

# MRT Dosimetry Methodology



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# Declaration of interest

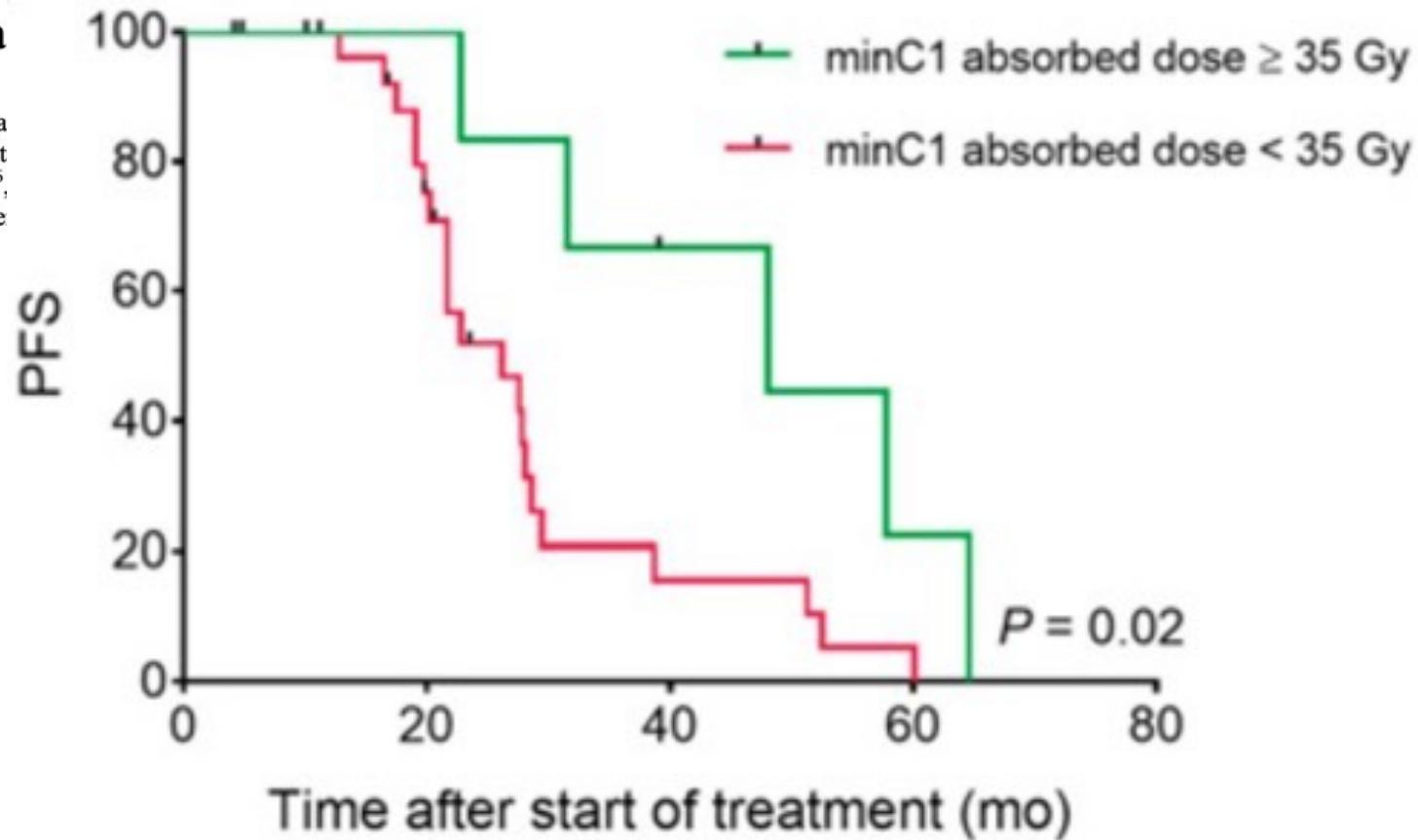
- M Bardiès supervises 2 PhD students (JA Fragoso and S Veloza Awad) sponsored by DOSIsoft
- M Bardiès is a consultant for CLARIO

## **Prediction of $^{177}\text{Lu}$ -DOTATATE PRRT Outcome Using Multimodality Imaging in Patients with Gastroenteropancreatic Neuroendocrine Tumors: Results from a Prospective Phase II LUMEN Study**

Magdalena Mileva<sup>1</sup>, Gwennaëlle Marin<sup>2</sup>, Hugo Levillain<sup>2</sup>, Carlos Artigas<sup>1</sup>, Camille Van Bogaert<sup>3</sup>, Clémentine Marin<sup>2</sup>,  
Rachele Danieli<sup>2</sup>, Amelie Deleporte<sup>4</sup>, Simona Picchia<sup>5</sup>, Konstantinos Stathopoulos<sup>5</sup>, Christiane Jungels<sup>4</sup>,  
Bruno Vanderlinden<sup>2</sup>, Marianne Paesmans<sup>6</sup>, Lieveke Ameye<sup>6</sup>, Gabriela Critchi<sup>1</sup>, Loubna Taraji-Schiltz<sup>1</sup>, Chloe Velghe<sup>6</sup>,  
Zéna Wimana<sup>1,7</sup>, Maria Bali<sup>5</sup>, Alain Hendlisz<sup>4</sup>, Patrick Flamen<sup>1</sup>, and Ioannis Karfis<sup>1</sup>

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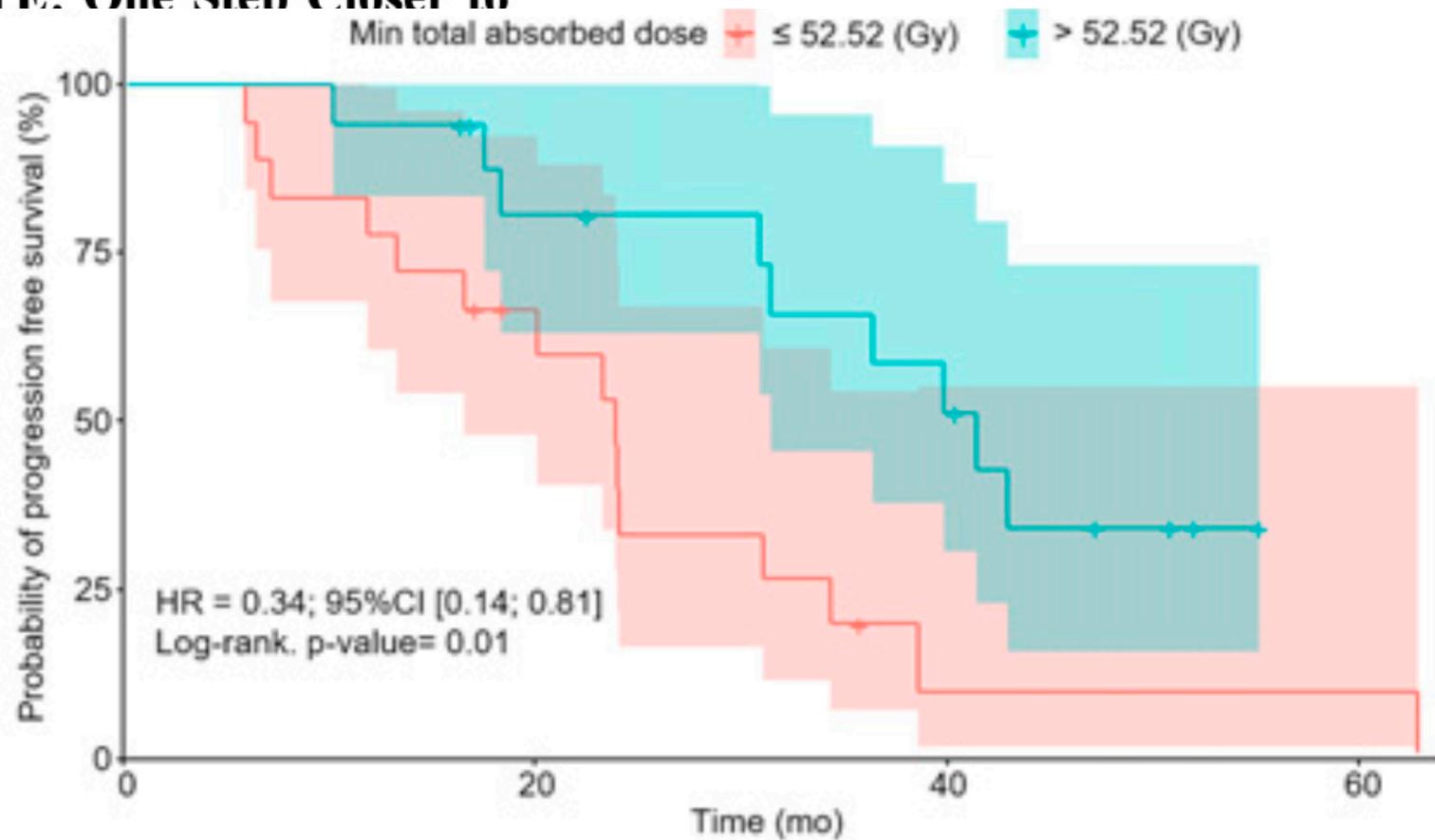


## **Absorbed Dose–Response Relationship in Patients with Gastroenteropancreatic Neuroendocrine Tumors Treated with [<sup>177</sup>Lu]Lu-DOTATATE: One Step Closer to Personalized Medicine**

Kévin Hebert\*<sup>1</sup>, Lore Santoro\*<sup>1,2</sup>, Maeva Monnier<sup>3</sup>, Florence Castan<sup>3</sup>, Ikrame Berkane<sup>1</sup>, Eric Assénat<sup>4</sup>, Cyril Fersing<sup>1–5</sup>, Pauline Gélibert<sup>6</sup>, Jean-Pierre Pouget<sup>2</sup>, Manuel Bardès<sup>1,2</sup>, Pierre-Olivier Kotzki<sup>1,2</sup>, and Emmanuel Deshayes<sup>1,2</sup>

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# The LUTADOSE trial: tumour dosimetry after the first administration predicts progression free survival in gastro-entero-pancreatic neuroendocrine tumours (GEP NETs) patients treated with [<sup>177</sup>Lu] Lu-DOTATATE

Marco Maccauro<sup>1</sup>  · Mariarosaria Cuomo<sup>1,2</sup> · Matteo Bauckneht<sup>3,4</sup>  · Matteo Bagnalasta<sup>1</sup>  · Stefania Mazzaglia<sup>1</sup> · Federica Scalorbi<sup>1</sup>  · Giovanni Argiroffi<sup>1</sup> · Margarita Kirienko<sup>1</sup>  · Alice Lorenzoni<sup>1</sup> · Gianluca Aliberti<sup>1</sup> · Sara Pusceddu<sup>5</sup> · Calareso Giuseppina<sup>6</sup> · Garanzini Enrico Matteo<sup>6</sup> · Ettore Seregni<sup>1</sup> · Carlo Chiesa<sup>1</sup> 

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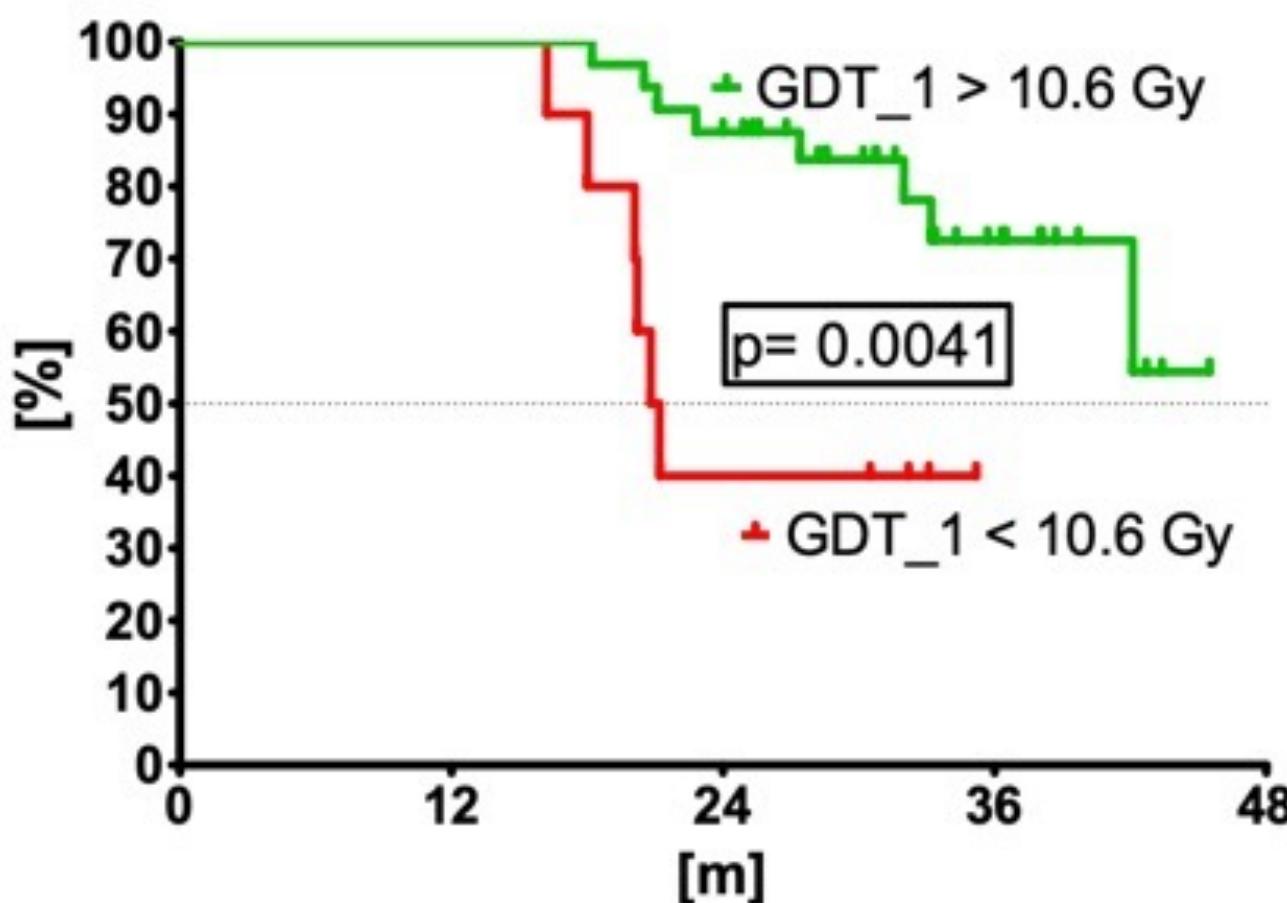


## The LUTADOSE trial: tumour dosimetry after Lu-DOTATATE predicts progression free survival in gastroenteropancreatic neuroendocrine tumours (GEP NETs) patients

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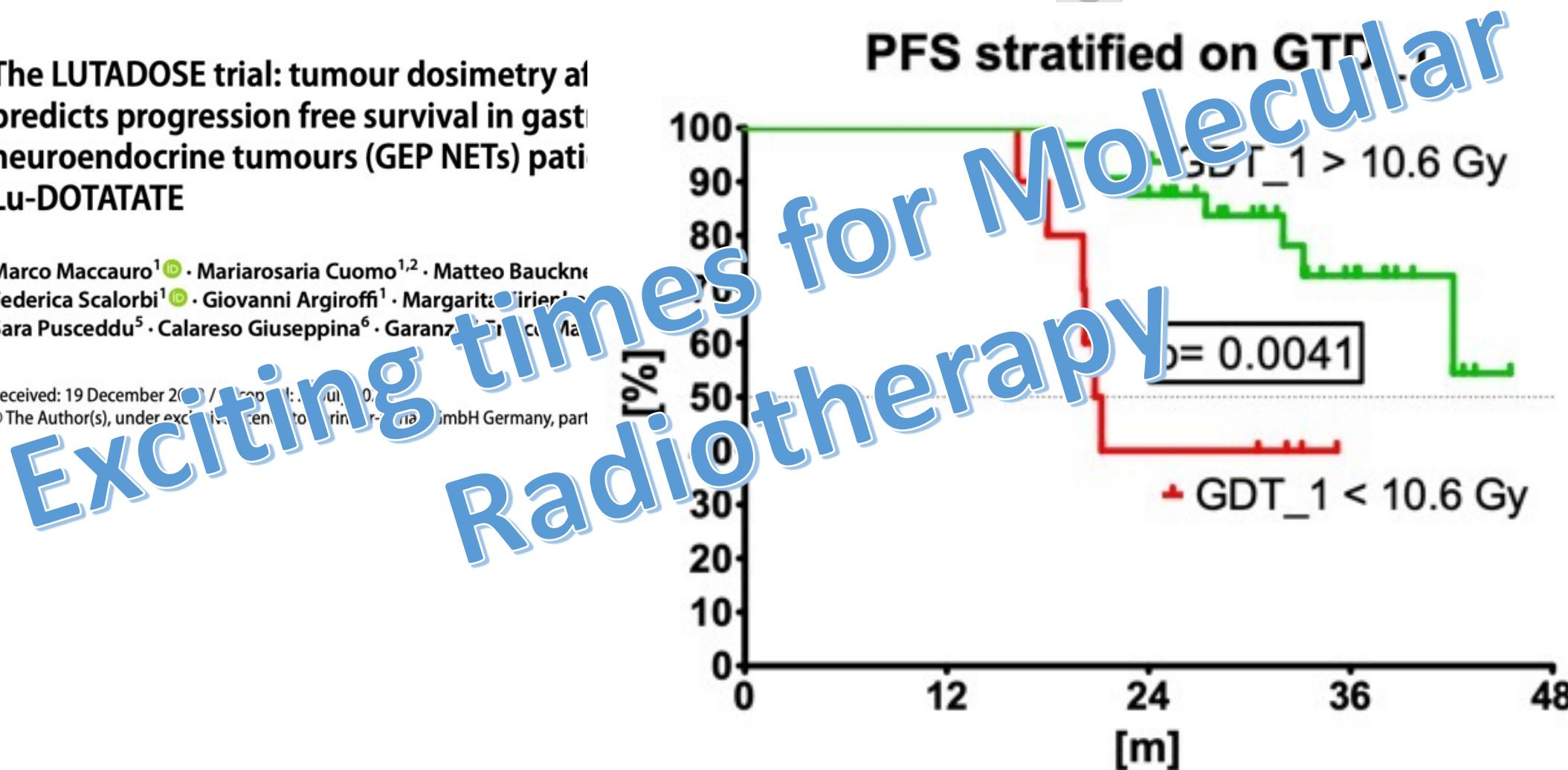
### PFS stratified on GDT\_1



## The LUTADOSE trial: tumour dosimetry at baseline predicts progression free survival in gastroenteropancreatic neuroendocrine tumours (GEP NETs) patients treated with Lu-DOTATATE

Marco Maccauro<sup>1</sup>  · Mariarosaria Cuomo<sup>1,2</sup> · Matteo Baucknecht<sup>3</sup> ·  
Federica Scalorbi<sup>1</sup>  · Giovanni Argiroff<sup>1</sup> · Margarita Tirivel<sup>4</sup> ·  
Sara Pusceddu<sup>5</sup> · Calareso Giuseppina<sup>6</sup> · Garanzini<sup>7</sup> · Riccardo Mancuso<sup>8</sup>

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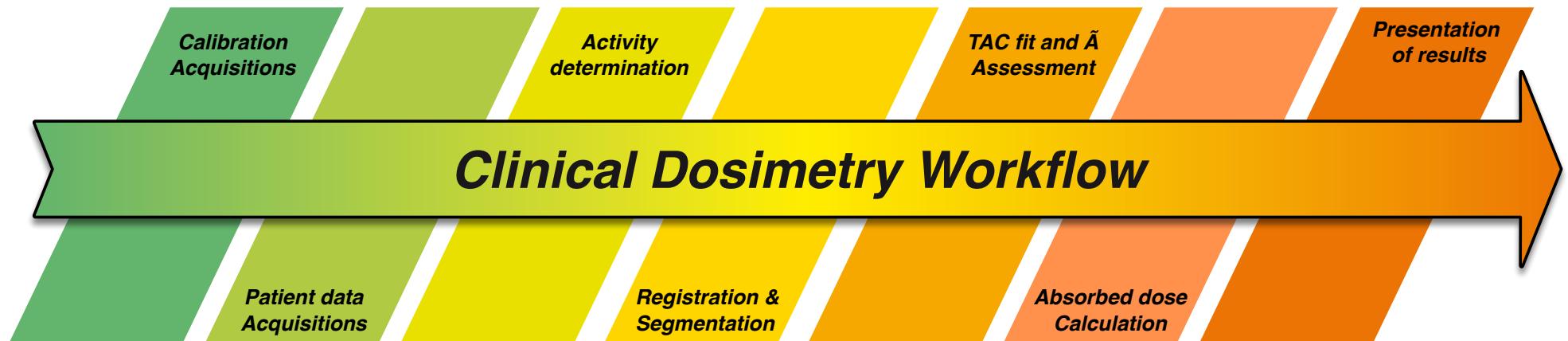


## Same pathology, different approaches, similar conclusions...

	Mileva et al.	Hebert et al.	Maccauro et al.
Modality	SPECT/CT	SPECT/CT	SPECT/CT
Time points	3	4	2
Patients	35 patients/83 lesions	35 patients/146 lesions	35 patients/165 lesions
Segmentation	SPECT from PET $^{68}\text{Ga}$ pretherapy	CT tag pretherapy	SPECT or CT during therapy
Dosimetric Index	$D_{n,1} \cdot \tau_1$	$D_{\text{Cumulated},1}$	GTG (GTD) Tumour Dose (GTD) at $C_1$

Standardisation & Traceability:  
Quality Assurance

# Clinical Dosimetry Workflow



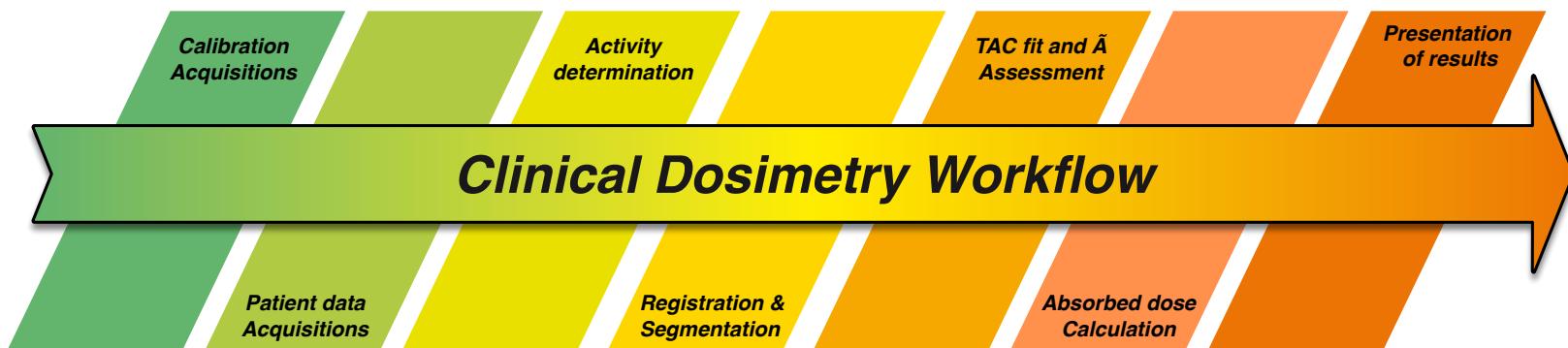
Adapted from: Bardies and Gear (2021)

Scientific Developments in Imaging and Dosimetry for Molecular Radiotherapy. Clinical Oncology 33(2) 117-124

- Clinical dosimetry is a sequence of steps:
- All steps should be treated with the same care!
- Software may address some parts of the clinical dosimetry workflow (CDW)

# RATIONALE COST Deliverable 4.1

- **Clinical dosimetry workflow (CDW):**
  - Ensemble of steps that lead from Calibrations to Reporting
  - CDW is composed by Individual Building Blocks



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- **Clinical dosimetry workflow (CDW):**
  - Ensemble of steps that lead from Calibrations to Reporting
  - CDW is composed by Individual Building Blocks
- **Individual Building Blocks (IBB)**
  - Independent steps that compose the CDW.
  - Example: Reconstruction, Registration, Radiation transport and energy deposition, etc.
  - IBBs have an input and an output

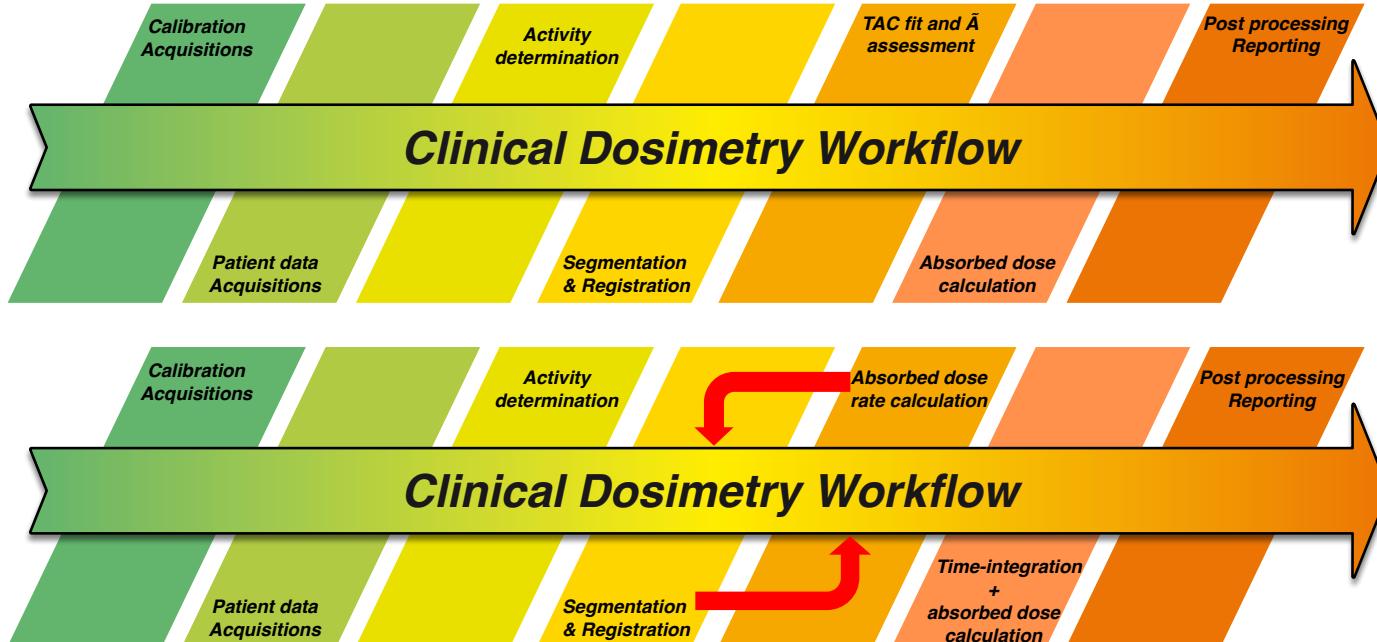
# Examples of IBB

- **Registration**
- **Input:** Images or Structures, for the whole FOV or for specific VOIs  
Rigid, elastic, or AI-based
- **Output:** Images or Structures

- **S Value Calculation (part of calibrations)**
- **Input:** Segmented anthropomorphic models (mathematical or voxel-based or hybrid), radionuclide emission data (radiation type, yield and energy)  
Radiation transport and energy deposition algorithm
- **Output: SAFs or S Values** tables for the segmented structures of the model

IBBs are independent, but may be connected (Registration and Segmentation)

# Examples of Clinical dosimetry workflows:



**“Conventional”**  
**Activity workflow**

**ADR workflows**

Different Clinical Dosimetry Workflow if:

- Changing IBBs in the CDW,
- Changing the order of the IBBs in the CDW
- Changing how IBBs are treated (rigid vs. elastic segmentation for example)

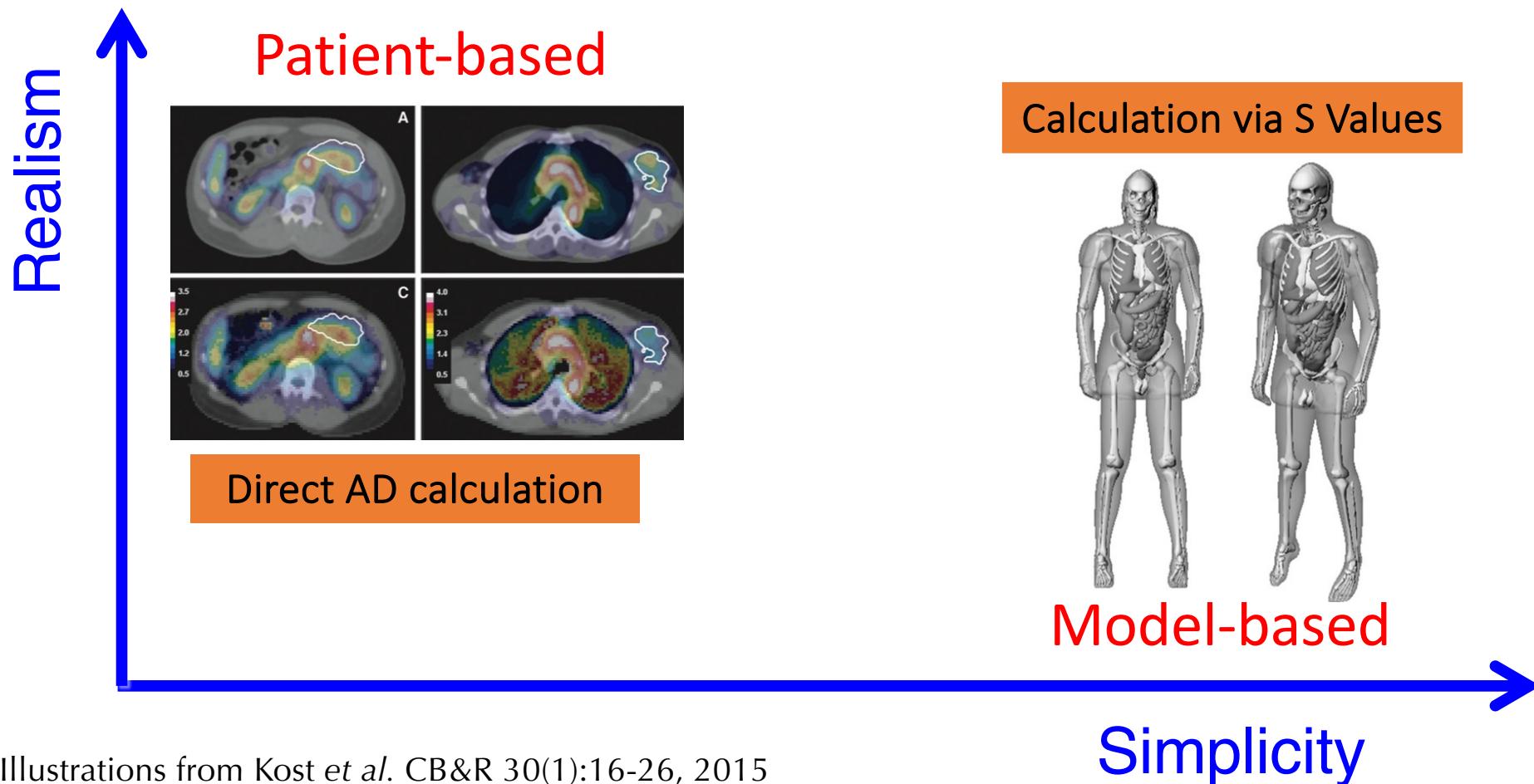
# Approaches

- Group CDWs that share a common characteristic that impacts the CDW
- Examples:
  - Treatment planning vs. Verification dosimetry
  - Model-based vs. Patient-based dosimetry
  - Reference dosimetry vs. Patient-specific dosimetry
  - Imaging-based vs. Non-imaging-based dosimetry
  - Multi-time points vs. Single time point...

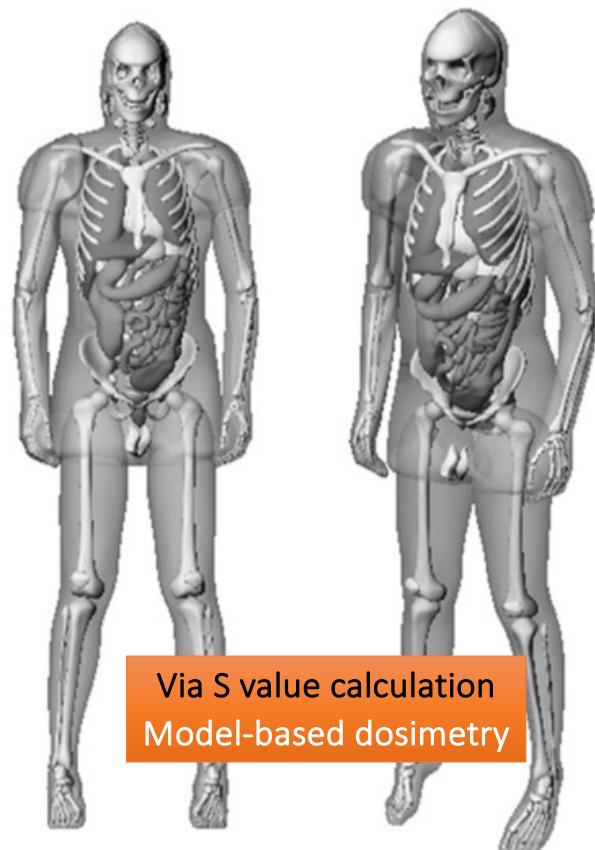
# Patient dosimetry procedures

- **3 levels of description:**
  - Individual Building Blocks
  - Clinical Dosimetry Workflows
  - Approaches
- Should allow characterising ALL patient dosimetry procedures reported in the literature
- Dosimetry reporting should ALWAYS document IBBs, CDWs and Approaches
- A step in direction of traceability...

# Patient-based vs. Model-based

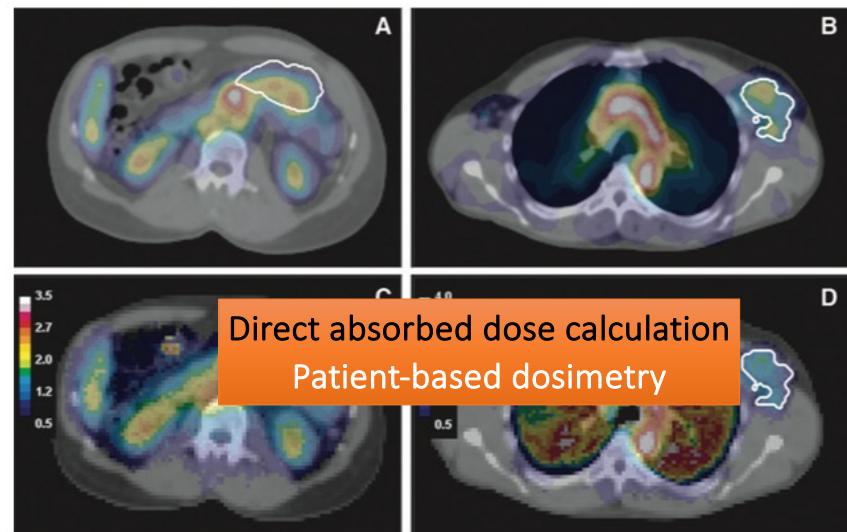


# Patient-based vs. Model-based



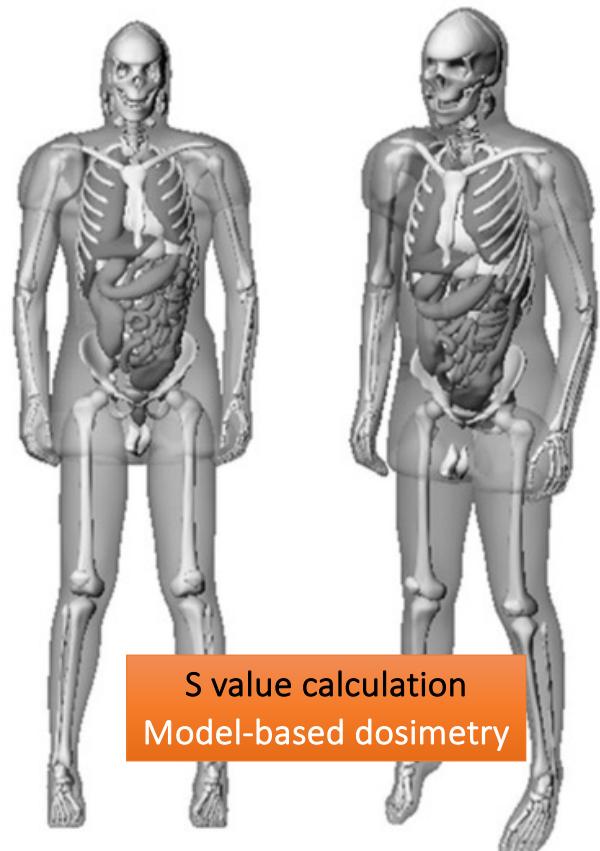
**FIG. 3.** Anterior views of the RADAR adult male NURBS phantom. NURBS, Non-Uniform Rational B-Spline; RADAR, Radiation Dose Assessment Resource.

- Different clinical dosimetry workflows!
- Different software



**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](http://www.liebertpub.com/cbr)

# Model-based approach



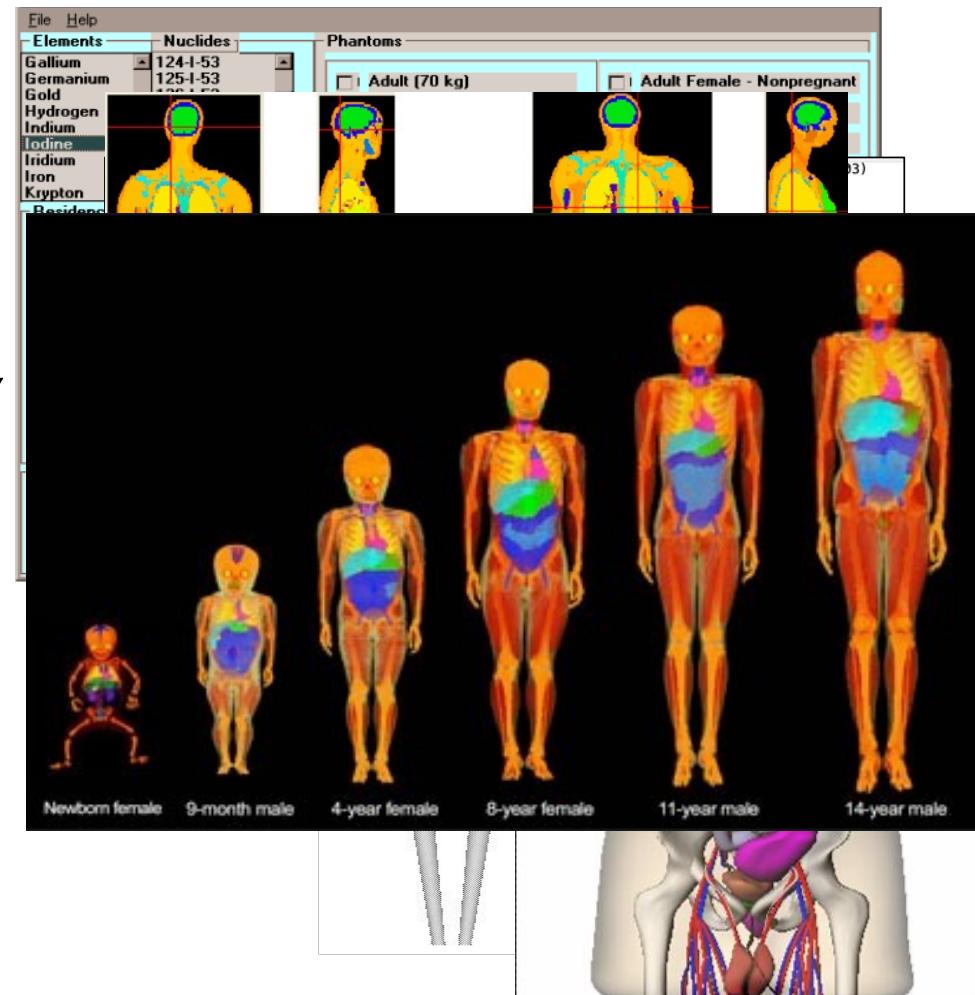
**FIG. 3.** Anterior views of the RADAR adult male NURBS phantom. NURBS, Non-Uniform Rational B-Spline; RADAR, Radiation Dose Assessment Resource.

- S: absorbed dose in the target per decay in the source
- **Consequences:**
  - S: for one radionuclide & one model
  - ≠ algorithms (LED, Conv., Monte Carlo)
  - Pre-computation: 1 source, many targets (may take a while – calibration IBB)
  - Allows for absorbed dose calculation for targets outside image FOV!
  - Allows for reference dosimetry (diagnostics)
  - For a reference model, not your patient, but...

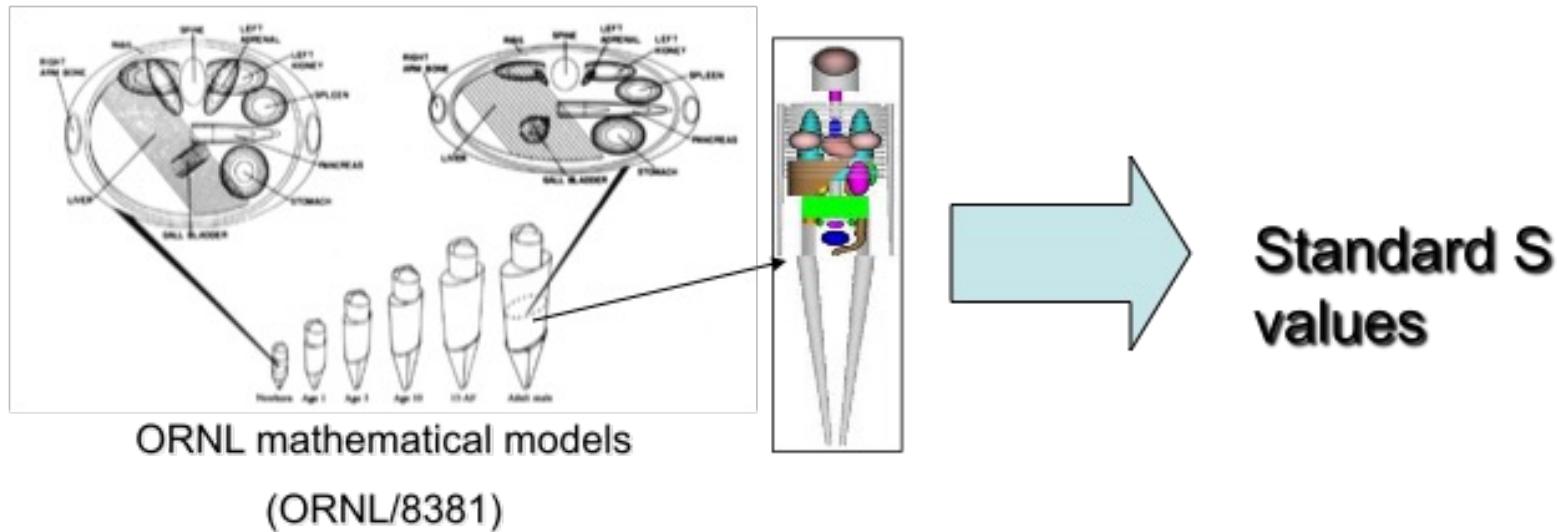
# Model-based dosimetry software

First software to have been proposed:

- MIRDOSE:  
Stabin MG J Nucl Med. 1996 37(3):538-46
- OLINDA V1:  
Stabin et al. J Nucl Med. 2005 46(6):1023-7
- IDAC-DOSE 2.1:  
Andersson et al. EJNMMI Research 2017
- OLINDA V2:  
Stabin Health Phys. 2023 124(5):397-406.
- MIRDcalc:  
Kesner et al. J Nucl Med. 2023 64(10):1668



# Mass adjustment: A means to go towards personalisation



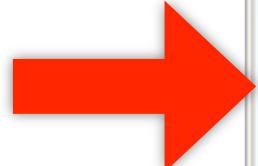
$$S_{Patient} = S_{Model} \times \frac{m_{Model}}{m_{Patient}} \quad (\text{for } \alpha, \beta, \bar{e})$$

Different scaling for X and  $\gamma$

For self irradiation only!

# Example: OLINDA mass adjustment

Model-based to “adjusted-model-based”



Input Data:

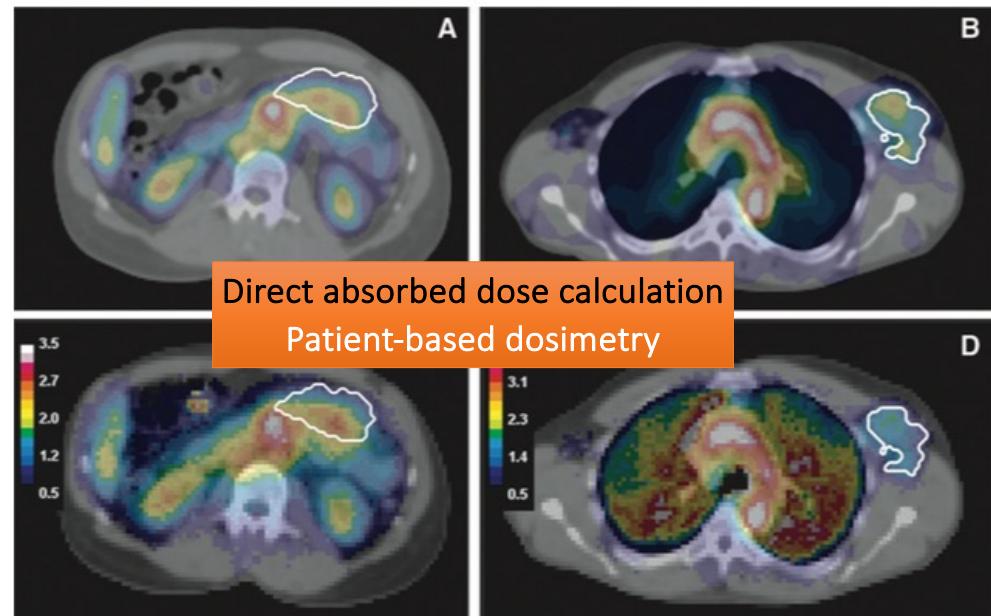
1420.0	Brain	1120.0	Red Marrow
351.0	Breasts	120.0	Osteogenic Cells
10.5	Gallbladder Wall	3010.0	Skin
167.0	LLI Wall	183.0	Spleen
677.0	Small Intestine	39.1	Testes
158.0	Stomach Wall	20.9	Thymus
220.0	ULI Wall	20.7	Thyroid
316.0	Heart Wall	47.6	Urinary Bladder Wall
299.0	Kidneys	79.0	Uterus
1910.0	Liver	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
Multiply all masses by:	1.0	

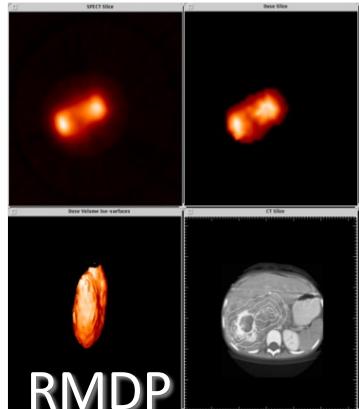
# Patient-based dosimetry

- Fully based on patient images:
  - (Cumulated) activity maps (SPECT or PET)
  - Density maps (CT)
- No need for S but still MIRD formalism!
- One pass calculation!
  - ≠ algorithms (LED, Conv., Monte Carlo)
- Accuracy (vs. time)?
  - Debatable (rapidly changing panorama)
- Implemented in most commercial software

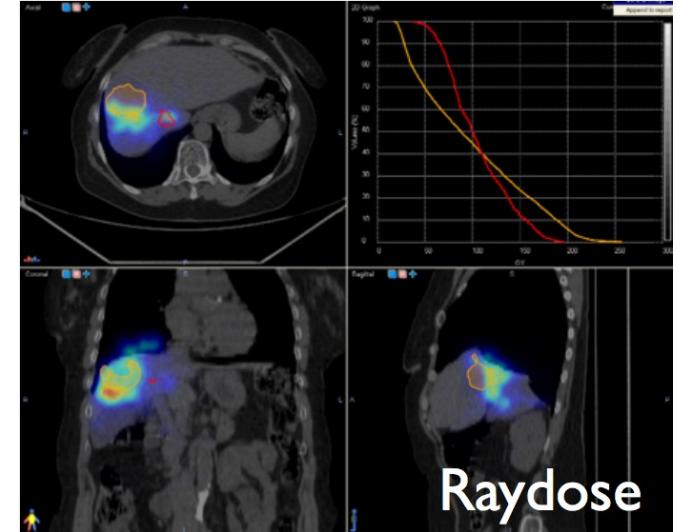
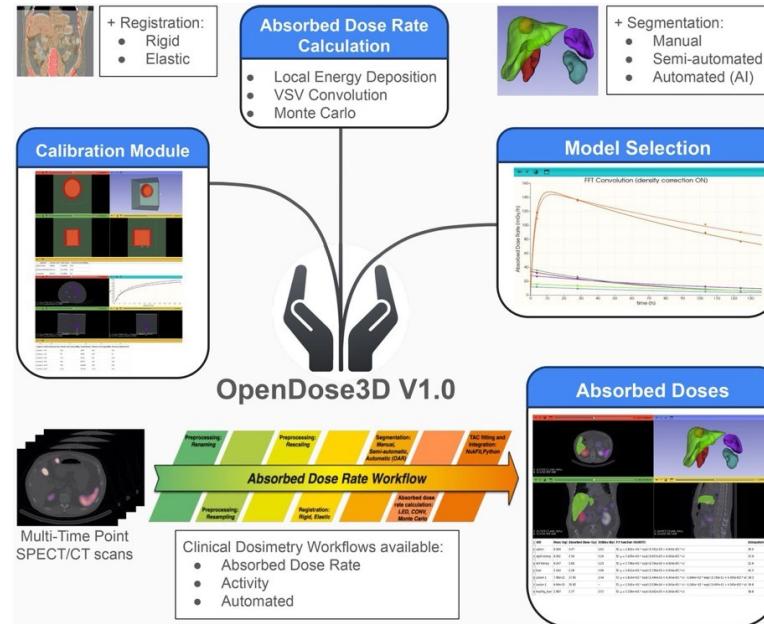


# Patient-based dosimetry software

- Fully image-based
- Address “some” parts of the clinical dosimetry workflow
- **Academic** or commercial software



NukDOS



# Patient-based dosimetry software

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HERMES Dosimetry Software



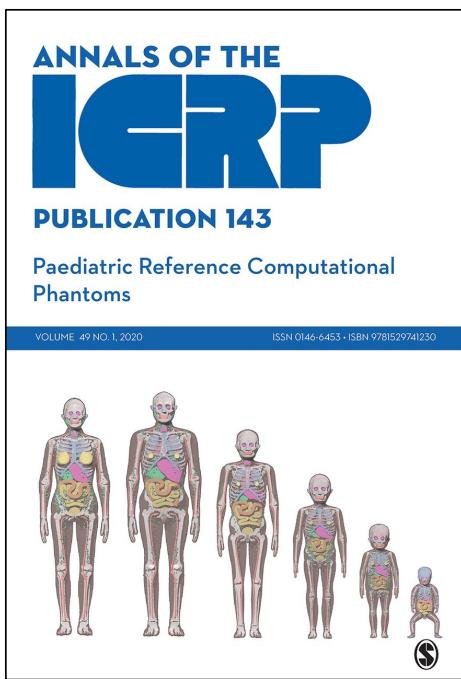
HERMES *Medical Solution*



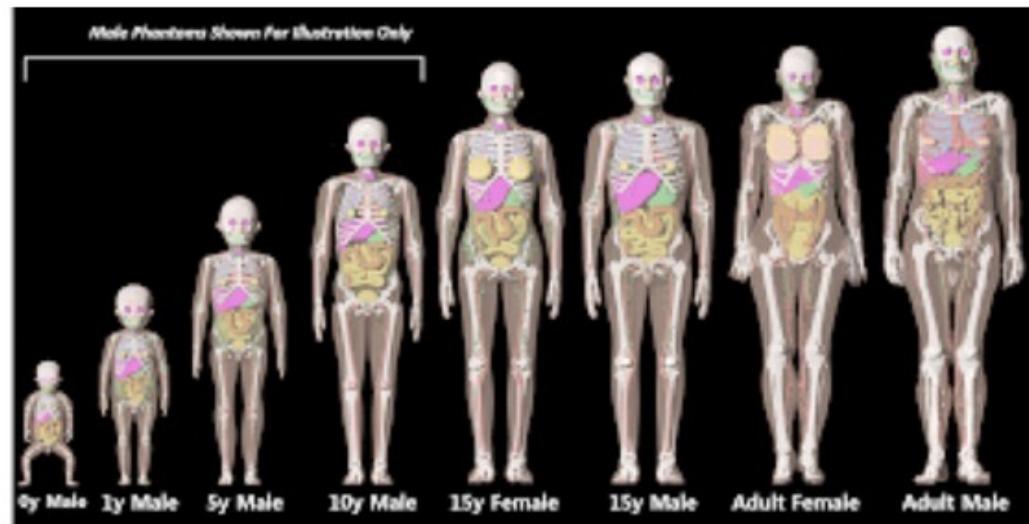
# Organ vs. Voxel-based approaches?

## MIRDcalc organ level dosimetry

- 333 isotopes (ICRP Publication 107),
- Family of 12 ICRP phantoms with 79 source organs and 43 target organs each



## *ICRP voxelized phantoms used in MIRDcalc software*



- [www.mirdsoft.org](http://www.mirdsoft.org) (MIRD pamphlets 28a and 28b 2023)

## Conclusions

- Traceability means documenting all steps of patient dosimetry
  - Individual Building Blocks
  - Clinical Dosimetry Workflows
  - Approaches
- Store ALL relevant data (patient dosimetry may require a lot!)
  - Need of a specific DICOM format for MRT dosimetry
  - Ongoing Joint EFOMP/AAPM/EANM/SNMMI Workgroup on QSPECT and MRT dosimetry standards (Jaroslav Ptacek)
- Document, document, document...
  - Lassmann *et al.* EANM Dosimetry Committee guidance document: good practice of clinical dosimetry reporting. *Eur J Nucl Med Mol Imaging* **38**, 192–200 (2011)

# Thank you

