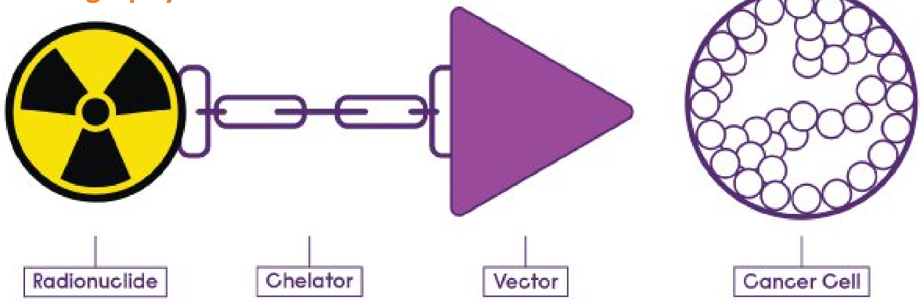
SPECT Imaging and Dosimetry of ^{155}Tb and ^{161}Tb and Evaluation of the Impact of ^{156}Tb Contamination

Mohammed Hussein and Marc-Antoine Verdier.

- Radiotherapy uses ionizing radiation to damage tumour cells while sparing normal tissues as much as possible.
- Internal radiotherapy:
  - The radioactive source is injected inside the body.
  - Dose is delivered closer to disease and supports targeted oncology.
  - High LET low dose rate.



Why VIR ?

- High precision, personalized treatment, targeting diffused tumors.
- Vectorized: need of imgaing for treatment planning, estimating the injected dose and following the bio distribution (Theranostic approach).

➢ Requires development of more specific radiopharmaceuticals and adapted imaging systems (SPECT, PET and gamma camera).

SPECT Scan

PET Scan

- Some available theranostic pairs:
  $^{64}Cu/^{67}Cu$, $^{44}Sc/^{47}Sc$, $^{86}Y/^{90}Y$.

Terbium Isotopes and PRALINE project

- Terbium (Tb): promising theranostic element with four isotopes[1].

➡ Interest in ^{155}Tb-^{161}Tb potential theranostic pair (~similar $t_{\frac{1}{2}}$).

- Challenge: medical cyclotron production (p < 30 MeV) of ^{155}Tb frpm ^{155nat}Gd induces co-production of ^{156}Tb (and some ^{154}Tb) emitting high energy γ-rays.

Isotope	Diagnosis	Therapy	1/2 life
^{149}Tb	? β+ 14.2%, γ	✓ (α)	4.12 h
^{152}Tb	✓ (β+)		17.48 h
^{155}Tb	✓ (γ)		5.32 d
^{161}Tb	? Low energy γ	✓ (β-)	6.96 d

γ - rays energy (keV)		
^{155}Tb (5.32 d)	^{156}Tb (5.35 d)	^{161}Tb (6.96 d)
86.54 (32%) 105.3 (25.1%) 180.1 (7.5%) 262.3 (5.3%)	88 (18%) 199.2 (41%) 356.3 (13.6%) 534.3 (67%) 1065.1 (10.8%) 1154.1 (10.4%) 1222.4 (31%) 1421.7 (12%)	48.9 (17.0%) 74.6 (10.2%)

SPECT

- PRALINE project: Production RAdioisotopes et Ligands pour l'Imagerie NucléairE

➢ Integrated project aims to develop new methodologies of radioisotopes production availability in large quantity with high chemical and isotopical purities and new ligands, and develop approaches and methods for nuclear imaging.

[1] Naskar N, Lahiri S. Theranostic Terbium Radioisotopes: Challenges in Production for Clinical Application. Front Med (Lausanne). 2021 May 31;8:675014.

Objective and Methodology

- Evaluate by simulation the impact of contamination of ^{156}Tb on ^{155}Tb SPECT images to determine acceptable contamination limit, in terms of:
  - Quantitative SPECT imaging.
  - Dosimetry.
- Evaluate capabilities of ^{161}Tb in termes of imaging and dosimetry

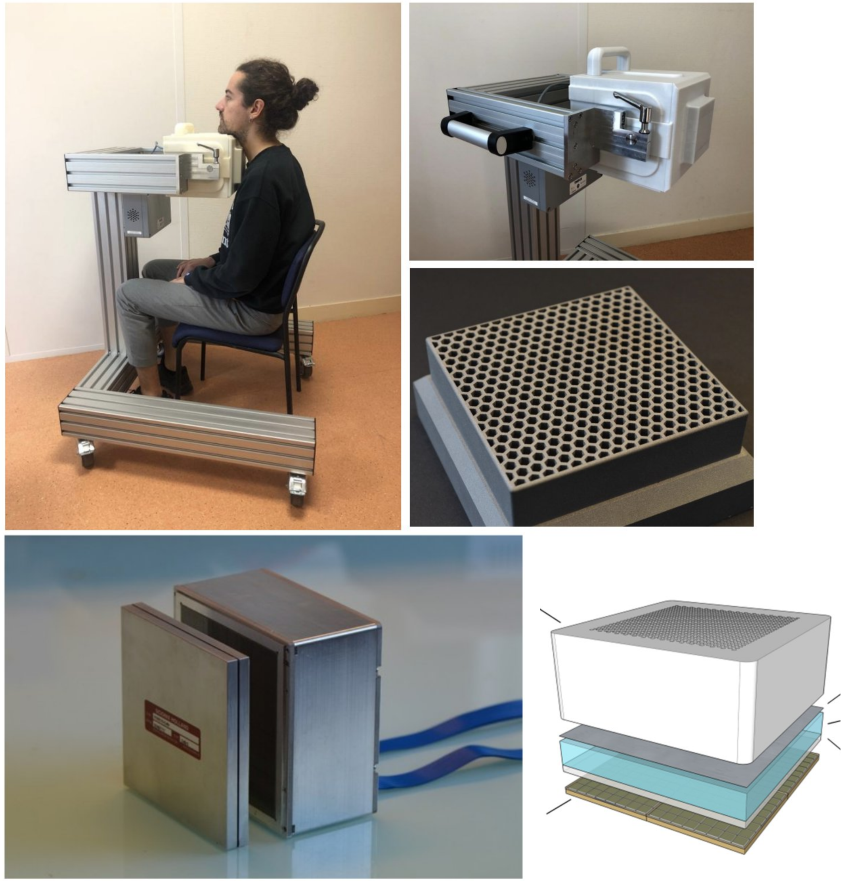
How?

- SPECT imaging Monte Carlo simulation experimentally validated of ^{155}Tb phantom contaminated with 0-10% ^{156}Tb using:
  - Low energy camera: ALBIRA (BRUKER).
  - Medium energy camera: THIDOS (homemade high performance camera).
  - Geometric preclinical phantom NEMA NU-4 2008.
- SPECT imaging of ^{161}Tb in geometric phantom
- Dosimetry using mouse phantom simulation with exp. bio-kinetic data (not addressed in this presentation).

Material and methods

Experimental Setup: THIDOS[1]

- Medium energy gamma camera - 364 keV ^{131}I - molecular radiotherapy of thyroid diseases.
  - Developed completely in REV group - Health pole - IJCLab.
- Detector:
  - 10×10×1 cm^3 $CeBr_3$ scintillator
  - Coupled to 16×16 SiPM array (256 channels)
- Collimators:Tungsten parallel-hole collimators
  - high-sensitivity (planning) or high-resolution (post-treatment)
- Shielding: Optimized tungsten + lead for high energy gamma rays.
- Performance:
  - Spatial resolution: 1.15 mm FWHM (intrinsic)
  - Energy resolution: 8% at 356 keV

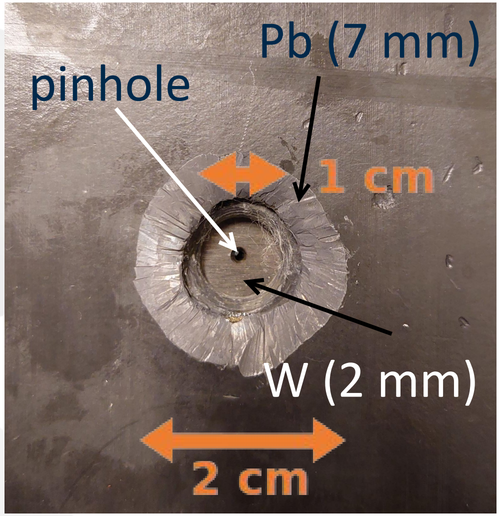


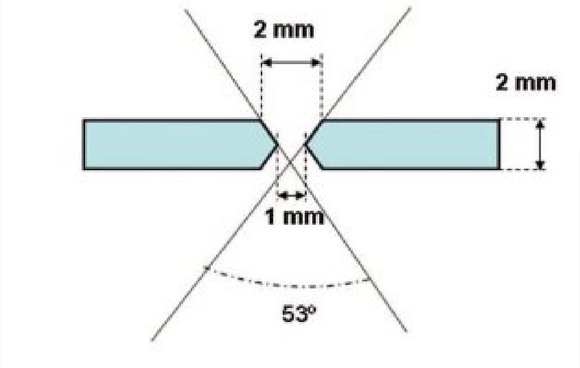
[1]A High-Resolution Portable Gamma-Camera for Estimation of Absorbed Dose in Molecular Radiotherapy, Théo Bossis et al.

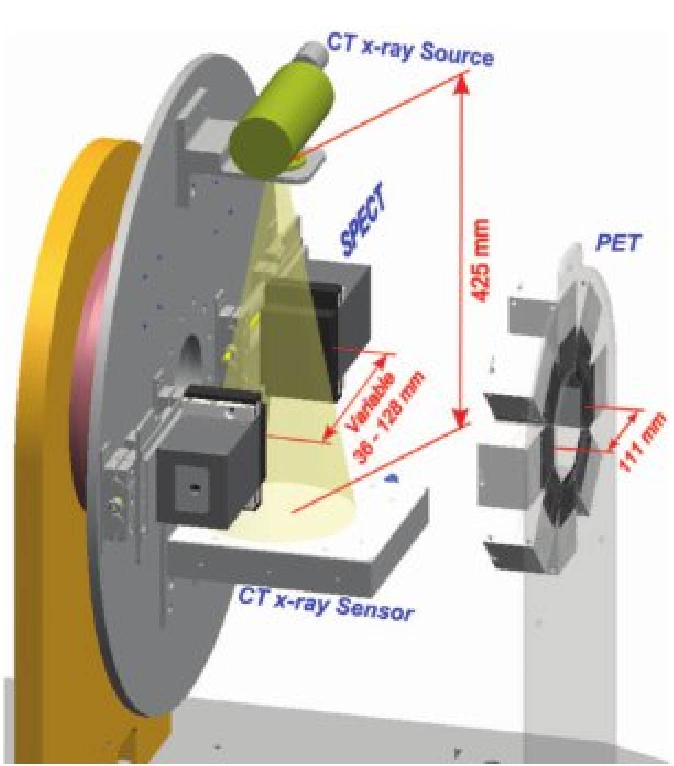
➢ Used in the simulation as SPECT head camera.

- ○ Detector: ALBIRA S108 small animal PET/SPECT/CT (industrial) imaging system (BRUKER)[1] at CHUV, Lausanne.
- ○ 2 rotating SPECT heads, 30 positions/camera (6°).
  - – Camera optimized for ^{99m}Tc (140 keV).
  - – Single pinhole collimator (2 mm W).
  - – Spatial res.(FWHM) : ~1.5 mm (BRUKER).
  - – Energy res.(FWHM): 17% at 140 keV (BRUKER).
- • Shielding and collimation adapted for ~ 140 keV ➡ high potential scattering and penetration for for high energy gamma rays.
- ○ Tomo-Reconstruction program implemented.

➢ **Study and understand camera performance, include corrections in reconstruction.**



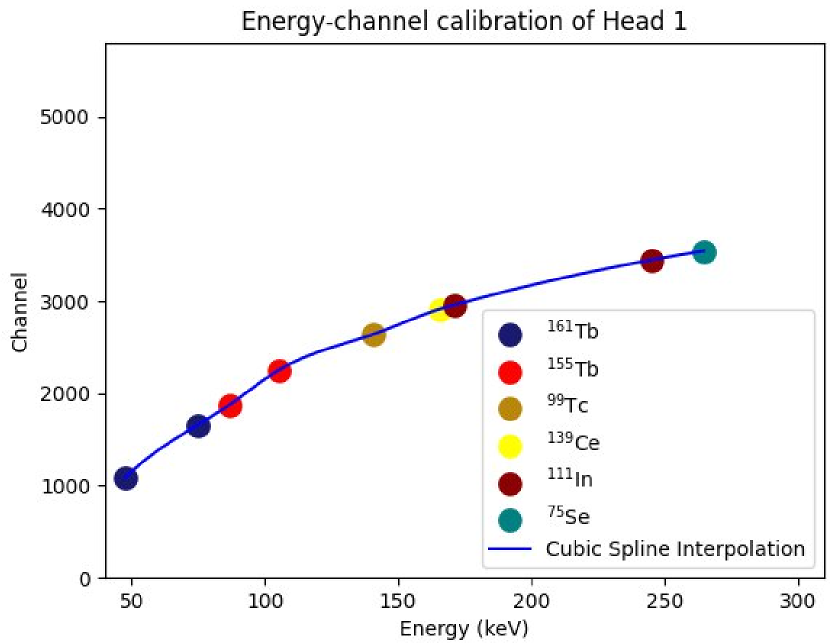


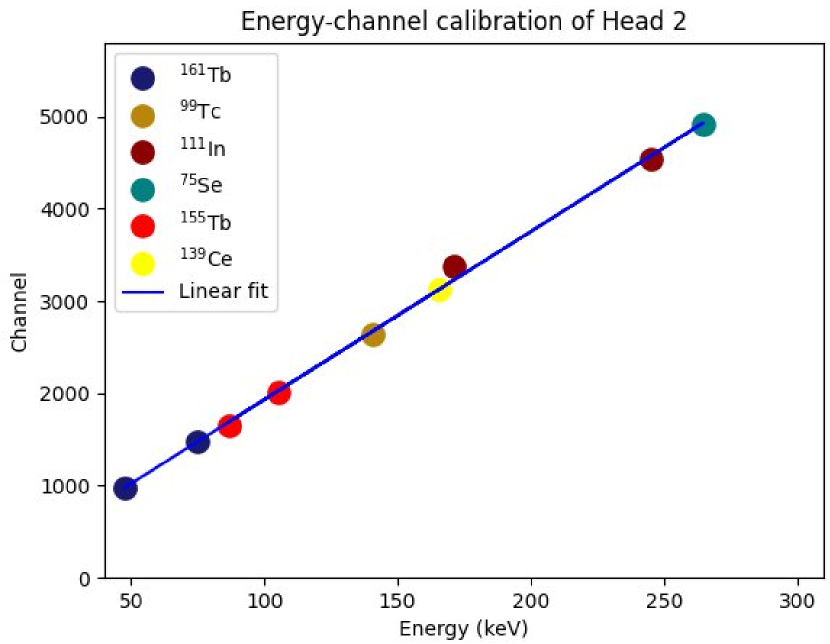


[1] Sánchez et al. Med. Phys, 40, No. 5, May 2013.

- Calibration:
  - Current calibration optimized for ^{99m}Tc only (BRUKER) ➡ need improvement.
  - New calibration, different acquisition with various isotopes performed.
  - Unlike head 2, calibration of head 1 is non-linear ➡ Complicate treatment and analysis ! (to present only Head 2)

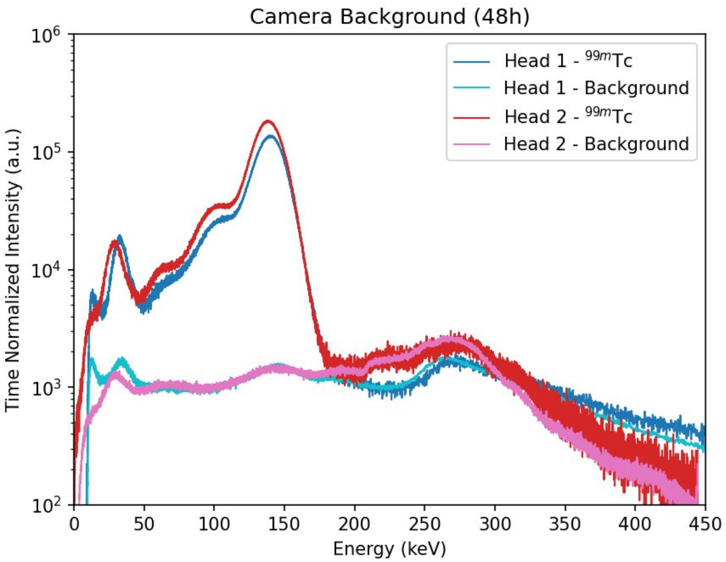
➢ An external reconstruction performed to include all these corrections.

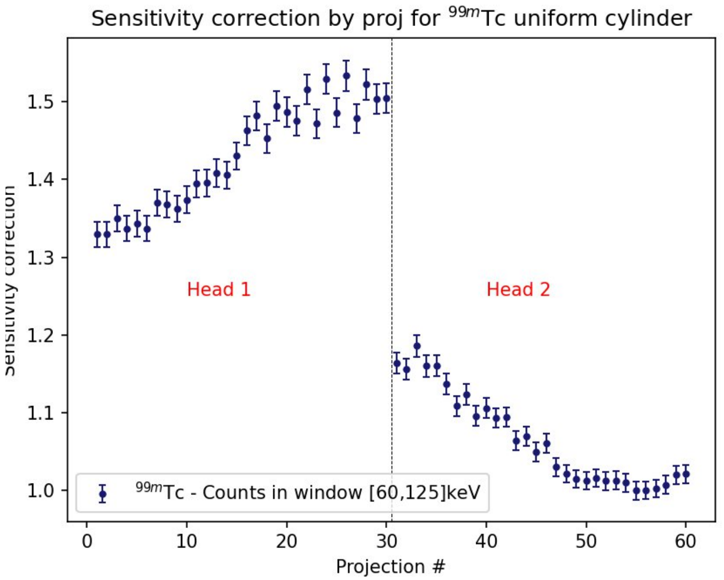


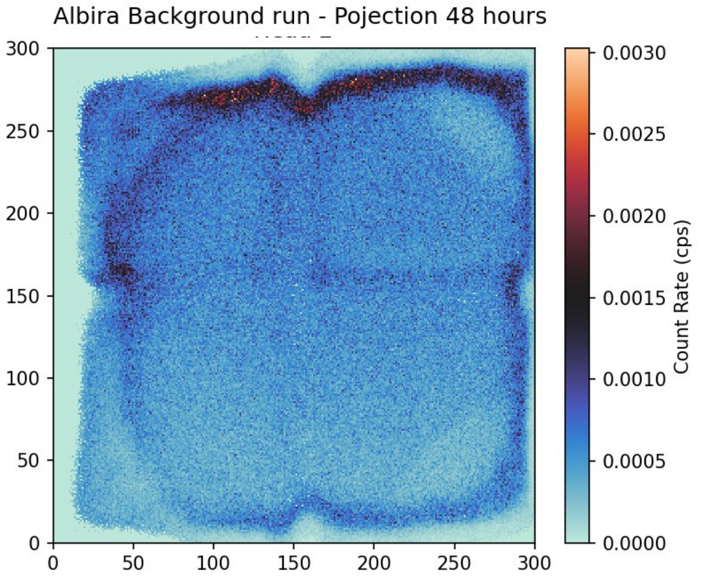


Experimental challenges - ^{99m}Tc camera assessment

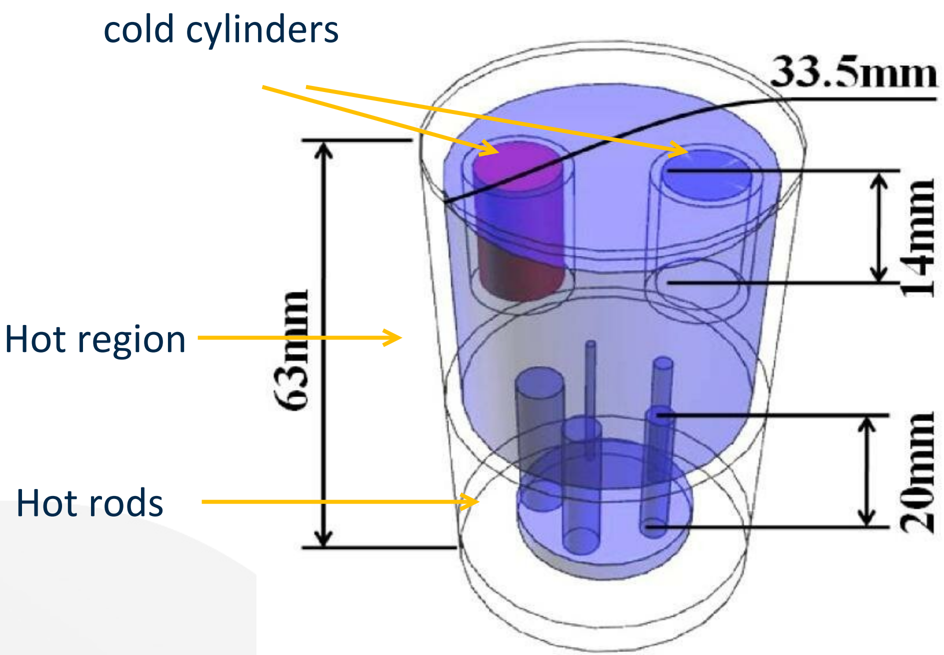
- Background studying ➡ count rate 30-40 cps (negligible).
- Sensitivity disparity between the two heads + geometrical effect ➡ corrected for each projection.
- Sensitivity drop below ~ 50 keV, and above ~ 200 keV.
- Measured energy resolution : ~~13.5~~ 17% at 140 keV.
- Projection image in-uniformity cause artifacts in reco images and lower SNR !





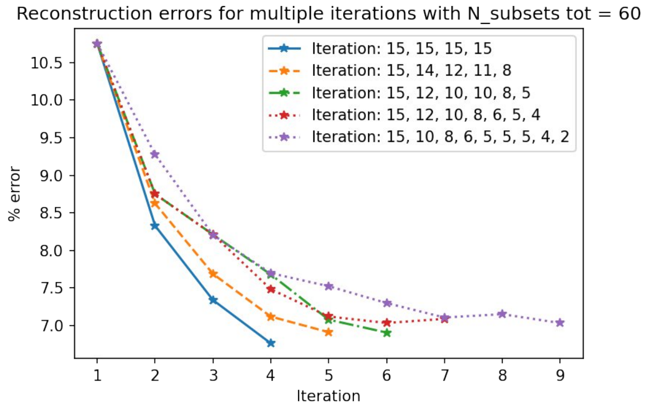


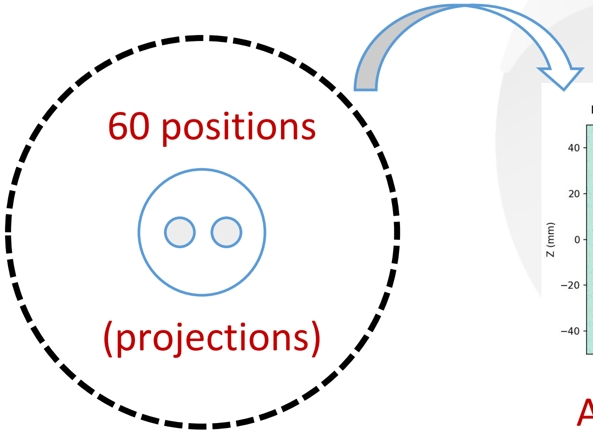
- **Phantom**: NEMA NU 4-2008, a standard small-animal imaging phantom designed for quantitative performance evaluation.[1]
  - Includes rods (1–5 mm) for spatial resolution testing.
  - Cold and uniform regions for contrast, uniformity, and SNR analysis.

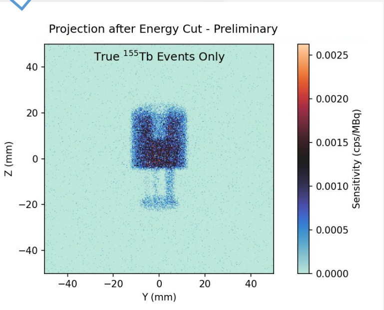


[1] NEMA Standards Publication NU 4-2008 Performance Measurements of Small Animal Positron Emission Tomographs National Electrical Manufacturers Association 1300 N. 17th Street, Suite 1752 Rosslyn, VA 22209.

- **Tomographic SPECT reconstruction** performed using CASToR platform.[1]
- Data converted from GATE 10 form to CASToR form.
- Ordered Subset Expectation Maximization (OSEM) algorithm, an MLEM variant.
- Camera geometry defined, correction added and parameters optimized.

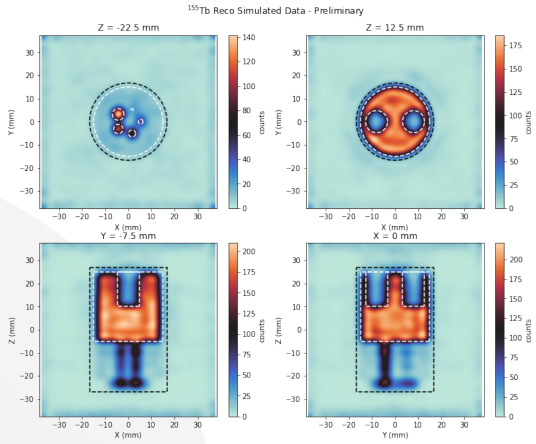






A 2D Projection

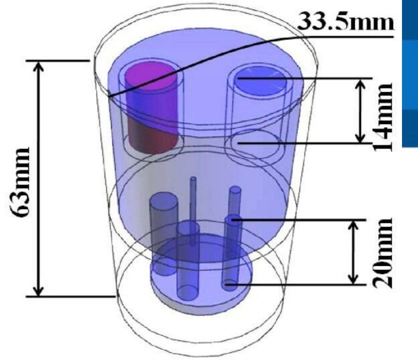
3D image reconstruction (OSEM)



3D reconstructed image

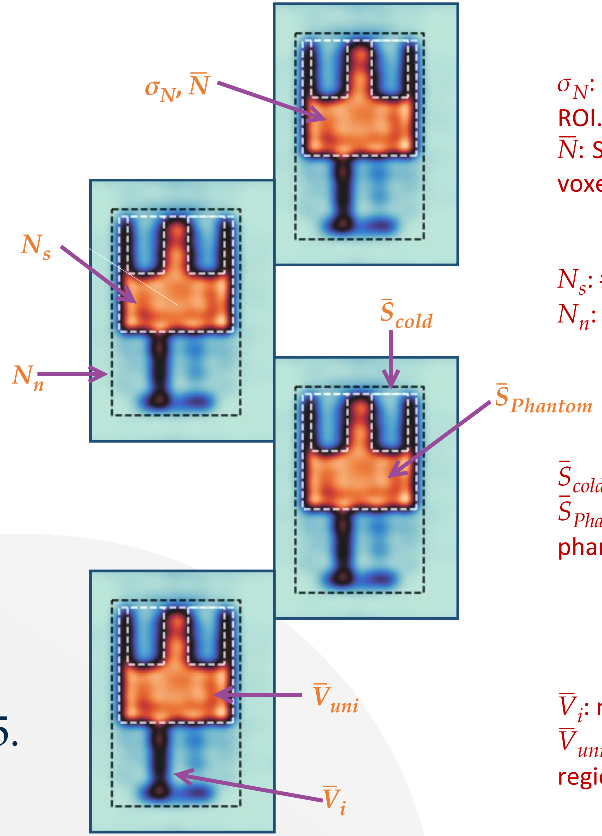
[1] CASToR: a generic data organization and processing code framework for multi-modal and multi-dimensional tomographic reconstruction, Thibaut Merlin et al., 2018.

Quantification



To quantify the reconstructed images, multiple factors were calculated:

- Integral uniformity [%]: $IU = \frac{\sigma_N}{\bar{N}}$
- Signal to noise ratio: $SNR = \frac{|N_s - N_n|}{N_n}$
- Contrast factor of the cold cylinders [%]: $Q_{cold} = [1 - \frac{\bar{S}_{cold}}{\bar{S}_{Phantom}}]$
- Recovery coefficients: $RCs = \frac{\bar{V}_i}{\bar{V}_{uni}}, \mathrm{i} = 1,\ldots 5.$



σ_N: Standard deviation of voxels values in ROI.
$\bar{N}$: Sum of counts in ROI averaged by # of voxels.

N_s: # of counts considered as signal in ROI.
N_n: # of counts considered as noise in ROI.

$\bar{S}_{cold}$: average counts in the cold cylinder.
$\bar{S}_{Phantom}$: average counts in the ROI of the phantom.

$\bar{V}_i$: mean voxel value in the rods.
$\bar{V}_{uni}$: mean voxel value in the uniform region of the phantom.

- 3 experiments performed at CHUV, Lausanne for simulation validation (Thanks to PRISMAP program):

  - 7 MBq of ^{155}Tb phantom (12 h acquisition) – Produced by MEDICIS/CERN, contaminated with ^{139}Ce .
    ➡ Subtracted by ^{139}Ce only later acquisition.

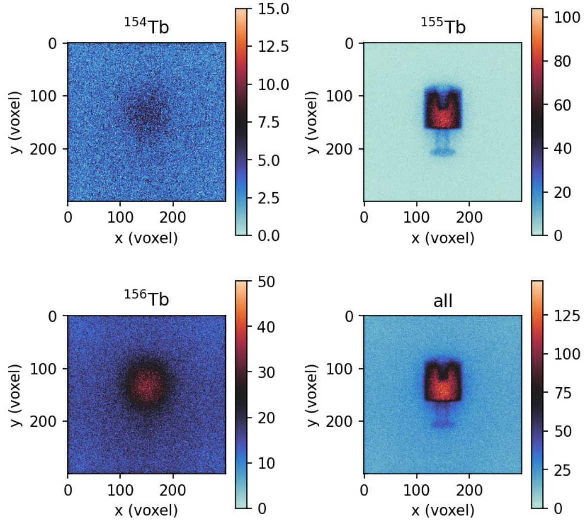
  - 32.4 MBq (~89%-8%) ^{155}Tb -^{156}Tb phantom (12 h acquisition) – Produced by PSI. (+3% ^{154}Tb).

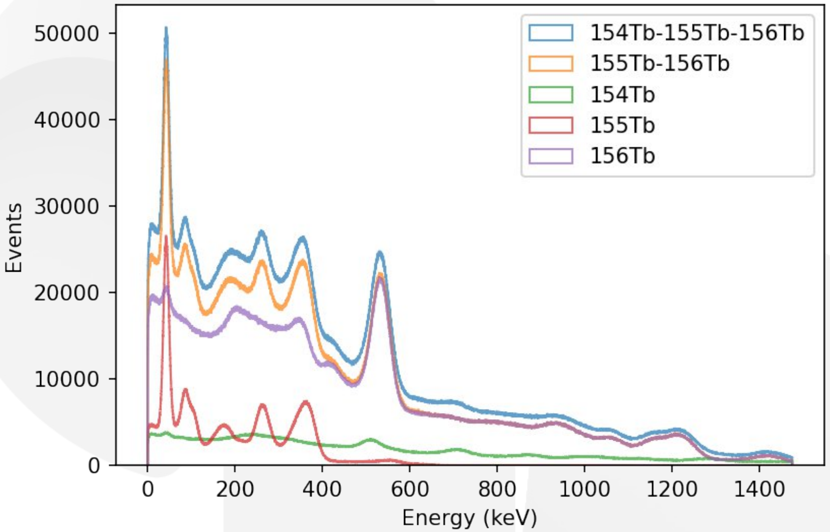
  - 12 MBq of ^{161}Tb phantom (4 h acquisition) – Produced by PSI.

Isotope	Half life
^{154}Tb	21.5 h
^{155}Tb	5.32 d
^{156}Tb	5.35 d
^{161}Tb	6.96 d
^{139}Ce	160.xx d

GATE Simulation

- **Monte Carlo simulation** performed GATE 10 Platform (Geant4 based) for both imaging and dosimetry.
- With GATE 10: Reproduced cameras parts and movement, phantom and all sources (isotopes and contaminants).





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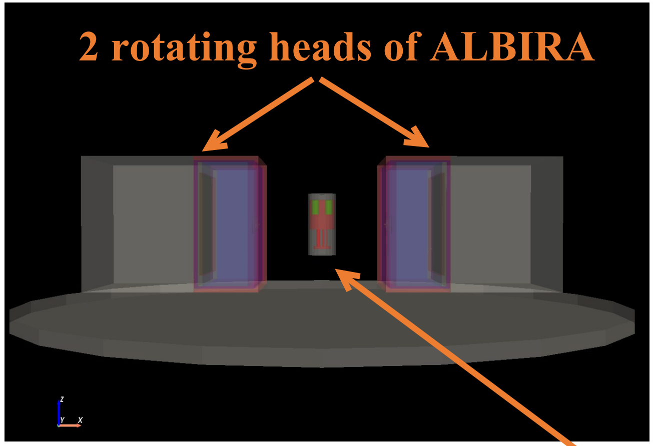
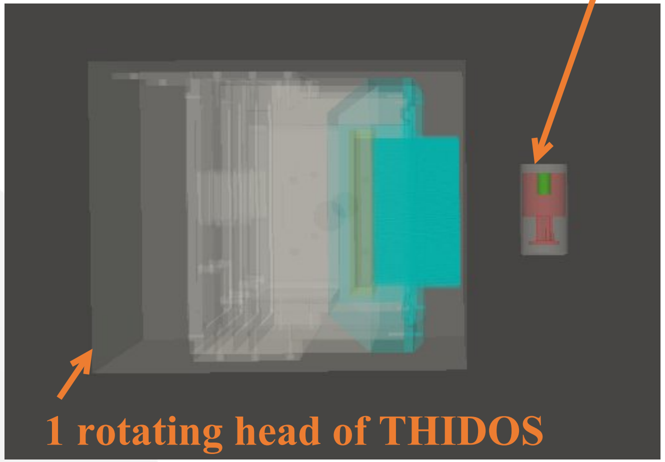
ALBIRA



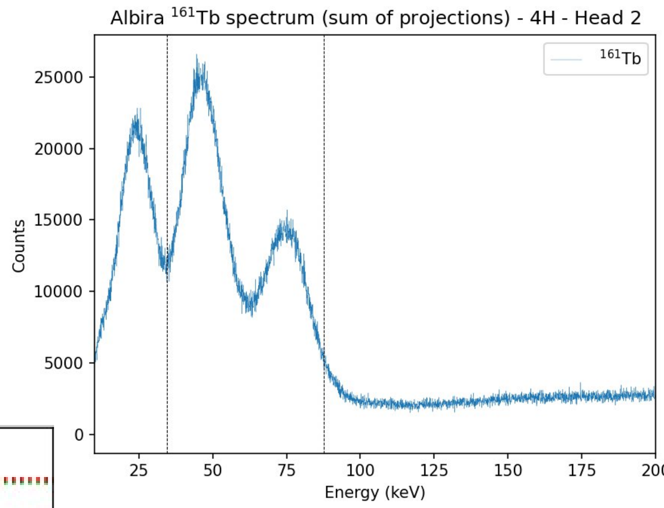
THIDOS

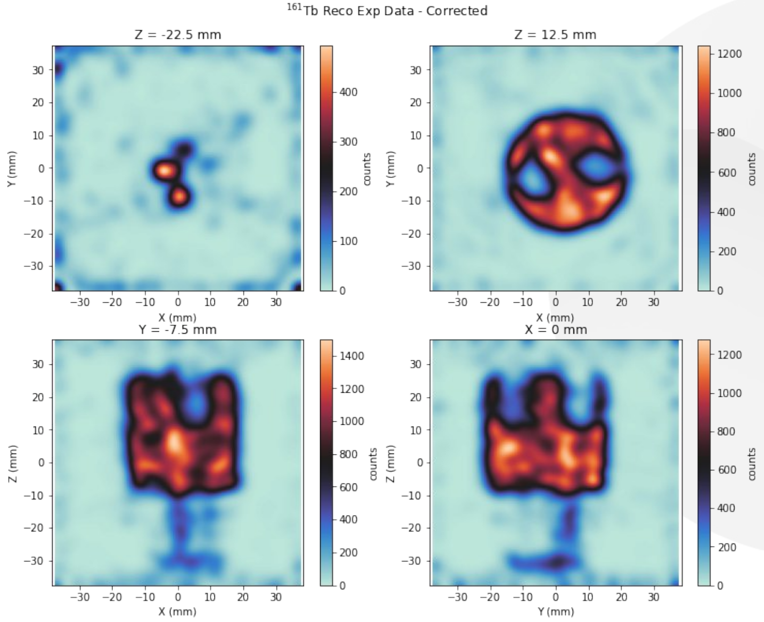


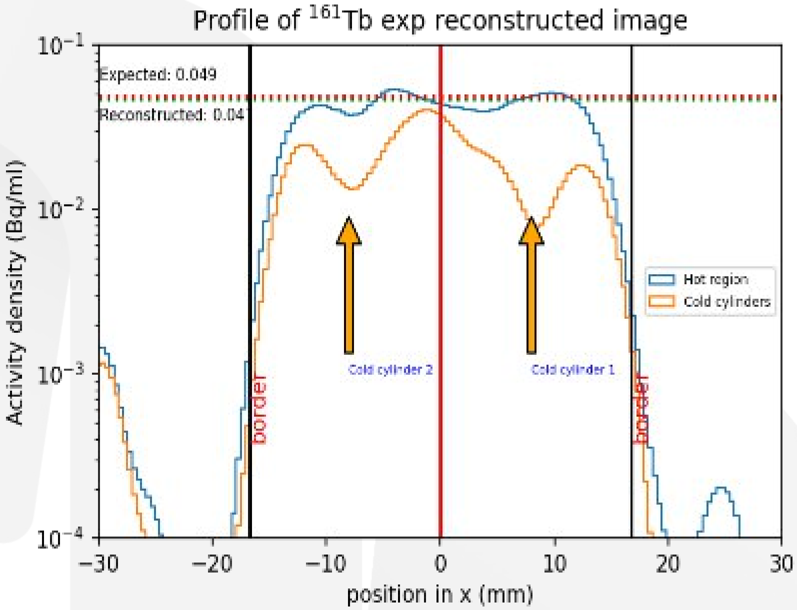
Study ^{161}Tb SPECT imaging capability: Results

- 2 γ peaks (48.9 keV, 74.6 keV) utilizable for SPECT tomographic reconstruction.
- Despite the notable in homogeneity & BG, largest rods reconstructed & high SNR.

➡ **Strong potential of ^{161}Tb in imaging clinical application (THERANOSTIC by itself).**





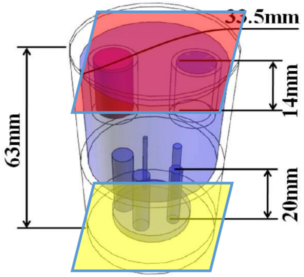


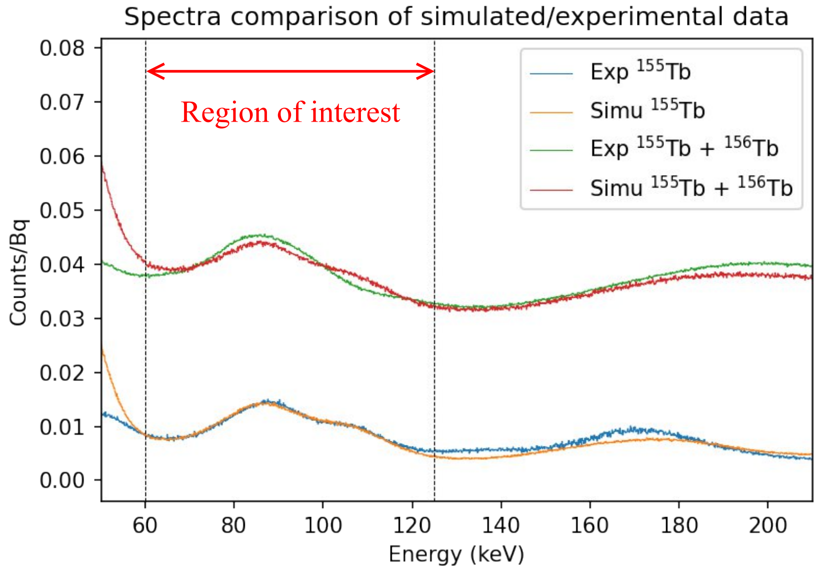
Quantification factor	^{161}Tb Pure
SNR	104.5
IU (%)	16.31
Q_{cold} (%)	88.97

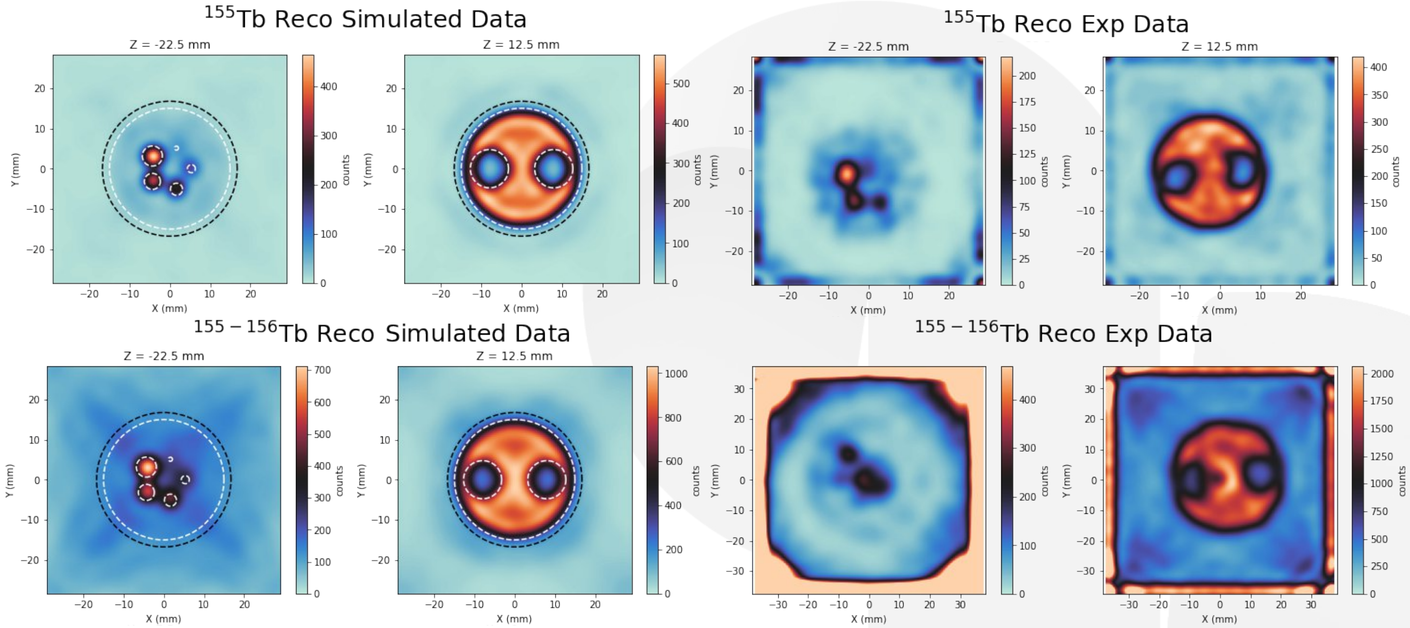
Simulation Validation

➢ Simulation validation :

- Agreement between spectra in [60,125] keV window.
- Some discrepancies between experiment and simulation due to residual artifacts.







Quantification factor	^{155}Tb exp	^{155}Tb +8% ^{156}Tb exp	^{155}Tb simu	^{155}Tb+8% ^{156}Tb simu
SNR	50.86	7.12	103.9	15.86
IU (%)	8.39	7.54	4.49	4.08
Q_{cold} (%)	84.48	63.19	89.73	83.93

Simulation Results

Conclusion and perspectives

- ^{161}Tb imageable with LE SPECT camera using its LE γ emissions.

- ^{156}Tb strongly degrades ^{155}Tb SPECT images, especially with LE collimation/shielding.
- ^{156}Tb contamination limit is system dependent; not only affected by activity contribution.
  - For LE imaging systems: acceptable ^{156}Tb limit: about 1–2% to limit the loss in SNR.
  - For ME imaging systems even a 10% ^{156}Tb contamination is tolerated if the system is well collimated.

Perspectives:

- ➢ A dedicated collimator could be optimized for the mixed ^{155}Tb/^{156}Tb, as a quality/sensitivity trade-off.
- ➢ To study how to extend ^{161}Tb for clinical imaging.
- ➢ Dosimetric study of ^{156}Tb contamination.

Thank You

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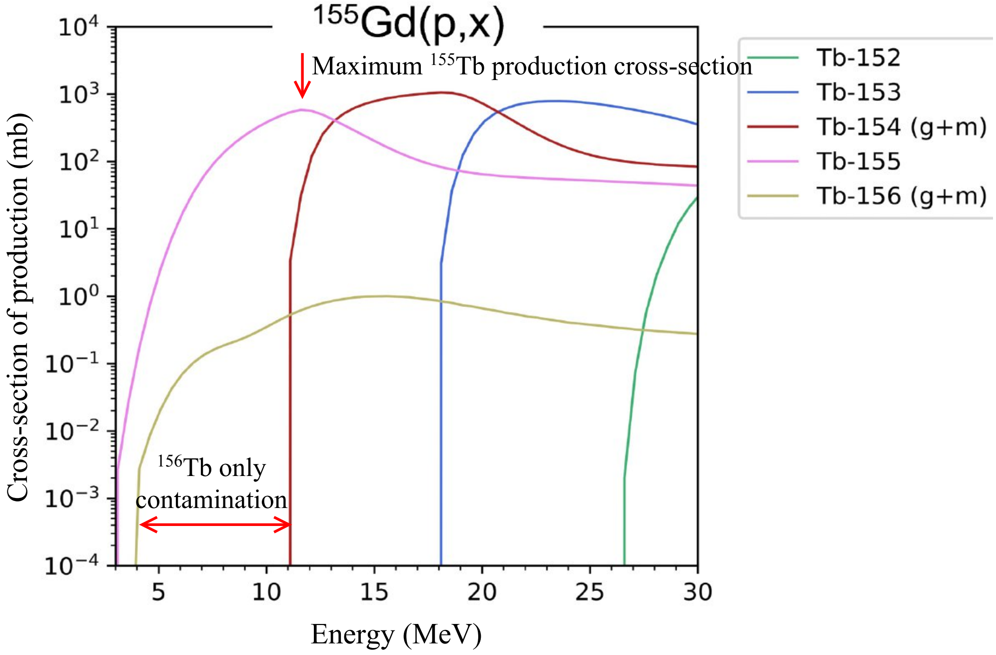
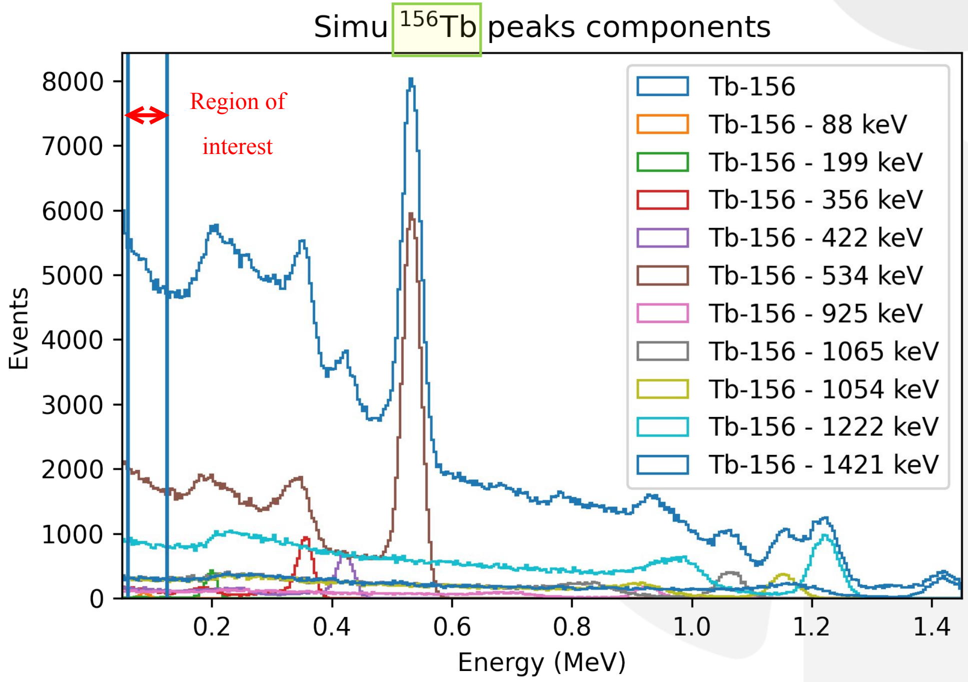
- PRALINE project: Production RAdioisotopes et Ligands pour l’Imagerie NucléairE
    - ➢ Aims to develop new methodologies of radioisotopes production availability in large quantity with high chemical and isotopical purities and new ligands, and develop approaches and methods for nuclear imaging.
- Production part:
    - Determination of the optimal parameters for the isotopes production.
- Chemical part:
    - Chelator development & Physico-chemical properties
- Imaging part:
    - Develop approaches and methods for nuclear imaging.
    - Investigate contamination effect of produced radionuclides for imaging and Dosimetry.



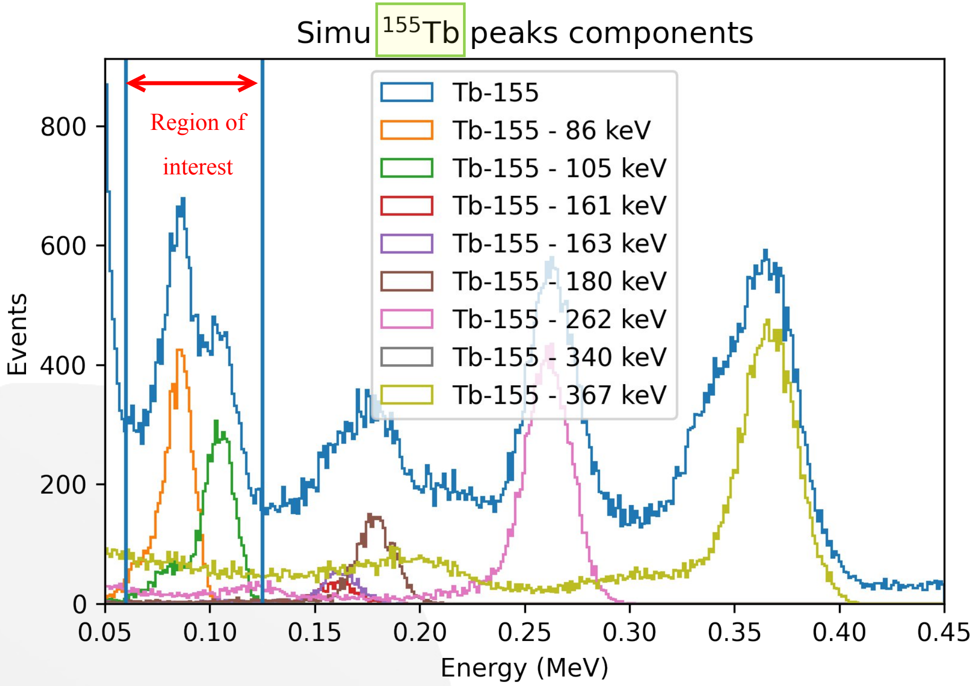
De la cible de ^{199}Gd au ^{199}Tb, un radionucléide pour la santé, M. BOUTECULET (Ph.D, Université Paris-Saclay, 2025)

GATE Simulation

- We can dissemble rays contribution for each isotope in simulation.
- ➢ High contribution of 156Tb high energy rays within region of interest (figures for ALBIRA).



Careful! Different Scales



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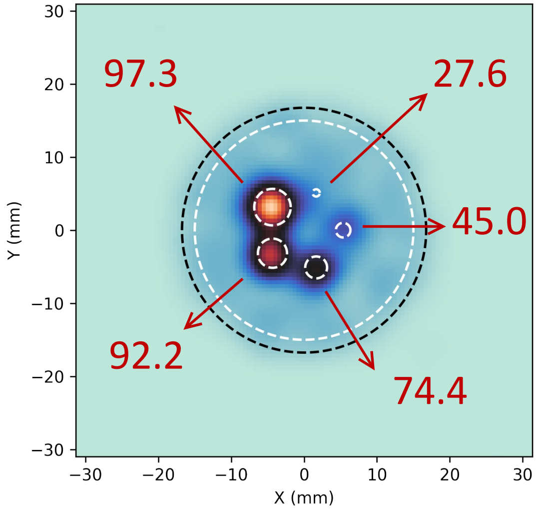
Images Quantification

- Recovery coefficients (RCs) for the 3–5 mm rods are relatively high and close for both systems (slightly higher for THIDOS).

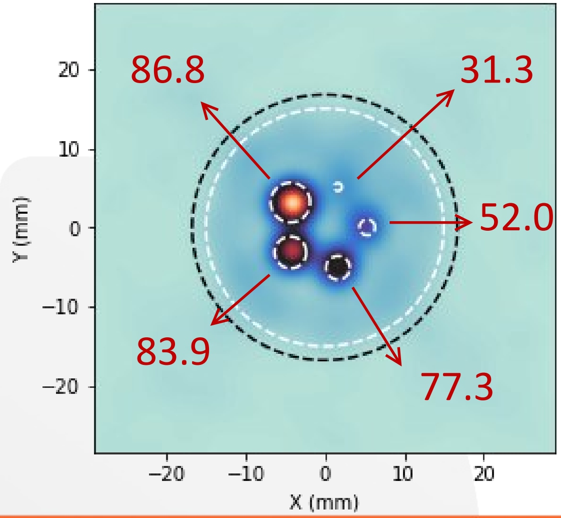
➢ Estimated spatial resolution of 3 mm.

- As contamination increases, ALBIRA shows a rise in RCs → consistent with contamination derived counts biasing the measured rod activity.

- THIDOS shows only a modest increase in RCs with contamination → stronger blocking of contamination contribution



RCs [%] of THIDOS

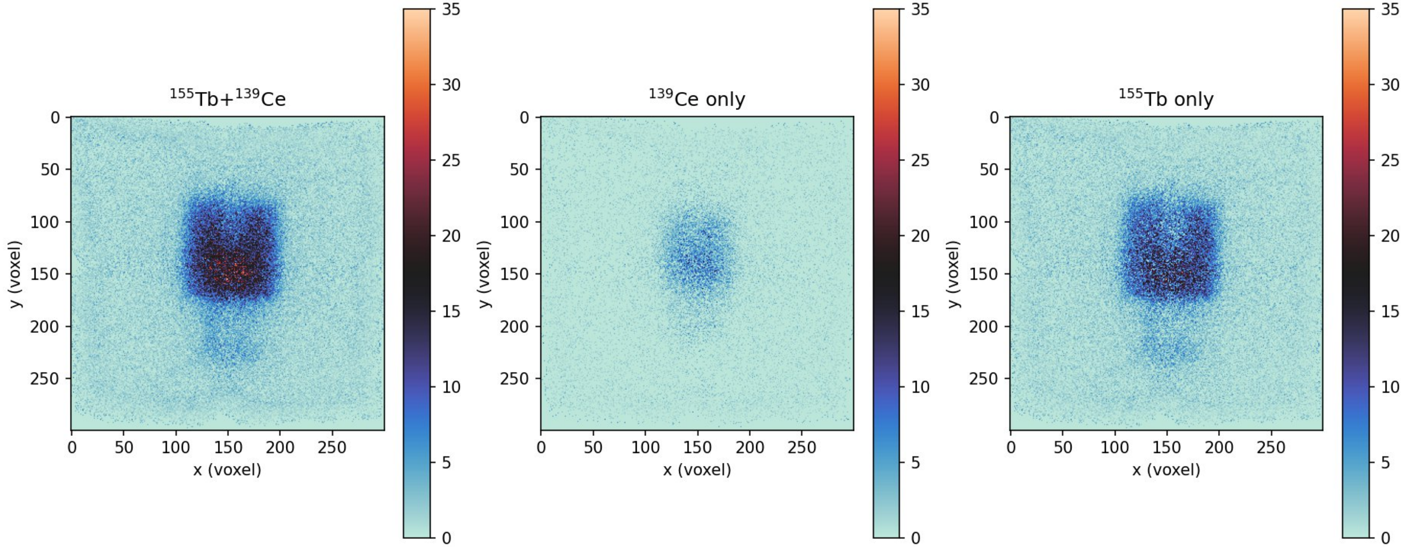


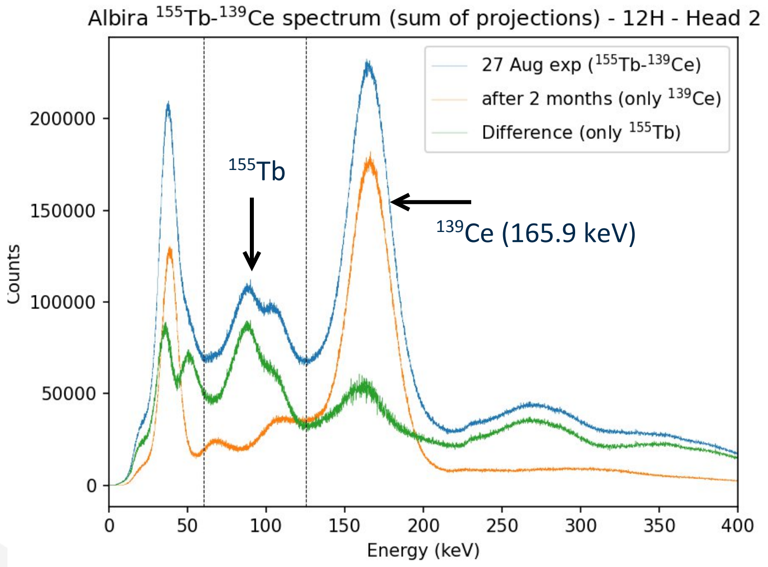
RCs [%] of ALBIRA

- Produced by MEDICIS:
  - ^{155}Tb (5.9 MBq, $T_{1/2}$: 5.32 d).
  - Contaminated by ^{139}Ce (11.9 MBq, 137.64 d).
- Only ^{139}Ce acquisition performed after ^{155}Tb decay (2 months after).

➢ Simple subtraction performed → to optimize subtraction method (ongoing).

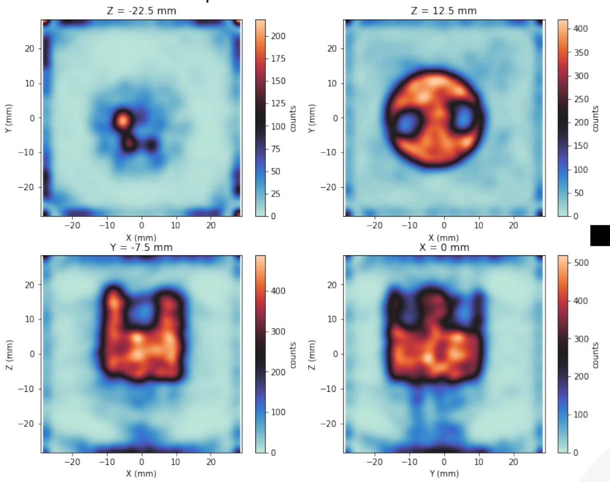
1 2D projection comparison

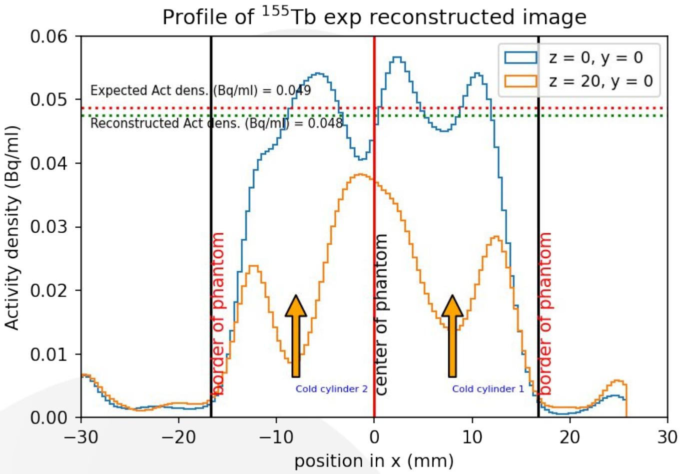




^{155}Tb - $^{154\text{-}155\text{-}156}$Tb experimental results

^{155}Tb Reco Exp Data - subtracted and corrected

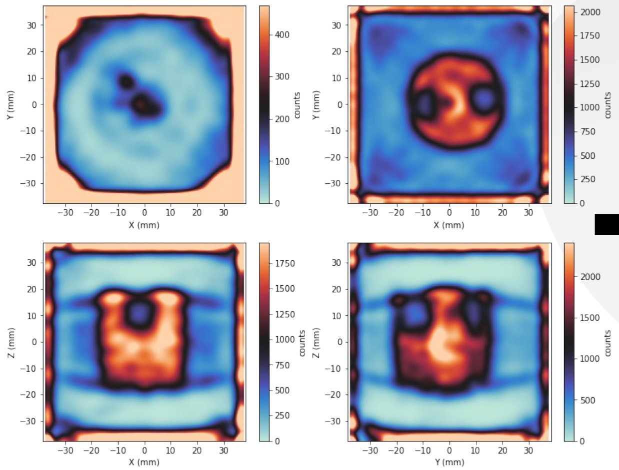


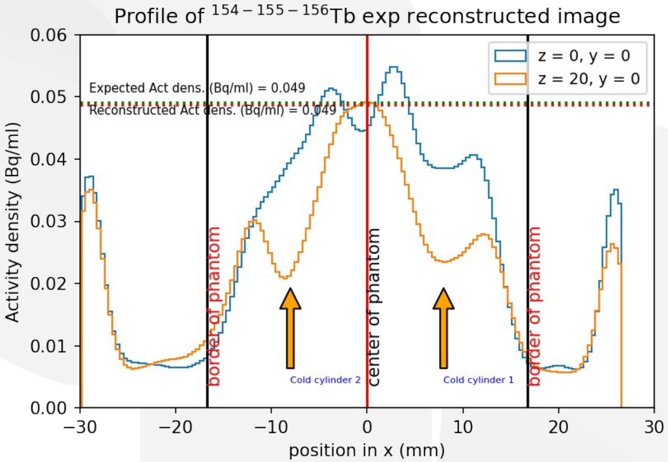


Quant. factor	^{155}Tb exp	$^{154\text{-}155\text{-}156}$Tb exp
SNR	50.86	7.12
IU (%)	8.39	7.54
Q_{cold} (%)	84.48	63.19

➡ ~ 7 times worse

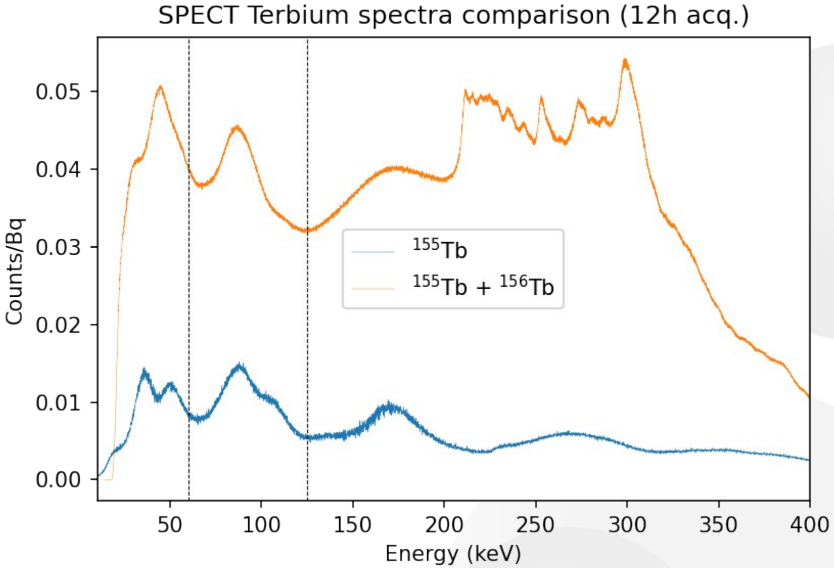
$155-156$Tb Reco Exp Data

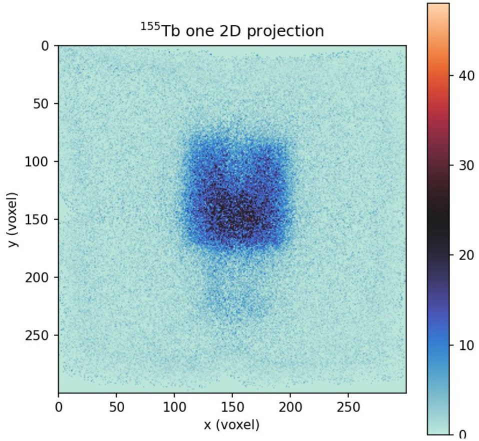


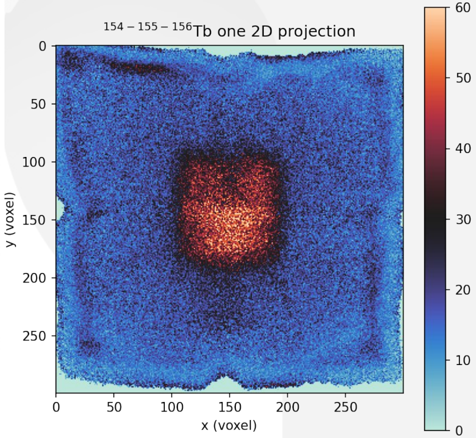


- Pure ^{155}Tb is eligible for SPECT imaging.
- Image immensely polluted with ^{156}Tb, could not be reconstructed.

➡ Shielding and collimation ?

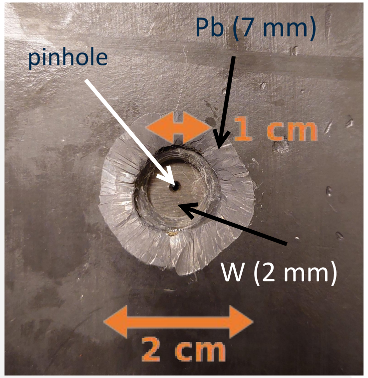


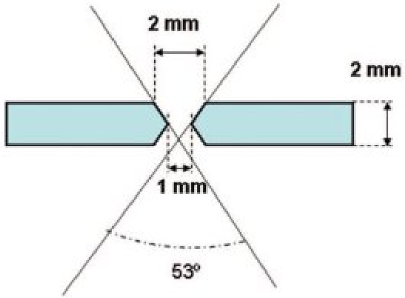




- 79.8% ^{156}Tb detected counts in ROI for 8% activity cont.
- Shielding and collimation not adapted for these high energies.
- We are not able to reconstruct well the images due to dense scattering and septal penetration.

➡ **To study it using simulation.**

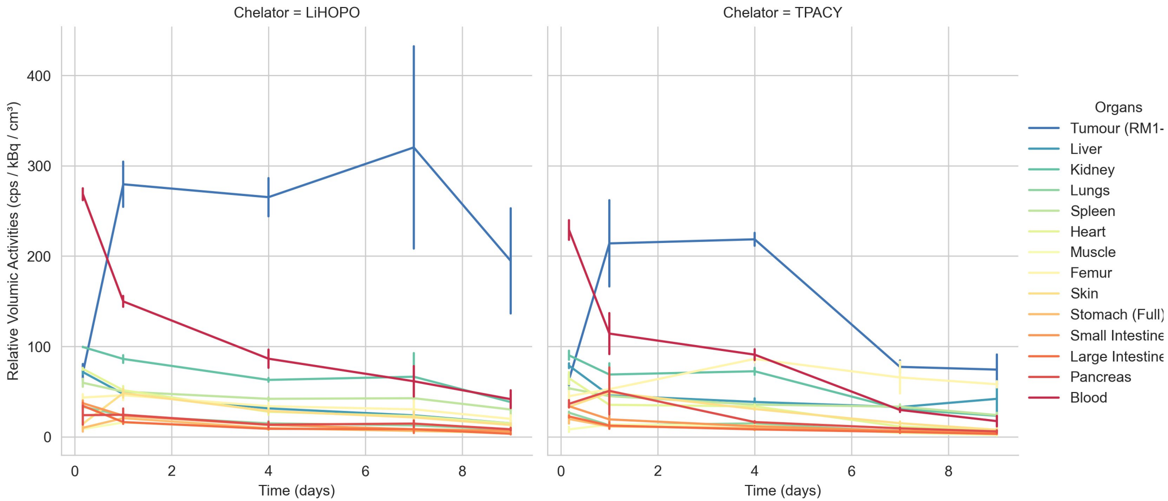


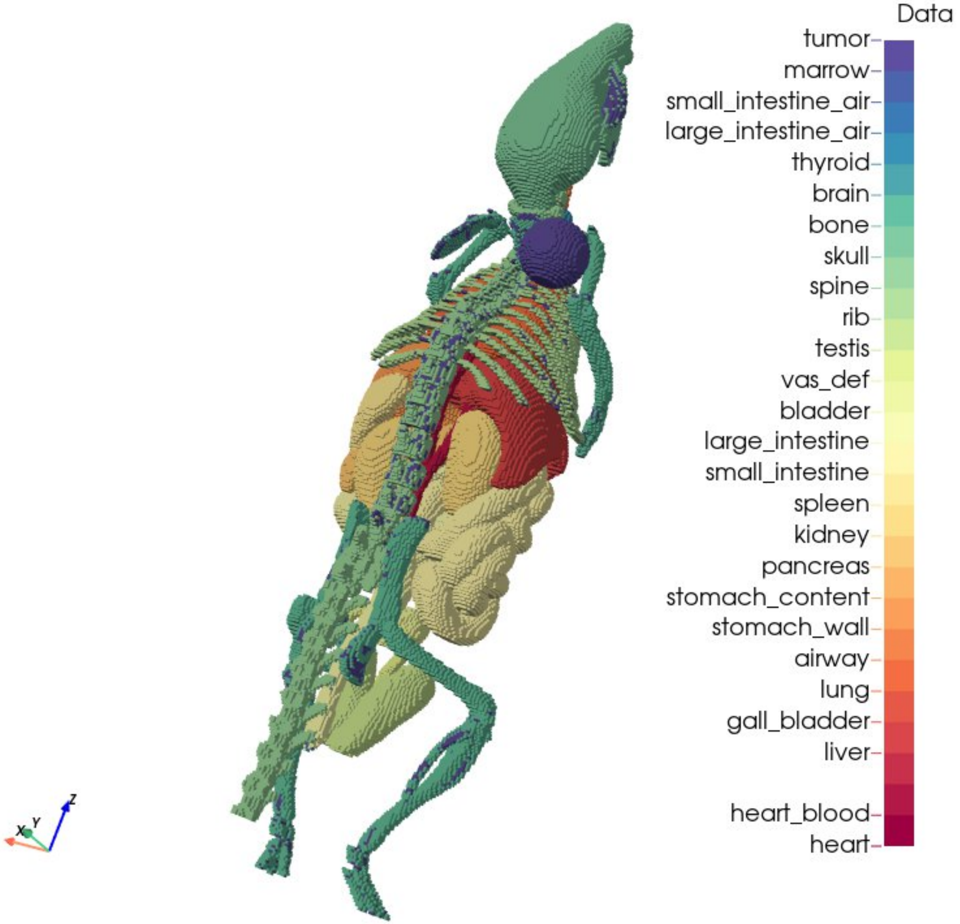


Knife-edge pinhole

Dosimetry

- Ongoing dosimetric study for:
  - ^{161}Tb (β-, γ).
  - ^{155}Tb + ^{156}Tb contamination (γ).
- Combining simulation (GATE 10) of a voxelized phantom with experimental biokinetic data from real mice taken place at CHUV, Lausanne.





Dosimetry: Experimental Data

- Aim: To evaluate dosimetric effect of:
  - ^{161}Tb (β-, γ).
  - ^{155}Tb + ^{156}Tb contamination (γ).

- Dosimetry: measurement, calculation and assessment of the ionizing radiation dose absorbed by an object
- Unit: Gray (Gy) = kJ/kg

- Medical Internal Radiation Dosimetry (MIRD) equation:

$\bar{\mathbf{D}}$:	mean absorbed dose
$\bar{D}_{t\leftarrow s} = S_{t\leftarrow s}\,\tilde{A}_s$	source (s) and target (t) organ
S-values:	mean absorbed dose in unit t per cumulated activity in s
$\tilde{\mathbf{A}}$:	cumulated activity $\tilde{\mathbf{A}} = \int \mathbf{A(t)\,dt}$ $\quad \tilde{\mathbf{A}}_s = \int \mathbf{A}_s \,\mathbf{exp\text{-}}(\lambda_p + \lambda_b)\mathbf{t\,dt}$ time integral of the activity

$$\bar{\mathbf{D}}_{t\leftarrow s} = \mathbf{S}_{t\leftarrow s} \int \mathbf{A}_s \,\mathbf{exp\text{-}}(\lambda_{\mathbf{phys}} + \lambda_{\mathbf{biol}})\mathbf{t\,dt}$$

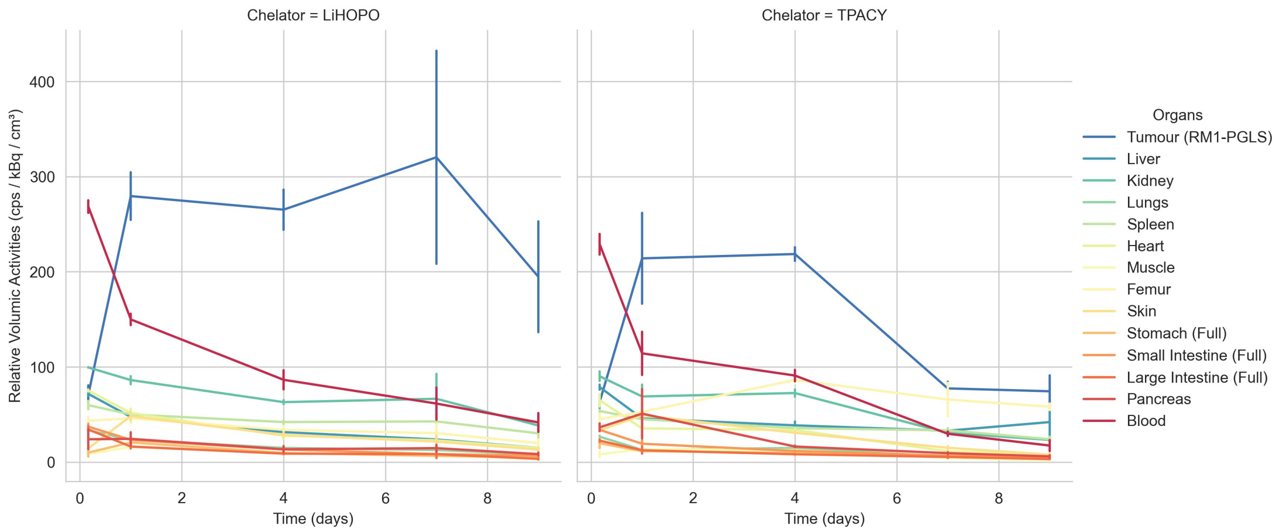
MIRD:
→ S factors
→ $T_{1/2}$

PET:
absolute activity in source organ
→ (Bq / ml)

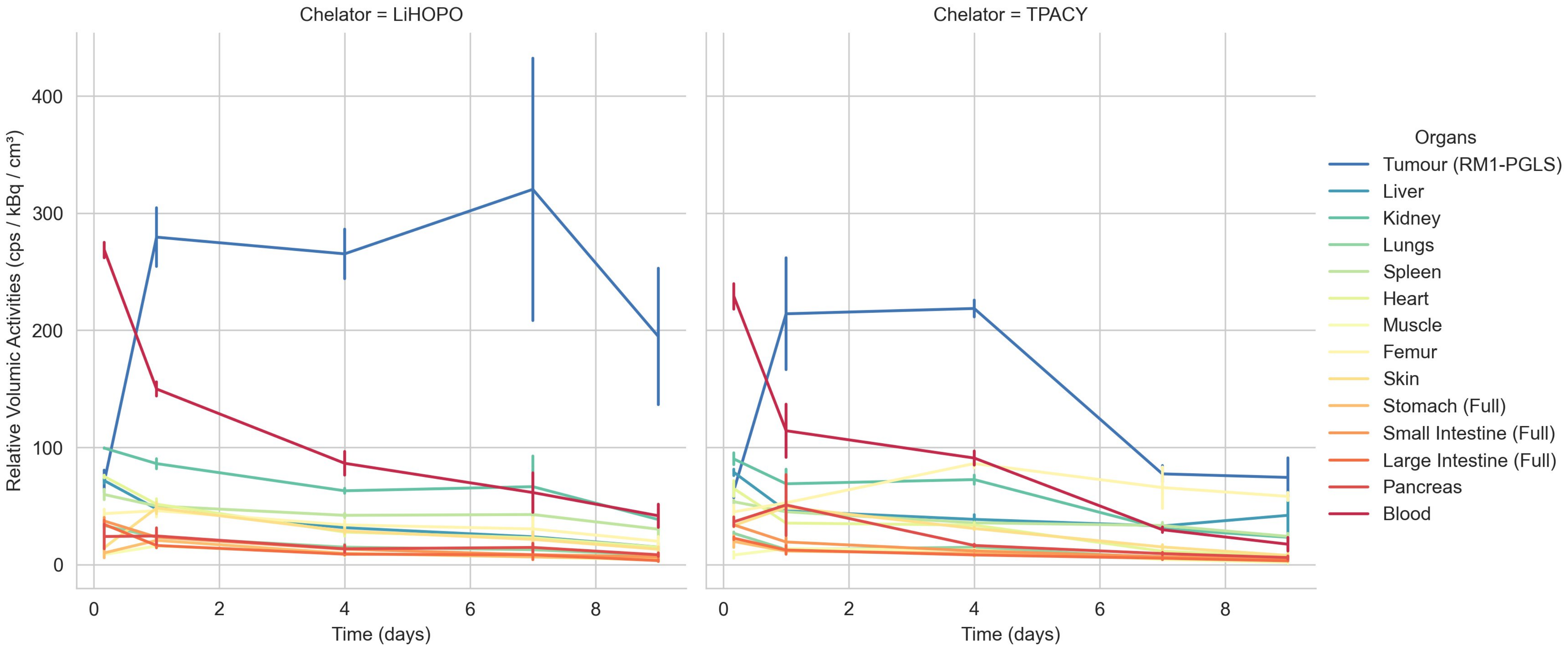
PET:
uptake kinetics
→ (Bq / ml / min)

Dosimetry: Experimental Data

- Simulation combined with experimental biokinetic data taken place at CHUV, Lausanne with collaboration with ICMUB Dijon.
- PSMA vector with 2 different chelators:
  - LiHOPO
  - TPACY
- Black 6 male mice (12 weeks).
- 9 days of ^{161}Tb dose.
- 3 mice sacrificed / time point / chelator !
- Extract dose/(vol.Bq) & use it to evaluate time activity curves (TACs) for each organ.

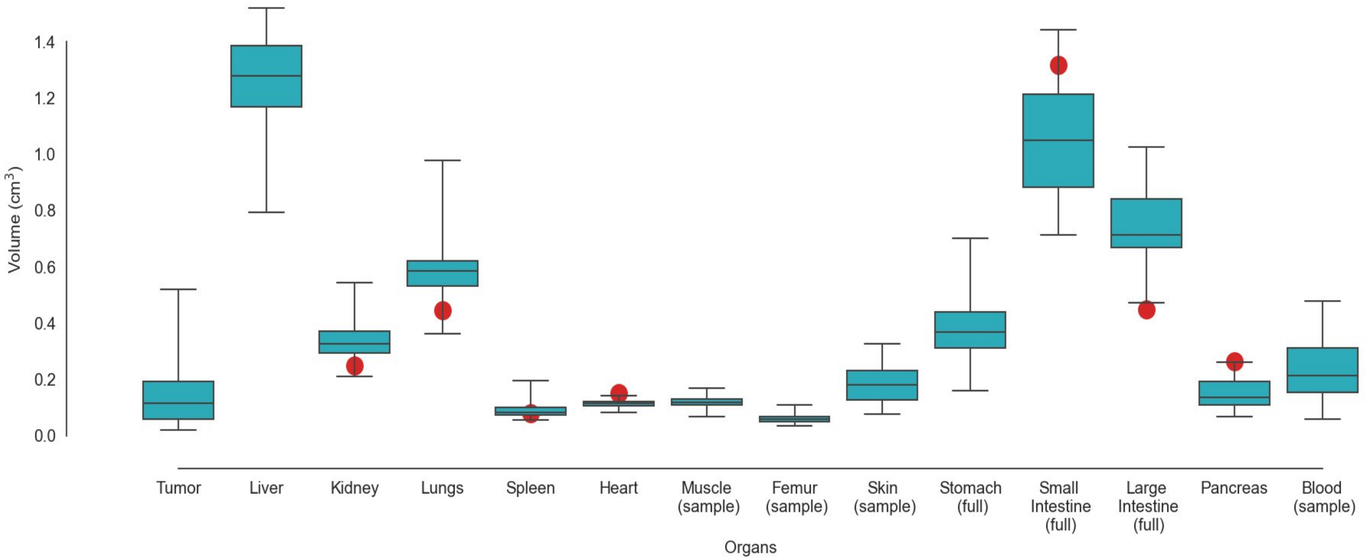


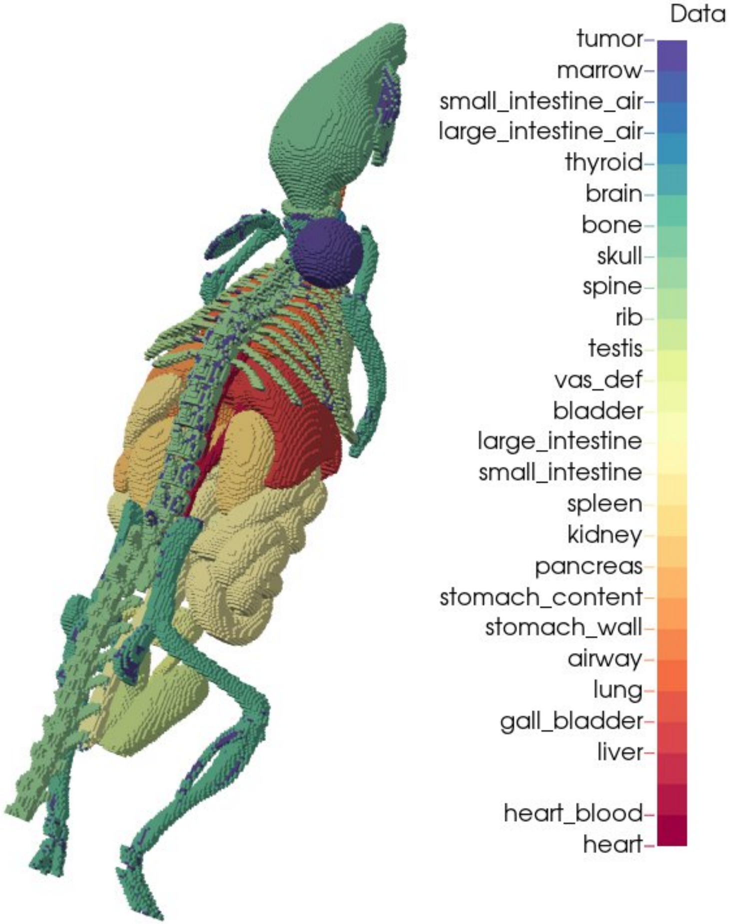
Dosimetry: Experimental Data



Dosimetry: Mouse Phantom and Simulation

- Dosimetry GATE 10 study using a voxelized mouse phantom (MOBY):
  - 140 x 140 x 400 voxels, 0.25 mm size
  - Added tumour manually.
  - Re-scaled to mimic experimental organs volumes.
  - Output: 3D dose map/voxel in Gy + uncertainties (dose actor).





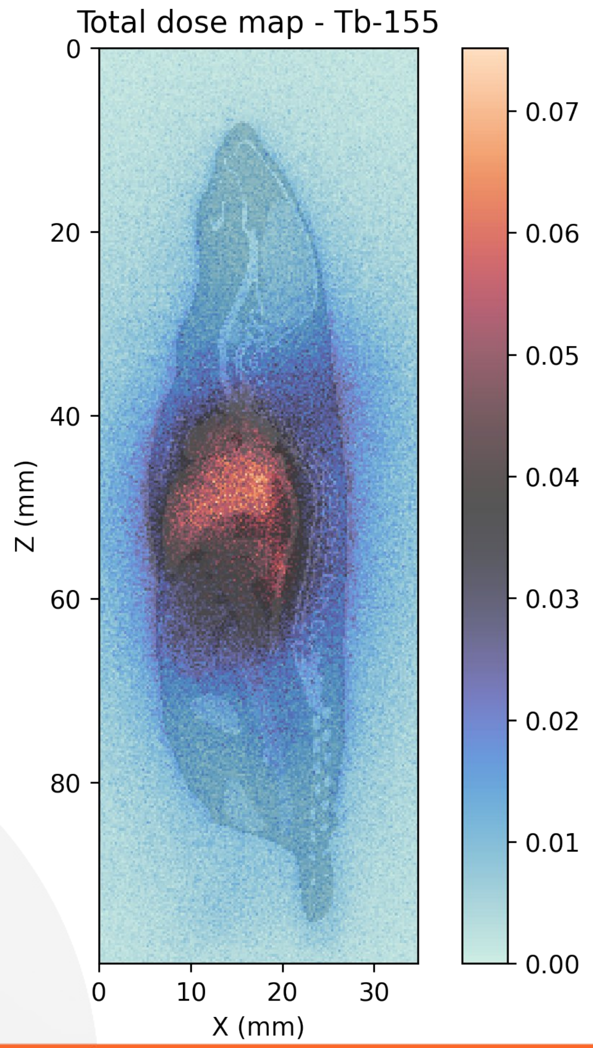
Dosimetry: Simulation and Results

- Different mouse organs simulated using biokinetic information for TACs, to evaluate the effect of contamination on dosimetry.

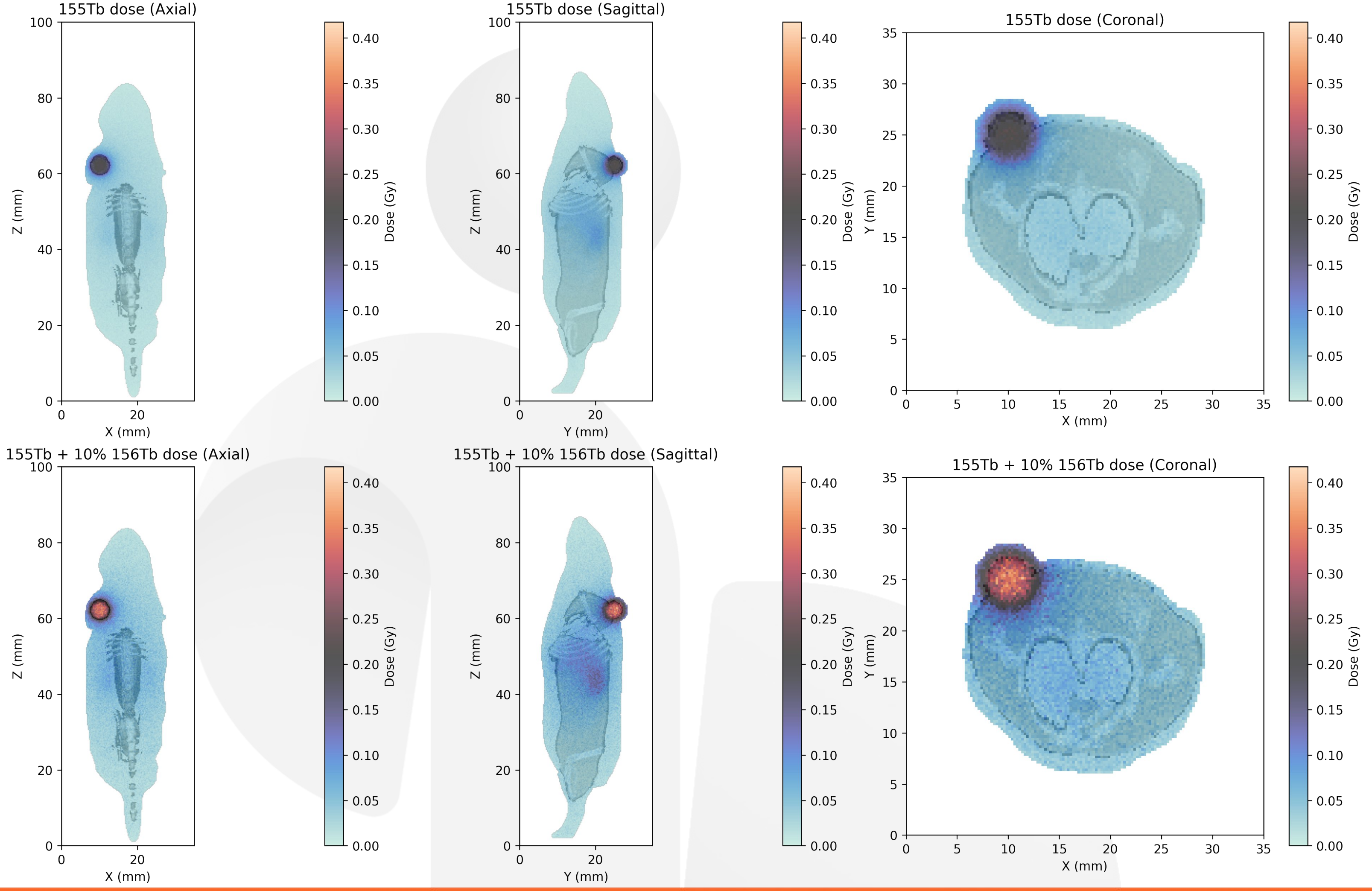
- Local (self) dosimetry: coming from activity in the organ itself.
- Global (total) dosimetry: coming from activity in all organs.

- Most of the dose is distributed globally as it is only from gammas.

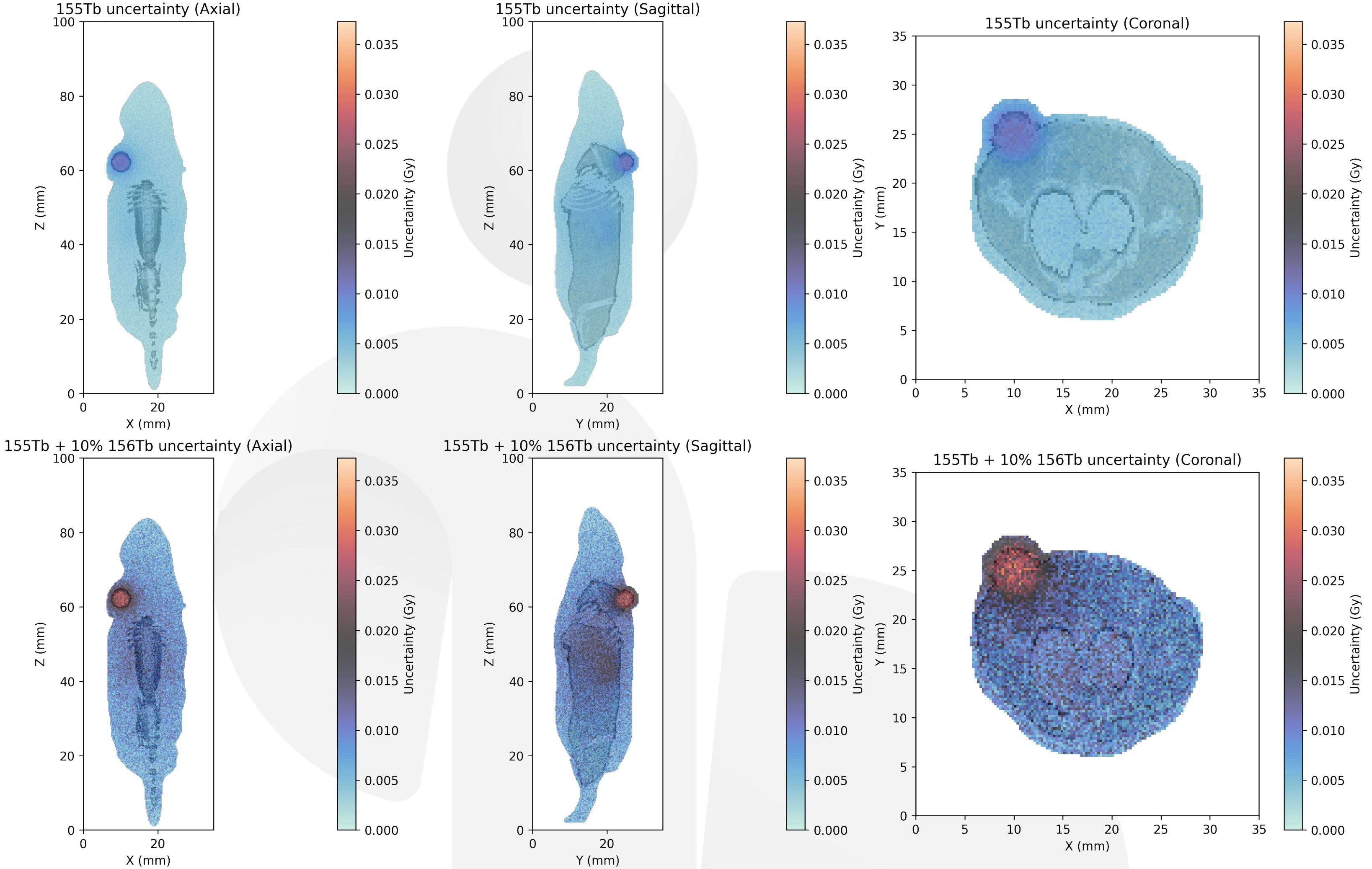
- Large organs → Larger total deposited energy.
- Close organs → Larger volumic deposited energy.



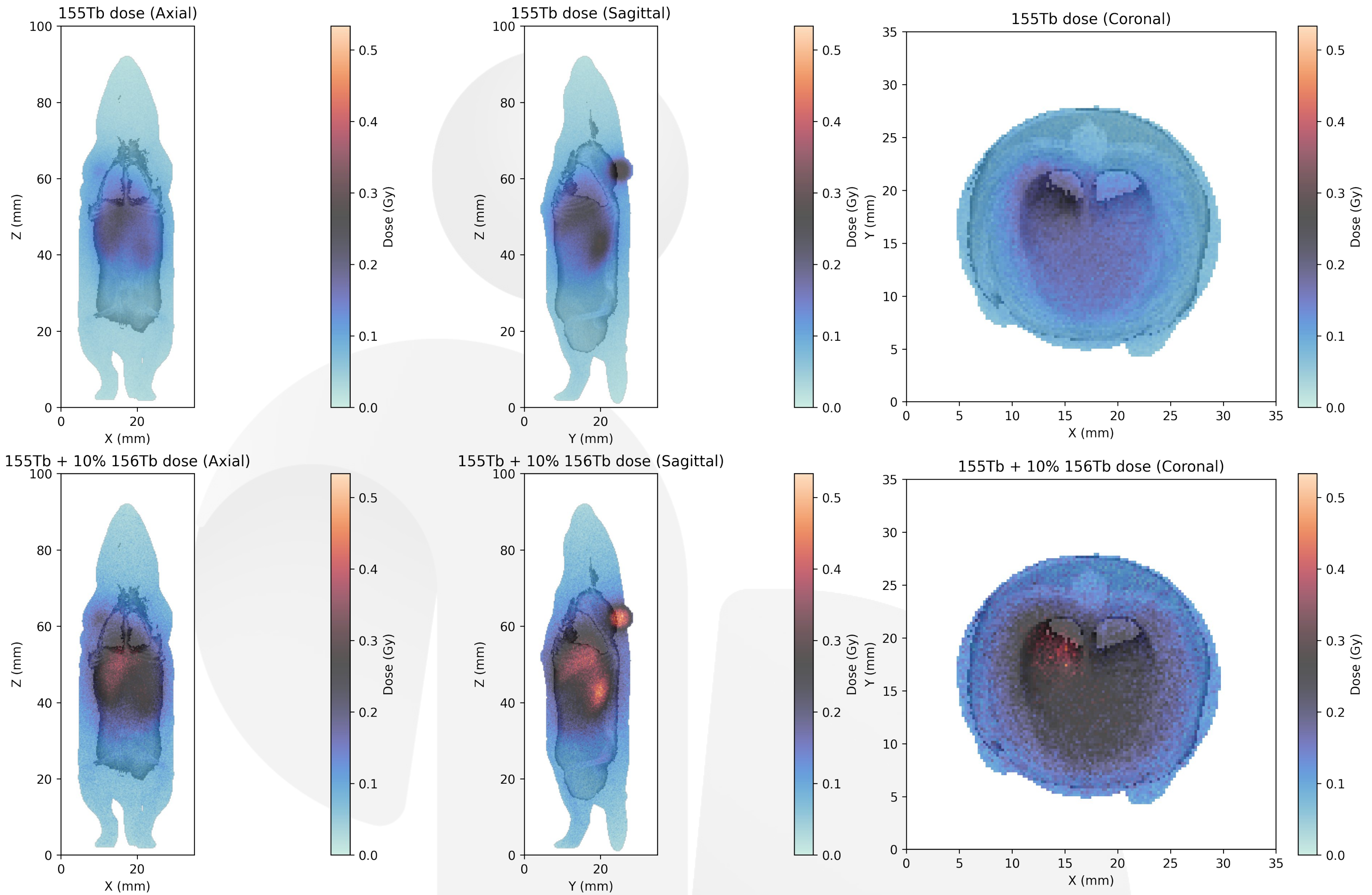
Dosimetry Map: Tumour Slice



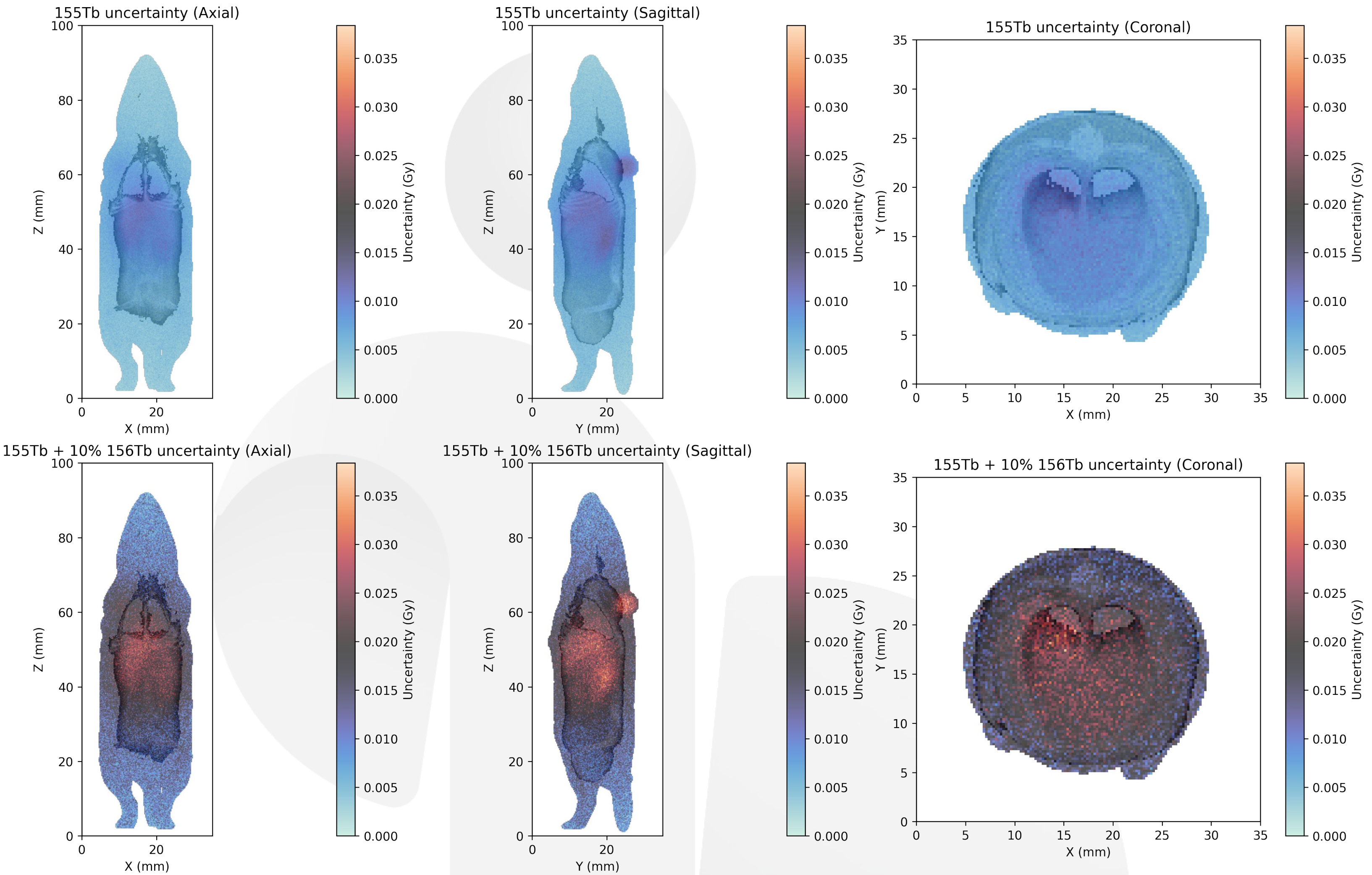
Dosimetry Uncertainty Map: Tumour Slice



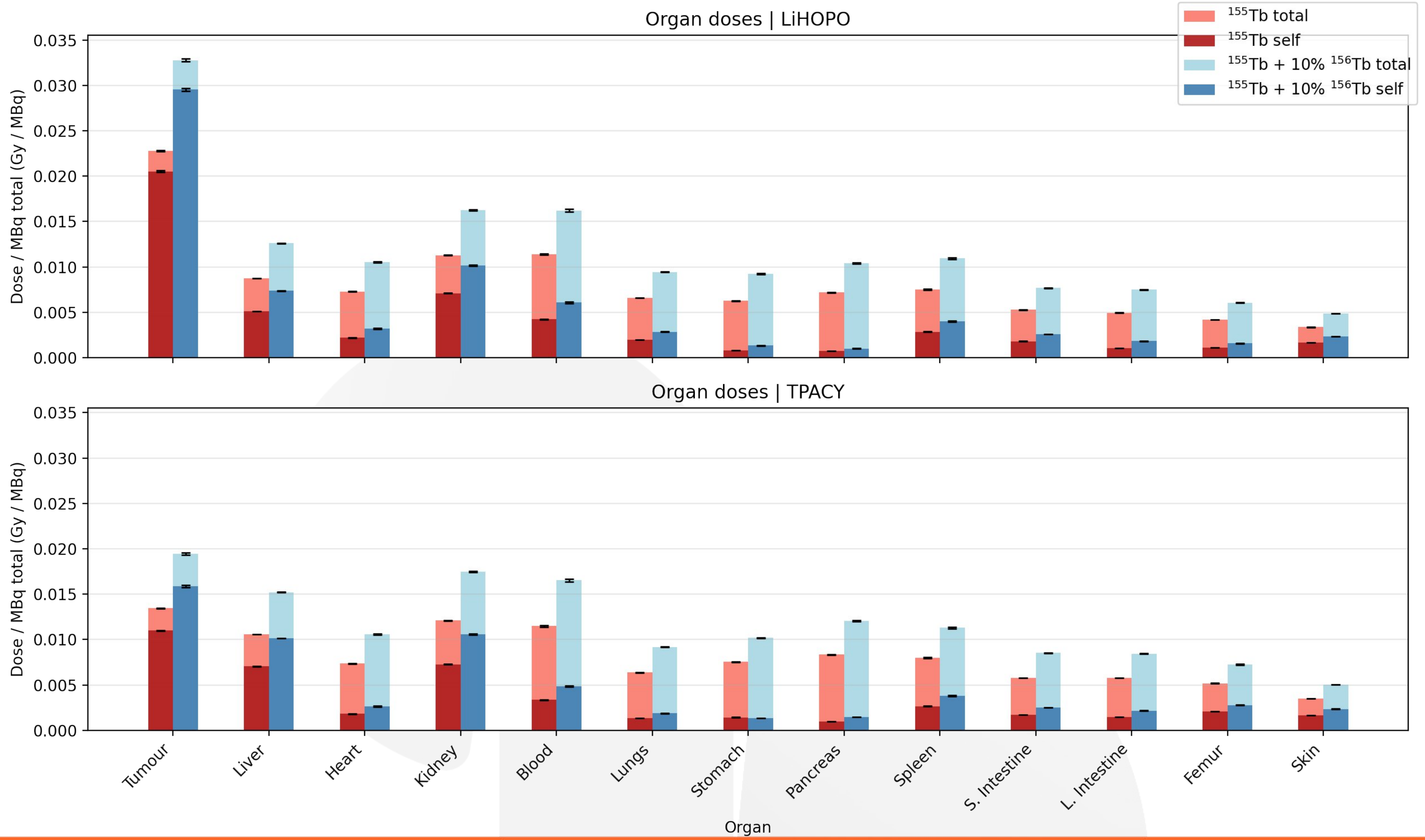
Dosimetry Map: Liver Slice



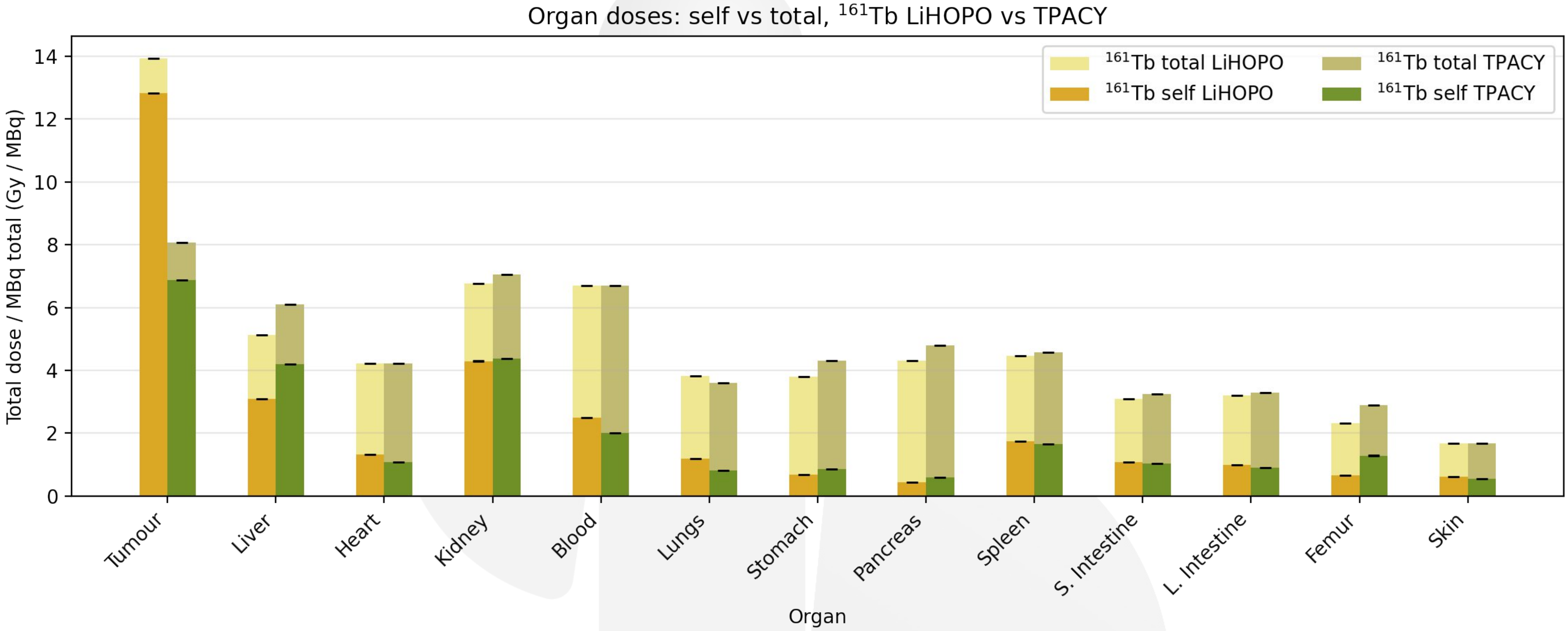
Dosimetry Uncertainty Map: Liver Slice



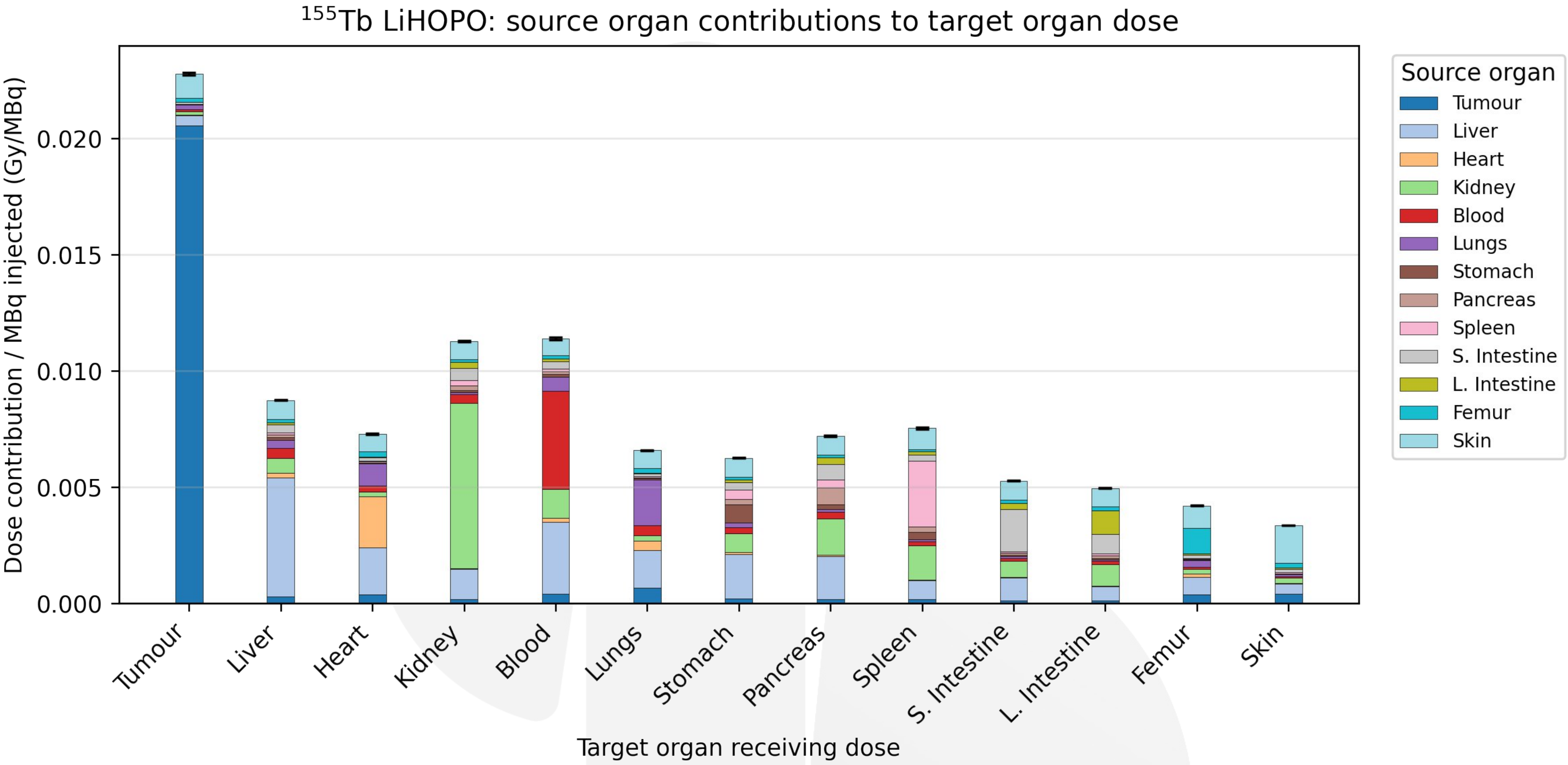
Total Dosimetry by Organ ^{155}Tb-^{156}Tb



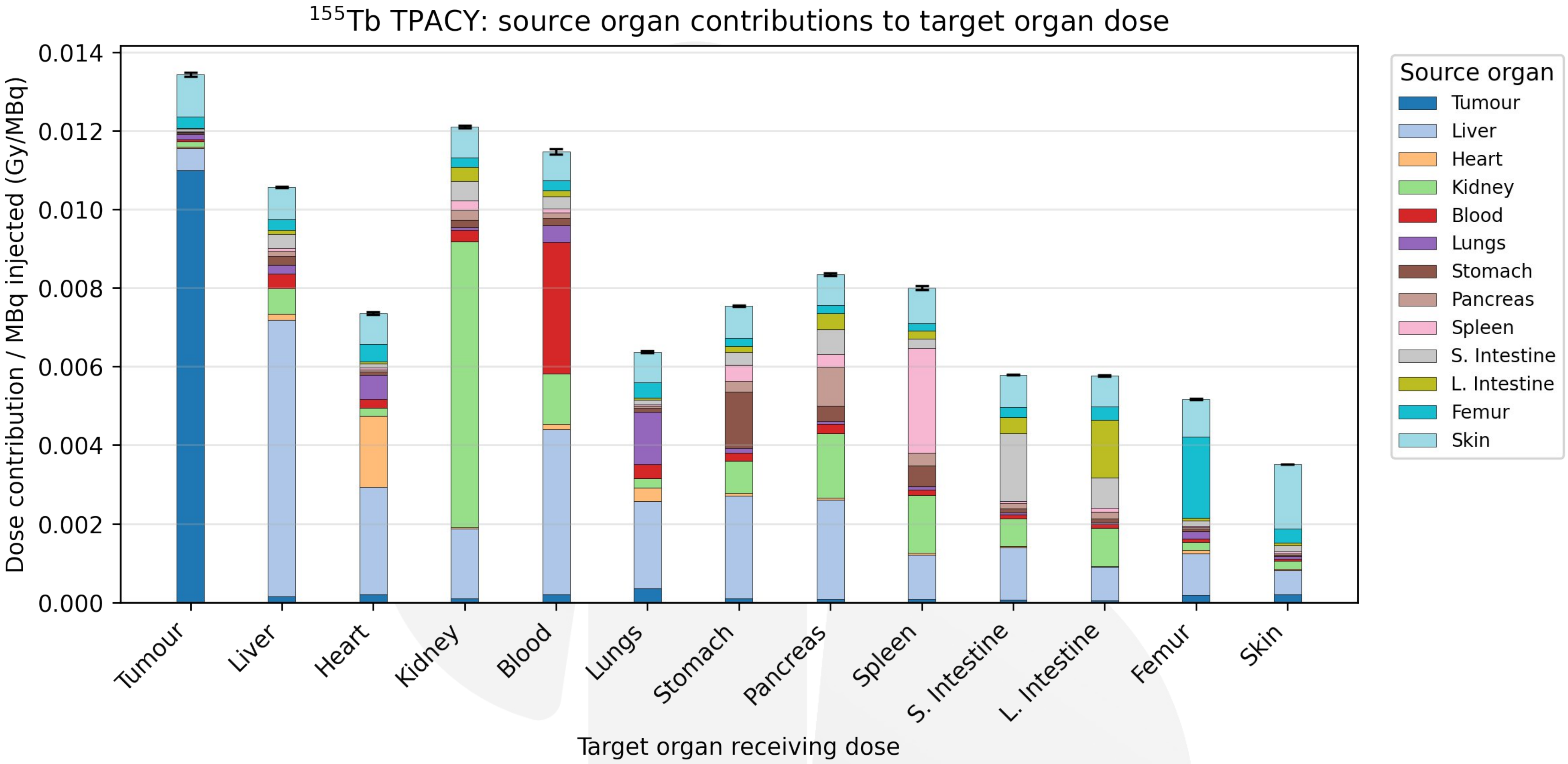
Total Dosimetry by Organ ^{161}Tb



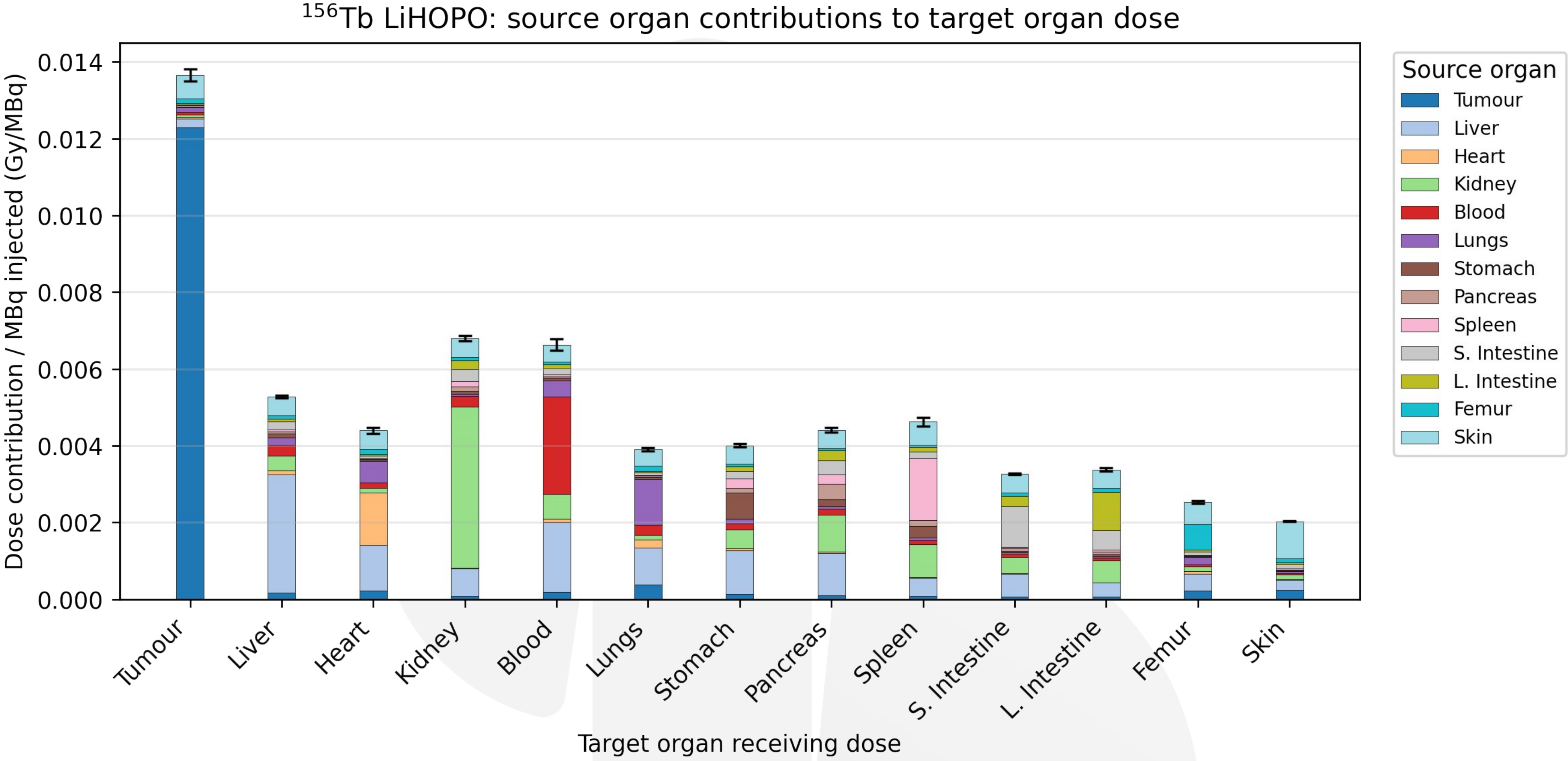
Dosimetry source by Organ ^{155}Tb - LiHOPO



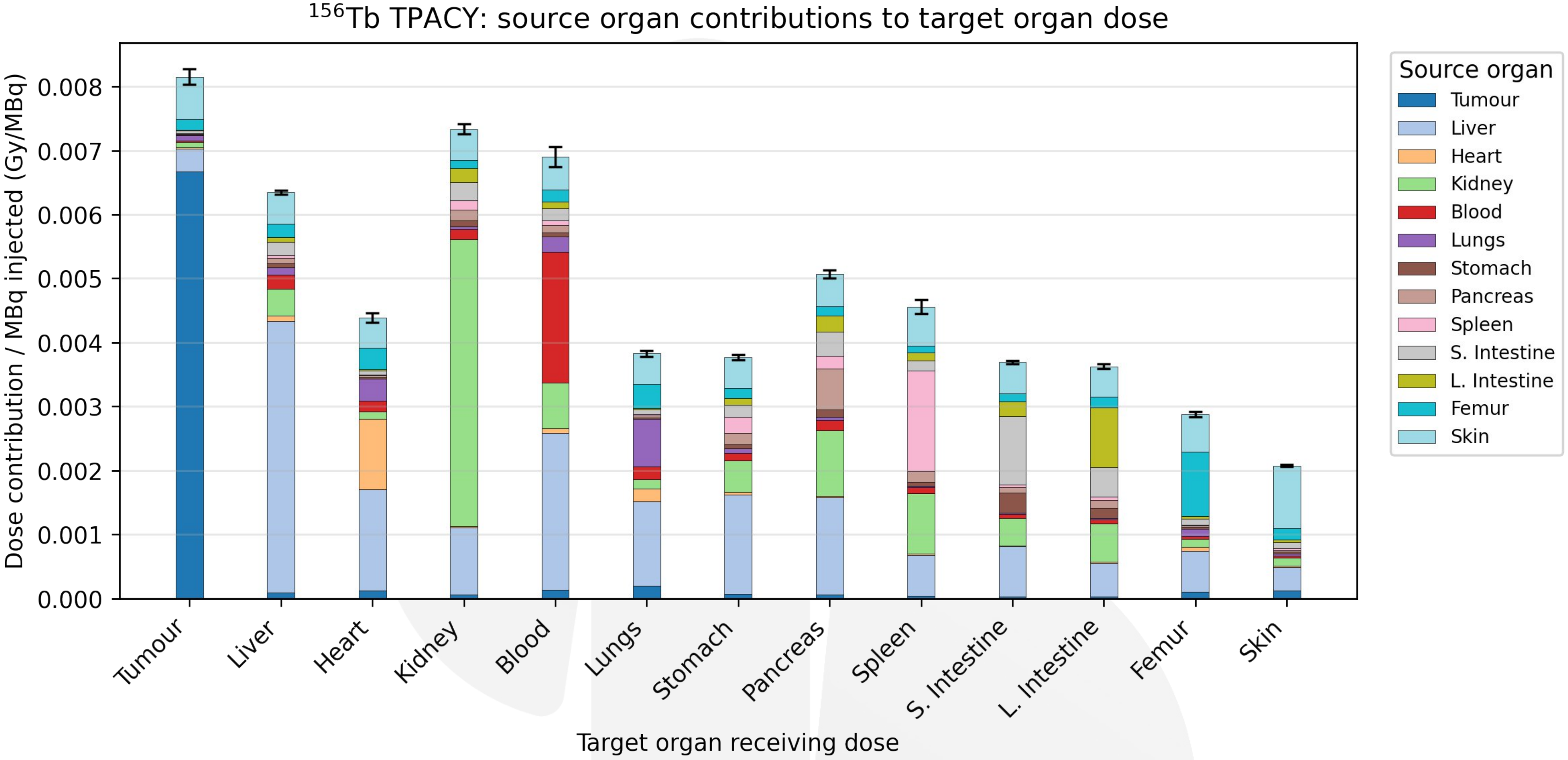
Dosimetry source by Organ ^{155}Tb - TPACY



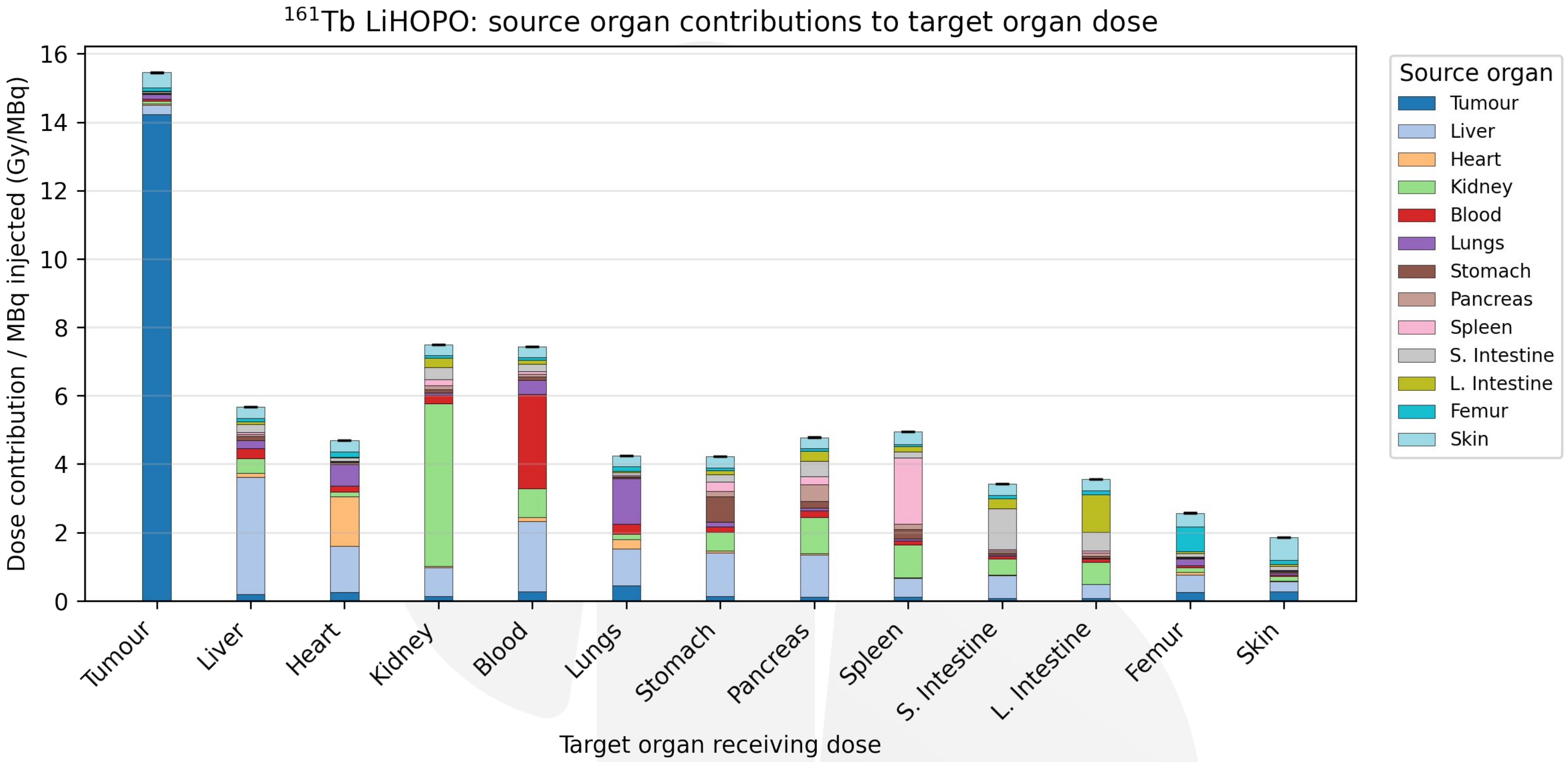
Dosimetry source by Organ ^{156}Tb - LiHOPO



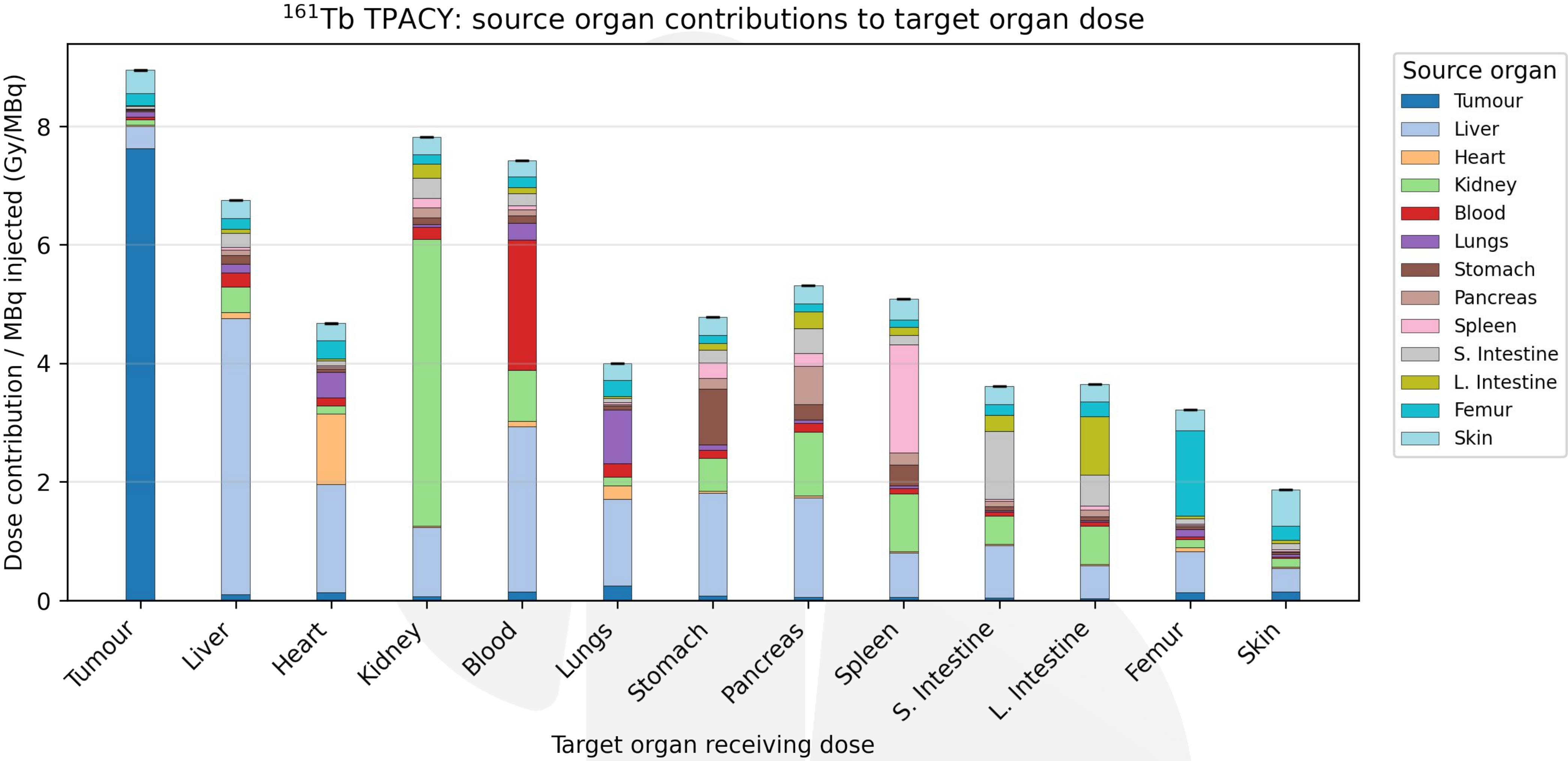
Dosimetry source by Organ ^{156}Tb - TPACY



Dosimetry source by Organ ^{161}Tb - LiHOPO



Dosimetry source by Organ ^{161}Tb - TPACY



Dosimetry: Simulation and Results

- 10% 156Tb lead to ~+50% dose
- Dose/Mbq ~ twice a large for LIHOPO compared to TPACY
- Main organs at risk:
  - Kidneys (~20-25 Gy).
  - Liver (~25-30 Gy).
  - Bone marrow (6-7 Gy, sometimes less).
  - Gastrointestinal tract (stomach/small bowel/colon) (20-25 Gy).
  - Lungs (~15-20 Gy).
  - Others in some cases.
- Must be compared to dosimetric models (Silvano) and litterature