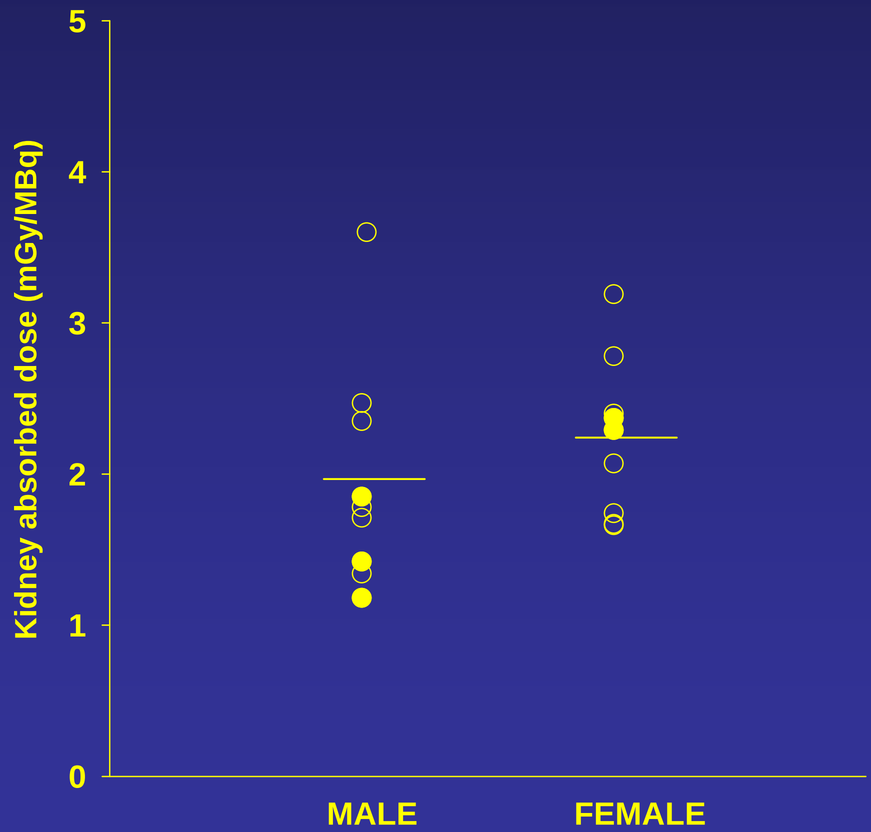
Equivalent Uniform Dose (EUD)

- **Accounts for non-uniform absorbed dose distribution**
- **Provides a single value that may be used to compare different dose distributions**
- **Reference value relates to uniform distribution**

$$EUD = -\frac{1}{\alpha}\ln\left(\sum_{i=1}^{N}\frac{e^{-\alpha BED_i}}{N}\right)$$

Prideaux *et al* JNM '07,
Hobbs, *et al* Med Phys '09
Baechler, *et al* Med Phys '08

Individual kidneys absorbed dose of ^{90}Y-DOTATOC Using 86Y-DOTATOC quantitative imaging and MIRDOSE3.1 for dosimetric calculations (assuming a standard kidney volume)



→ **Therapy planning: activities delivering 27 Gy to the kidneys**

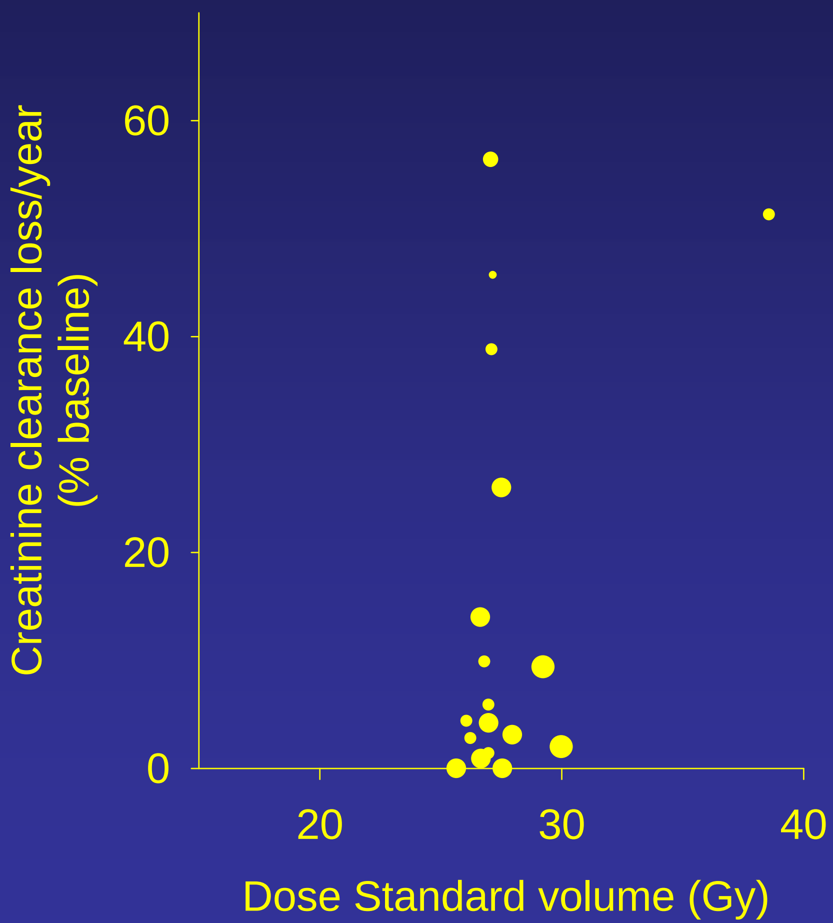
↓

Toxicity assessment

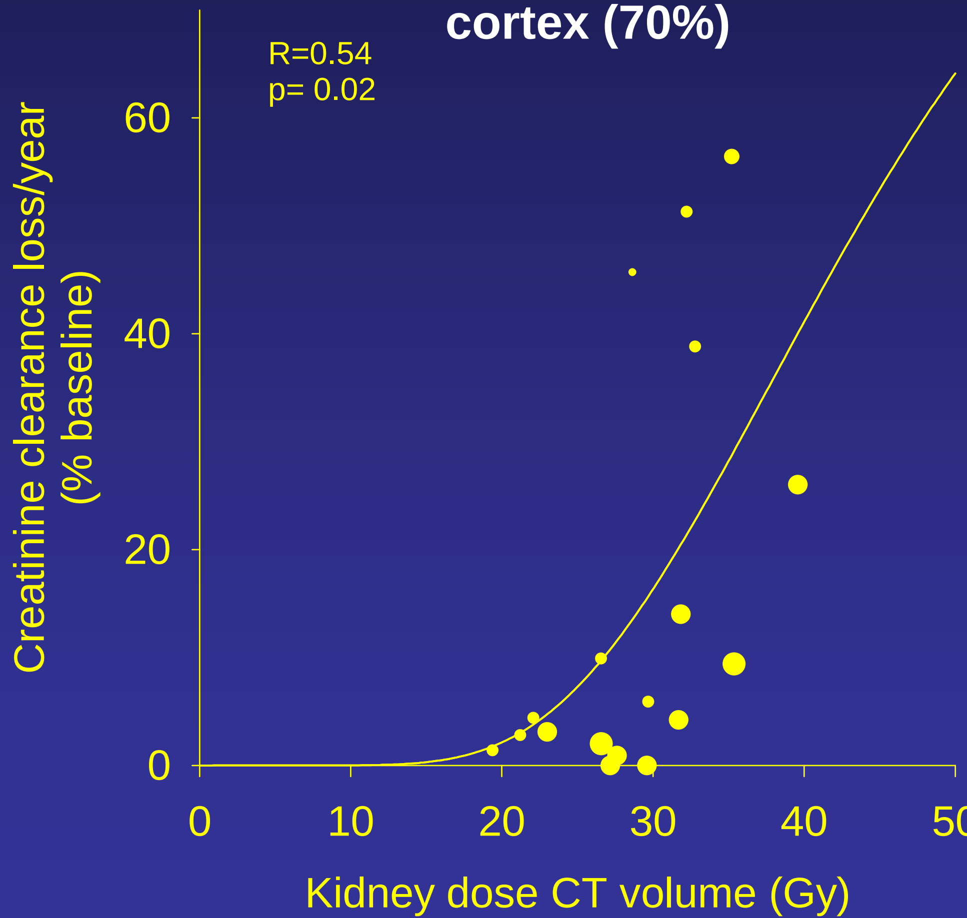
Importance of organ volume in self irradiation

**Correlation between kidney dose (Gy)
and creatinine clearance loss/year (% baseline) N=18**

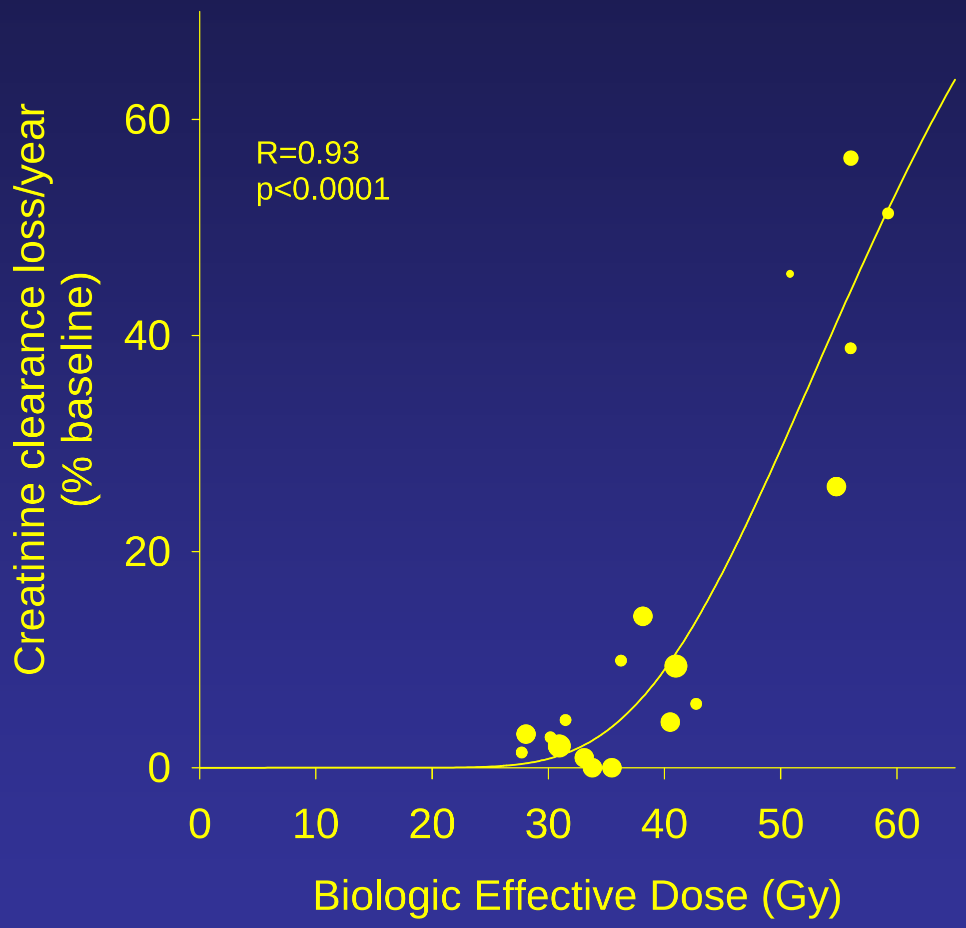
Standard kidney volumes



Kidney volumes measured by CT cortex (70%)



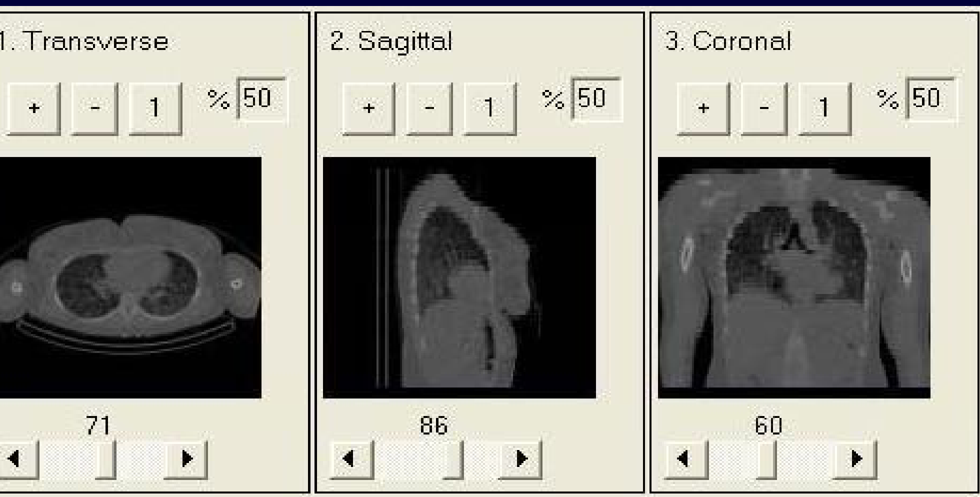
Correlation between BED and creatinine clearance loss/year



Barone R, Borson-Chazot F, Valkema R, et al. J Nucl Med. 2005 Jan;46 Suppl 1:99S-106S

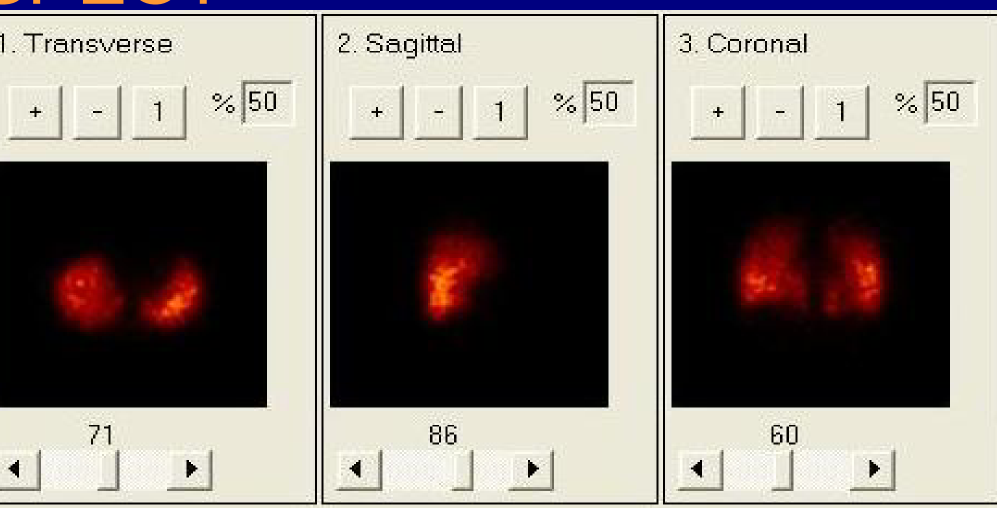
Clinical Thyroid Case

CT



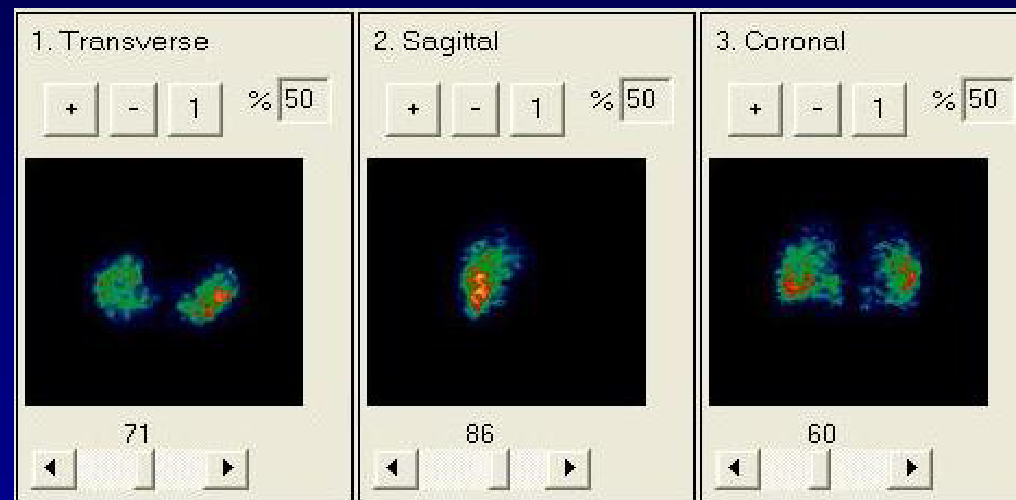
Non Uniform Density in Lungs

SPECT



•Non Uniform Activity Distribution

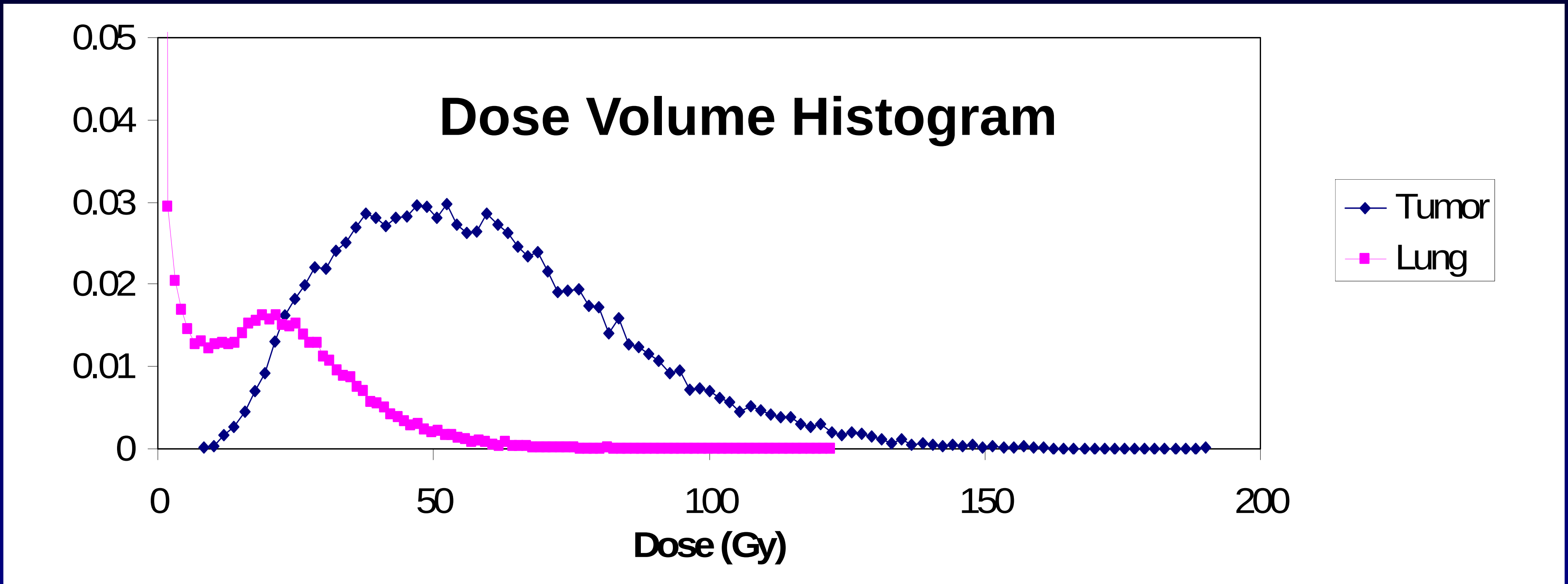
Eff. Half-life



•Non Uniform Clearance

Prideaux et al. J Nucl Med

Clinical Thyroid Case



	Tumor	Lung	
Mean Dose =	57.7 Gy	9.5 Gy	
Mean BED =	58.5 Gy	9.8 Gy	dose rate
EUD =	25.0 Gy	8.3 Gy	uniformity

Prideaux et al. J Nucl Med '07

3D-RD Clinical Implementation

- Real time (1 week) ^{131}I treatment planning for an 11 year-old girl with metastatic differentiated papillary thyroid cancer using patient specific 3-dimensional dosimetry (3D-RD).
- Heavy lung involvement meant concern about pulmonary toxicity and concern for overdosing
- Other considerations: tumor dose and brain toxicity
- Patient had prior ^{131}I for diagnostic and still retained significant quantities especially in two brain tumors
- Use ^{124}I and PET/CT for dosimetric assessment

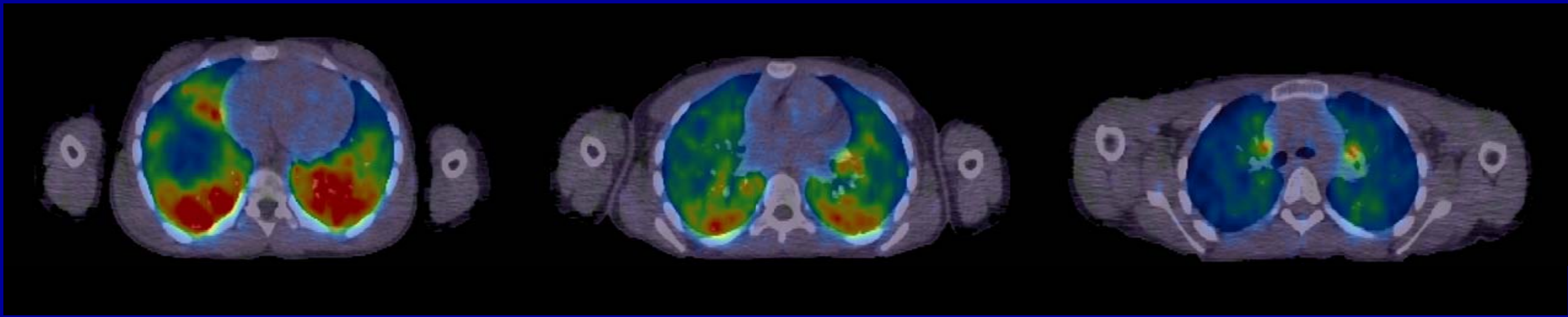
Hobbs, *et al* JNM

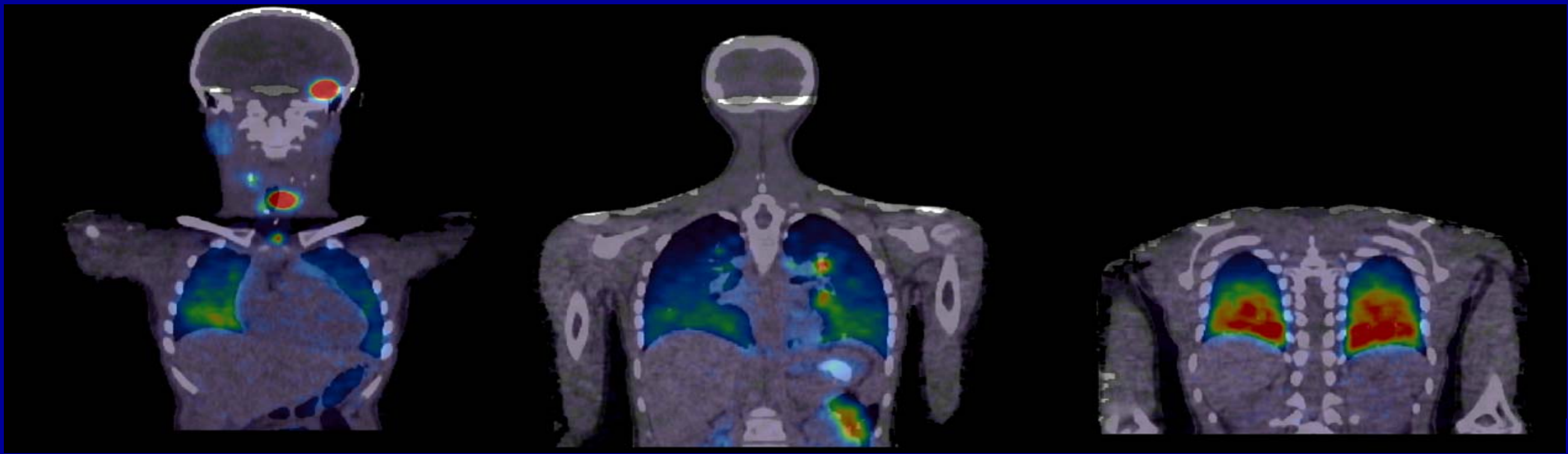
Method

- The patient received 92 MBq (2.5 mCi) of ^{124}I
- Whole body PET/CT scans were performed at 1, 24, 48, 72, and 96 h.
  - 2D mode with tungsten septa in place
  - Calibration with a standard measured in counting well
- 3D-RD calculation includes
  - longitudinal co-registration
  - compensation for different half-lives
  - EGS-based Monte Carlo simulation of ^{131}I decay for each time point.
- The dose rate results were fitted and an estimated absorbed dose per administered (^{131}I) activity to lungs was obtained and scaled to MTD of 27 Gy to normal lung
- Other methods (absorbed fraction with OLINDA and Benua-Leeper) were used for comparison using PET activity maps

Hobbs, *et al* JNM

PET/CT images

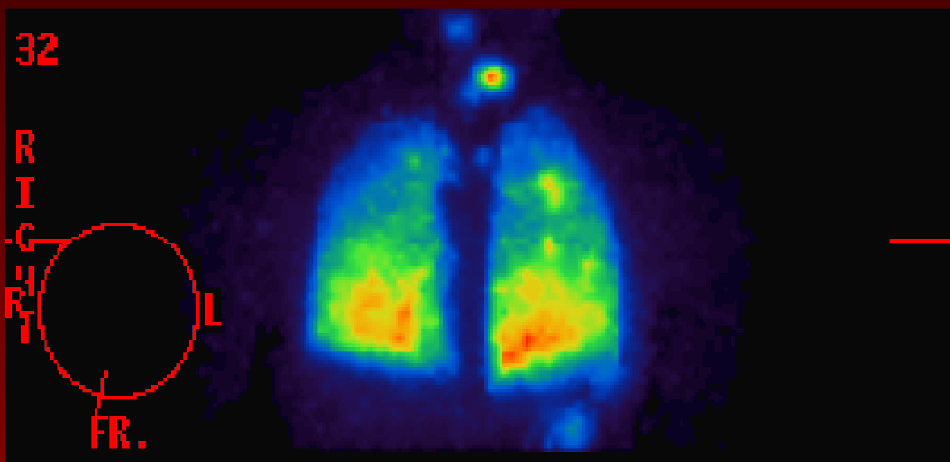




Hobbs, *et al* JNM

PET-based thyroid dosimetry

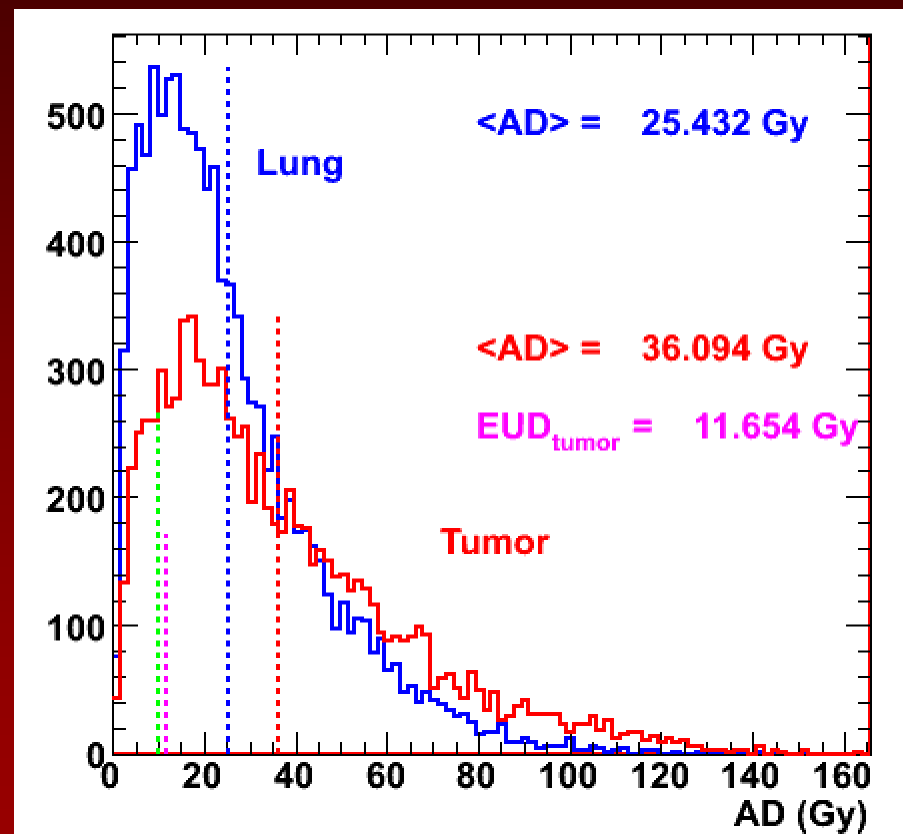
Absorbed Dose Map



- Example dosimetry analysis, patient was administered 5.1 GBq so as not to exceed 25-27 Gy to lungs
- Physician was thinking of 7.4 GBq
- Patient temporal lobe tumor has shrunk
- family is very happy

- Based on dosimetry calculation
- MC started after first acquisition
- Calculation completed within 48 h of last time-point
- Absorbed dose to T lobe lesion ≈ 325 Gy
- Lung tumor dose 36 Gy
- Equivalent uniform dose (EUD) = 11.6 Gy

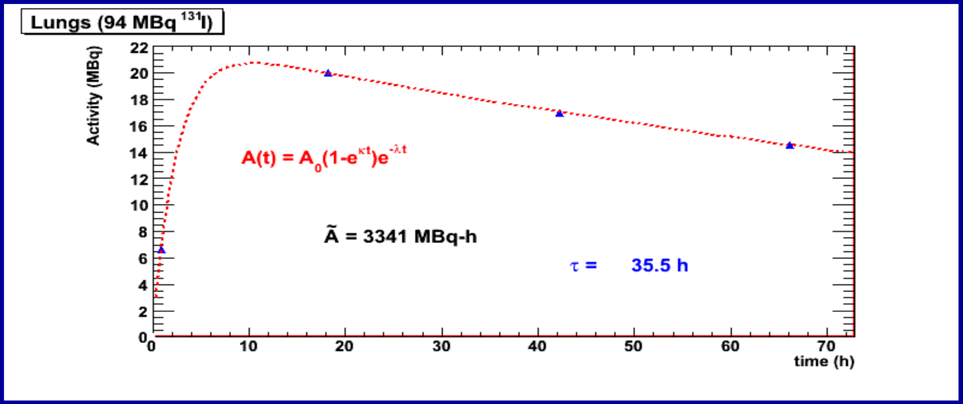
Dose-Volume histograms

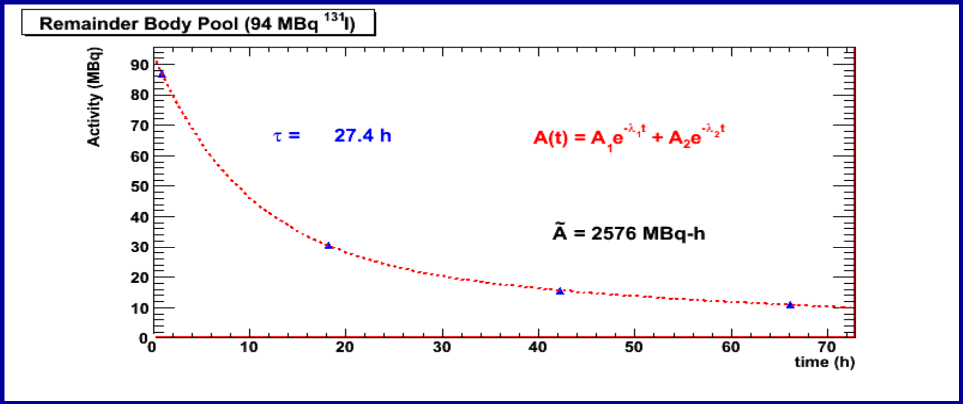


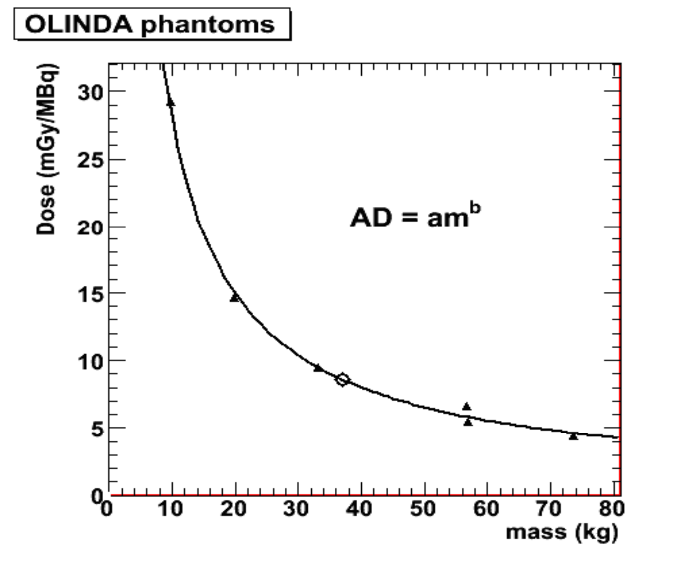
Absorbed dose distribution for 5.1 GBq ^{131}I administration

OLINDA-absorbed fraction

- Residence times from lungs and rest of body pool
- Input into OLINDA for all phantoms
- Phantom results as a function of mass and fit
- Input patient mass
- Scale to 27 Gy MTD constraint
- **AA: 2.89 GBq (78 mCi)**







Hobbs, *et al* JNM '09

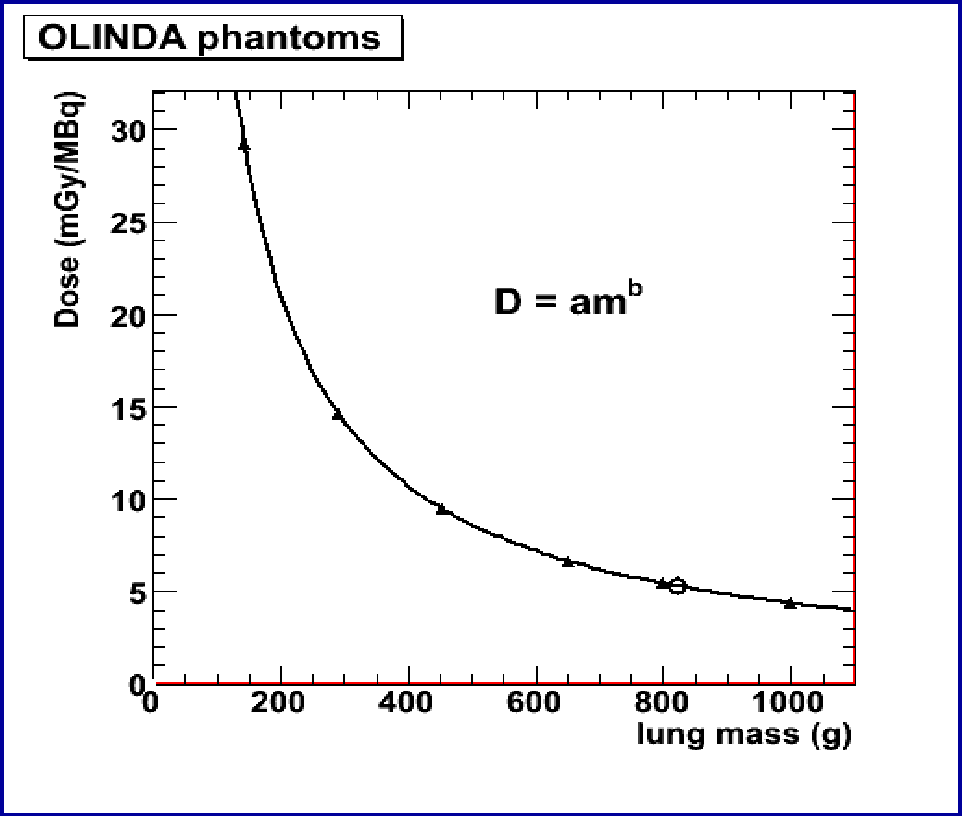
Methodological Comparison

- What activity to administer?
- OLINDA: 2.9 GBq
- 3D-RD: 5.1 GBq
- Retrospective re-examination

Hobbs, *et al* JNM

OLINDA reviewed

- Patient lung mass greater than typical
  - Tumor increases density
  - Higher mass means lower dose for same activity
  - Plot OLINDA phantom results as a function of lung mass
  - Input patient lung mass
  - Scale to 27 Gy MTD
  - **AA: 5.18 GBq (140 mCi)**
- Convergence of results!



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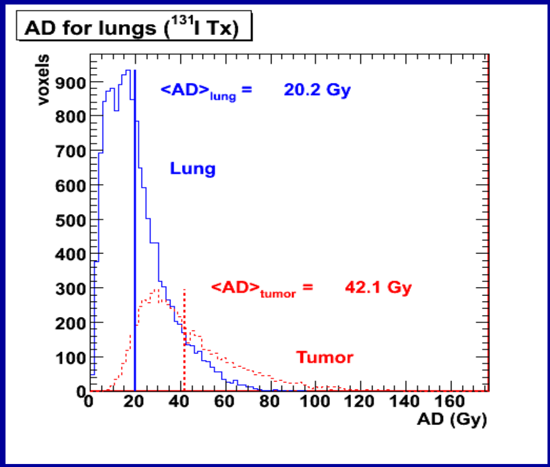
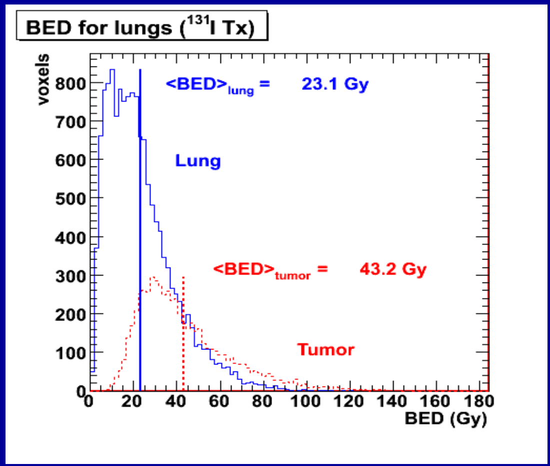
Lung/Tumor Discrimination

- 27 Gy Constraint to "normal lung tissue" rather than lung VOI
- Define "normal lung"
- Discriminate based on activity uptake at 48 h (overlap with anatomical position, density)
- BED uses numeric integration
  - α/β parameters different – less variation in the BED
- AA = 6.83 GBq (185 mCi)





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3D-RD for pediatric case

- Feasibility of real time treatment planning using 3D-RD, patient-specific dosimetry.
- A higher recommended AA than by an S-value based method (with a highly favorable clinical outcome) was obtained.
- Re-visitation of methods led to convergence (for this case).
- Further investigation of lung/tumor discrimination in future

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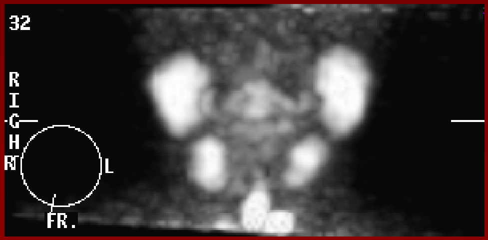
Salivary Gland ^{124}I-PET dosimetry

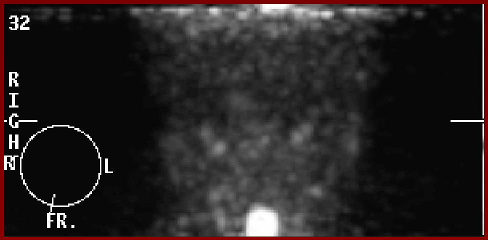
Collaboration with Prof.
Andreas Bockisch, M.D. and Dr.
Walter Jentzen, Ph.D.
University of Duisburg-Essen,
Essen, Germany

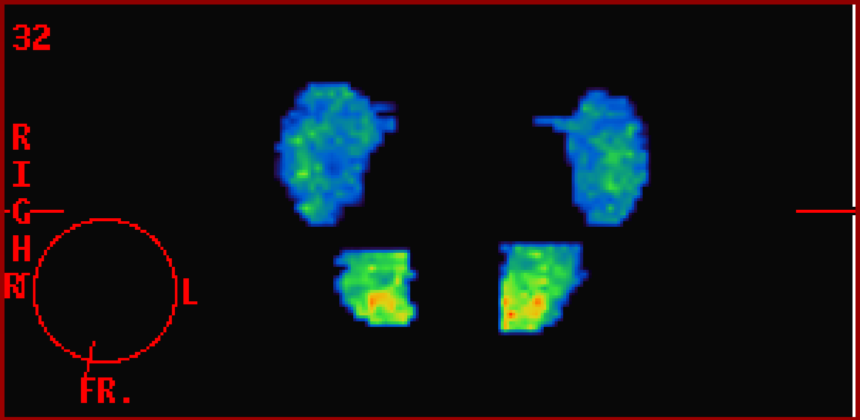
- Dose-Response for Salivary gland toxicity
- 7 ^{124}I PET scans over 4 days
- Compare w/ absorbed fraction calculation
- Impact of spatial dose distribution

~2 h



~72 h





Absorbed dose map for dose contribution due to decays after the first 24 h

The Problem defined

“Calculate energy deposition density (i.e., absorbed dose) in a particular organ or tumor volume”

The Problem defined

Index of response and toxicity:

- absorbed dose, D(x,y,z)
- absorbed dose rate, DR(x,y,z)
- Radiosensitivity, R(x,y,z)
- proliferation rate, P(x,y,z)
- Criticality (importance in likely organ failure), C(x,y,z)

Response = F(D,DR,R,P,C); F ?