

From Model-based to Patient-specific dosimetry in Nuclear Medicine



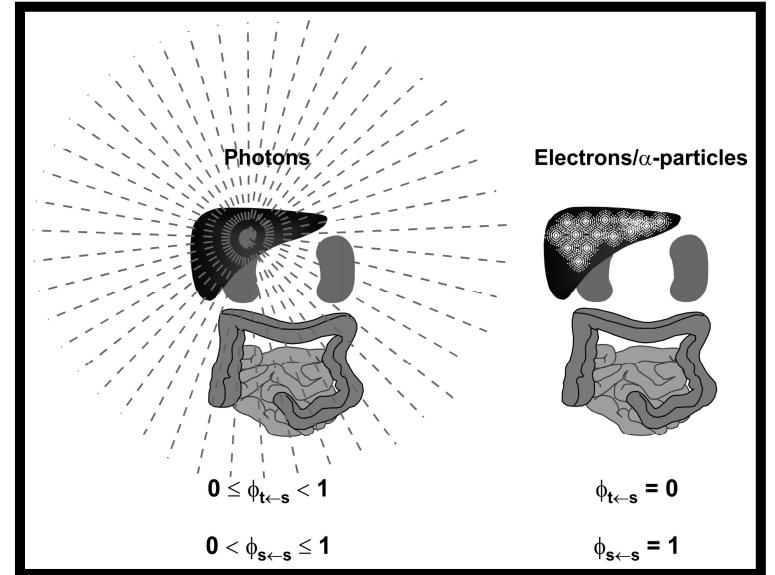
Manuel Bardiès (manuel.bardies@inserm.fr)
Centre de Recherches en Cancérologie de Toulouse, France



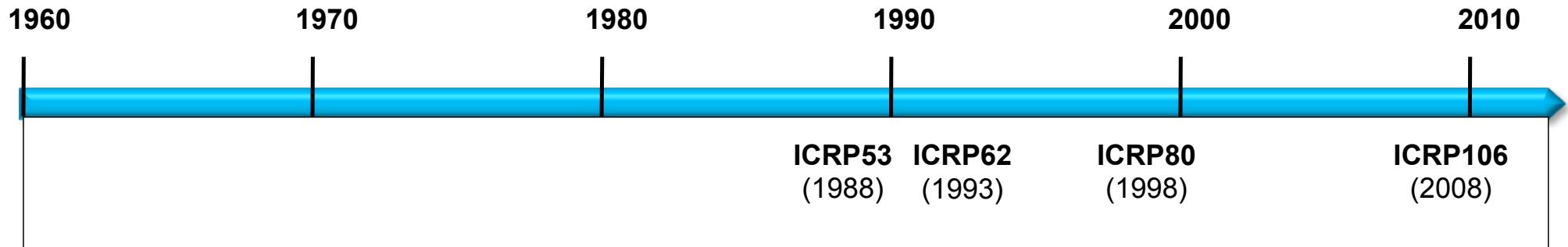
Nuclear Medicine Dosimetry

$$\bar{D}_k = \sum_h \tilde{A}_h \times S_{(k \leftarrow h)}$$

- MIRD formalism
 - \tilde{A} : Cumulated activity
 - Quantitative Imaging
 - Time-Activity Curve integration
 - S : Absorbed Dose Calculation
- And... global accuracy relies on both terms:
 - Improving \tilde{A} requires improving S (and vice-versa)



Diagnostics dosimetry

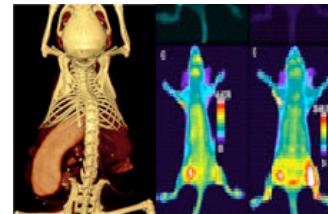
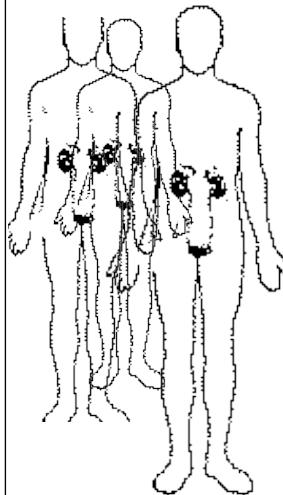


«Radiation dose to patients from radiopharmaceuticals»

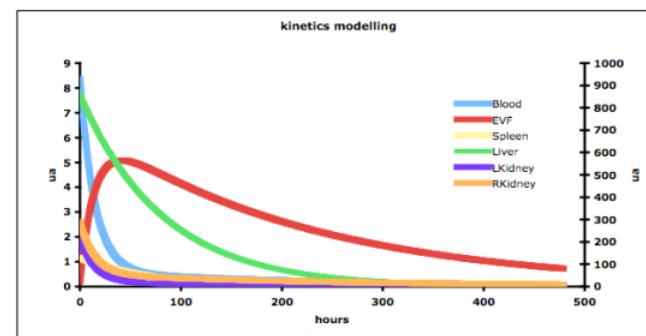
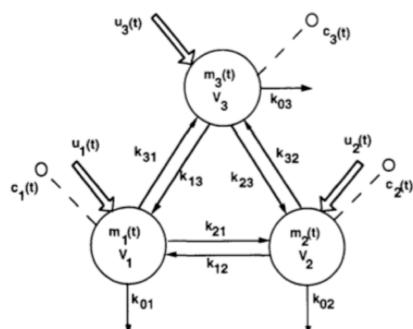
- 1988 ICRP Publication 53. Ann. ICRP 18 (1-4)
- 1993 Addendum 1 to ICRP Publication 53. Ann. ICRP 22(3)
- 1998 Addendum 2 to ICRP Publication 53. Ann. ICRP 28 (3)
- 2008 Addendum 3 to ICRP Publication 53. Ann. ICRP 38 (1-2)



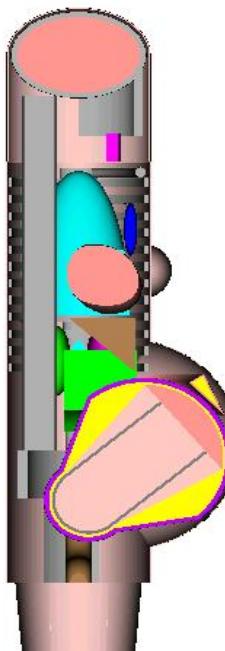
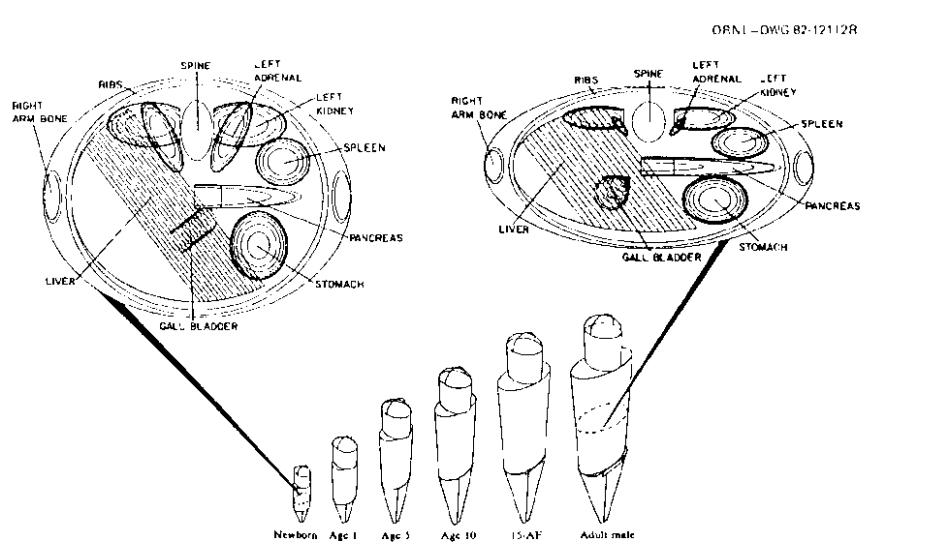
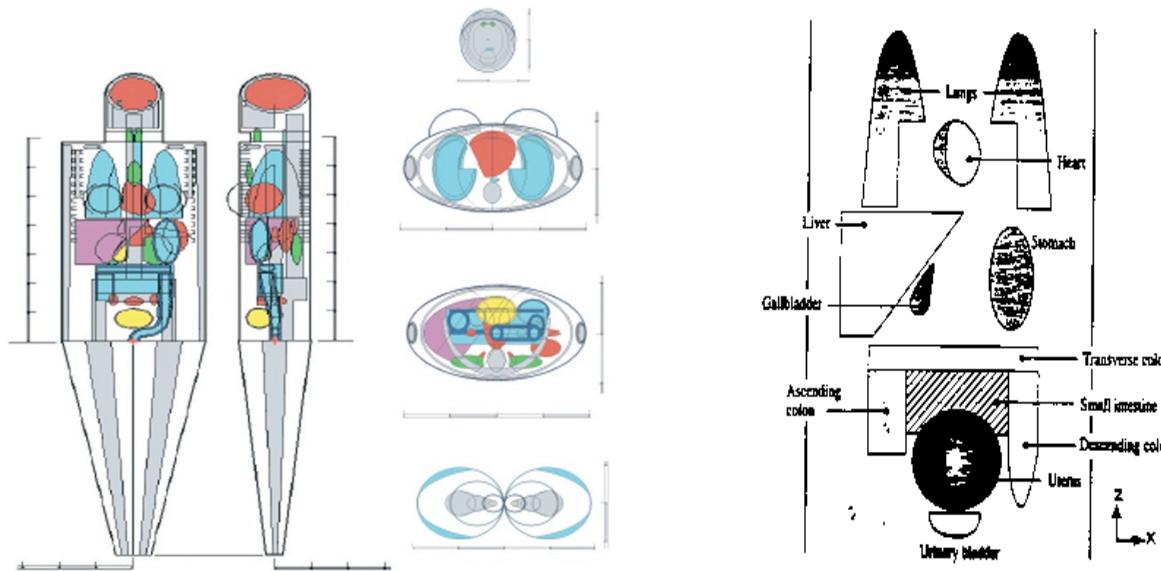
ICRP Approach (Diagnostics)



~A



ICRP Approach (Diagnostics)



S

Computing models

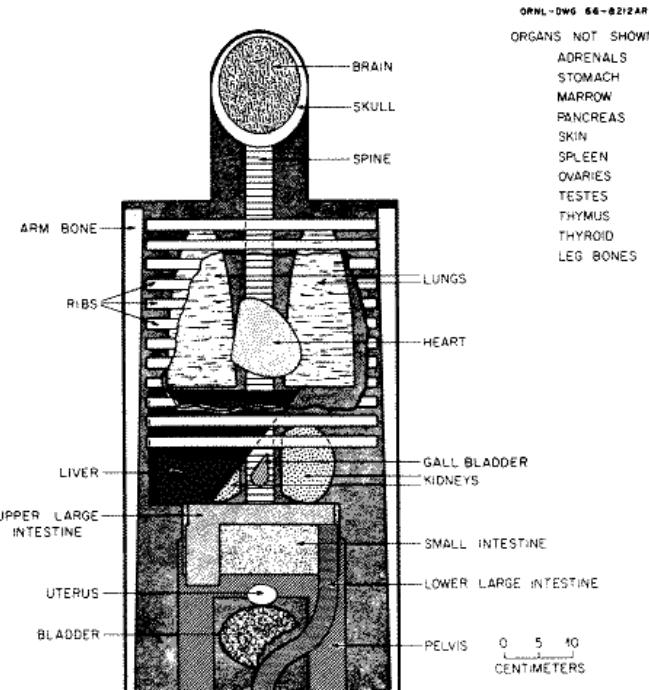
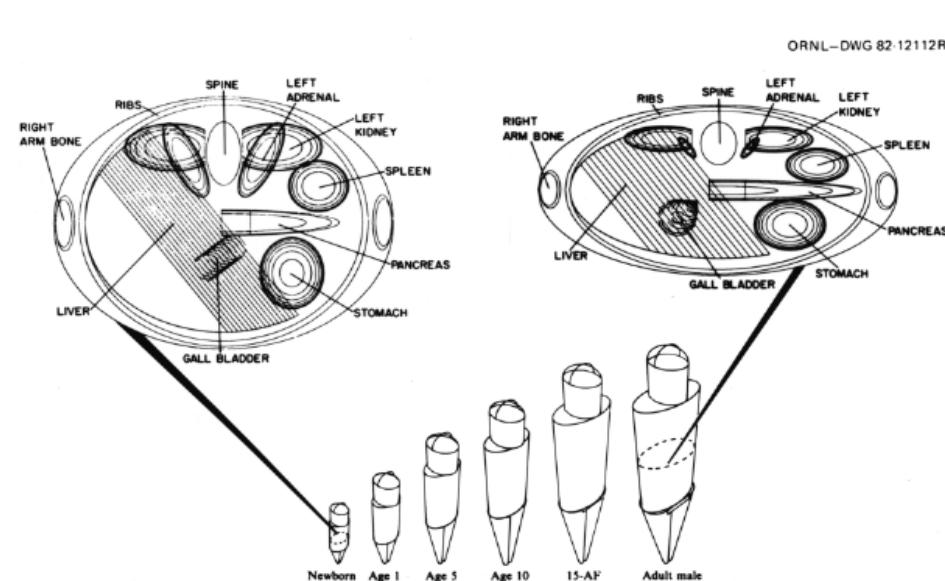
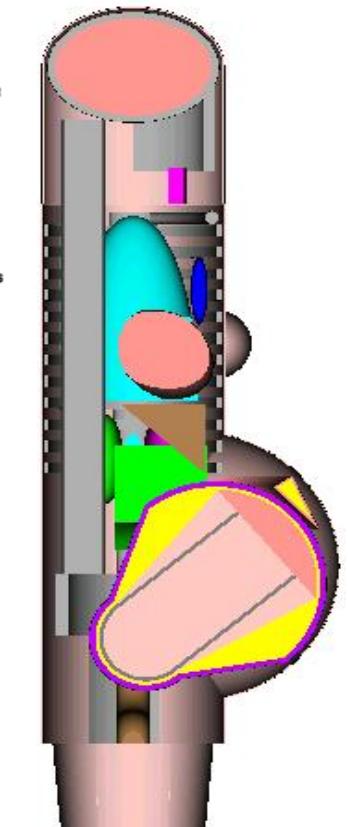


Fig. A-3. Anterior view of the principal organs in the head and trunk of the adult phantom developed by Snyder et al. (1974). Although the heart and head have been modified in this report, this schematic illustrates the simplicity of the geometries of the organs.

Snyder 1975

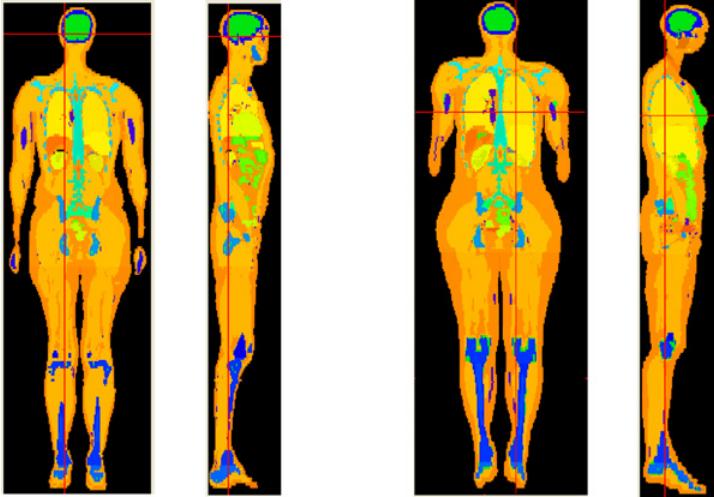


Cristy & Eckerman 1987



Stabin 1995

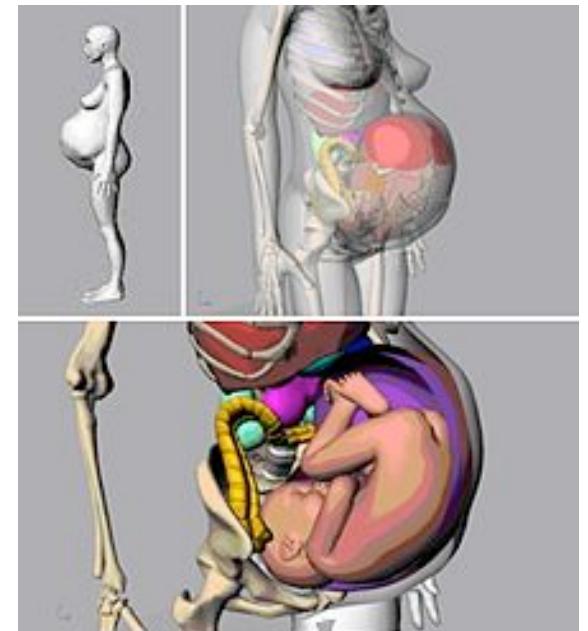
Computing models



Reference Adult
male/female
ICRP 110



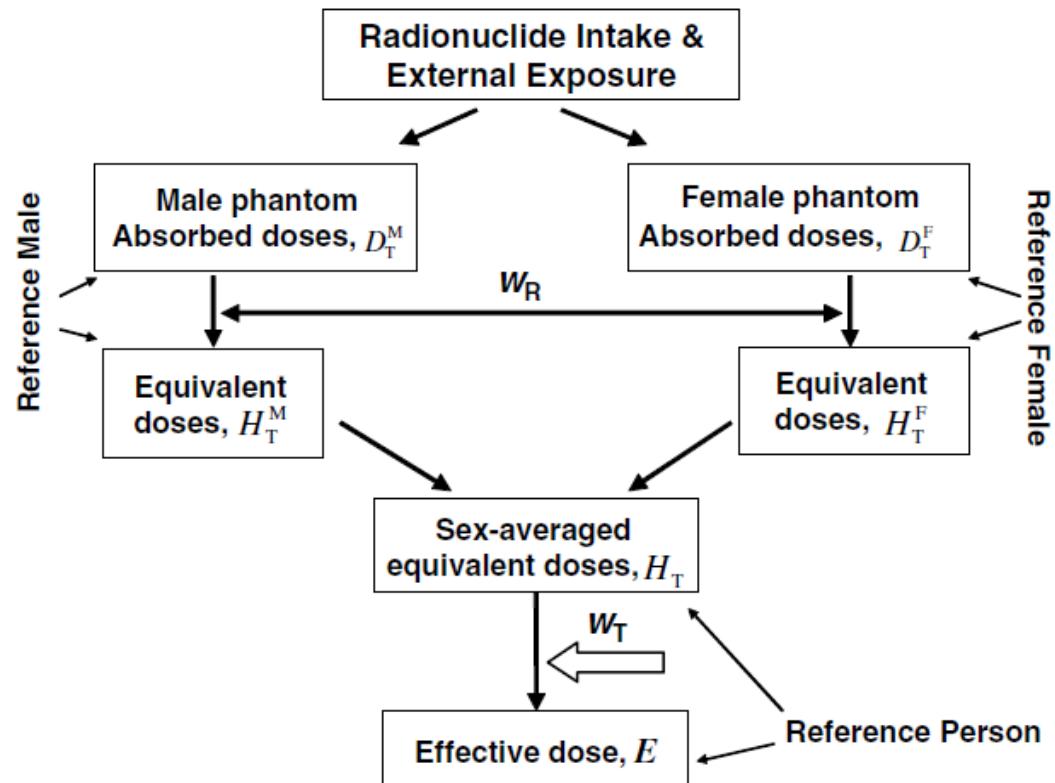
Paediatric series
Lee et al. (2010)
PMB 55(2):339-363



Pregnant female
Guo et al. (2010)
RPD 138(1):20-28

ICRP Evolution

- Recent reference report
(ICRP 103)
- New computing models
(ICRP 110 + ... ?)
- New calculation scheme
- New weighting factors
- Transition phase!
(ex: ICRP 106)



New ICRP 110 models

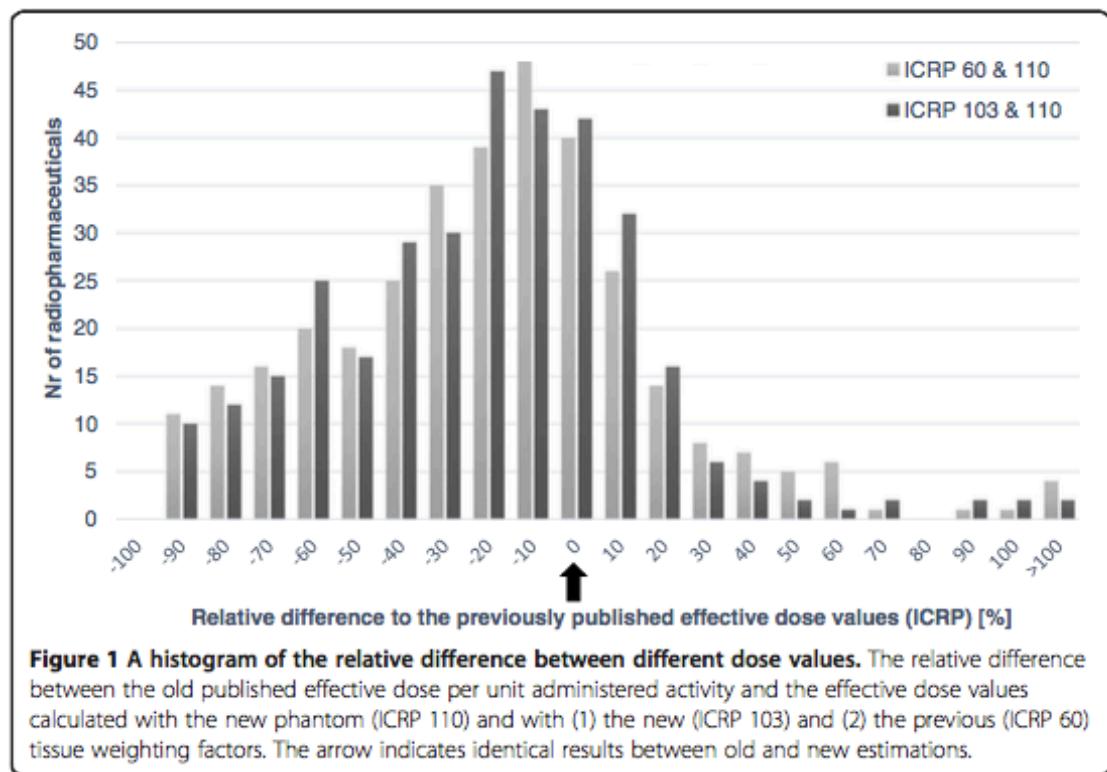
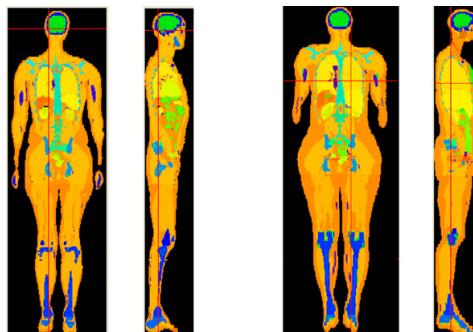
ORIGINAL RESEARCH

Open Access

Effective dose to adult patients from 338 radiopharmaceuticals estimated using ICRP biokinetic data, ICRP/ICRU computational reference phantoms and ICRP 2007 tissue weighting factors

Martin Andersson^{1*}, Lennart Johansson², David Minarik¹, Sigrid Leide-Svegborn¹ and Sören Mattsson¹

Andersson et al. EJNMMI Physics 2014 1:9



- Zankl et al. «Electron specific absorbed fractions for the adult male and female ICRP/ICRU reference computational phantoms» Phys Med Biol 2012, 57(14):4501–4526
- Andersson et al. «An internal radiation dosimetry computer program, IDAC2.0, for estimation of patient dose for radiopharmaceuticals» Radiat Prot Dosimetry 2013; doi: 10.1093/rpd/nct337

Diagnostics dosimetry: Conclusion

Group	Model	Model ICRP - MIRD DER

Molecular Radiotherapy



<http://www.youtube.com/watch?v=GRRmX5eTa8s>

Dosimetry for MRT:

Group	Model	Model ICRP - MIRD DER
Specific		

- Patient-specific dosimetry requires AT LEAST a specific determination of \tilde{A}_h

Quantitative imaging: \tilde{A}_h

Is quantitative imaging for dosimetric purposes different from 'conventional' quantitative imaging in NM?

Quick answer: No...

...but some aspects are specific...

What kind of quantitative imaging is required for dosimetry?

Quantitative imaging: \tilde{A}_h

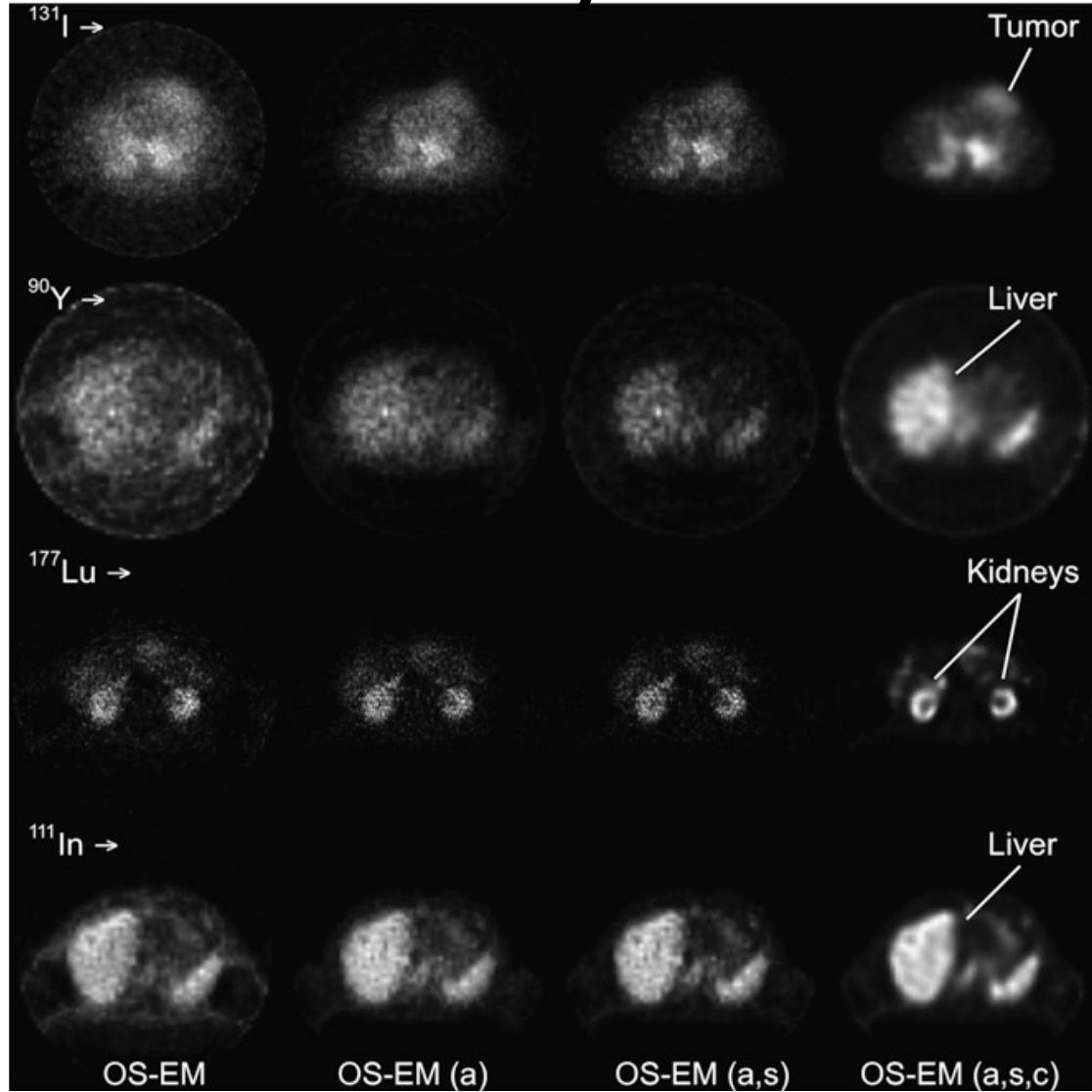
- What quantitative imaging implies:
 - On principle: Absolute quantification
 - Activity concentration in all voxels (Bq/cc)
 - Corrections OK for the whole FOV
- For the whole patient (space)
- Follow radiopharmaceutical kinetics (time)

Assessing errors: the main issue?

- Methodologies have been proposed to correct for several effects that degrade the quantitative content of NM images
- Many references are available in the literature!
 - Some approaches were implemented in clinical practice
 - Most remain as ‘one centre’ approach
- So who’s right?

Dewaraja YK et al. 2012, **MIRD pamphlet No. 23:**
Quantitative SPECT for patient-specific 3-dimensional dosimetry in internal radionuclide therapy. *J Nucl Med* 53(8), pp. 1310-25

SPECT: currently used isotopes



Dewaraja YK et al. 2012, MIRD pamphlet No. 23:

Quantitative SPECT for patient-specific 3-dimensional dosimetry in internal radionuclide therapy. *J Nucl Med* 53(8), pp. 1310-25

SPECT: currently used isotopes

Study	Radionuclide	System	Reconstruction	accuracy
Zeintl et al., 2010 (18)	^{99m} Tc	SPECT/CT	OS-EM, CDR, CT-derived AC, energy window-based SC, PVC	<6.8% error for 0.5- to 16-mL spheres
Dewaraja et al., 2010 (37)	¹³¹ I	SPECT/CT	OS-EM, CDR, CT-derived AC, energy window-based SC	<17% error for 8- to 95-mL spheres; 31% for 4-mL sphere
Assie et al., 2010 (23)	¹¹¹ In	SPECT and CT separate	OS-EM, CT-derived AC, energy window-based SC, PVC	<20% error for organs and 2- to 32-mL spheres; 48% error for 0.5-mL sphere
Shcherbinin et al., 2008 (49)	^{99m} Tc, ¹¹¹ In, ¹²³ I, ¹³¹ I	SPECT/CT	OS-EM, CDR, CT-derived AC, analytic scatter modeling	3%-5% error for 32-mL bottles
Minarik et al., 2008 (95)	⁹⁰ Y	SPECT/CT	OS-EM, CDR, CT-derived AC, ESSE	<11% error for liver and 100-mL sphere
Willowson et al., 2008 (19)	^{99m} Tc	SPECT/CT	OS-EM, CT-derived AC, transmission-dependent SC, PVC	<4% error for liver and cardiac chambers
de Wit et al., 2006 (59)	¹⁶⁶ Ho	SPECT	OS-EM, CDR, ¹⁵³ Gd transmission source-derived AC, Monte Carlo scatter modeling	16% average error for 220-mL bottles
Du et al., 2006 (62)	¹²³ I	SPECT/CT	OS-EM, CDR, CT-derived AC, ESSE, PVC	<2% error for putamen and caudate regions of brain phantom
He et al., 2005 (52)	¹¹¹ In	SPECT/CT	OS-EM, CDR, CT-derived AC, ESSE, PVC	<12% error for organs and 8- to 23-mL spheres
Koral et al., 2005 (50)	¹³¹ I	SPECT and CT separate	OS-EM, CDR, CT-derived AC, energy window-based SC, PVC	<7% average error for 100-mL sphere

Dewaraja YK et al. 2012, MIRD pamphlet No. 23:

Quantitative SPECT for patient-specific 3-dimensional dosimetry in internal radionuclide therapy. *J Nucl Med* 53(8), pp. 1310-25

Dosimetry for MRT:

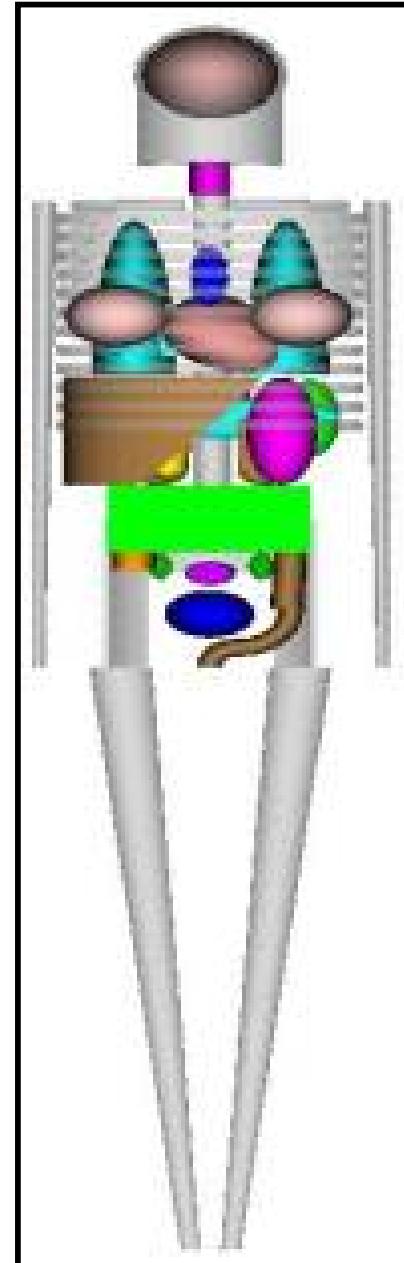
Group	Model	Model ICRP - MIRD DER
Specific		

- *Possibly the most important source of uncertainty?*

S factor calculation: $S_{(k \leftarrow h)}$

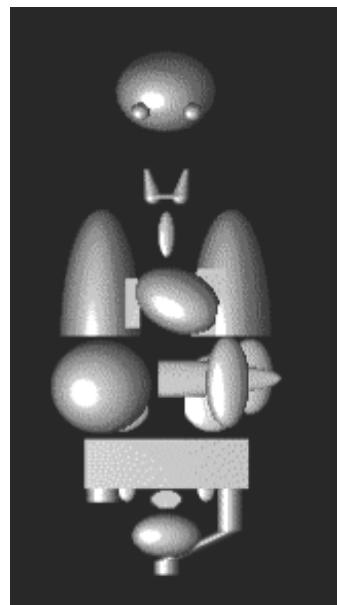
- From 'old' MIRD phantoms

MIRDOSE3
Olinda

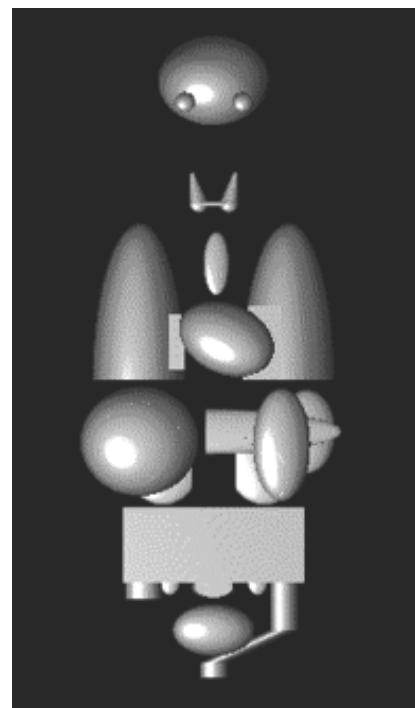


S factor calculation: $S_{(k \leftarrow h)}$

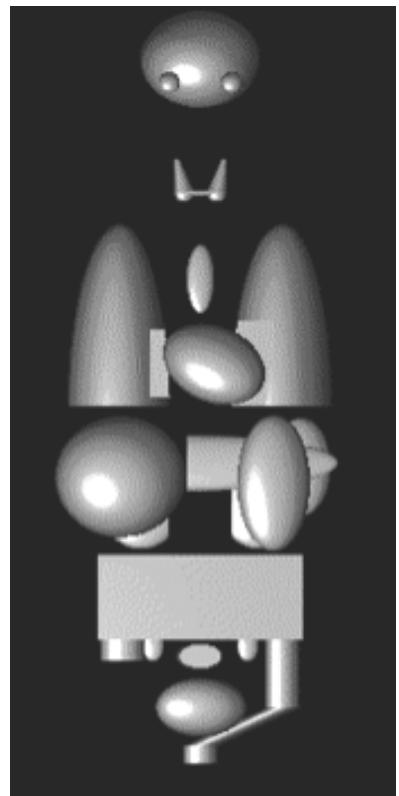
- From 'old' MIRD phantoms
- To more refined phantoms



150 cm



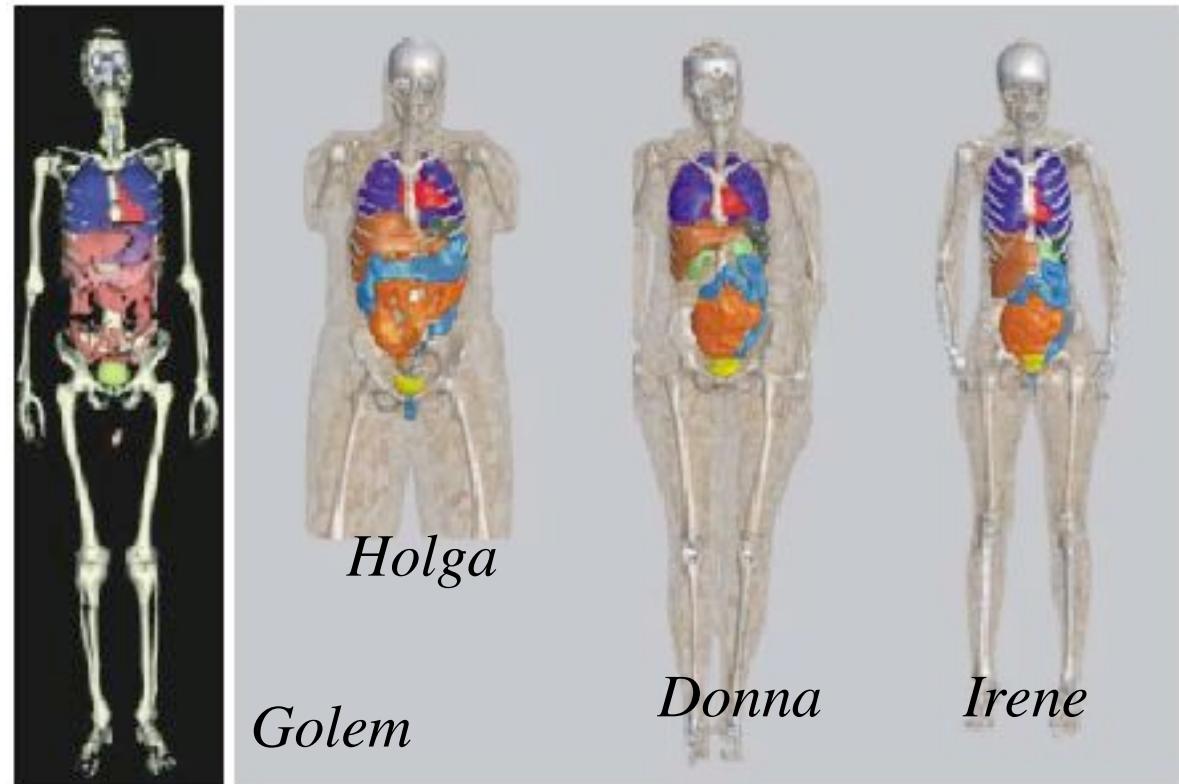
160 cm



170 cm

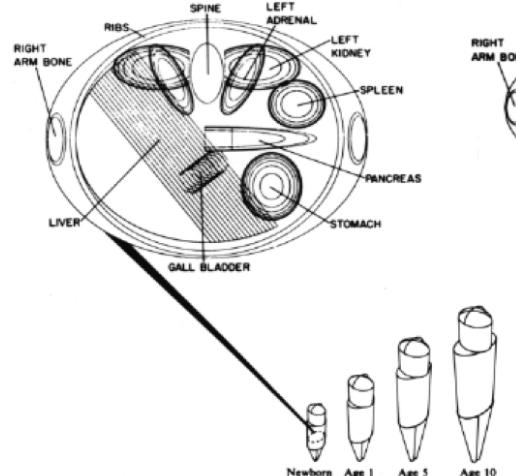
S factor calculation: $S_{(k \leftarrow h)}$

- From 'old' MIRD phantoms
- To more refined phantoms
- To voxel-based phantoms



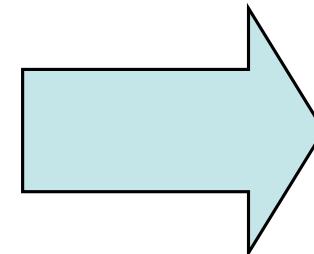
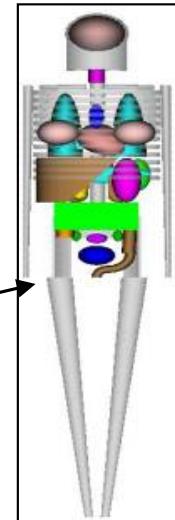
Radiat. Env. Biophys (2001) 40:153-162
PMB (2002) 47:89-106

Mass Adjustment



ORNL mathematical models

(ORNL/8381)



**Standard S
values**

For SELF Irradiation Only

$$S_{r \leftarrow r}(\text{patient}) = S_{r \leftarrow r}(\text{standard}) \cdot \frac{\text{Mass}_r(\text{standard})}{\text{Mass}_r(\text{specific})}$$

OLINDA mass adjustment

Input Data:

Model to adjusted-model!

1420.0	Brain	1120.0	Red Marrow
351.0	Breasts	120.0	Osteogenic Cells
10.5	Gallbladder Wall	3010.0	Skin
167.0	LLI Wall	183.0	Spleen
677.0	Small Intestine	39.1	Testes
158.0	Stomach Wall	20.9	Thymus
220.0	ULI Wall	20.7	Thyroid
316.0	Heart Wall	47.6	Urinary Bladder Wall
299.0	Kidneys	79.0	Uterus
1910.0	Liver	0.0	Fetus
1000.0	Lungs	0.0	Placenta
28000.0	Muscle	73700.0	Total Body
8.71	Ovaries		

Alpha Weight Factor Beta Weight Factor Photon Weight Factor

5.0 1.0 1.0 Reset organ values

Multiply all masses by: 1.0 DONE

Dosimetry for MRT:

Group	Model	Model ICRP - MIRD DER
Specific	Model \pm adjusted	Model \pm realistic

- Still «model-based» dosimetry - but easily implemented in a clinical environment!

Dosimetry for MRT:

Group	Model	Model ICRP - MIRD DER
Specific	Model \pm adjusted	Model \pm realistic
Specific		

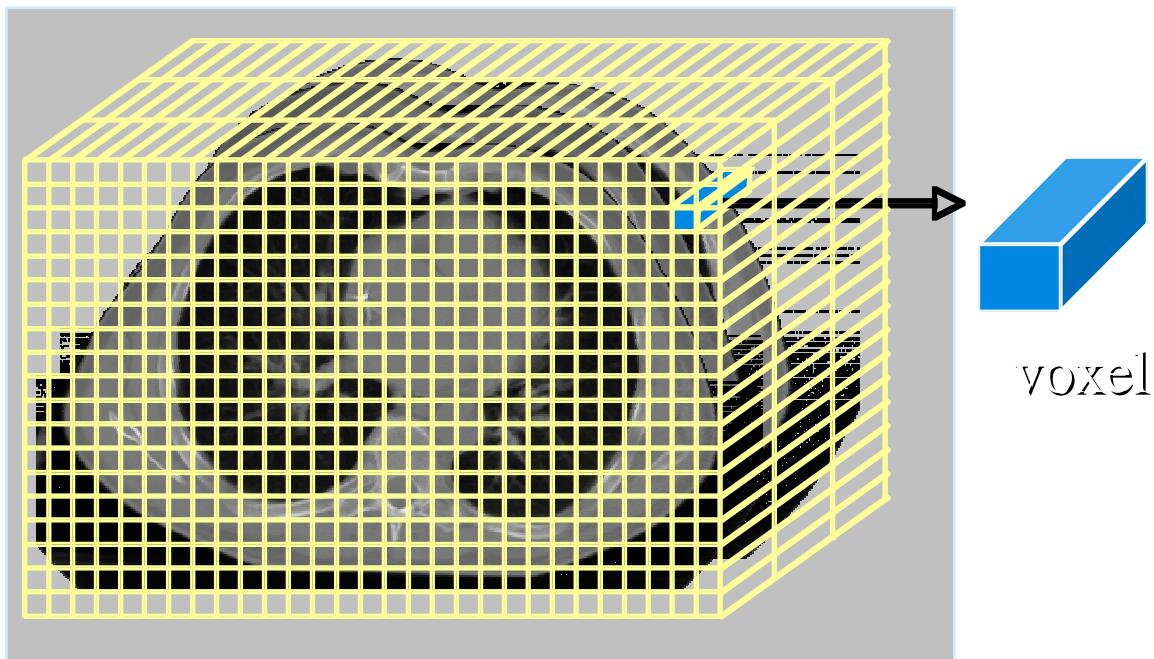
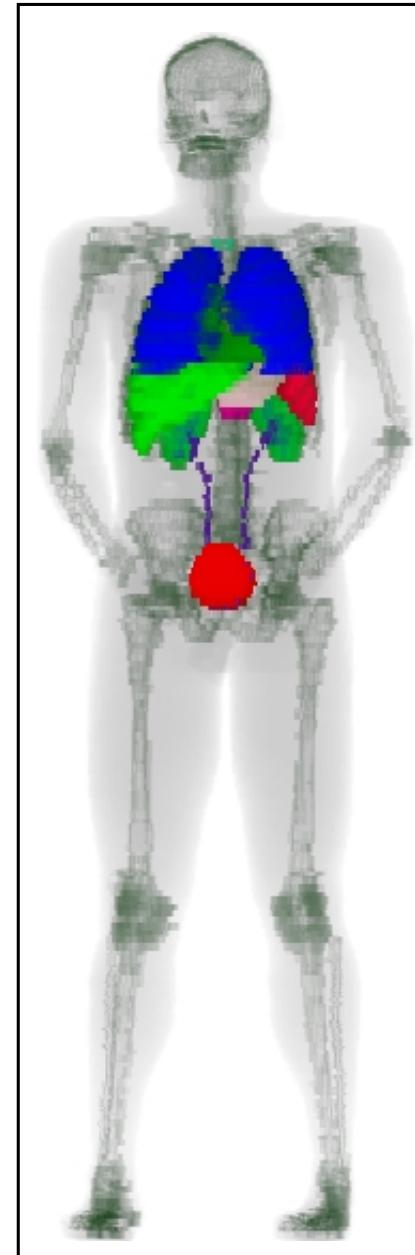
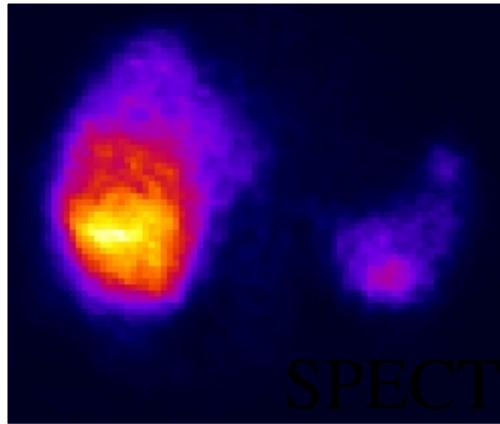
- *Patient-specific dosimetry requires AT LEAST a specific determination of \tilde{A}_h*

Dosimetry for MRT:

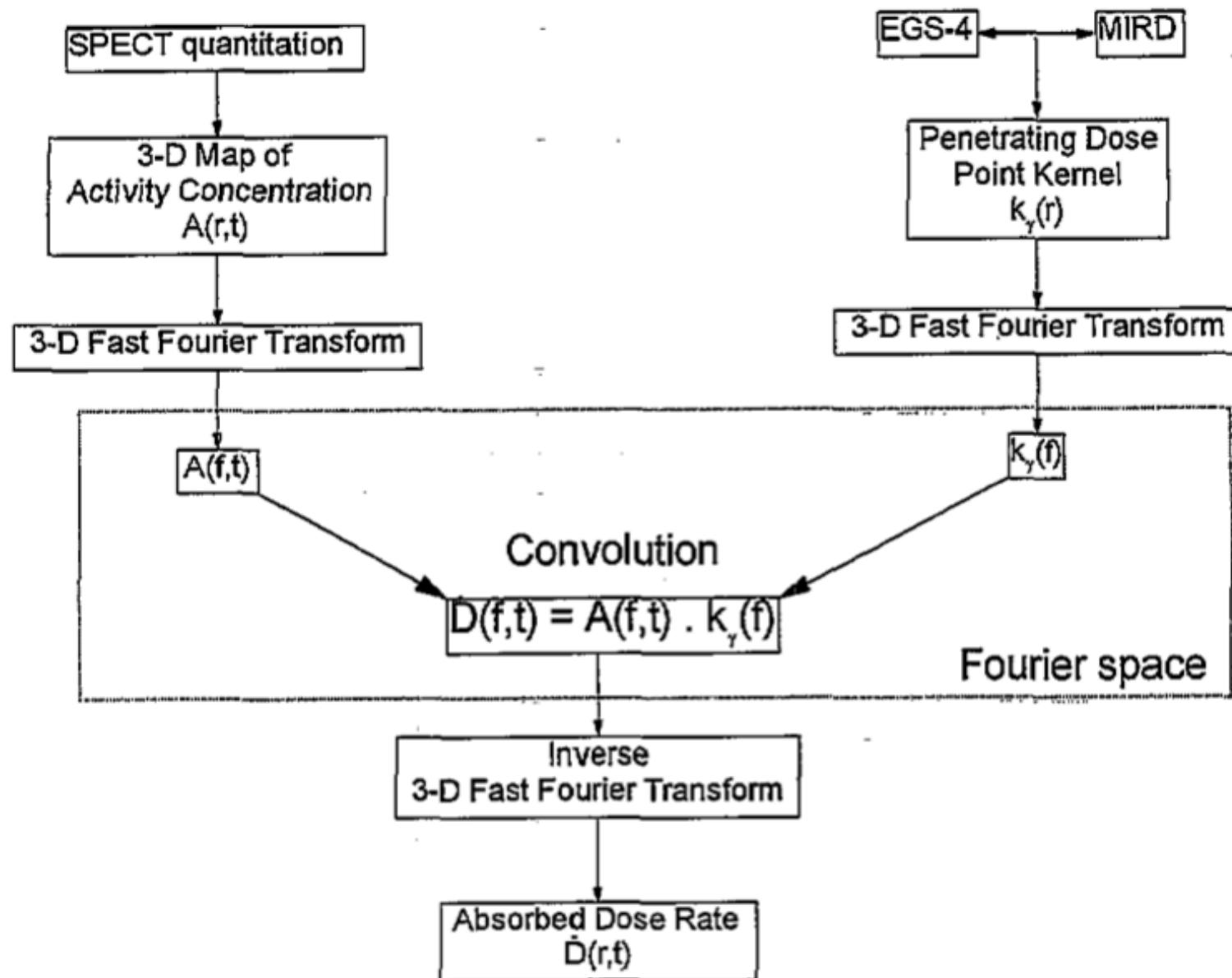
Group	Model	Model ICRP - MIRD DER
Specific	Model \pm adjusted	Model \pm realistic
Specific	Specific	

- *Specific S factor determination requires patient-specific geometry assessment*

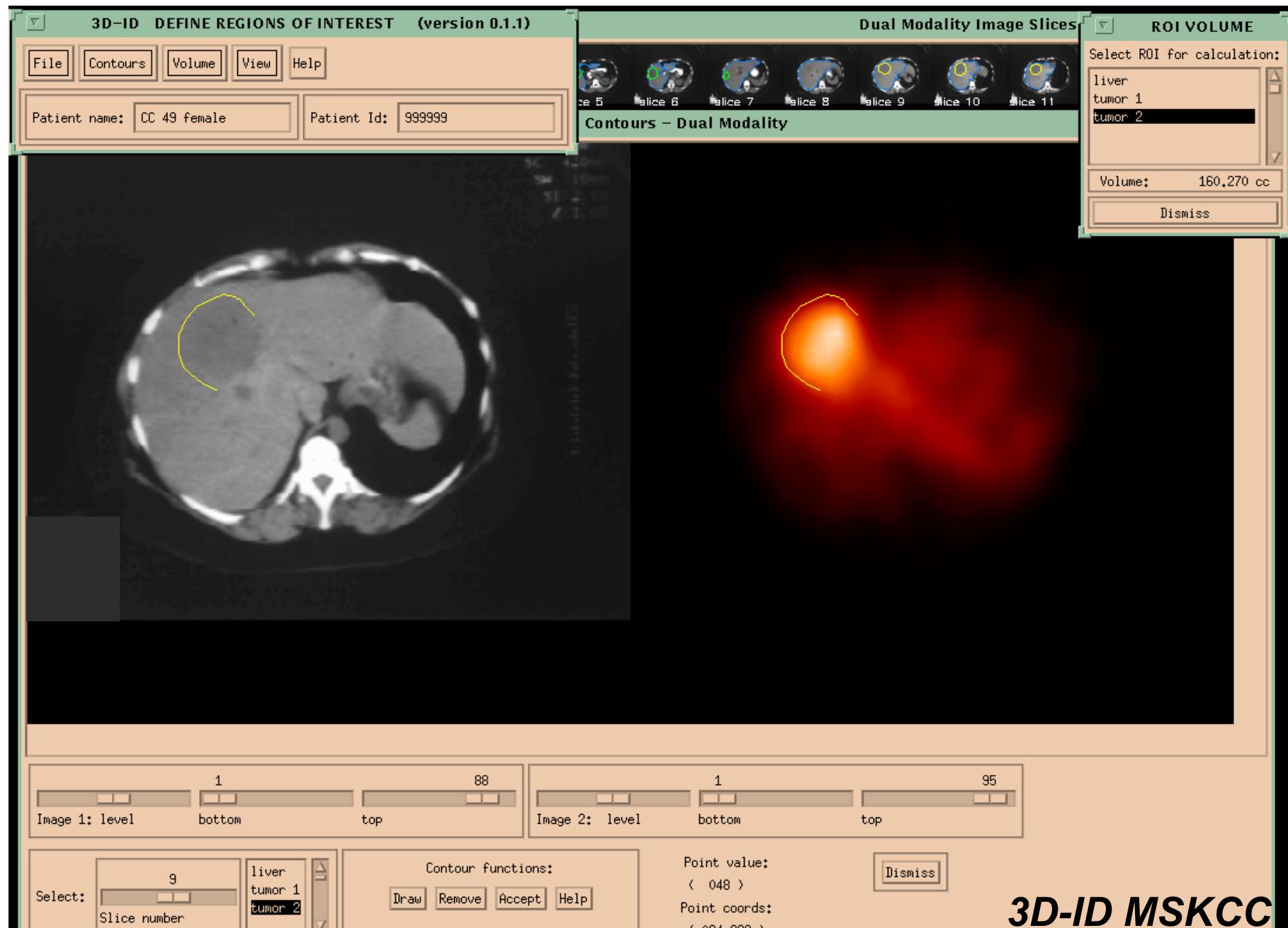
Patient-Specific dosimetry:



Patient specific dosimetry

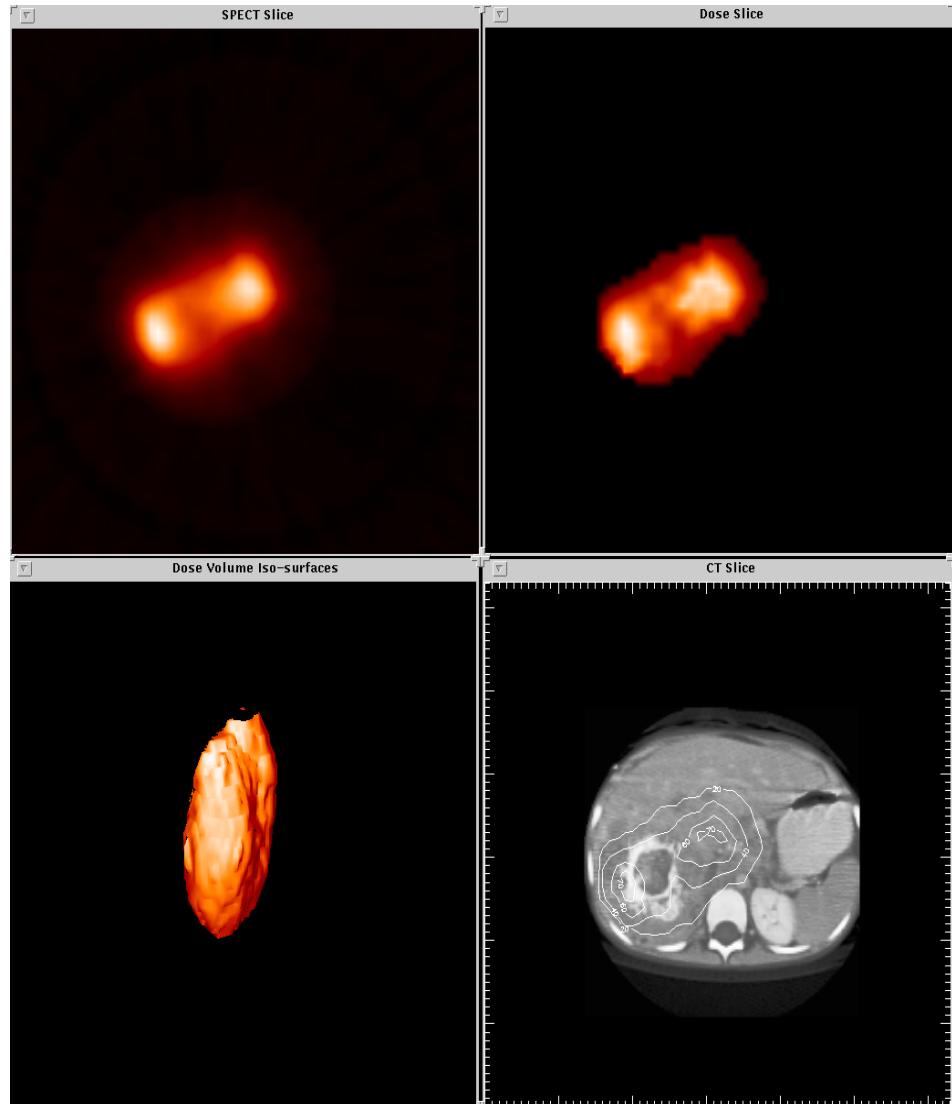


Patient specific dosimetry

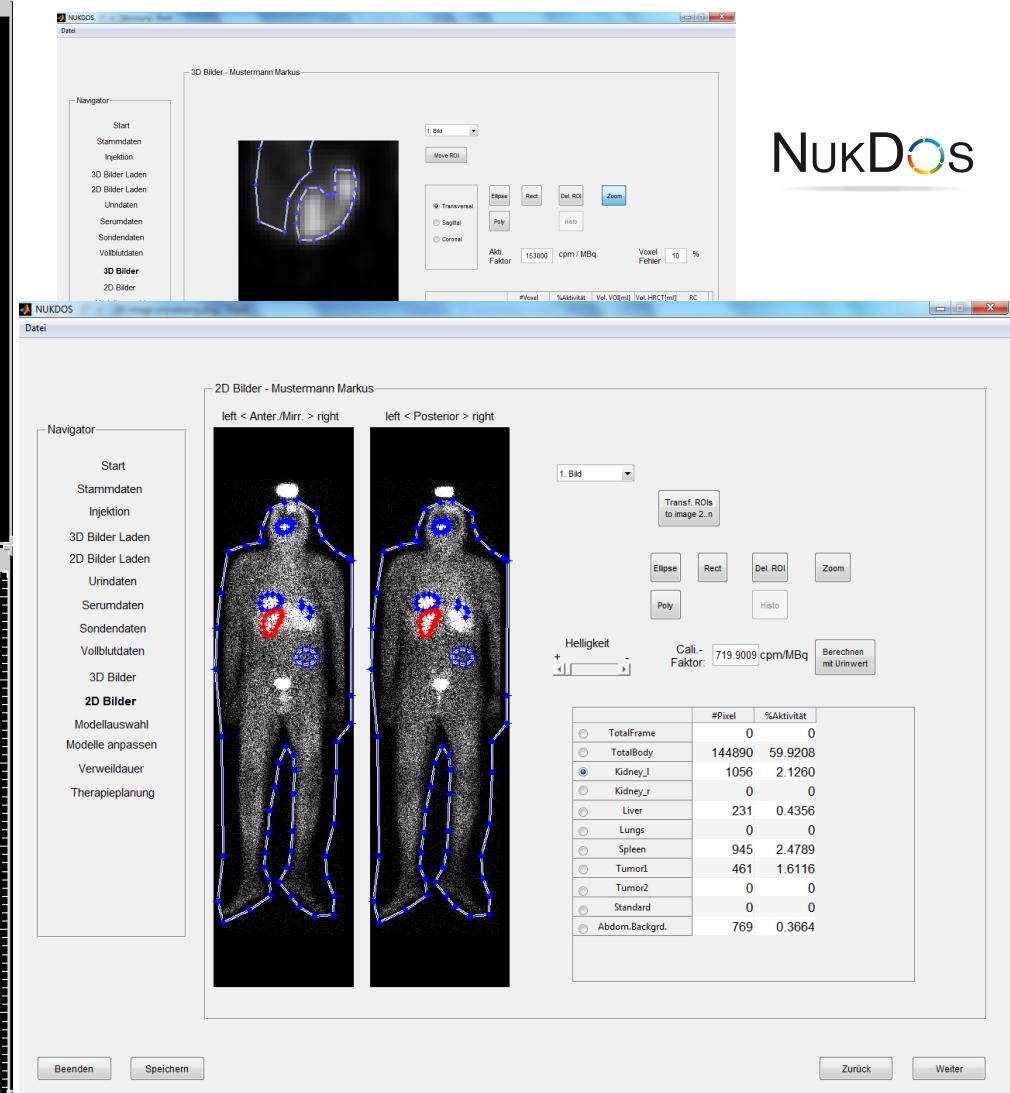


3D-ID MSKCC

Therapy dosimetry



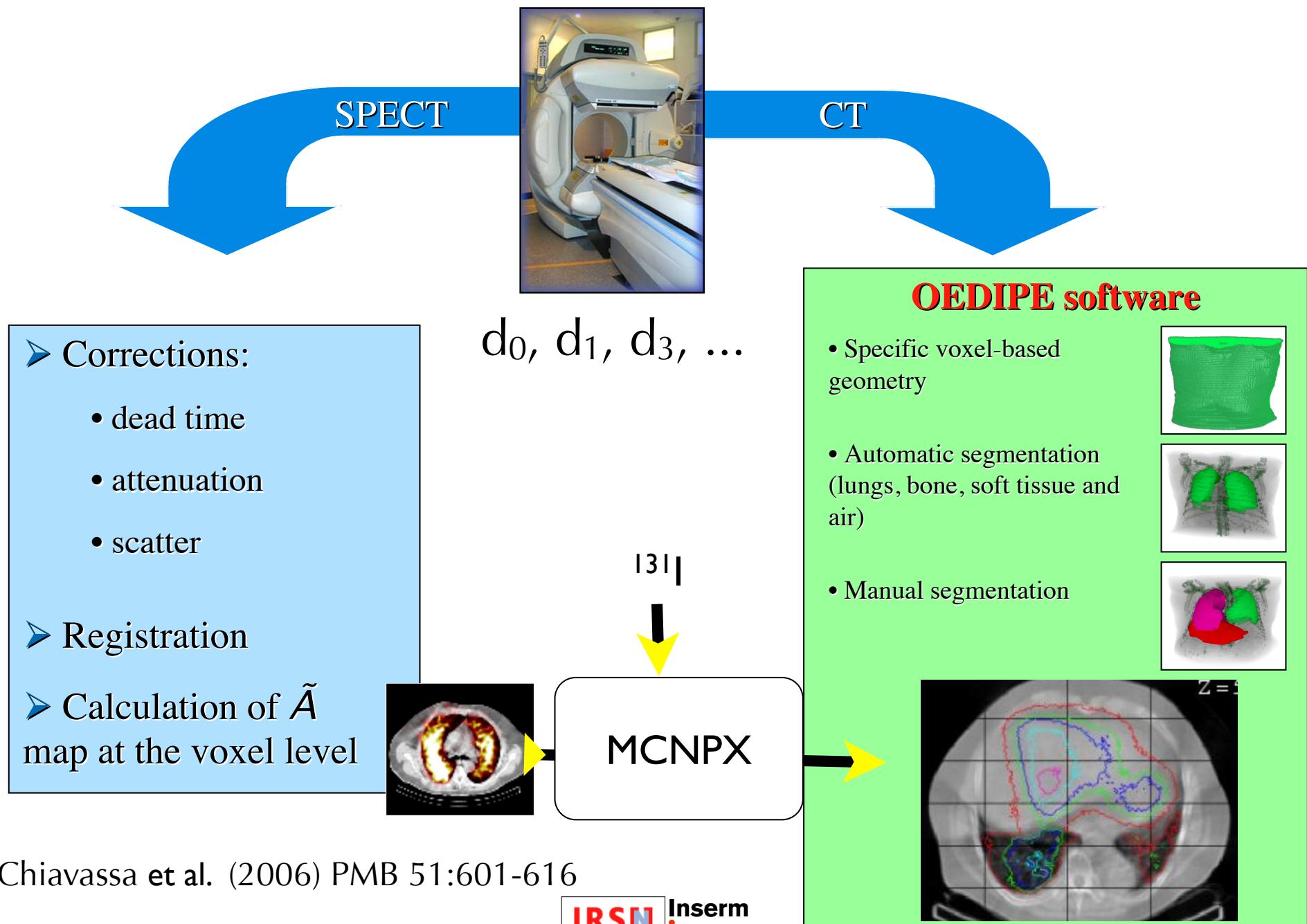
RMDP (M Guy, RMH)



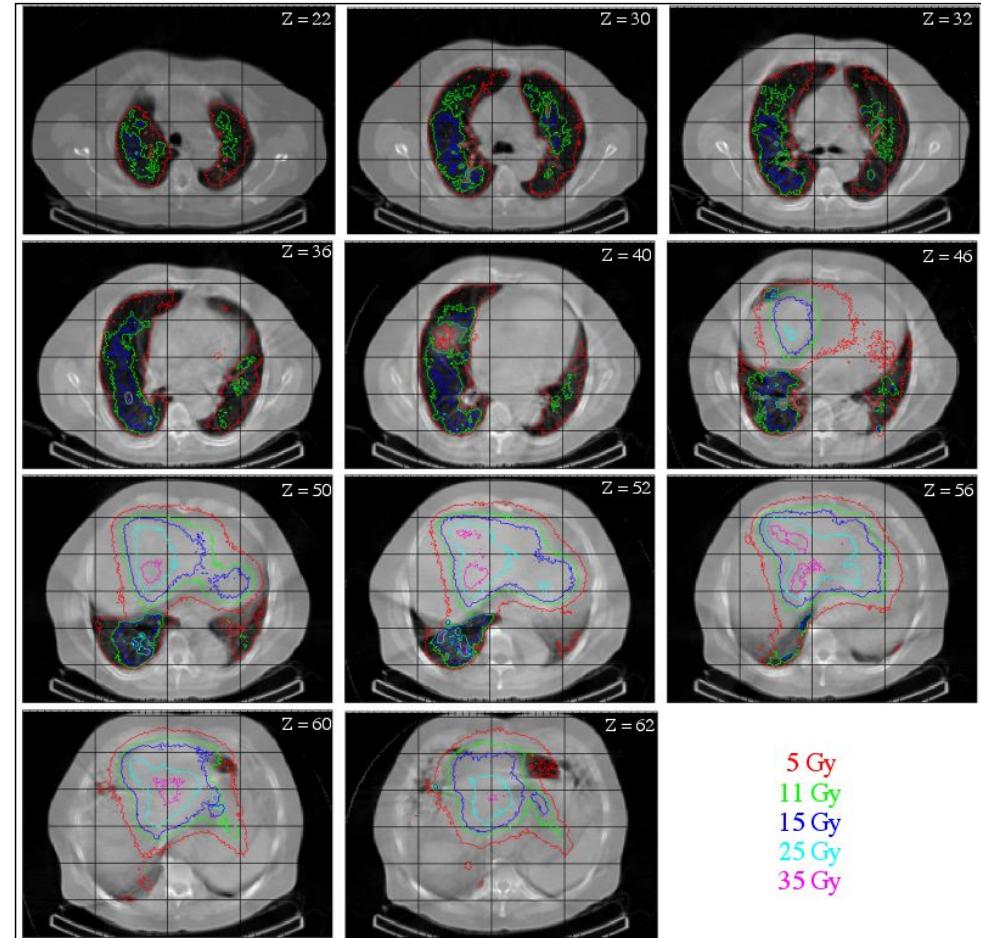
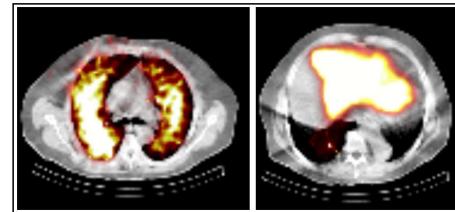
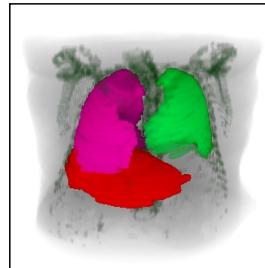
NukDos (M Laßmann, UKW)

NukDos

Patient-specific clinical dosimetry



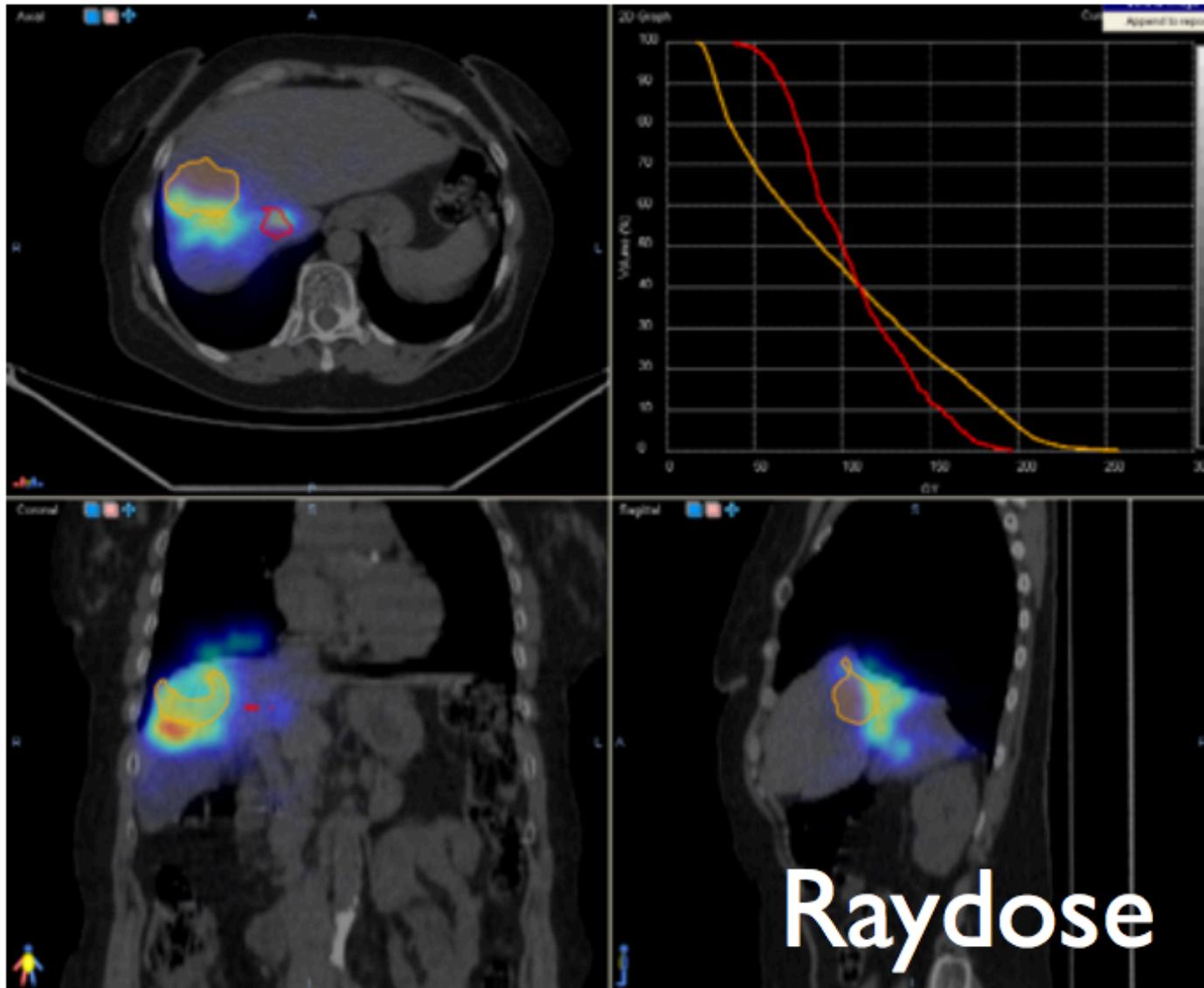
APPLICATION: LIPIOCIS™



- $194 \times 140 \times 90$ voxels
- $(2.21 \times 2.21 \times 4.42 \text{ mm}^3)$
- Organ: 45 min ($\sigma < 2\%$)
- Voxel: 3.8 d ($\sigma < 10\%$)

S Chiavassa et al. (2006) PMB 51:601-616

Monte Carlo based dosimetry



Courtesy: E Spezi (Velindre, Cardiff)

Marcatili et al. Phys Med Biol 2013 58 2491-2508

Monte Carlo based dosimetry

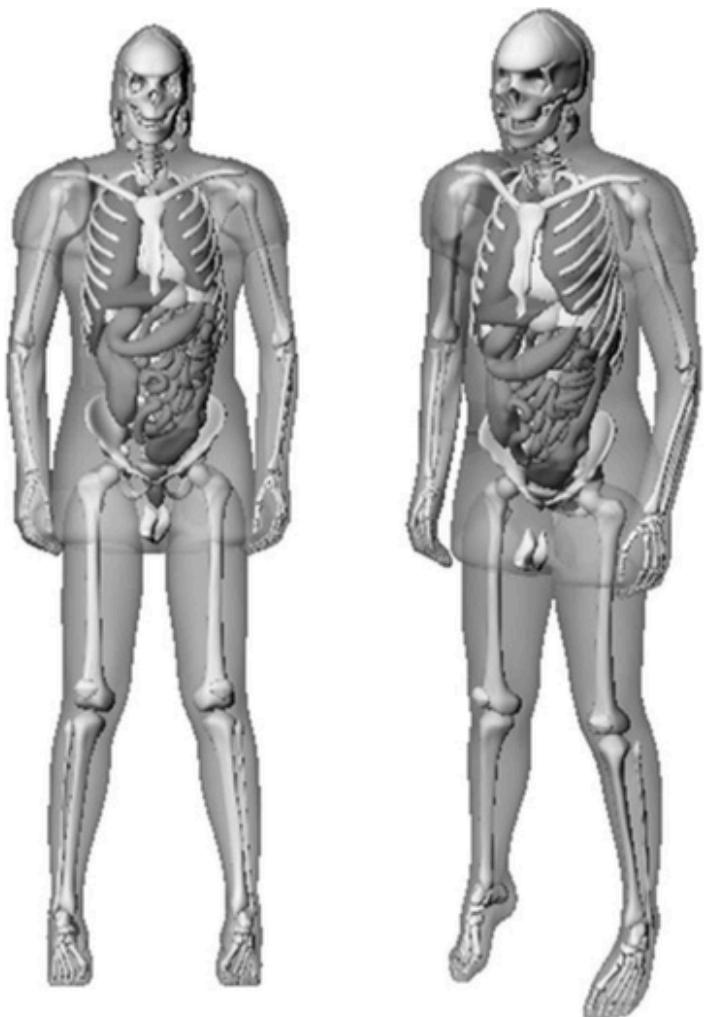


FIG. 3. Anterior views of the RADAR adult male NURBS phantom. NURBS, Non-Uniform Rational B-Spline; RADAR, Radiation Dose Assessment Resource.

CANCER BIOTHERAPY AND RADIOPHARMACEUTICALS
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DOI: 10.1089/cbr.2014.1713

Original Article

VIDA: A Voxel-Based Dosimetry Method for Targeted Radionuclide Therapy Using Geant4

Susan D. Kost,¹ Yuni K. Dewaraja,² Richard G. Abramson,³ and Michael G. Stabin³

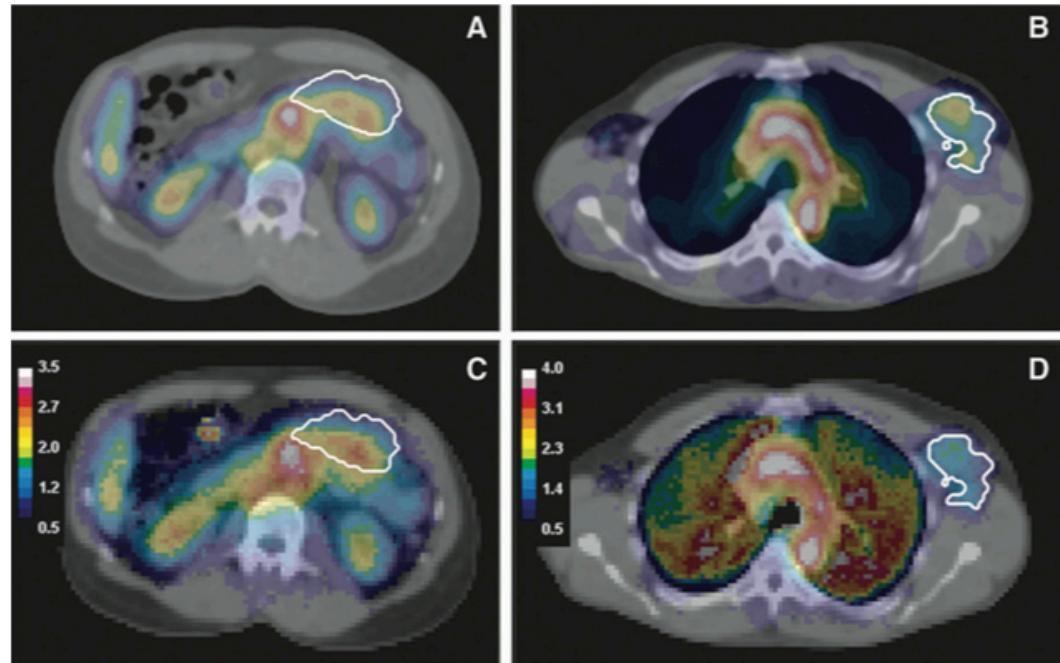


FIG. 5. Fused SPECT/CT images for patient 1 (**A**) and patient 2 (**B**) with matching 3D dose maps overlaid on CT for patient 1 (**C**) and patient 2 (**D**). The dose maps are displayed in units of Gy. Color images available online at www.liebertpub.com/cbr

Dosimetry for MRT:

Group	Model	Model ICRP - MIRD DER
Specific	Model ± adjusted	Model ± realistic
Specific	Specific	Specific

- *Patient-specific dosimetry: ALL steps must be patient-specific*

Conclusion

- Patient-specific dosimetry is feasible
- Huge literature in quantitative imaging/absorbed dose calculation (the methodology is there!)
- Patient-specific dosimetry requires ALL steps to be patient-specific
- BUT the biological/clinical end-point conditions the kind of approach that needs to be implemented!

Acknowledgements

- L Ferrer (CLCC & CHU, Nantes)
- Glenn Flux (ICR/RMH, Sutton)
- EANM Dosimetry & Therapy Committees

Special issue:

«Dosimetry in nuclear medicine therapy»

*The Quarterly Journal of Nuclear Medicine
and Molecular Imaging* 55(1-2), 2011



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Paul Sabatier
TOULOUSE III



manuel.bardies@inserm.fr

Thank you :-)