SAM Multidisciplinary Symposium

Dosimetry for Radionuclide Therapies: How do we get there and where can it take us?

Modeling strategies to improve Y-90 radioembolization dosimetry planning

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Learning objectives

At the end of this lecture you will be able to:

- **Explain** why precise and accurate Y-90 dosimetry is important
- **Describe** the new techniques under development and their promises
- **Contrast** challenges in Y-90 microsphere therapy with other radionuclide therapies

Outline

- Why do we need “good” dosimetry in Y-90 radioembolization?
  - dose-response relationship
  - Treatment efficacy and safety
- Image-based dosimetry for Y-90 microspheres
  - Pretreatment imaging (dose prediction)
  - Post treatment imaging (dose verification)
- Patient-specific dosimetry based on microsphere transport modeling and Y-90 physics

Dose-response relationship

Dose Matters: Y-90 liver radioembolization

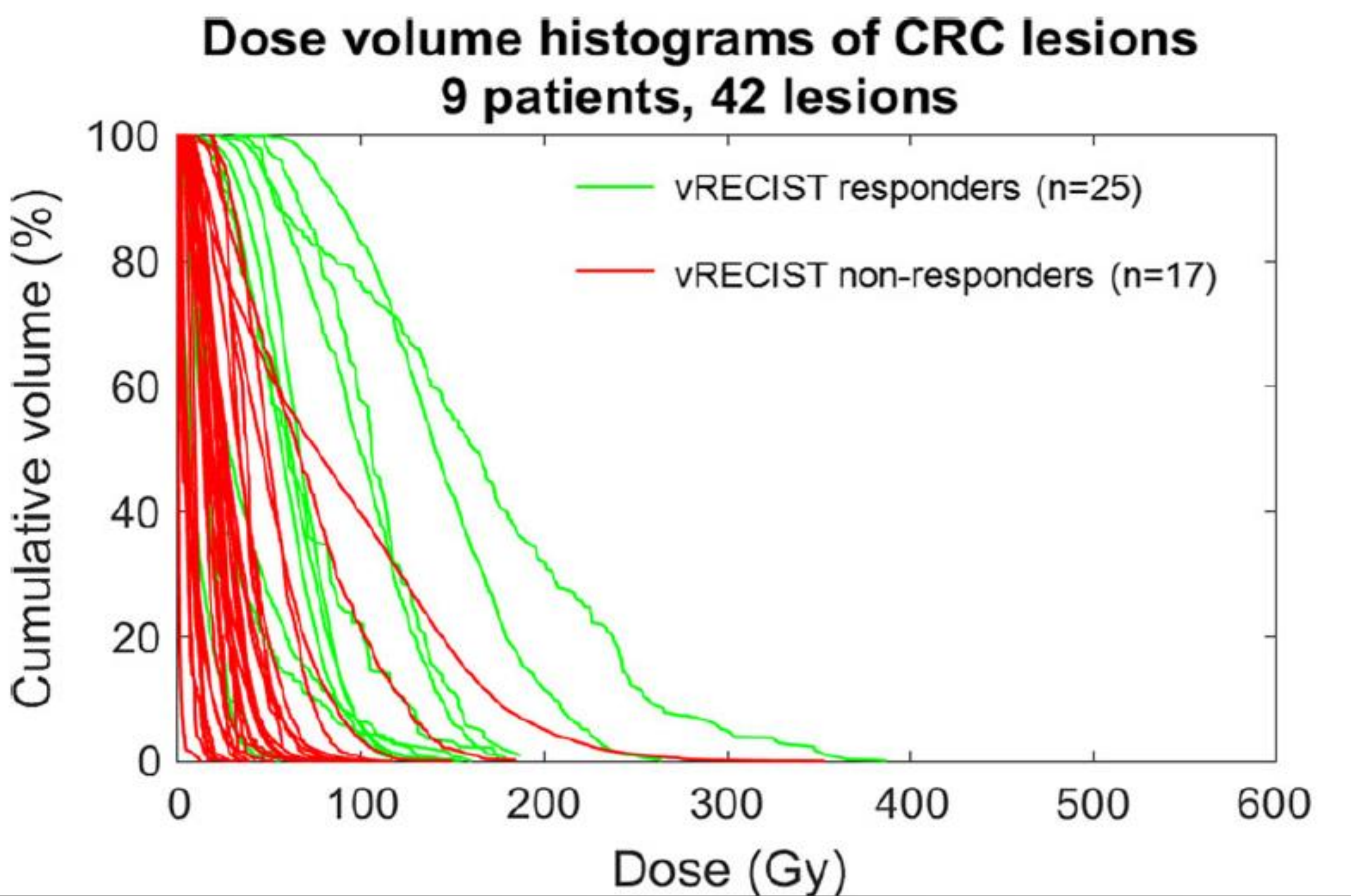
Cardiovasc Intervent Radiol (2016) 39:855–864
DOI 10.1007/s00270-015-1285-y

CIRSE CrossMark

CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

PET/MRI of Hepatic 90Y Microsphere Deposition Determines Individual Tumor Response

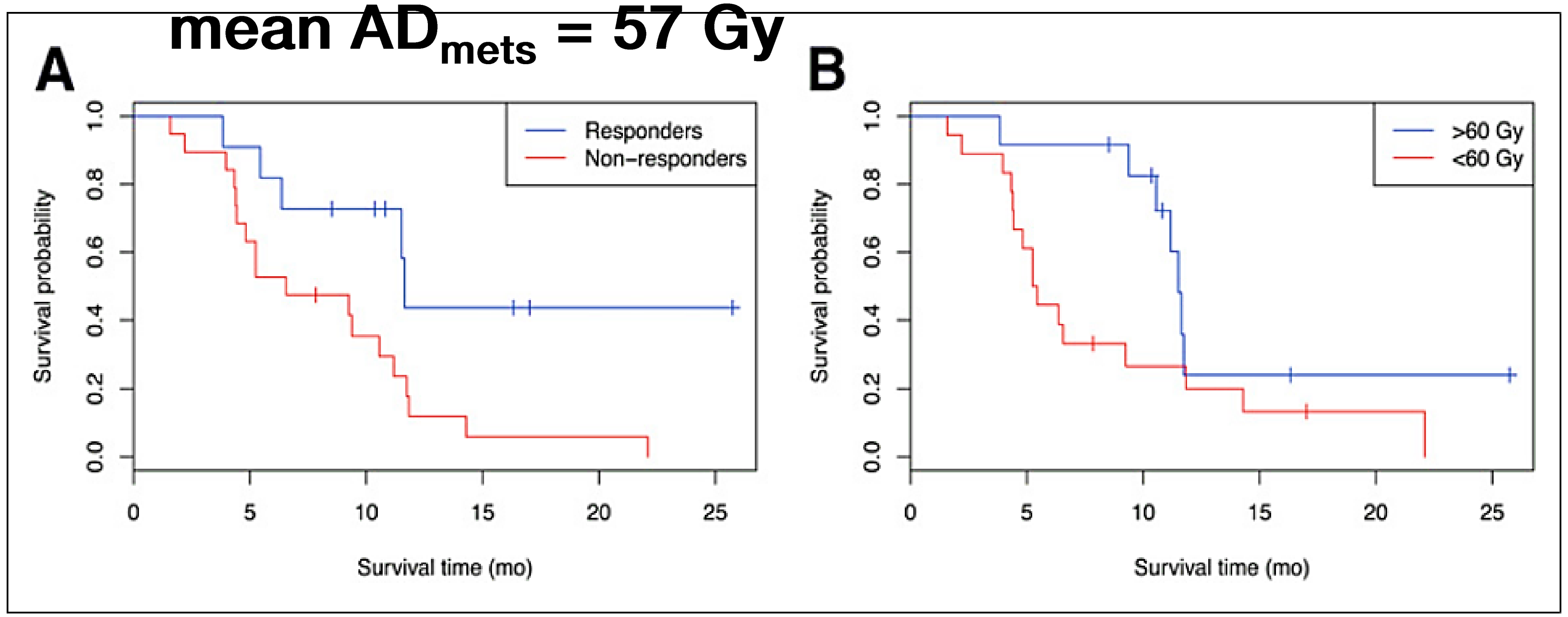
Kathryn J. Fowler[1] · Nichole M. Maughan[2] · Richard Laforest[3] · Nael E. Saad[1] · Akash Sharma[3] · Jeffrey Olsen[4] · Christina K. Speirs[4] · Parag J. Parikh[4]



Insights into the Dose–Response Relationship of Radioembolization with Resin ^{90}Y-Microspheres: A Prospective Cohort Study in Patients with Colorectal Cancer Liver Metastases

Andor F. van den Hoven[1], Charlotte E.N.M. Rosenbaum[1], Sjoerd G. Elias[1,2], Hugo W.A.M. de Jong[1], Miriam Koopman[3], Helena M. Verkooijen[1], Abass Alavi[4], Maurice A.A.J. van den Bosch[1], and Marnix G.E.H. Lam[1]

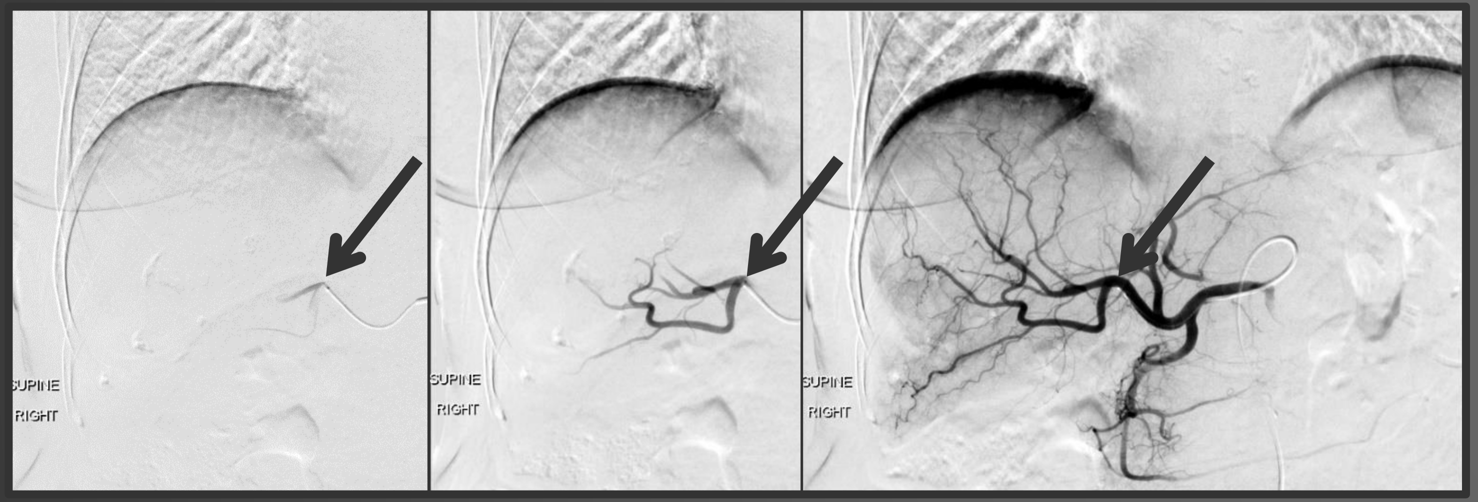
mean AD_{mets} = 57 Gy



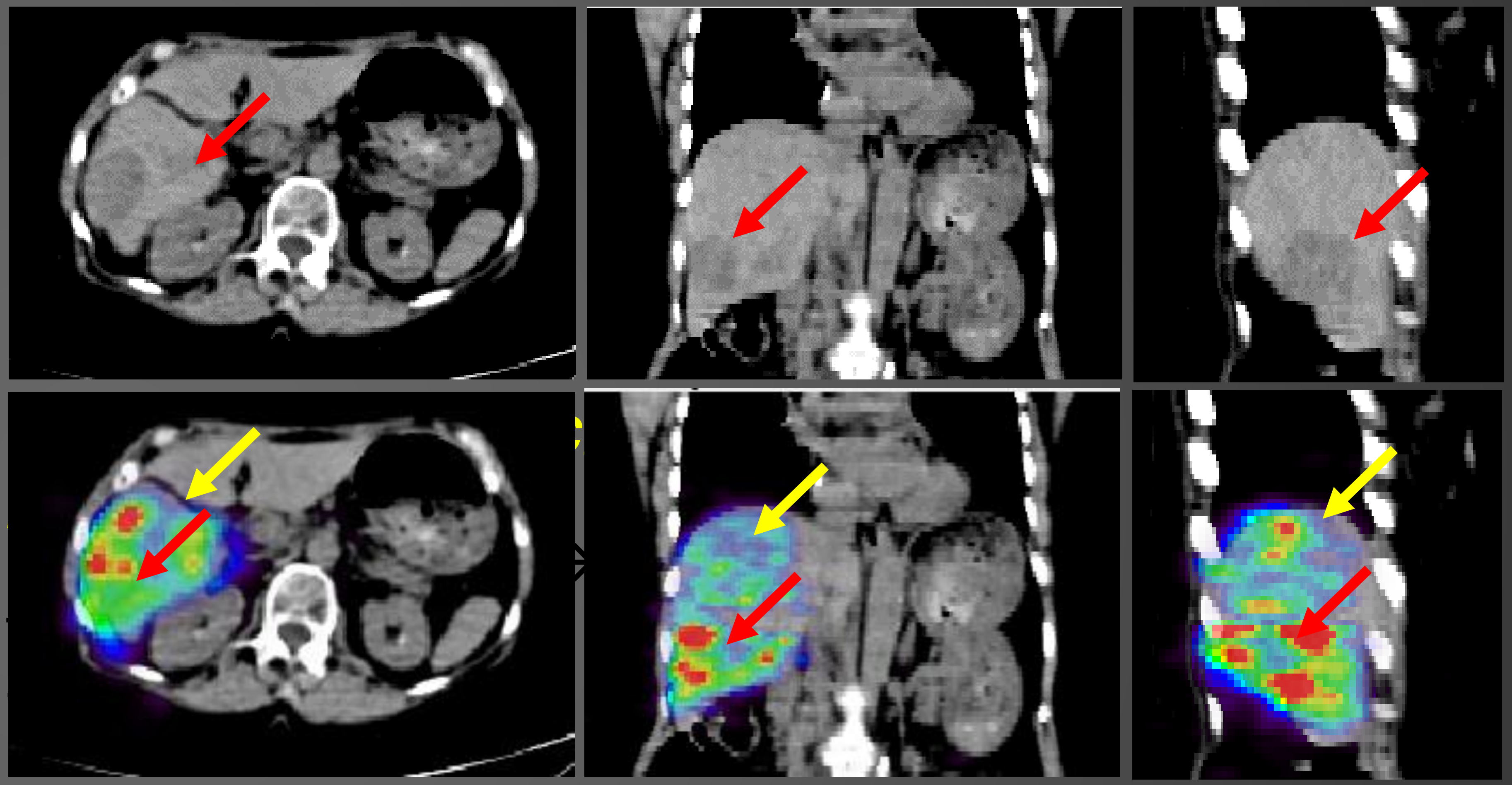
Improving treatment efficacy and safety through better planning

Clinical Questions

dose prediction: where to inject? how much?



X ray angiogram, pre-treatment



dose verification: how did we do? how much dose?

Dosimetry models for Y-90 radioembolization

Calculate the Absorbed Dose

Dosimetry systems

- Medical Internal Radiation Dose Committee from the Society of Nuclear Medicine (MIRD)
- Body Surface Area (BSA)
- Image-based dosimetry

Absorbed dose = cumulative dose

- Cumulative activity (activity x time), $\tilde{A}$
- Energy per radioactive decay E
- Absorbed fraction = fraction of energy absorbed within target, ϕ

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Y-90 Microsphere Dosimetry Models

MIRD

$$D\ (Gy) = 49.7\ \frac{AA(Bq)\ .\ (1 - LSF)}{mli\ (kg)}$$

BSA Method

$$AA\ (Bq) = (BSA - 0.2) + Tinvolv$$

Partition Model

$$AA\ (Bq) = \frac{D\ .\ mli\ (Vtu.TN + Vli)}{0.497\ .\ Vli\ .\ TN\ (1 - LSF)}$$

D = dose
AA = administered activity
mli = liver mass
LSF = lung shunt fraction
BSA = body surface area
Tinvolv = tumor involvement
Vli = liver volume
Vtu = tumor volume
TN = tumor to normal ratio

more information in: Bastiaannet, et al., EJNMMI Phys 5:22, 2018

Discrepancy Between models

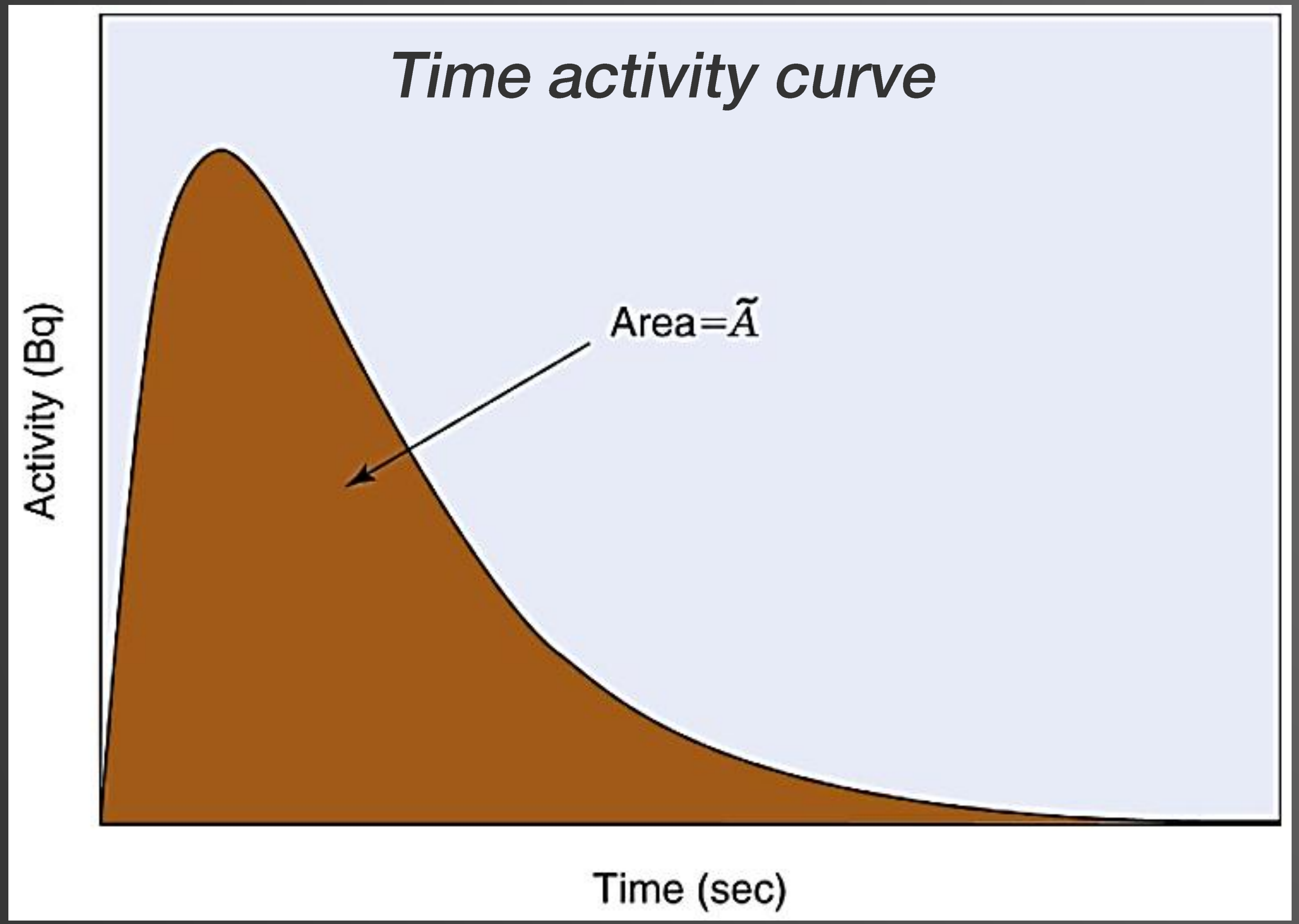
- Patient:
- 160 cm
- 74 kg
- Tumor involvement 0.60
- Lung shunt fraction LFS 0.044
- Target dose = 120 Gy
- Liver volume ~1.625 L
- TN 16.8 estimated from SPECT

	MIRD	BSA	Partition
Activity	3.9 GBq	1.7 GBq	5 GBq
Tumor	120 Gy	40 Gy	120 Gy
Liver	120 Gy	10.3 Gy	30.3 Gy
Lungs	8.5 Gy	3.7 Gy	10.8 Gy

Large variation in recommended administered activity and subsequent dose to target and organs-at-risk

Cumulative Activity in Y-90 microspheres

$\tilde{A} = AA \cdot \tau$ ← organ residence time



- Intra-hepatic injection → distribution primarily in the liver, with potential leak to lungs, abdomen
- Permanently implanted → no residence time

$$\tilde{A} = AA \cdot T_{1/2} / \ln 2$$

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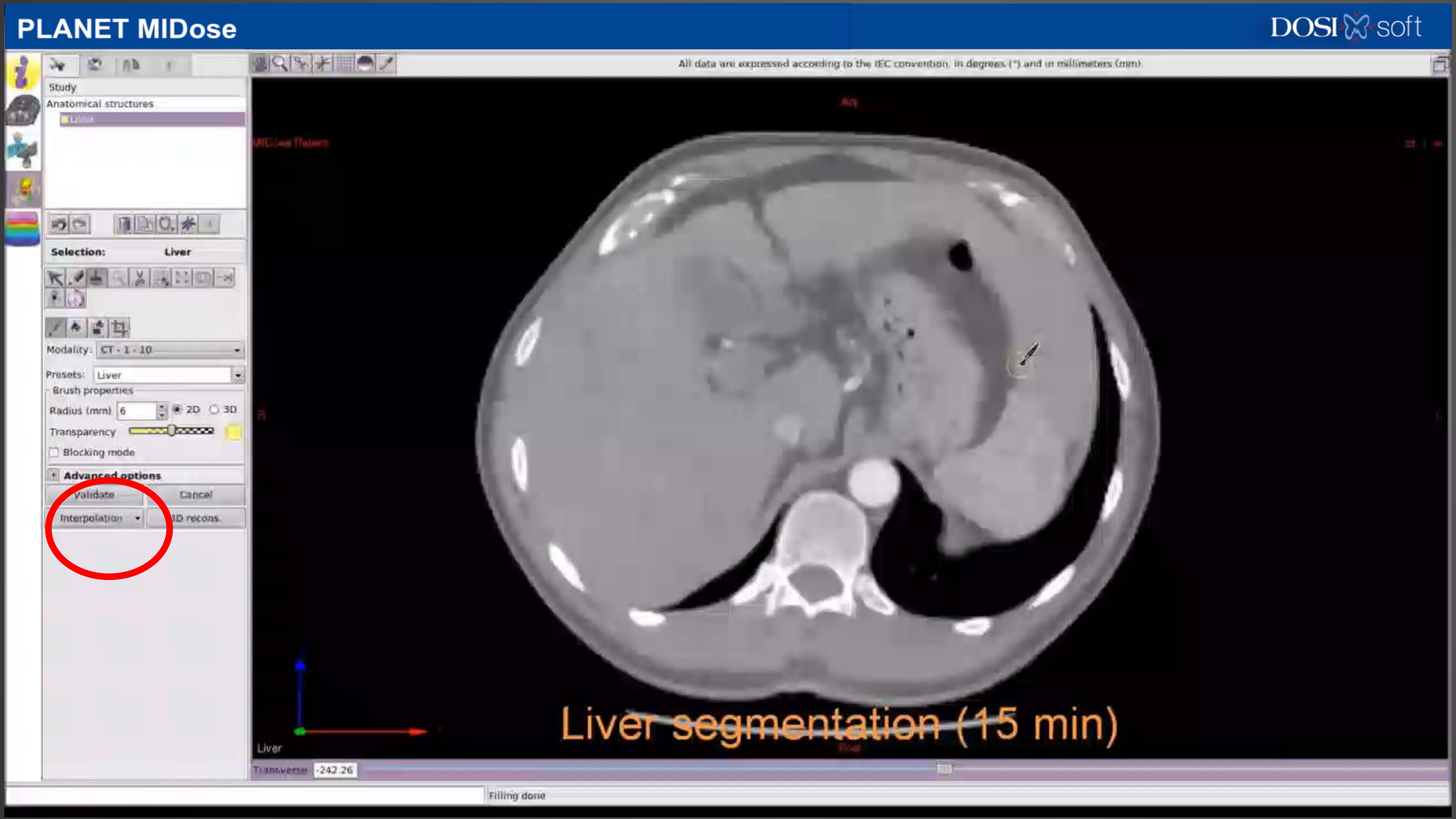
Image-based Dosimetry



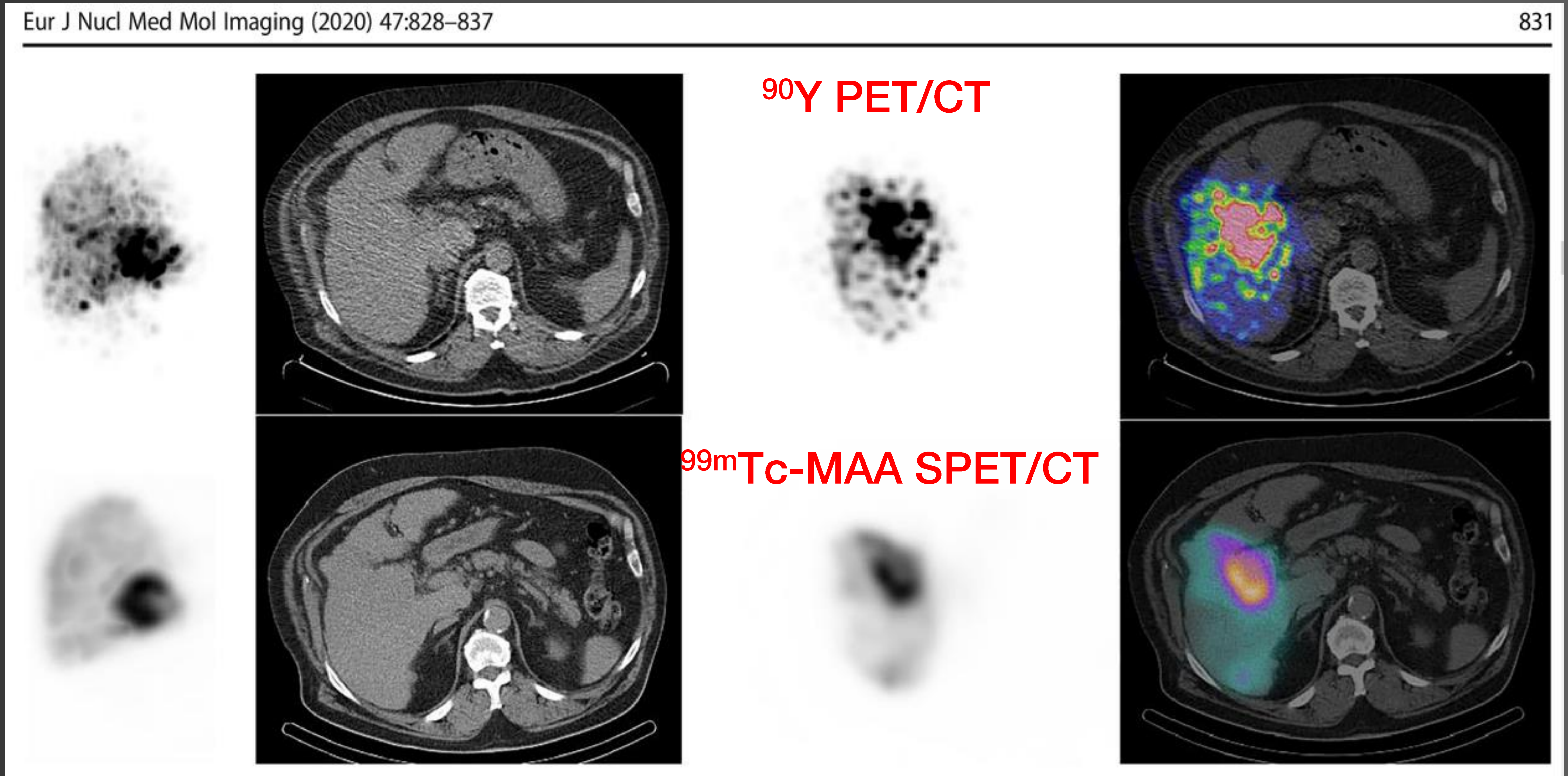
Anatomical imaging

Molecular imaging

- Spatial resolution for distribution within target
- Quantification
  counts → activity (Mbq)
  → dose (Gy)

Dose calculation

Pretreatment imaging with ^{99m}Tc-MAA



- Good accuracy in non-tumor tissue*
- Larger inaccuracy in lesions (>100s Gy in 5% patients)*
- Strong effect of catheter placement mismatch**

*Chiesa, et al. Eur J Nucl Med Mol Imaging, June 2020

*Jadoul, et al., Eur J Nucl Med Mol Imaging, 2019

**Haste et al., J Vasc Interv Radiol, 2017

An Engineering and Translational Perspective: Y-90 microsphere dosimetry with computational fluid dynamics

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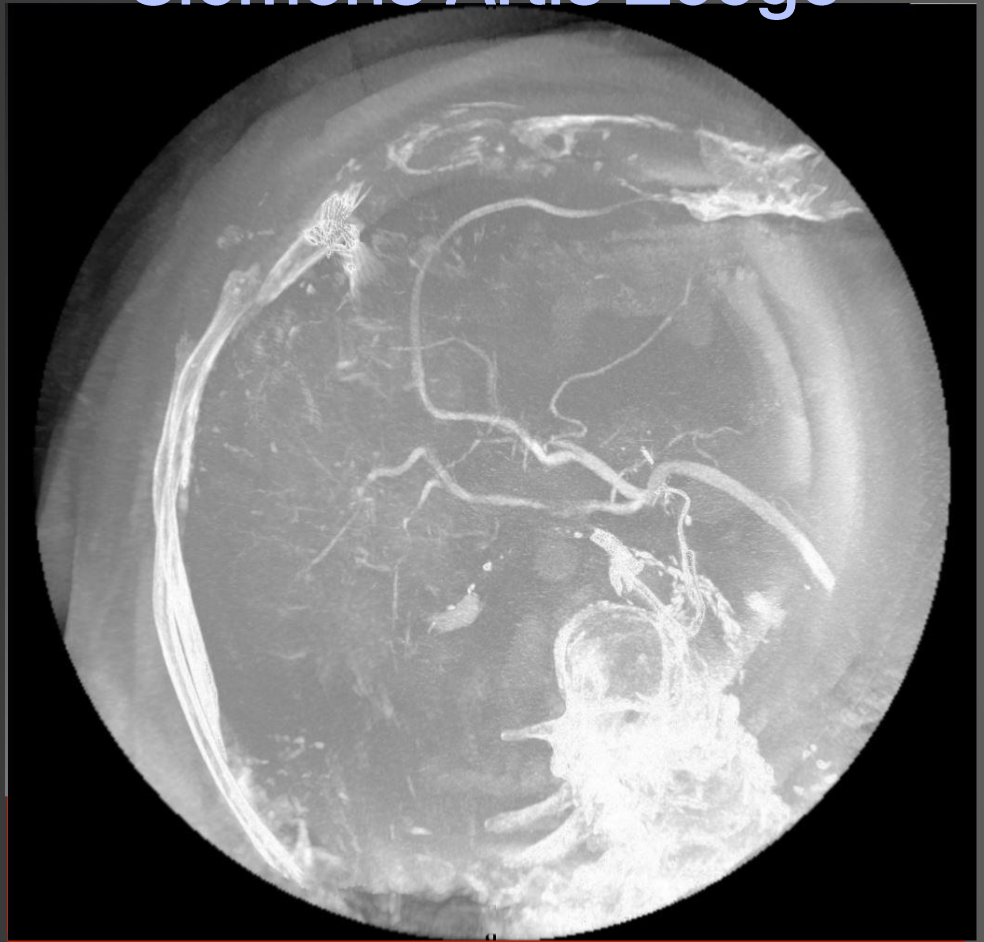
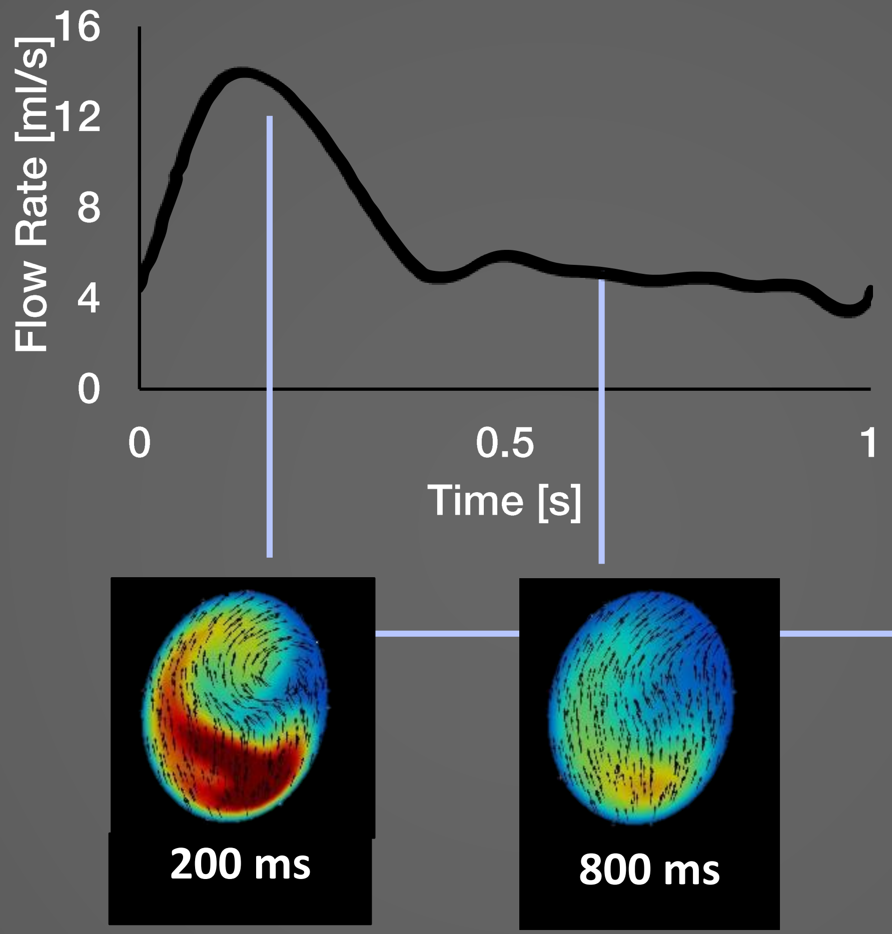
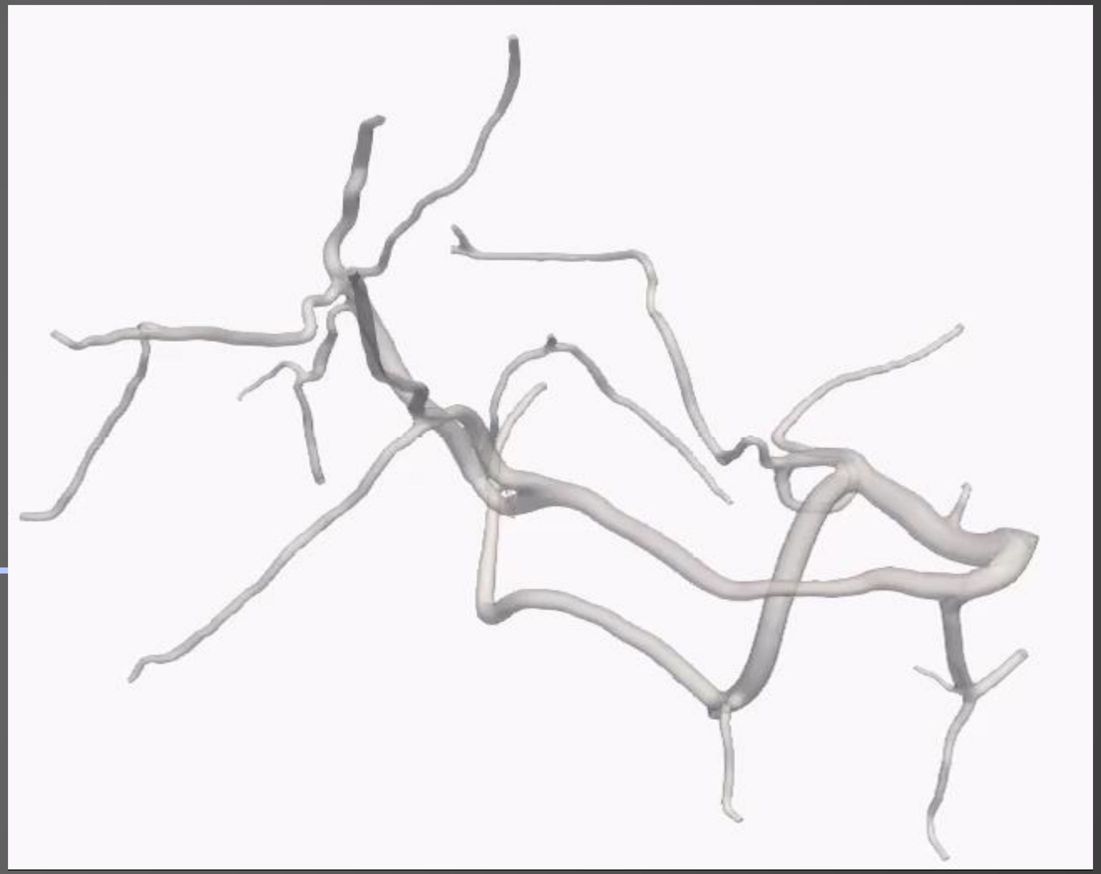
CFDose Overview

Planning CBCT,
Siemens Artis Zeego



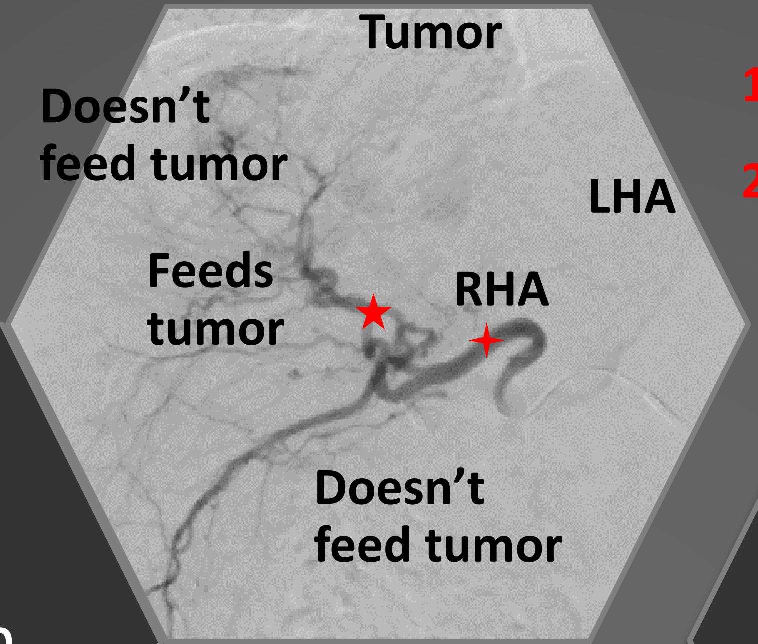
Blood fluid properties
Boundary conditions





Courtesy Amirtaha Taebi

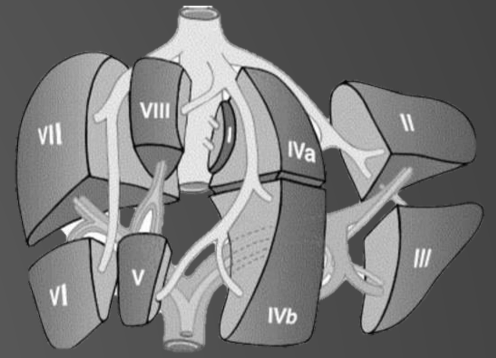
A Multimodal Imaging Approach



1st injection ✦

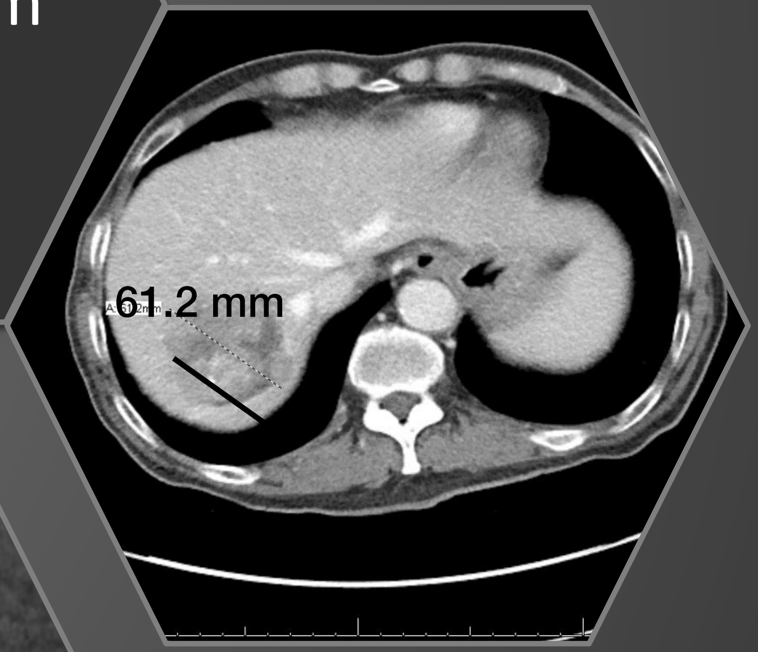
2nd injection ★

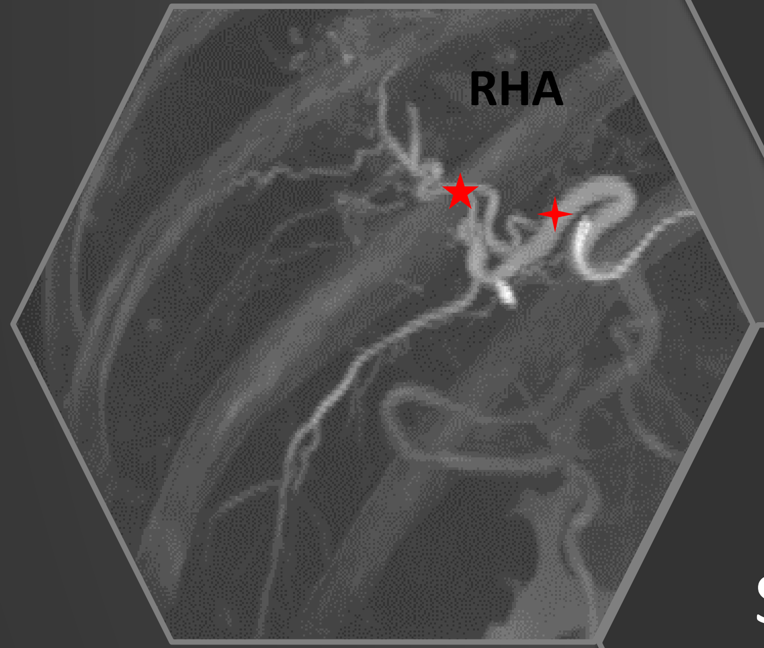
Couinaud segments



Analyze branching with DSA

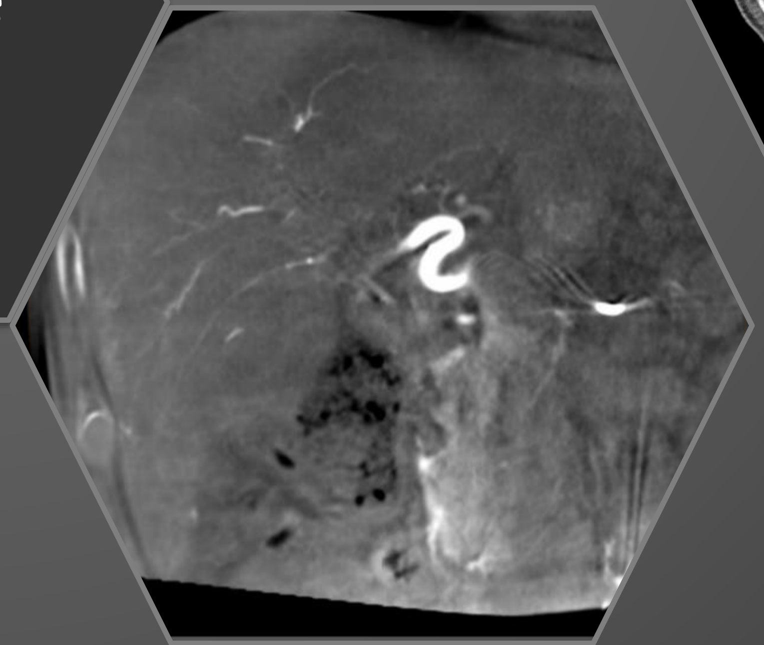
Localize tumors with equilibrium phase CECT



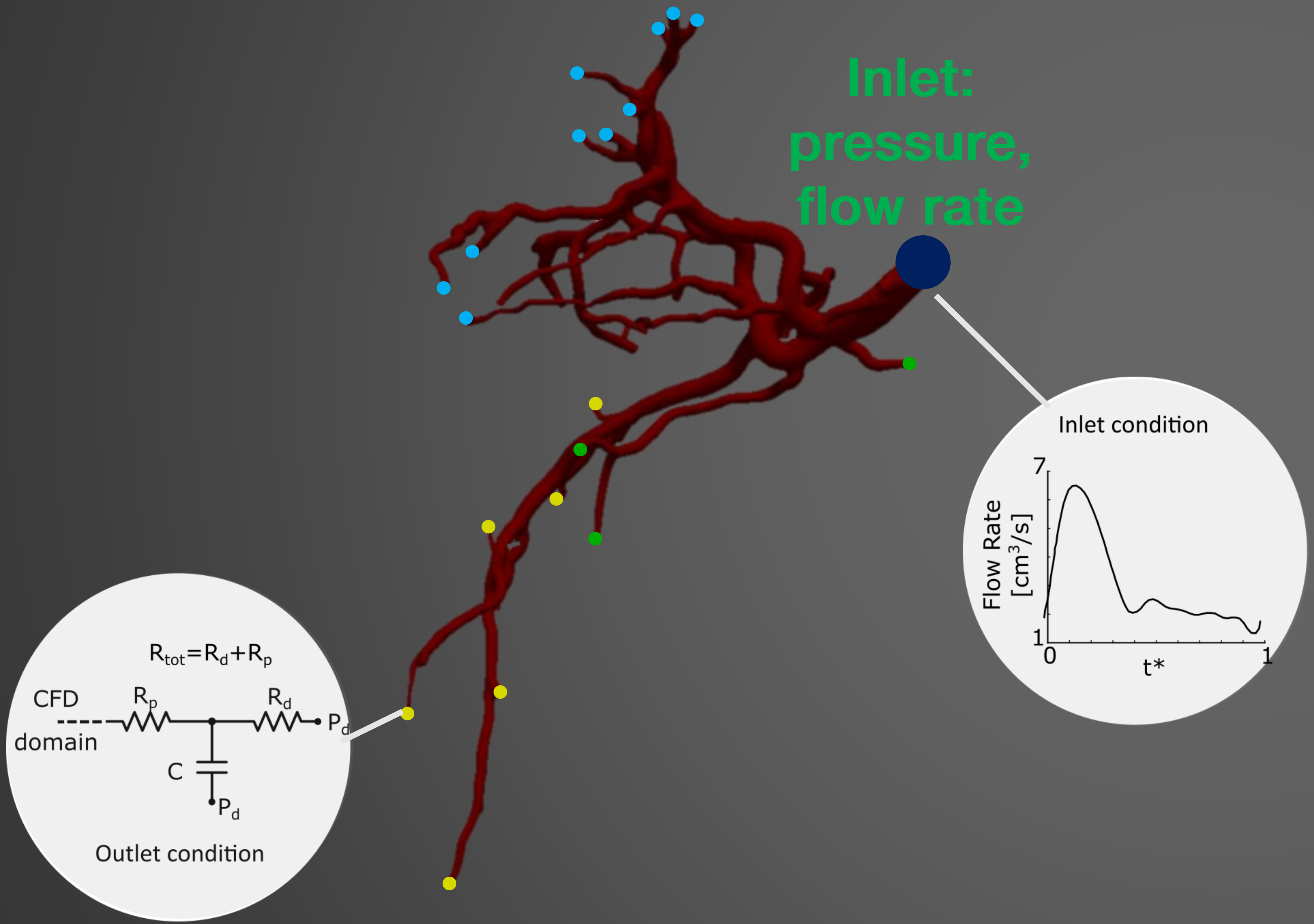


Identify HA on arterial phase CECT

Segment from CBCT



Flow Simulation: Multiscale Modeling

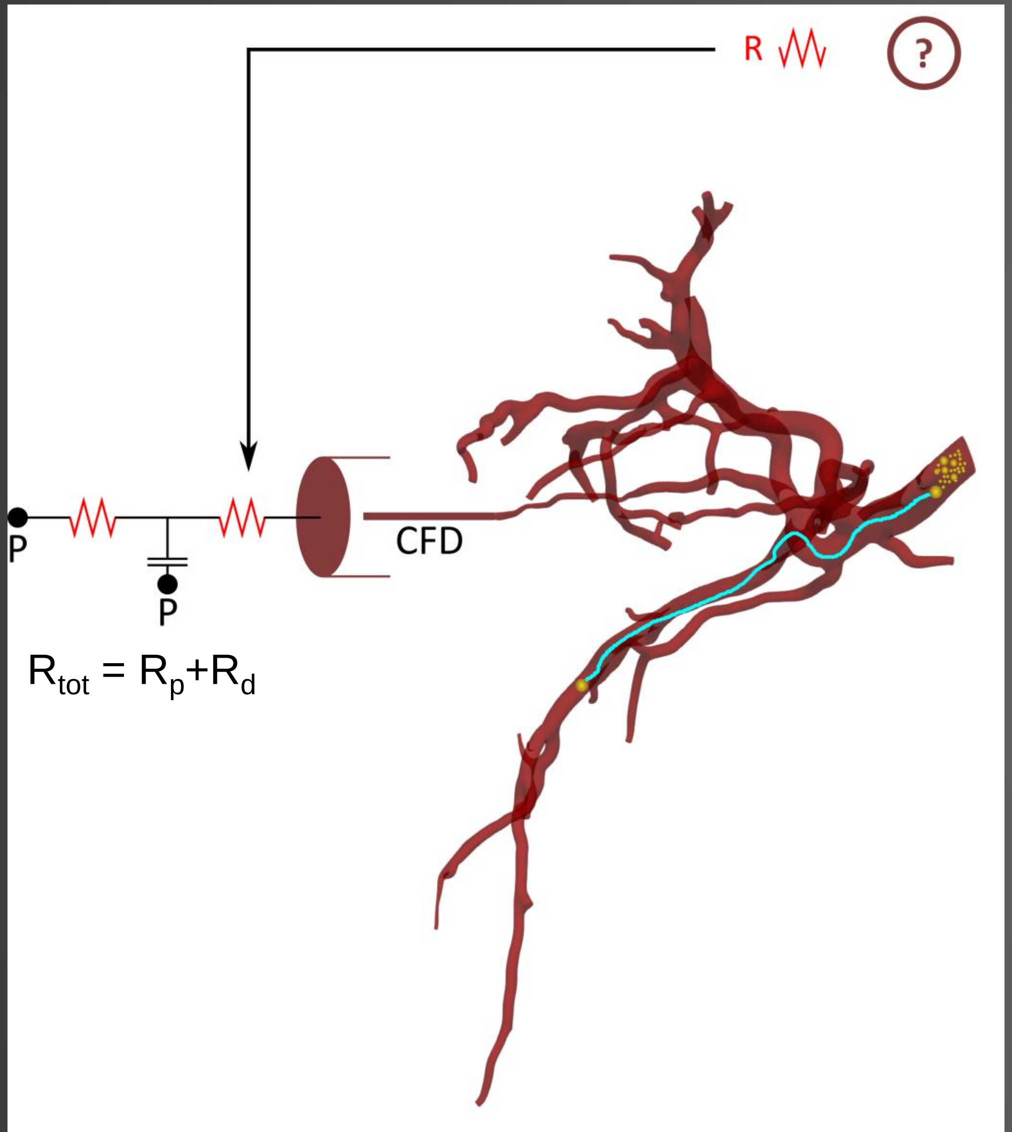


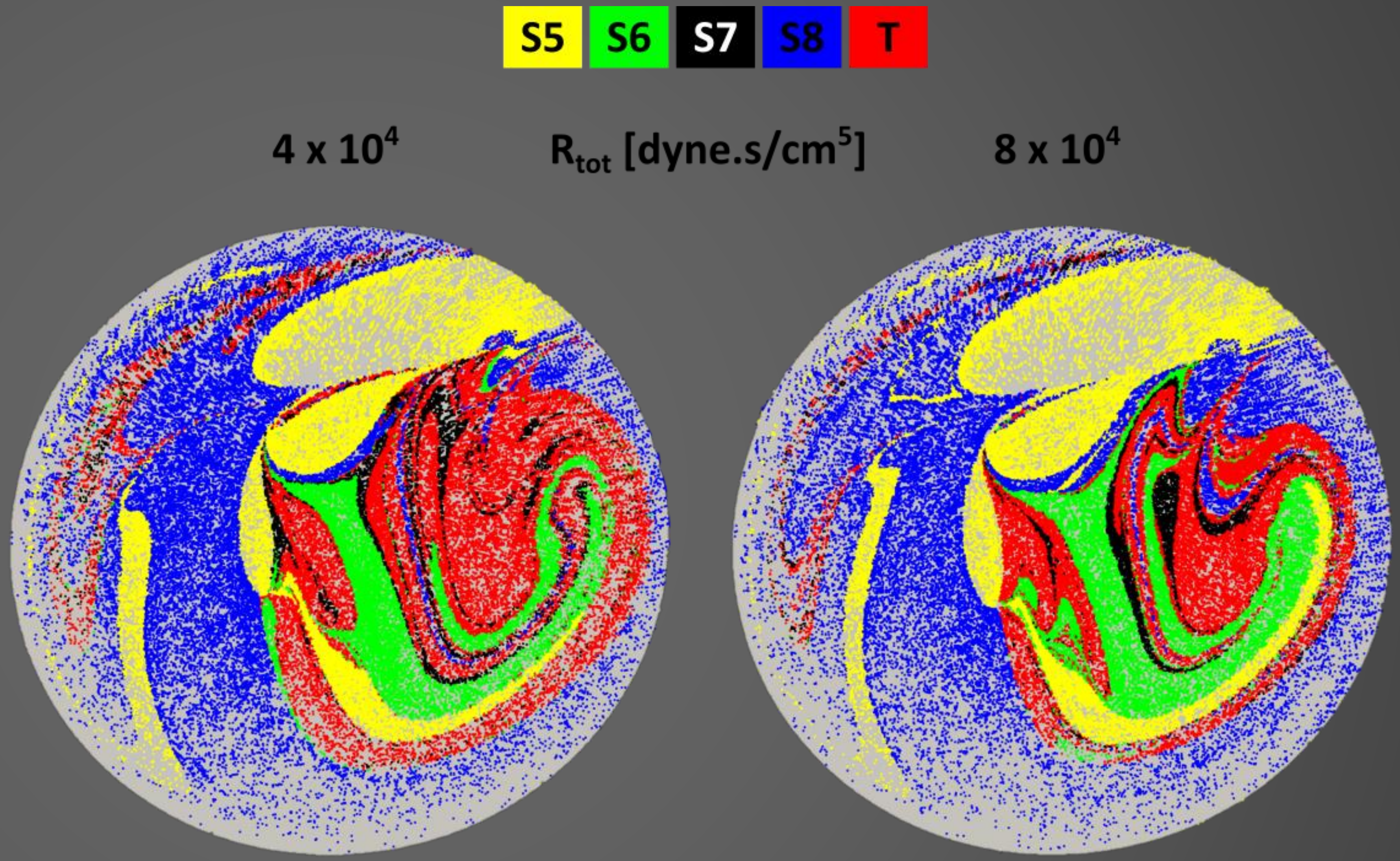
→ Segmented arterial tree combined with RCR Windkessel model for arterioles

- RCR circuit tuned using whole-body 0D model

Taebi, Vu, Roncali. J. Biomech. (in press)

Optimization of the Boundary Conditions





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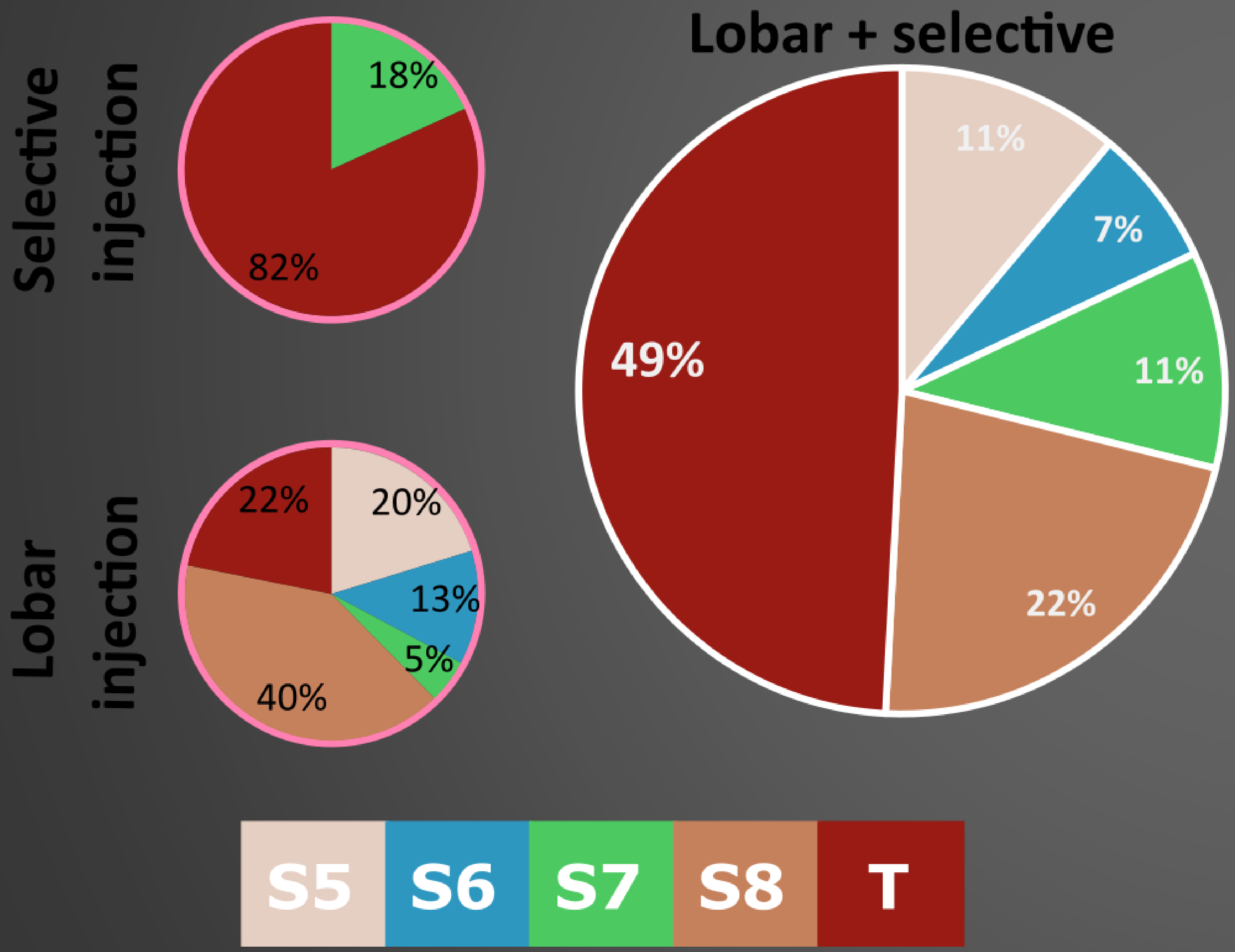
Blood Flow and Microsphere Distribution



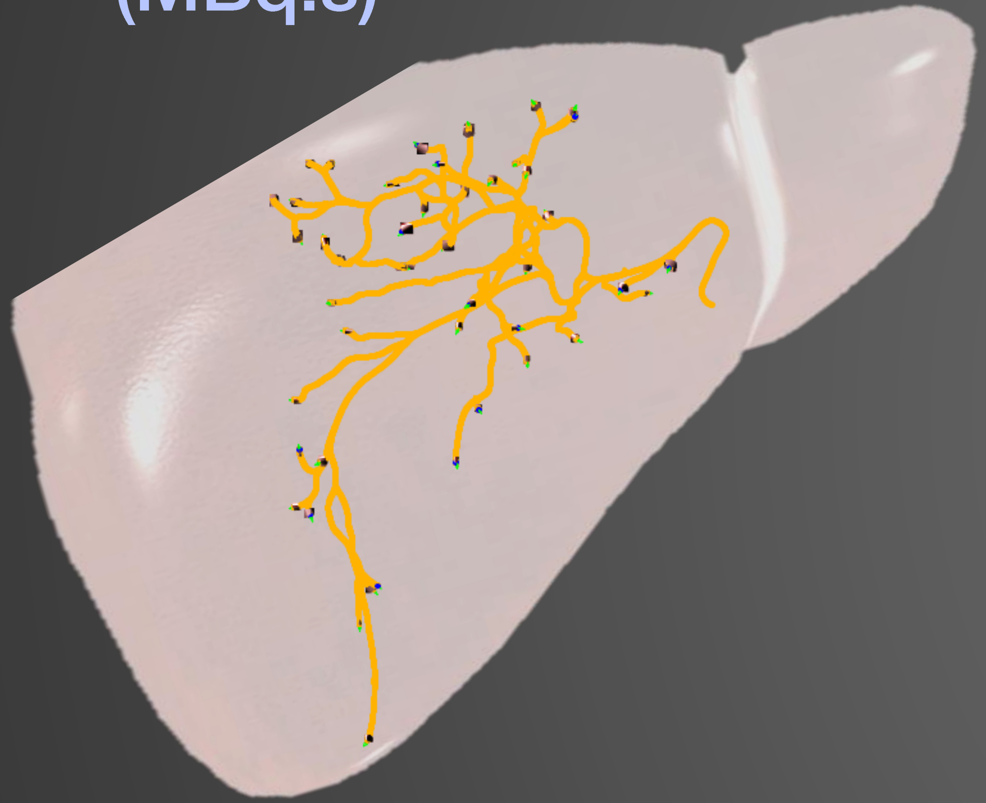
- Lobar injection: segments received 5%-40%
- Selective injection: tumor received 82%

→ Tumor received 49% of microspheres after both injections

Roncali et al. ABMES 2020

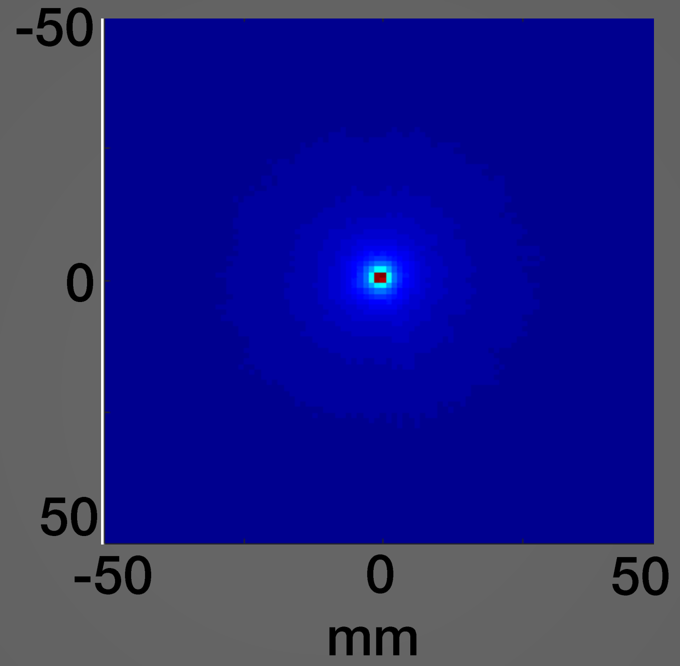
CFDose: Estimate Absorbed Dose distribution

Cumulative activity (MBq.s)



⊗

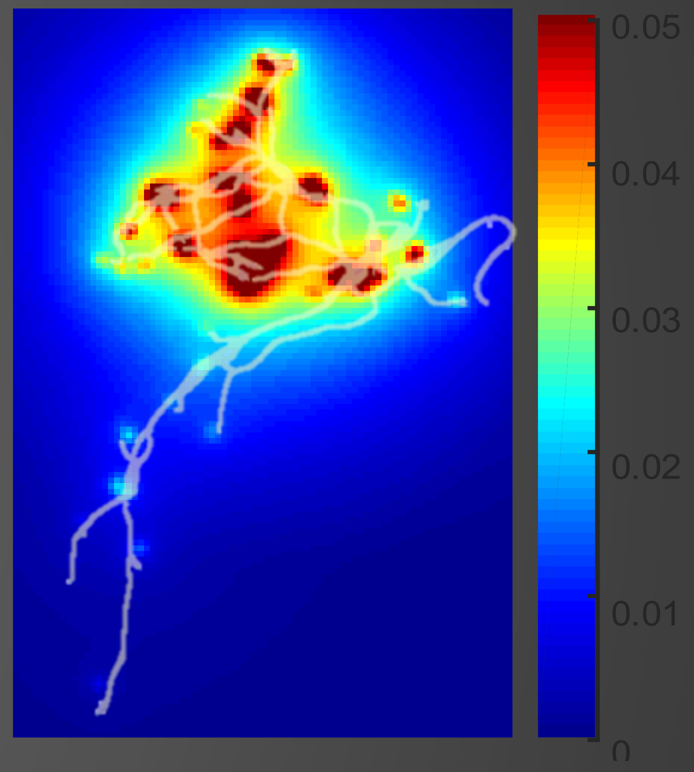
Gy / MBq.s



GATE/Geant4

=

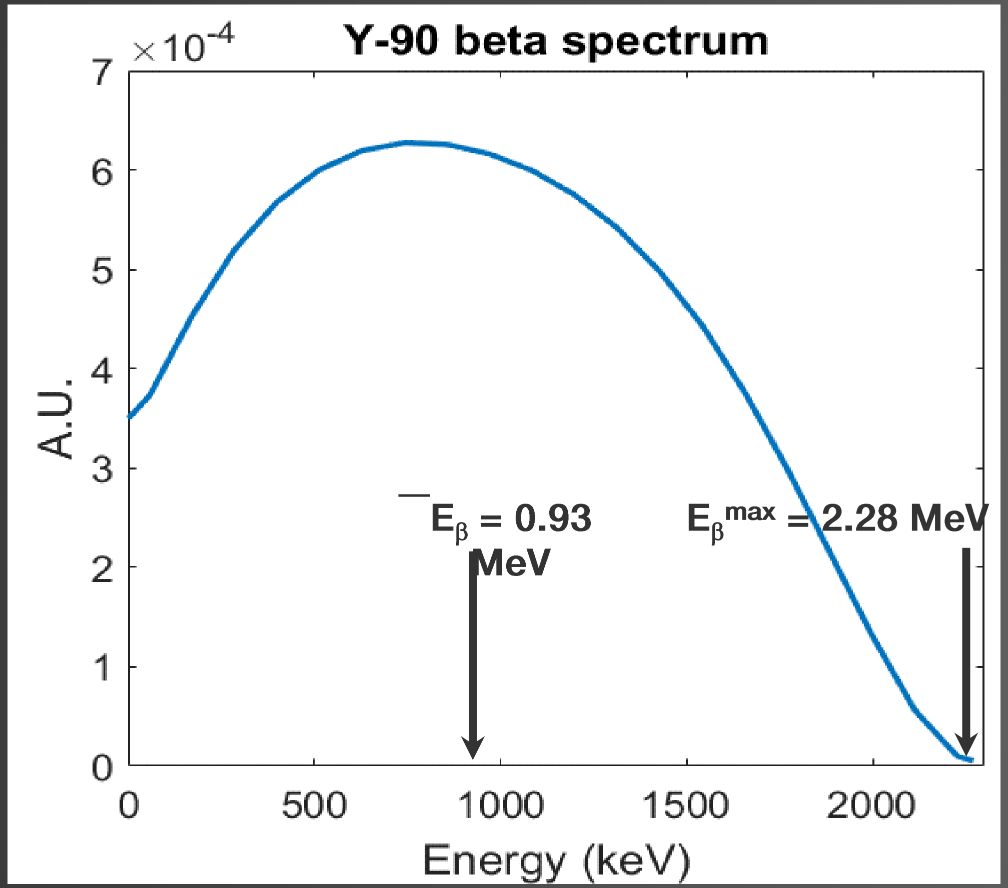
Gy



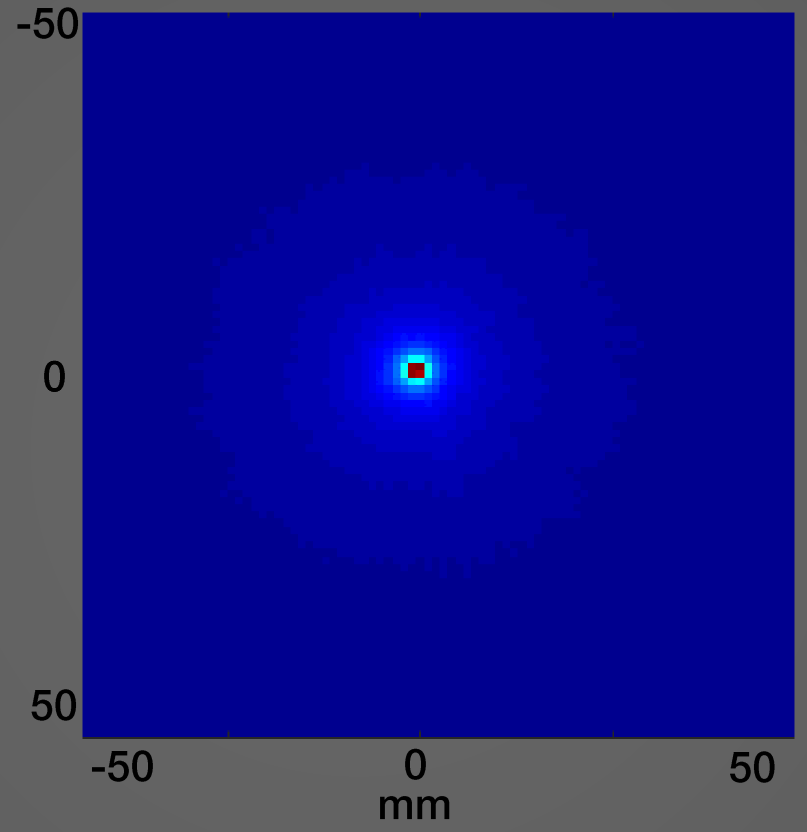
- Highly heterogenous dose distribution between segments
- Predicted total dose 125 Gy, consistent with MIRD 137 Gy

Roncali et. al. ABMES (2020), , Taebi et. al., J. Biomech. (2020)

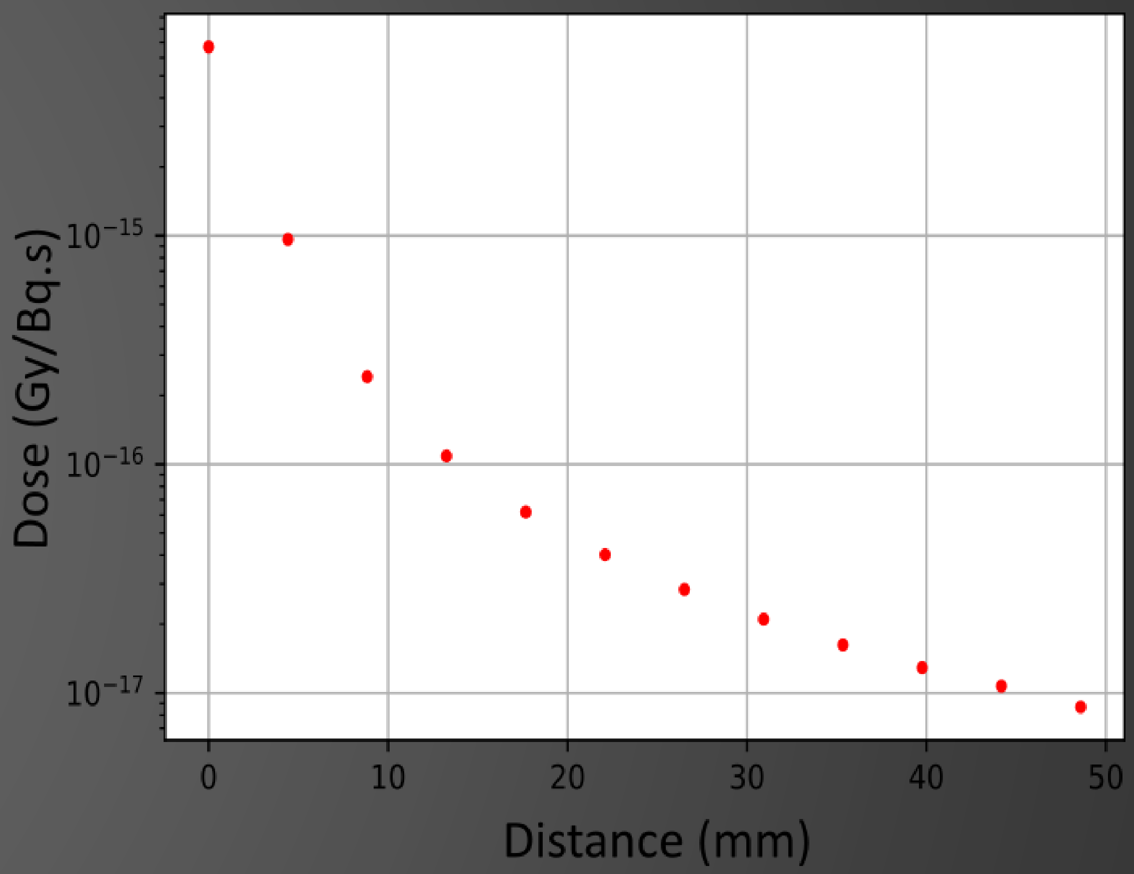
What is the energy of the β- ?



Dose point kernel



Kernel radial profile



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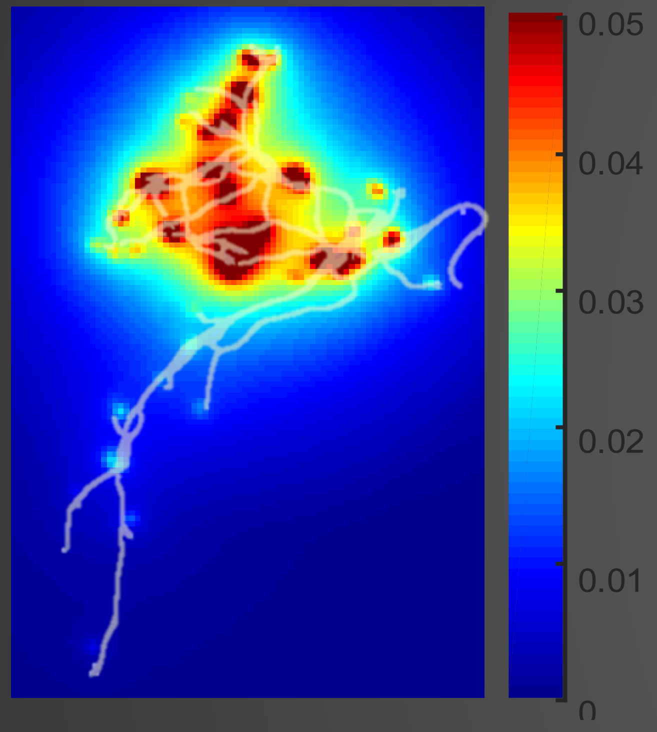
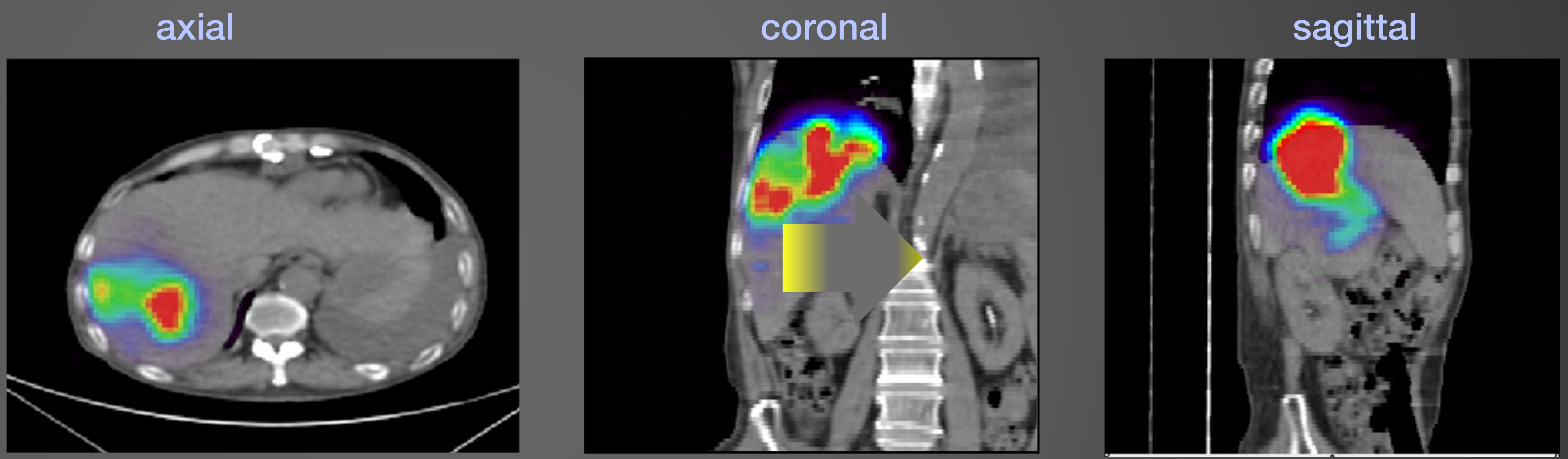
Y-90 PET/CT post treatment

Absorbed dose



Clinical Y-90 PET/CT

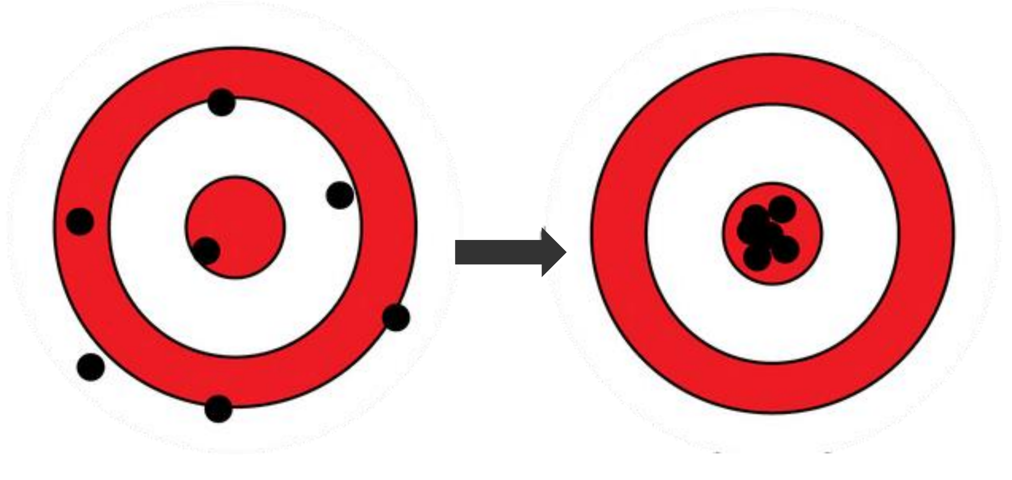


Qualitative agreement between predicted dose and Y-90 PET measured activity

- 6 patients scanned at UC Davis since September 2017
- Quantitative comparison of dose distribution in progress

Conclusions

Success of TRT relies on personalized treatment planning with high accuracy and precision



- Pre-treatment image-based dosimetry still limited by lesion inaccuracies → need for alternative approaches
- We leverage physics principles to predict dose distribution and develop CFDose
- Quantitative Y-90 PET post injection will provide validation at different levels

Acknowledgments

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