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Radiopharmaceutical Therapy (RPT) Dosimetry

Yuni K Dewaraja, PhD

Department of Radiology
University of Michigan

Joint DOE / NIH Workshop - Advancing Medical Care through Discovery in the Physical Sciences Workshop Series: Radiation Detection. Session 4 - Cameras, Detectors for Therapeutics

Disclosures

- Yuni Dewaraja
  - Grant support from Varian
  - Software support from MIM Software, Inc
  - Software support from Siemens Molecular Imaging
  - Consultant for MIM Software, Inc.

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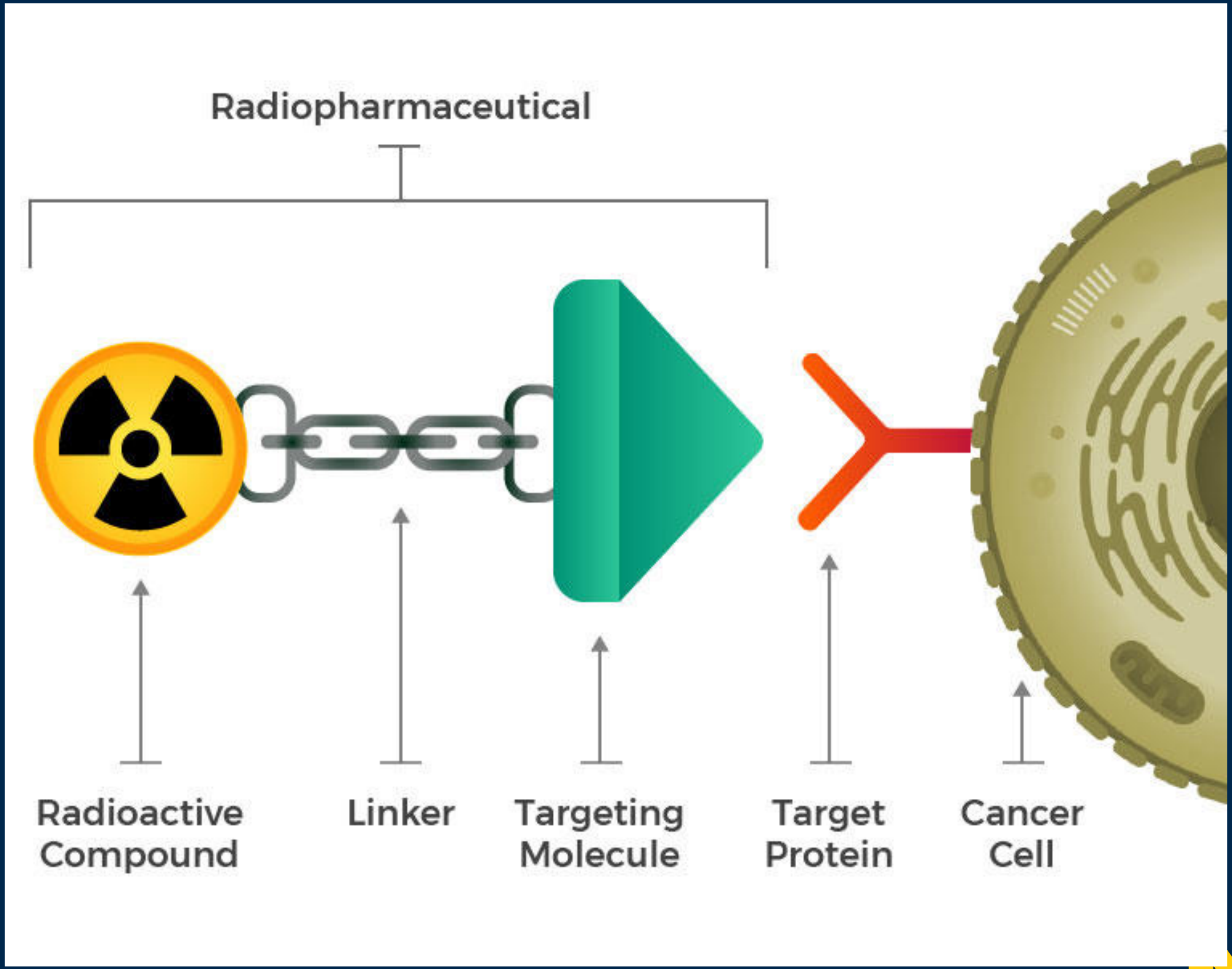
Radiopharmaceutical therapy (RPT)

- Also referred to as internal emitter therapy, radionuclide therapy, …
- Radiopharmaceuticals: consist of a radioactive molecule, a targeting molecule, and a linker that joins the two
  - 177Lu-PSMA , DOTATATE
  - Radioiodine therapy: the radioisotope (131I, 124I or 123I) can be directly mediated by the sodium-iodide symporter in the thyroid cells.
  - Radioembolization: intra-arterial administration of Y-90 microspheres



Credit: National Cancer Institute

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Radiopharmaceutical Therapy

- Current: Fixed activity ("one dose fits all") or weight-based
  - Convenient, but variability in pharmacokinetics & anatomy not considered
  - Potential for under-treatment or over-treatment
- Desired: Absorbed dose guided treatment planning
  - Adjust activity to keep absorbed dose to critical organ < MTD.
  - Adjust to deliver therapeutic absorbed dose to lesion at acceptable toxicity
- Why Change?
  - With fixed activity promising tumor control, but poor complete response and survival rates
  - Low/mild toxicity, but are we underdosing most patients?
  - Potential for improved efficacy with dosimetry guided treatment

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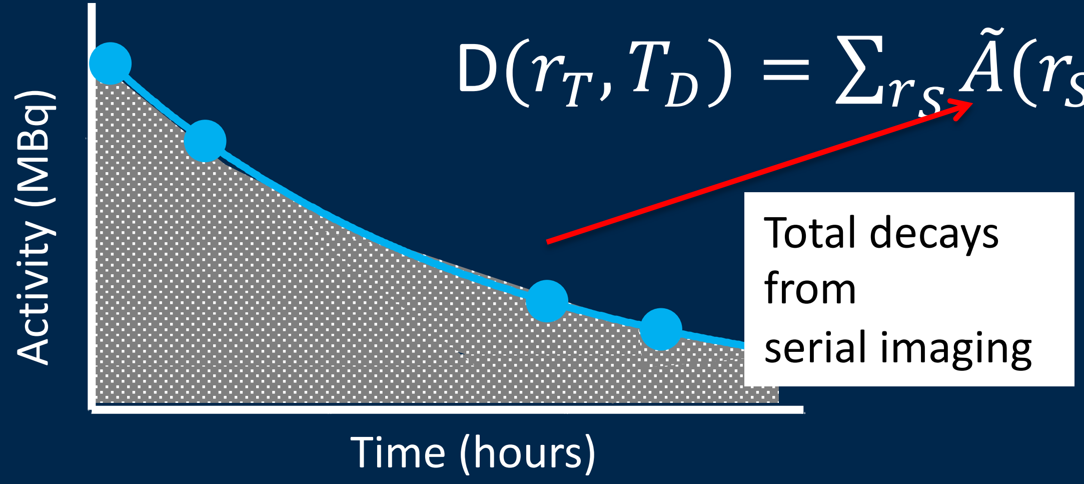
Absorbed Dose Estimation in RPT: Main Steps

- Image Acquisition usually at multi time points for kinetics
  - Pre-therapy usually with surrogate or post-therapy directly
- Image Reconstruction, Quantification,Partial Volume Correction
- Image Registration
- Organ/lesion Segmentation
- Time - activity fitting
- Absorbed dose estimation. MIRD schema widely used

$$\mathrm{D}(r_T, T_D) = \sum_{r_S} \tilde{A}(r_S, T_D) S(r_T \leftarrow r_S)$$



Absorbed dose to target per transformation in source. S-values can be at organ/ sub-organ/voxel/cellular levels

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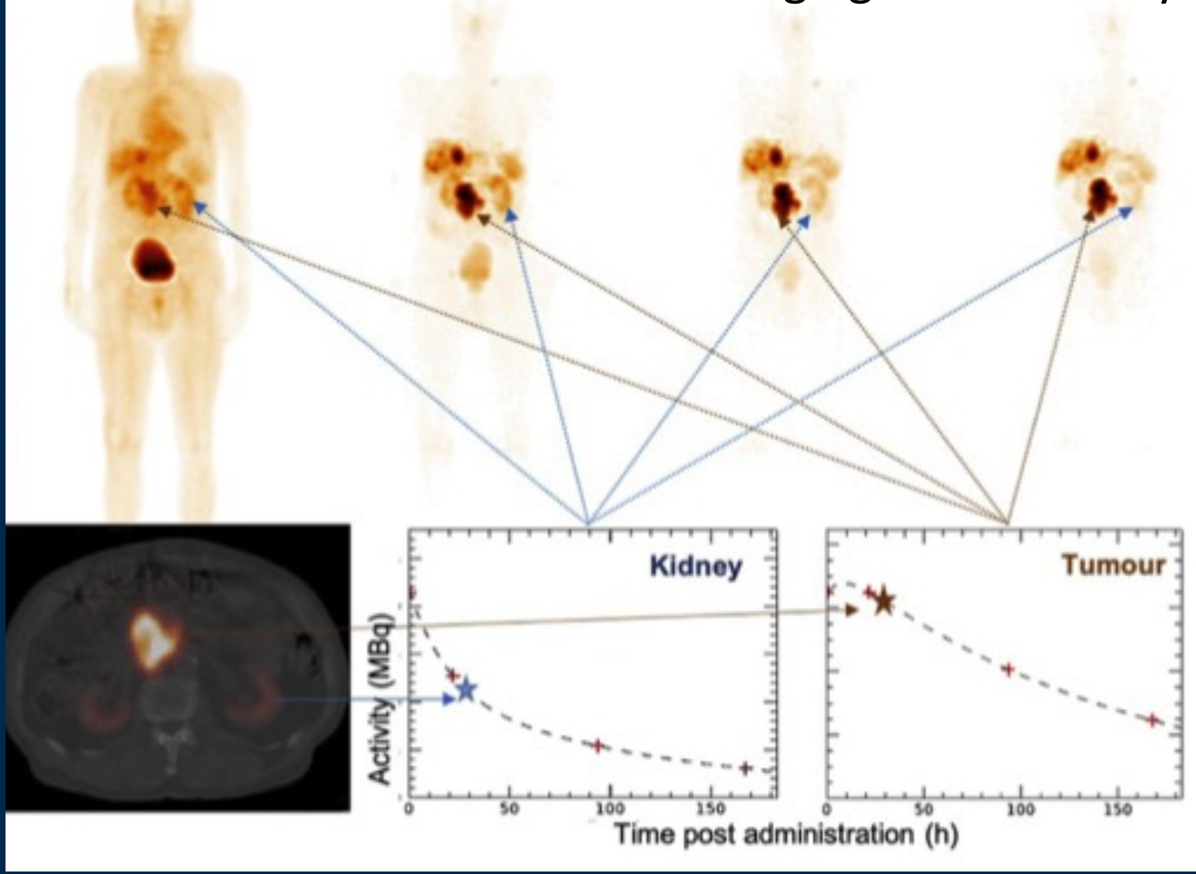
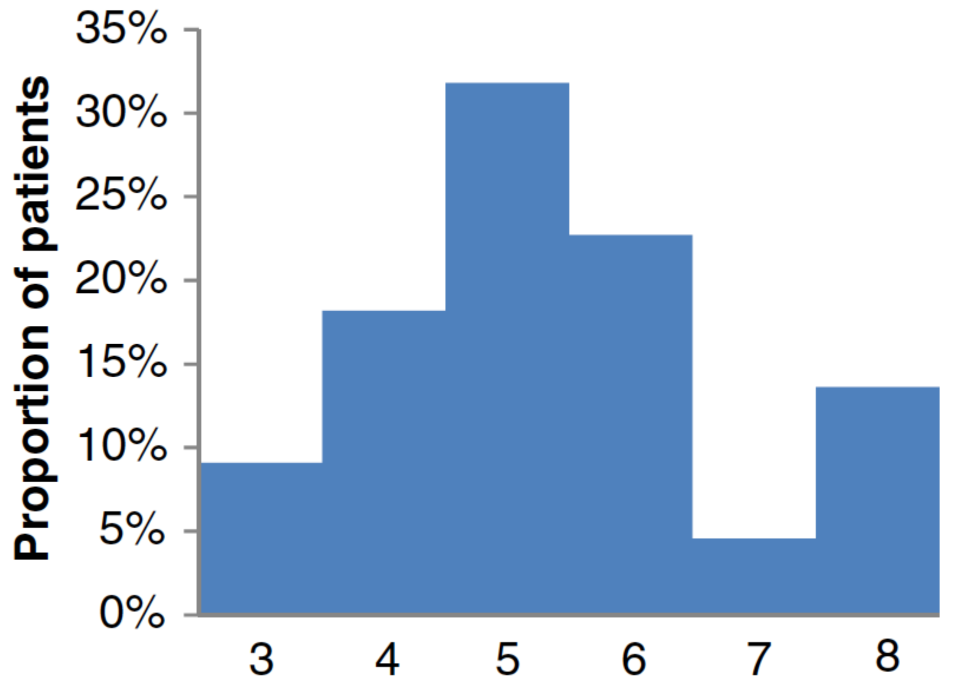
Example showing value of patient specific dosimetry: ^{177}Lu DOTATATE Trial

- Current standard: 4 cycles at 7.4 GBq/cycle
- Trial: As many cycles without exceeding kidney dose limit (MTD 27 Gy BED)
- Demonstrated: Cycles can be increased in most patients w/o reaching MTD

ILUMINET Trial: Planar + SPECT imaging for dosimetry





# of cycles within the protocol specified BED and AD limits

Sundlov et al, Eur J Nuc Med Mol Imag 2017

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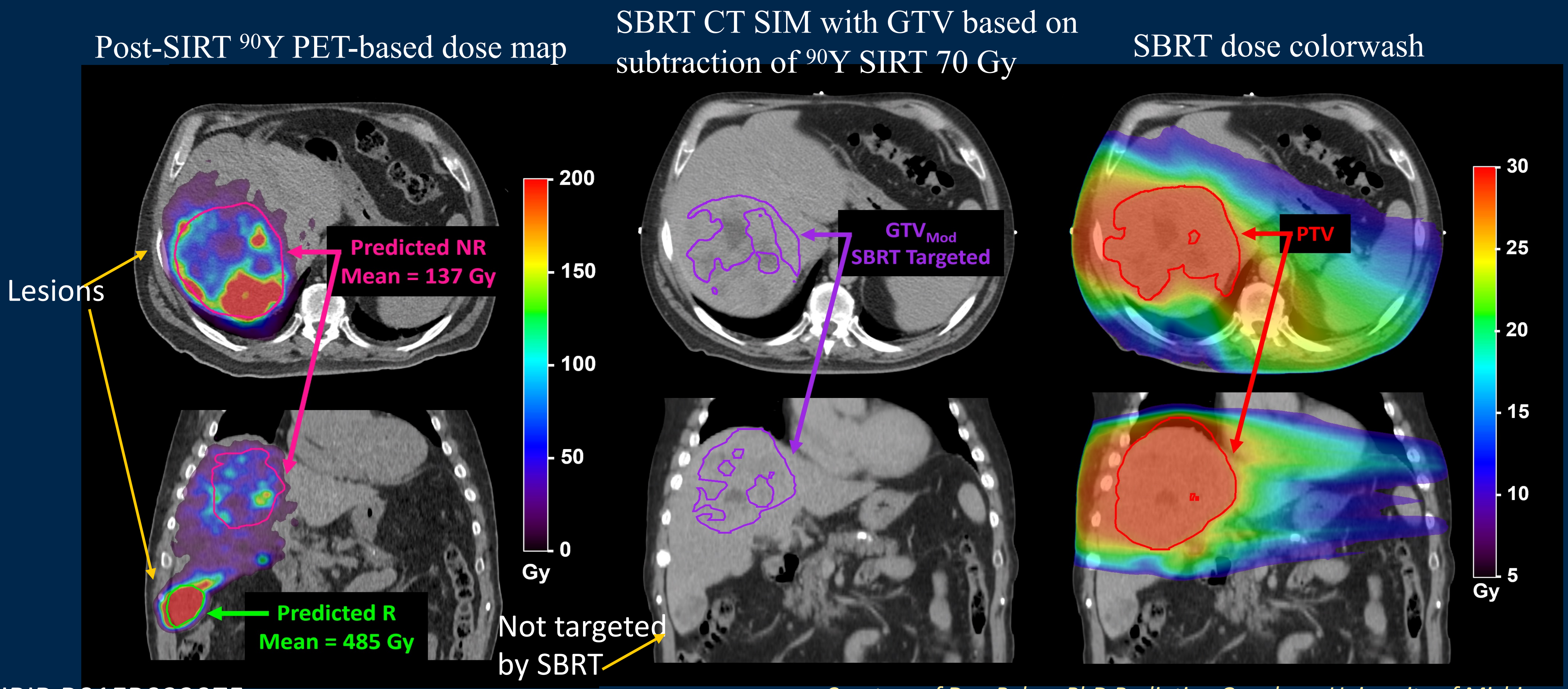
Value of patient specific dosimetry: U of Mich combined ^{90}Y SIRT + SBRT

Current: HCC lesions targeted by ^{90}Y selective internal radiation therapy or external radiotherapy

Trial: ^{90}Y PET absorbed dose map used to identify underdosed regions and boost with SBRT



NIBIB R01EB022075

Courtesy of Dan Polan, PhD Radiation Oncology, University of Michigan

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RPT: Why dosimetry guided treatment is not standard practice

- Unlike in external radiotherapy, not standard practice in RPT
- Why?
  - Imaging burden
  - Lack of accurate *and* clinic friendly tools
  - Scarcity of well established dose – effects relationships
    - Potentially related to insufficient data
- Recent developments
  - Potential for reduced time point imaging-based dosimetry and faster scans
  - AI-based tools for segmentation
  - Publicly available & commercial tools for patient specific dosimetry

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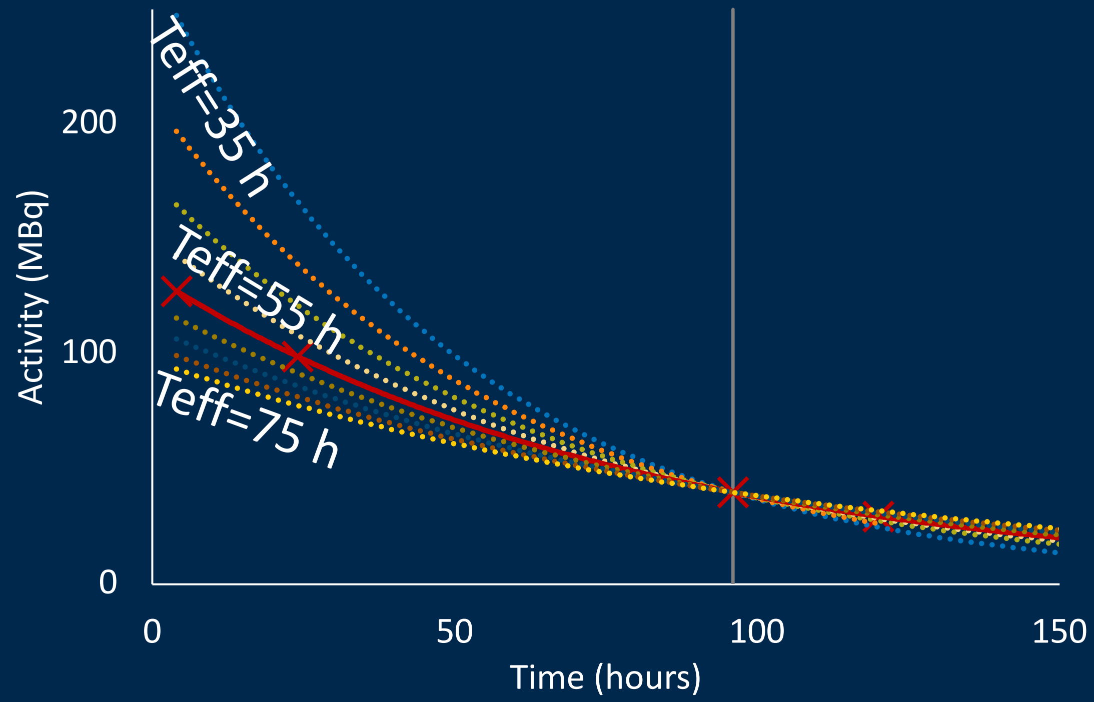
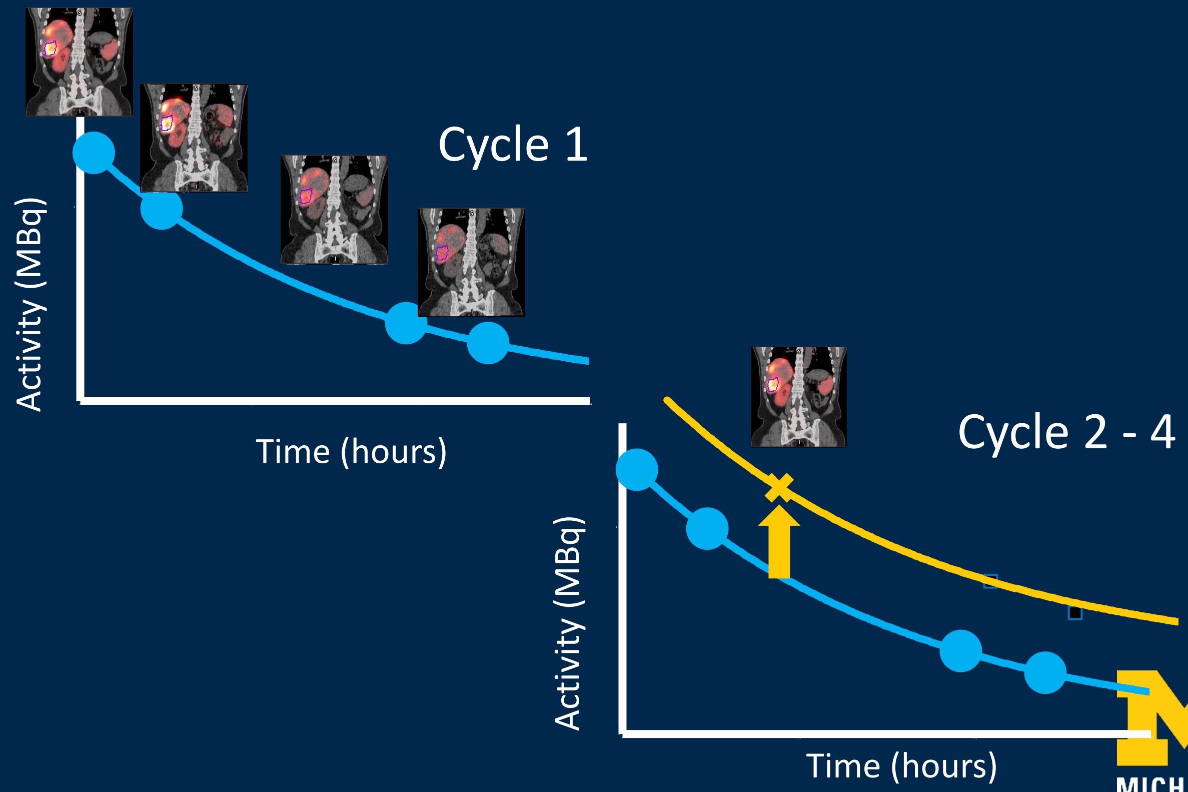
Single time point methods to reduce imaging burden of dosimetry

- Why it works? Even wide variations in effective half-life gives similar TIA

$$\bar{D}(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S)$$



- Full Imaging in Cycle 1 + Single Timepoint at Others
  - Assumes kinetics are unchanged between cycles but allows for cycle specific changes in uptake



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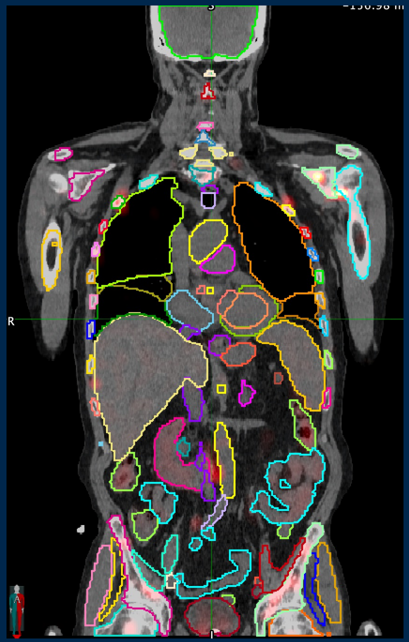
Madsen, Med Phys 2018; Hanscheid et al, JNM 2018

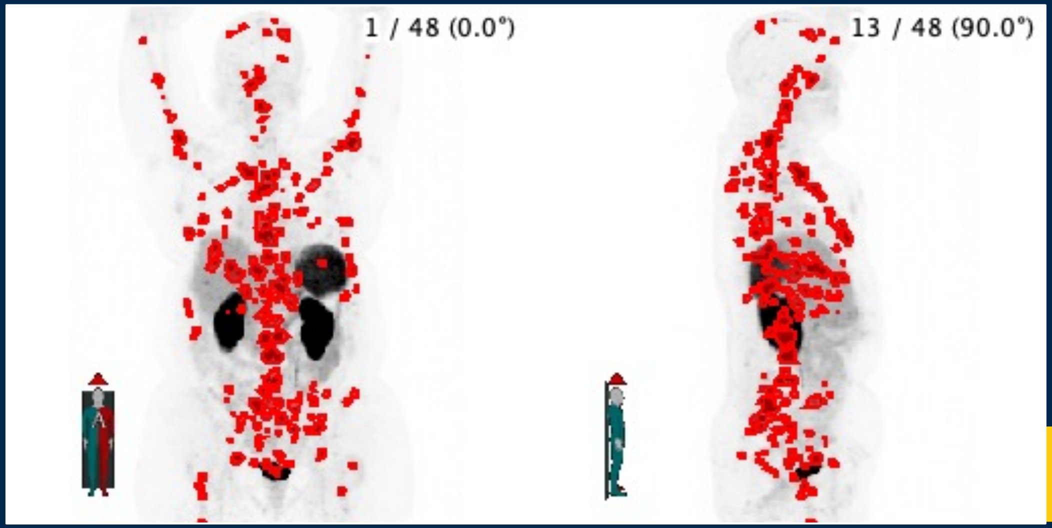
Developments that facilitate patient specific dosimetry: AI-Segmentation

- Well-validated for normal organs
- Coupled with some dosimetry packages

- Free-ware
  - TotalSegmentator: 104 structures in CT
- https://arxiv.org/pdf/2208.05868.pdf



- Individual lesion segmentation is more challenging
- Semi-automated tools available for whole-body tumor segmentation with and without AI for 'cleaning' physiological uptake



Kim et al, Evaluation of thresholding methods for the quantification of [^{68}Ga]Ga-PSMA-11 PET molecular tumor volume ... Eur J Nucl Med Mol Imaging. 2023

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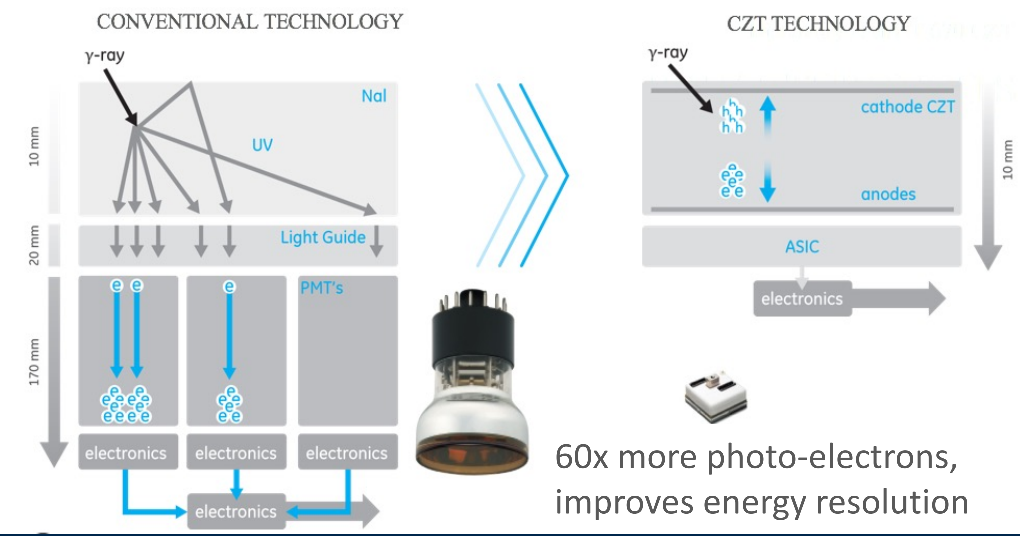
Developments that facilitate dosimetry: Advances in SPECT & PET

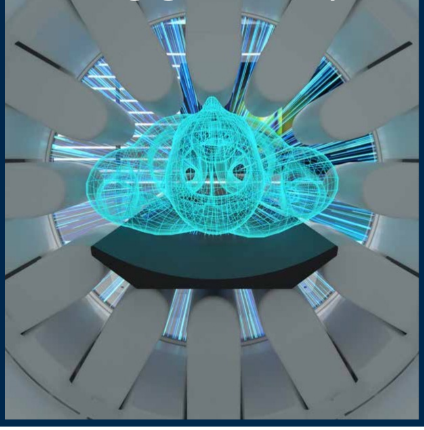
SPECT: Cadmium Zinc Telluride semiconductor for direct conversion of gamma energy to charge carriers



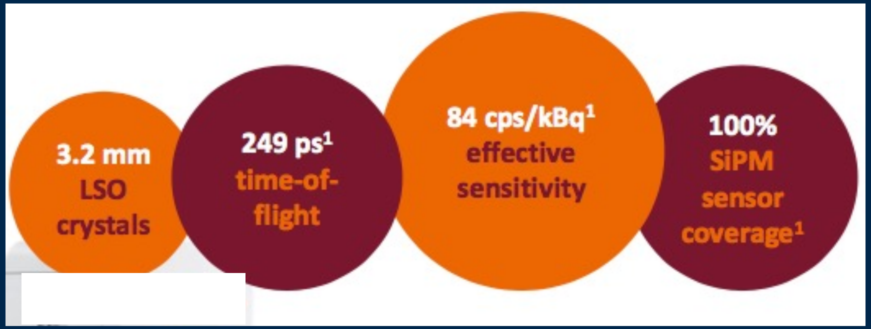
60x more photo-electrons, improves energy resolution

Built in source holders and calibration standards

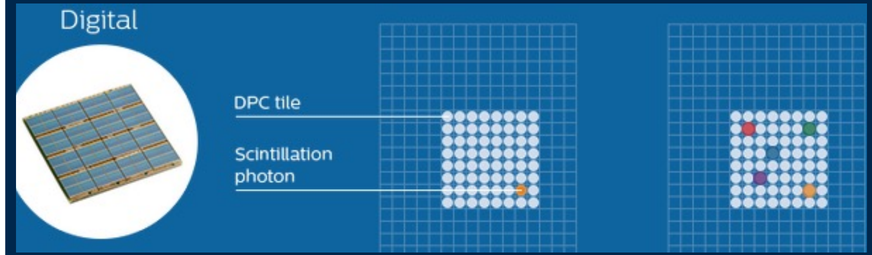
Multi-detectors in ring geometry

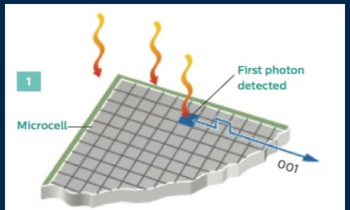


PET Si Photomultipliers. Reduced crystal size

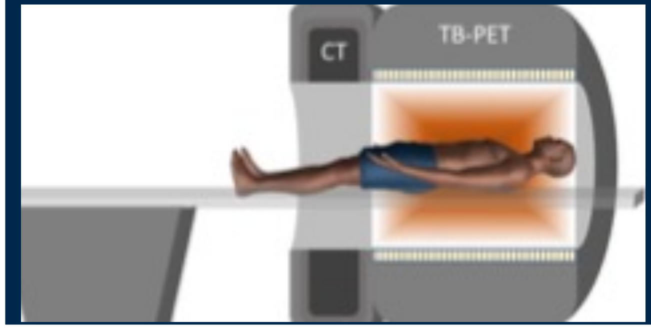


Photon Counting Technology. Array of single photon avalanche diodes convert light from the scintillator directly to a digital signal





Total body PET. Gain in sensitivity:
Improve SNR, reduce dose, or scan faster



Axial length	Gain in body sensitivity (1–2-m-long object) vs 20 cm axial length
70 cm	9–10 x
100 cm	15–20 x
140 cm	20–30 x
200 cm	30–40 x

GE CZT technology; StarGuide datasheet; xSPECT Quant and Biograph Vision, Siemens; Philips Vereos PET/CT, White Paper; State of the art in total body PET. EJNMMI Phys. 2020;7(1):35.

Developments that facilitate dosimetry: faster SPECT scans

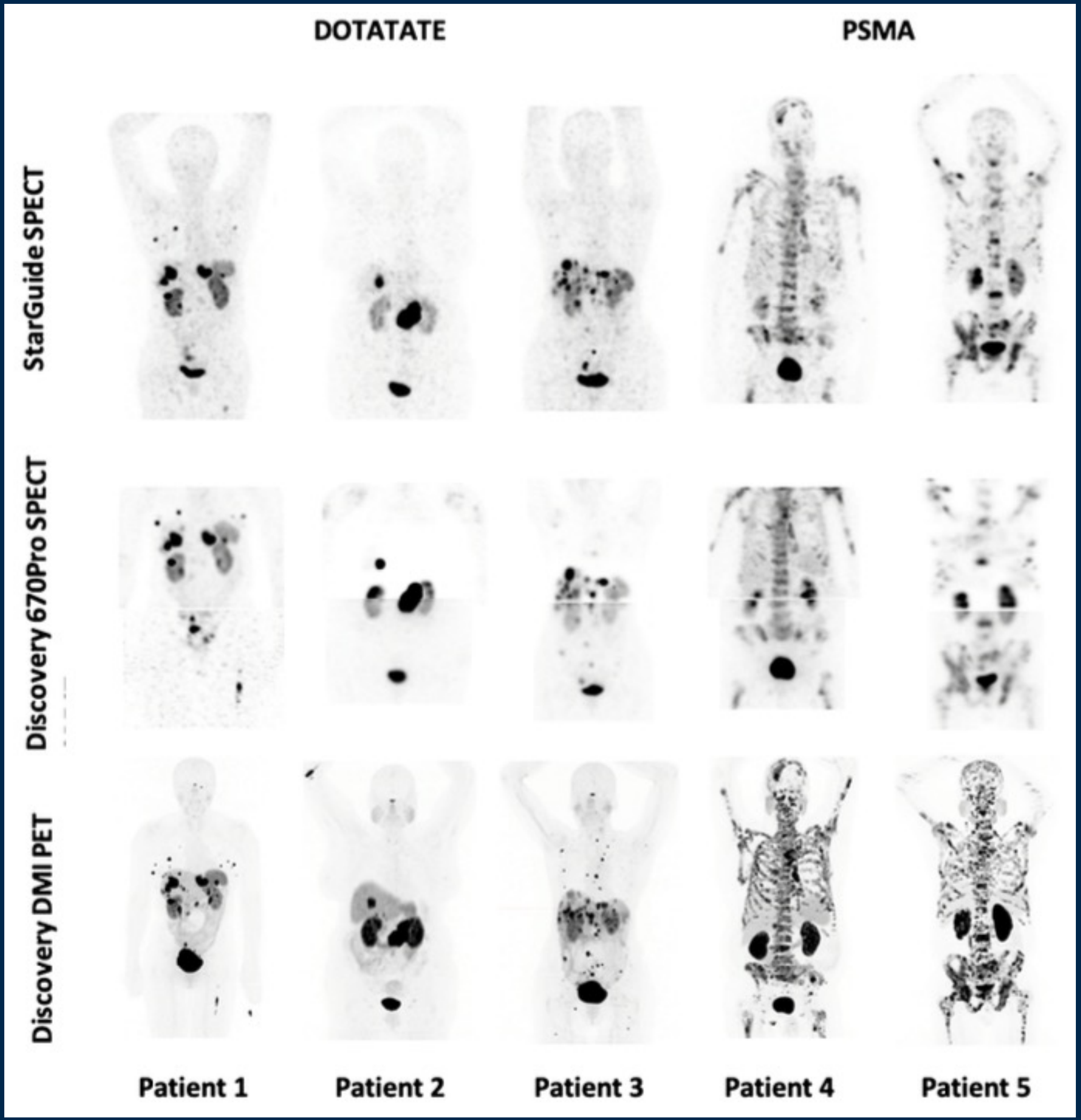
European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-023-06176-6

ORIGINAL ARTICLE

SPECT at the speed of PET: a feasibility study of CZT-based whole-body SPECT/CT in the post ^{177}Lu-DOTATATE and ^{177}Lu-PSMA617 setting

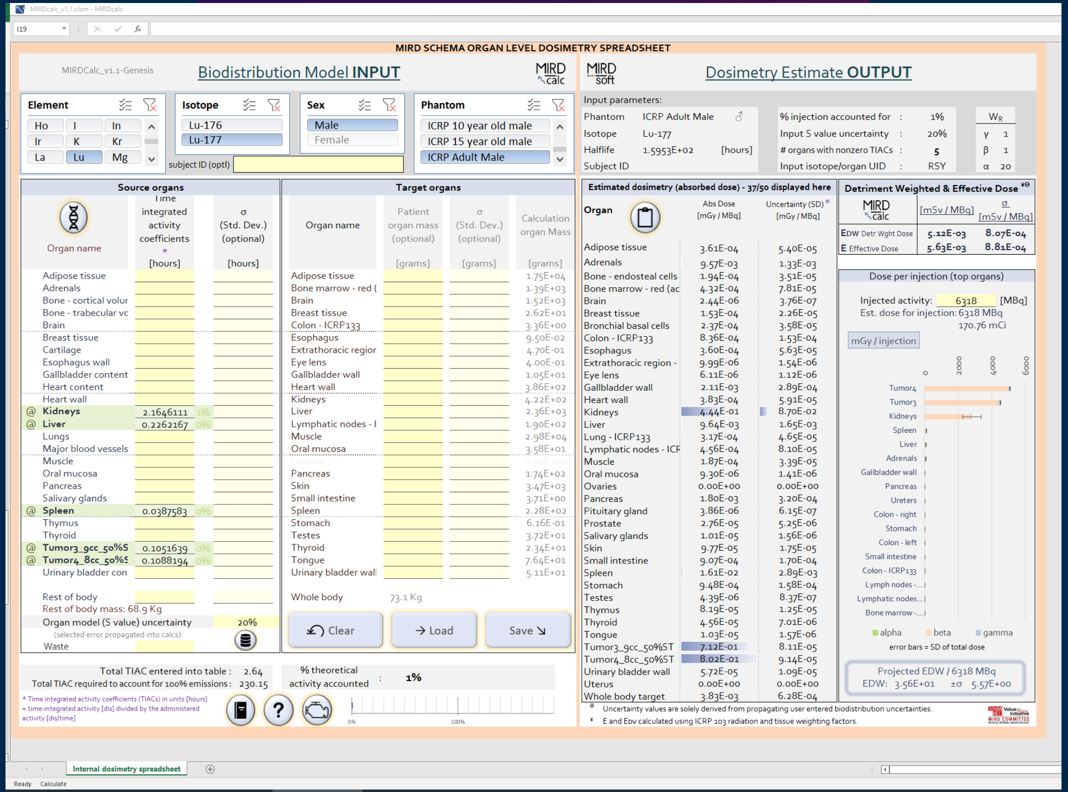
Hong Song[1] · Valentina Ferri[1] · Heying Duan[1] · Carina Mari Aparici[1] · Guido Davidzon[1] · Benjamin L. Franc[1] · Farshad Moradi[1] · Judy Nguyen[1] · Jagruti Shah[1] · Andrei Iagaru[1]

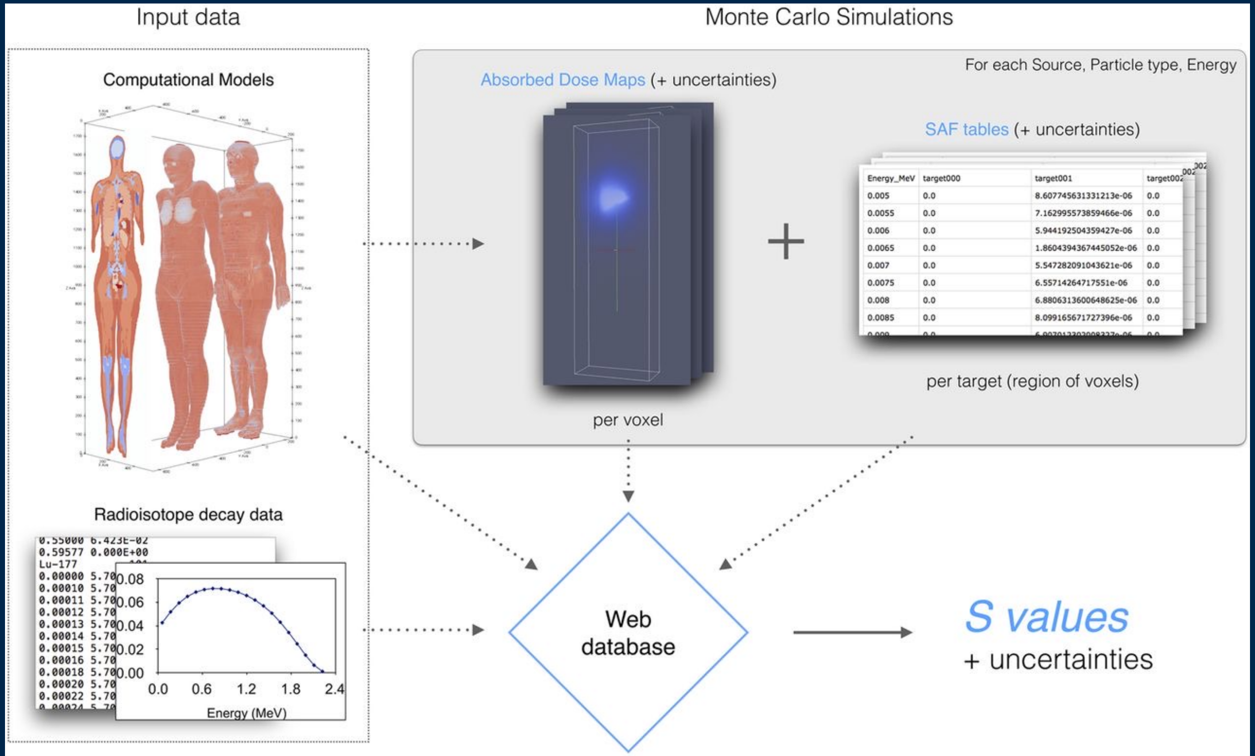
- New system: Vertex to mid-thighs post-therapy SPECT/CT scans with 4 bed positions, 3 min/bed and a total scan time of 12 min.
- Old system: 2 bed positions covering chest, abdomen, pelvis with total scan time of 32 min.
- Scans acquired with faster scanning time using new system had comparable detection/targeting rate



Publicly Available Dosimetry Software

- MIRDsoft https://mirdsoft.org/
- OpenDose https://www.opendose.org/





SAFs produced by MC simulations are stored in database along with input data. Web application allows calculation, and downloading of SAFs and S values

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Kesner et al. J Nuc Med, 59 (supplement 1) 473;

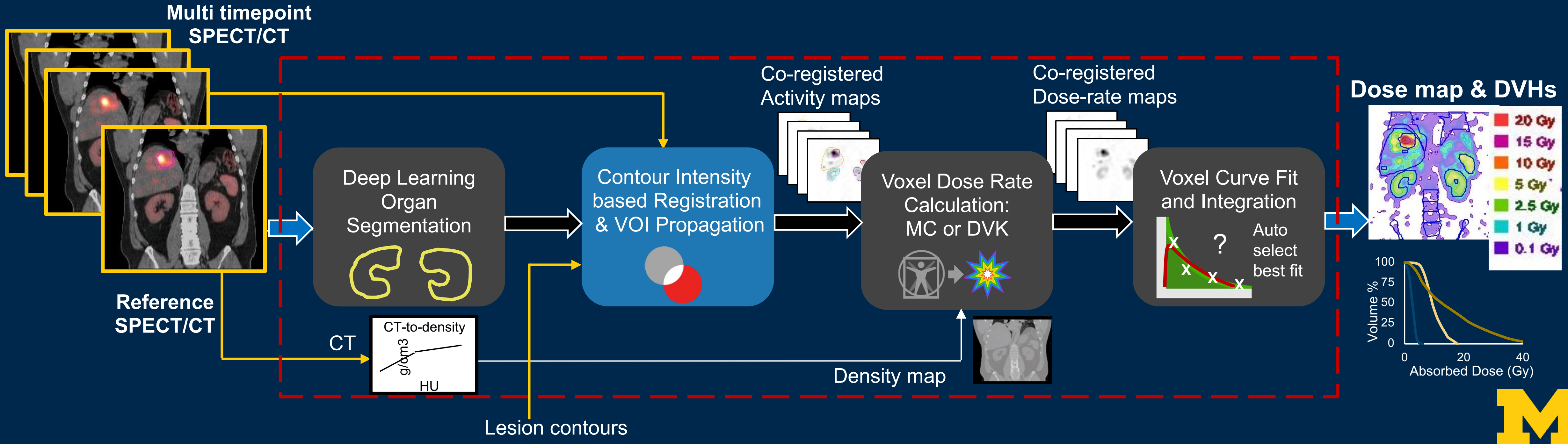
Chauvin et al. OpenDose. J Nuc Med 2020

Automated Monte Carlo voxel dosimetry in minutes

A Pipeline for Automated Voxel Dosimetry: Application in Patients with Multi-SPECT/CT Imaging After ^{177}Lu-Peptide Receptor Radionuclide Therapy

J Nucl Med 2022; 63:1665–1672

Yuni K. Dewaraja[1], David M. Mirando[2], Avery B. Peterson[1,3], Jeremy Niedbala[1], John D. Millet[1], Justin K. Mikell[4], Kirk A. Frey[1], Ka Kit Wong[1], Scott J. Wilderman[1], and Aaron S. Nelson[2]



NCI R01CA240706. NIBIB R01EB022075

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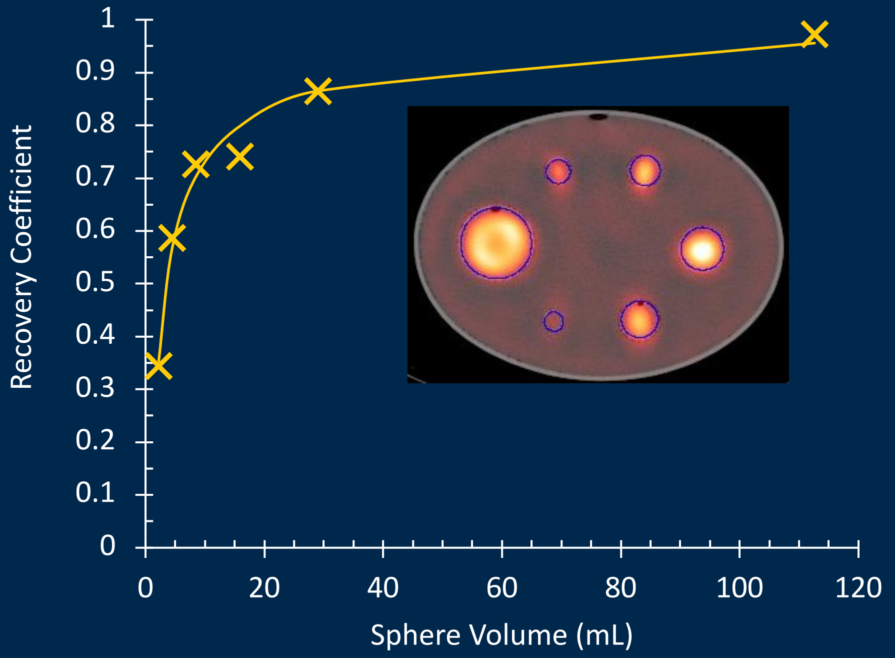
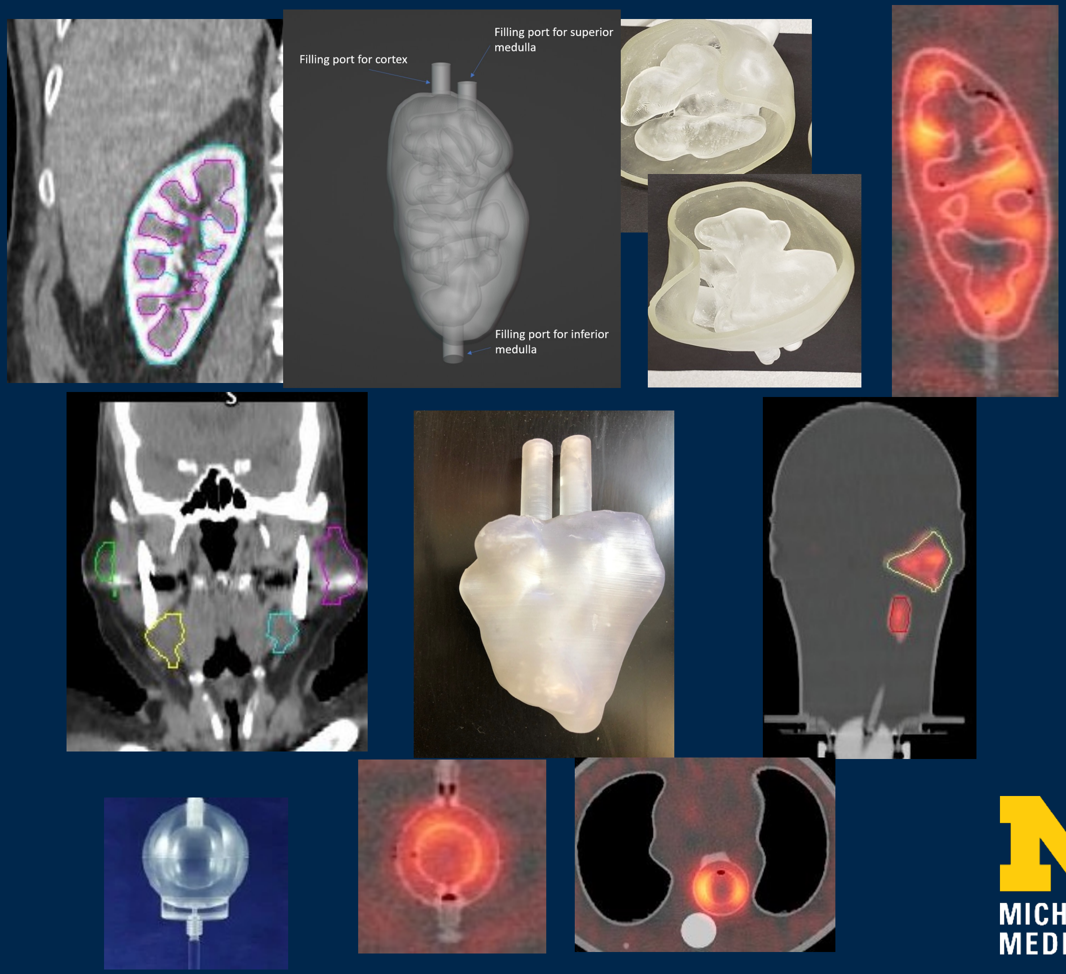
Poor SPECT resolution remains a challenge

- Recovery Coefficients for Partial Volume Correction
  - RC vs. volume curve using phantom meas.
  - Practical, but limitations, specially for small/complex structures
  - Mean value correction – not voxel level



- Structures in body are not spheres …
  - Limitations evident from phantom studies



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Absorbed Dose Estimation in RPT: What is possible & remaining challenges

- Image Acquisition
  - Reduced timepoints: Established for some therapies. Needed for others
  - Shorter scans: new detector systems & AI-based denoising
- Image Reconstruction, Quantification & Partial Volume Correction
  - Problematic for small/complex structures due to resolution and motion effects. Voxel-level PVC unresolved problem
  - Additional challenges when imaging alpha-emitters
- Organ/lesion Segmentation
  - Automated methods available for organs, under development for lesions
- Absorbed dose estimation
  - Multiple options including free-ware. Fast, accurate voxel-level calculation possible

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Thank You

yuni@umich.edu

Grant support from NIBIB R01EB022075, NCI 1R01CA240706 is acknowledged.

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