



Università degli studi di Padova
Master Degree in Physics

Introduction to Research



Geant4 Computational Dosimetry for the ISOLPHARM Project



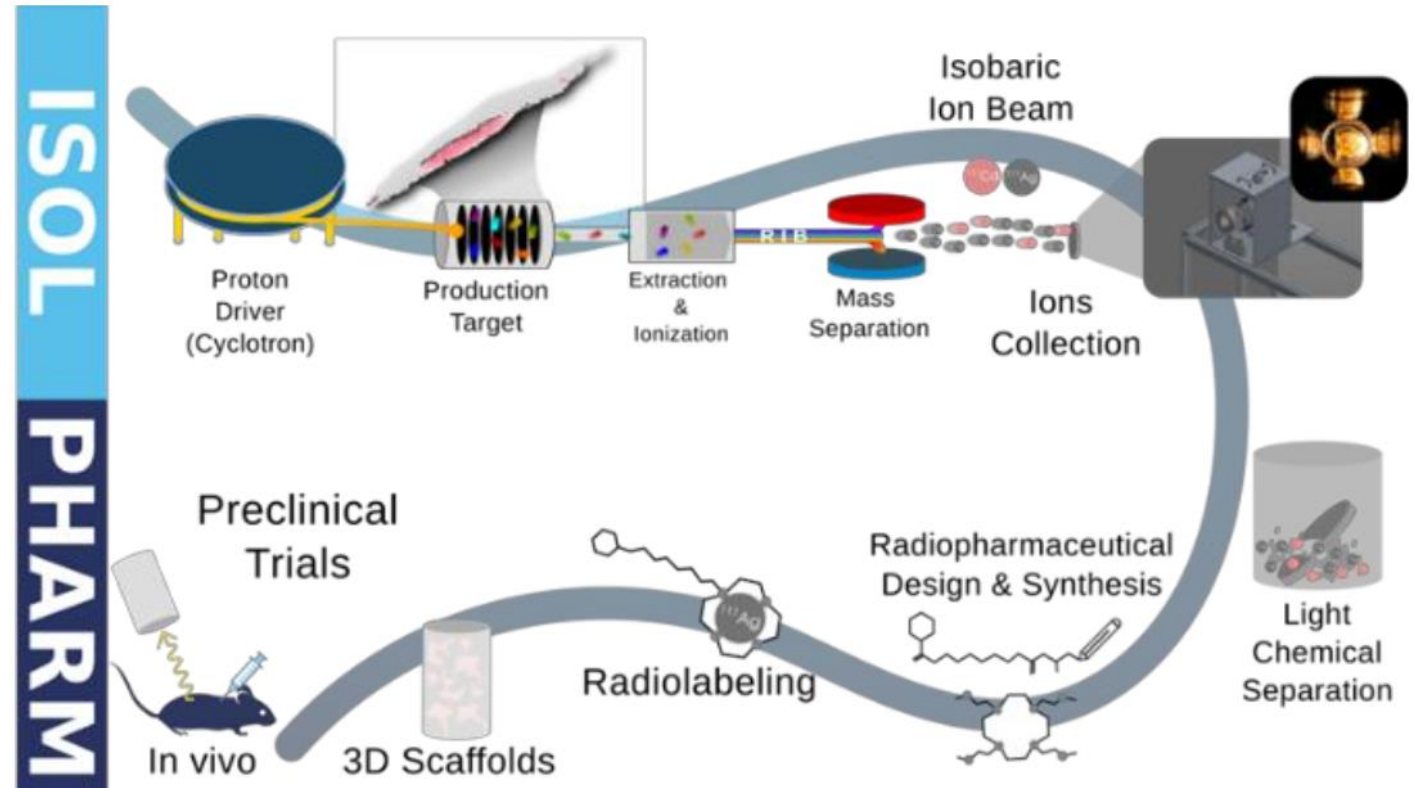
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ISOLPHARM Project

Production of radionuclides for targeted radiopharmaceuticals.

- A 30-70 MeV proton beam from a cyclotron hits a depleted Uranium Carbide target, generating neutron-rich radionuclides.

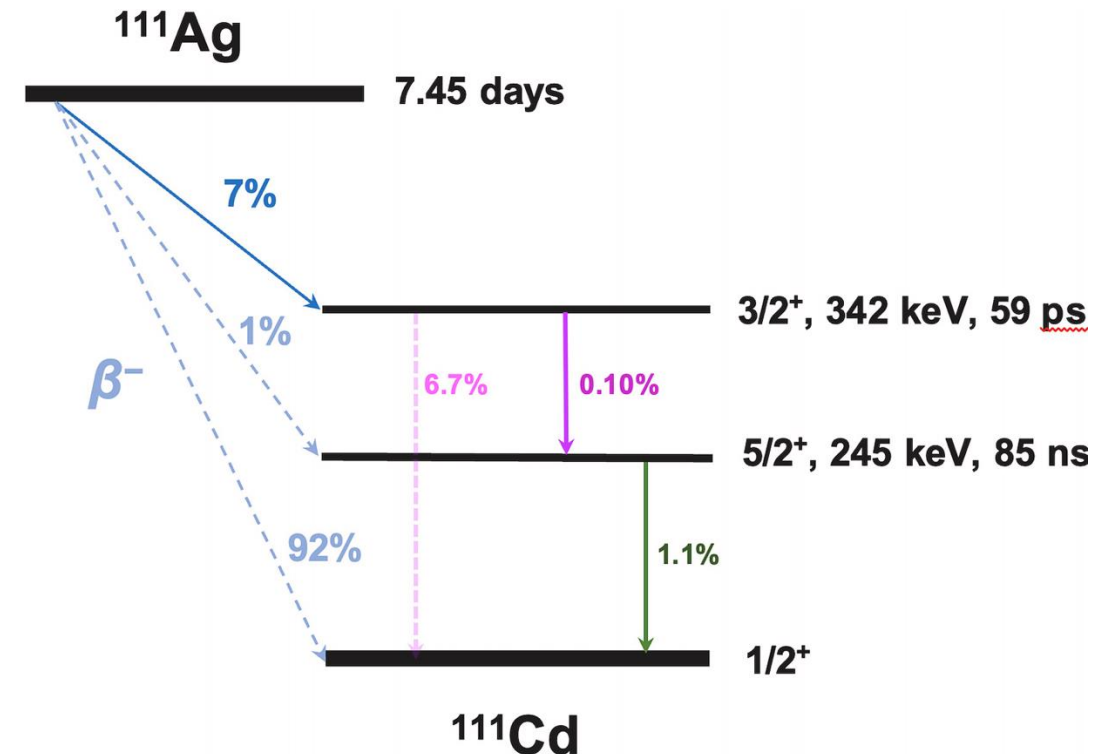


ISOL technique for radioPHARMaceuticals

Ag-111

The first chosen radionuclide for internal radiotherapy is Ag-111:

- β^- emitter (360 keV) -> induce cell death and deliver a cytotoxic radiation dose on the disease site;
- Medium half-life time (7.45 d);
- Medium tissue penetration (~ 1 mm);
- Low level of associated γ emission ($\sim 6\%$).



Objectives of this internship

The aim of this internship is to ***create a dataset of organ-to-organ S-values of Ag-111 radionuclide:***

we will use specific biodistributions with a whole body heterogeneous source based on MOBY's voxel-based phantoms with Geant4 simulations.

The developed dataset can be used to improve the accuracy of absorbed dose calculations in small animals dosimetry and highlight the impact of the mouse and organs size on S-values calculation.

Dosimetric Formalism

Our study uses the internal dosimetry standard provided by the *MIRD* (*Medical Internal Radiation Dose*) Committee.

- Absorbed Dose [1 Gy=1 J/kg]:

$$D = -\frac{dE}{dm}$$

- Cumulative Activity [Bq s]:

$$\tilde{A}(r_S, T_D) = \int_0^{T_D} A(r_S, t) dt$$

- S-values [Gy/Bq s]:

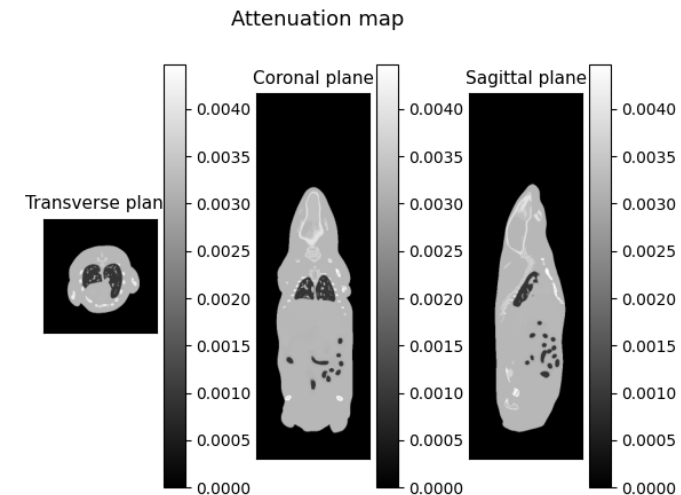
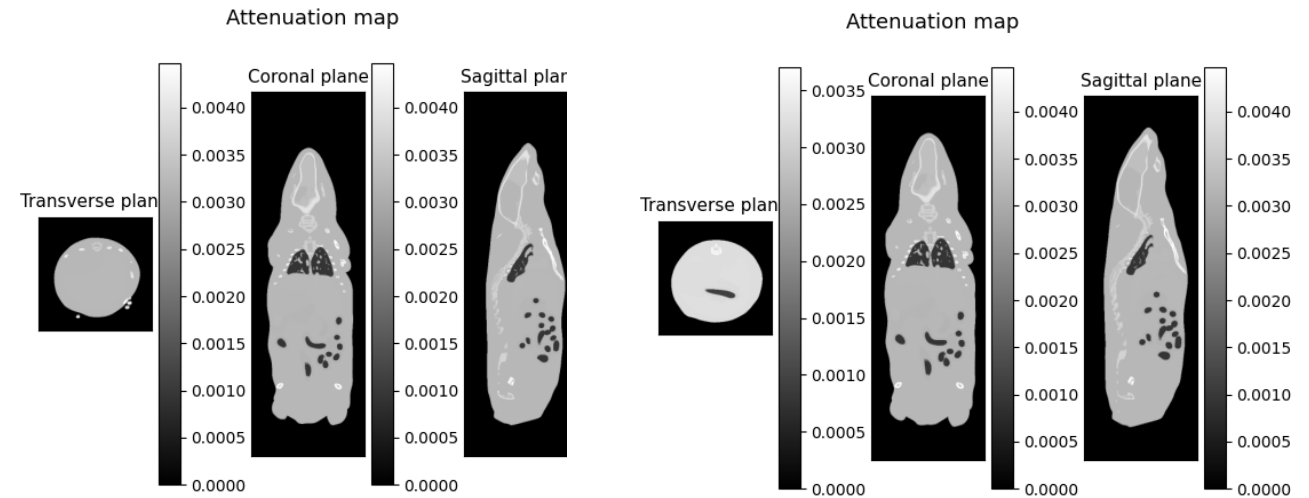
$$S(r_T \leftarrow r_S) = \sum_i \frac{n_i E_i \Phi(r_T \leftarrow r_S)}{m}$$

- Absorbed Dose Rate [Gy/s]:

$$D'(r_T, T_D) = \sum_{r_S} \tilde{A}(r_S, T_D) S(r_T \leftarrow r_S) \quad \text{MIRD Equation}$$

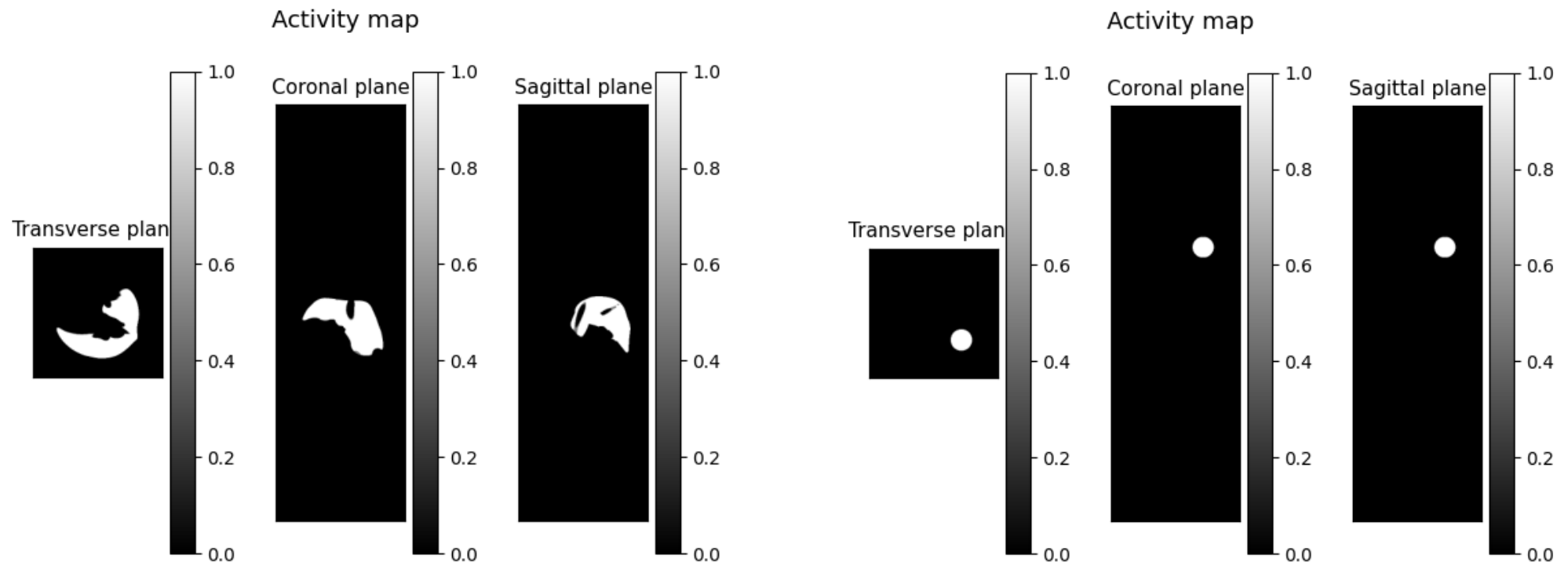
The MOBY Phantoms

- MOBY (*Mouse whole BodY*) phantoms are based on a high-resolution 3D Magnetic Resonance Microscopy (MRM) dataset for the organ/body surfaces;
- Voxel-based mouse models (**15, 20, 25 g**) -> **Attenuation Maps**: similar to a CT scan.



The MOBY Phantoms

- **Activity Maps** of single organs to recreate a PET- or SPECT- like matrix.
- A tumor can be generated as a sphere selecting its position and dimension.



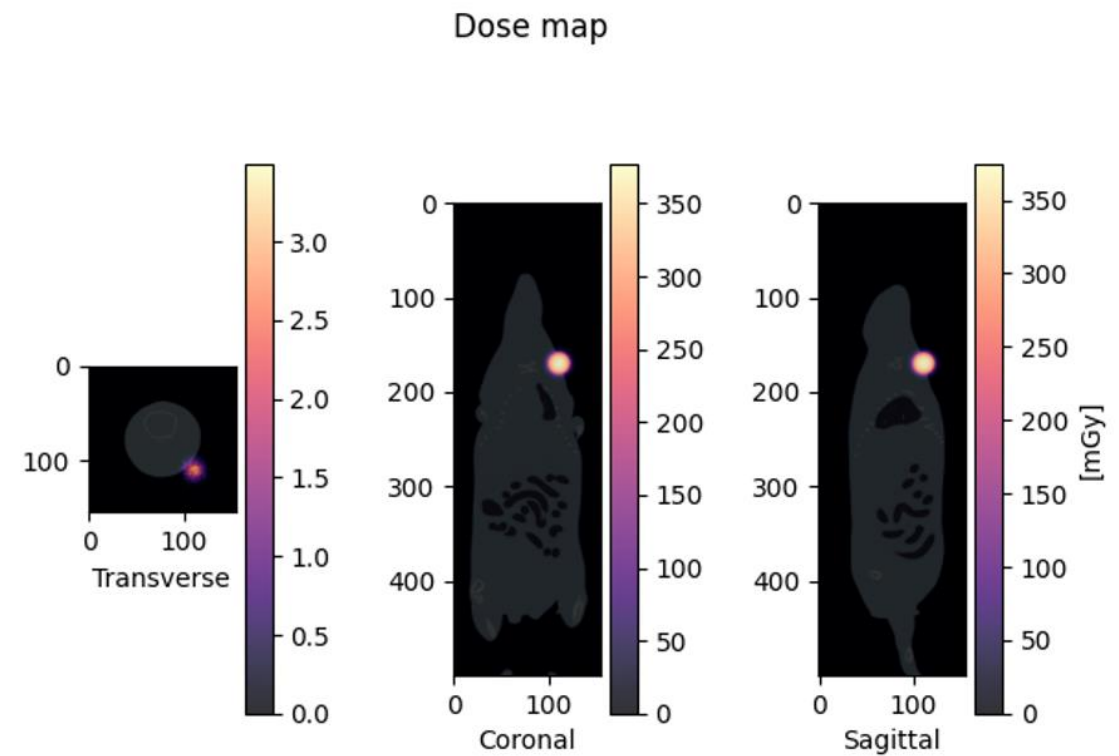
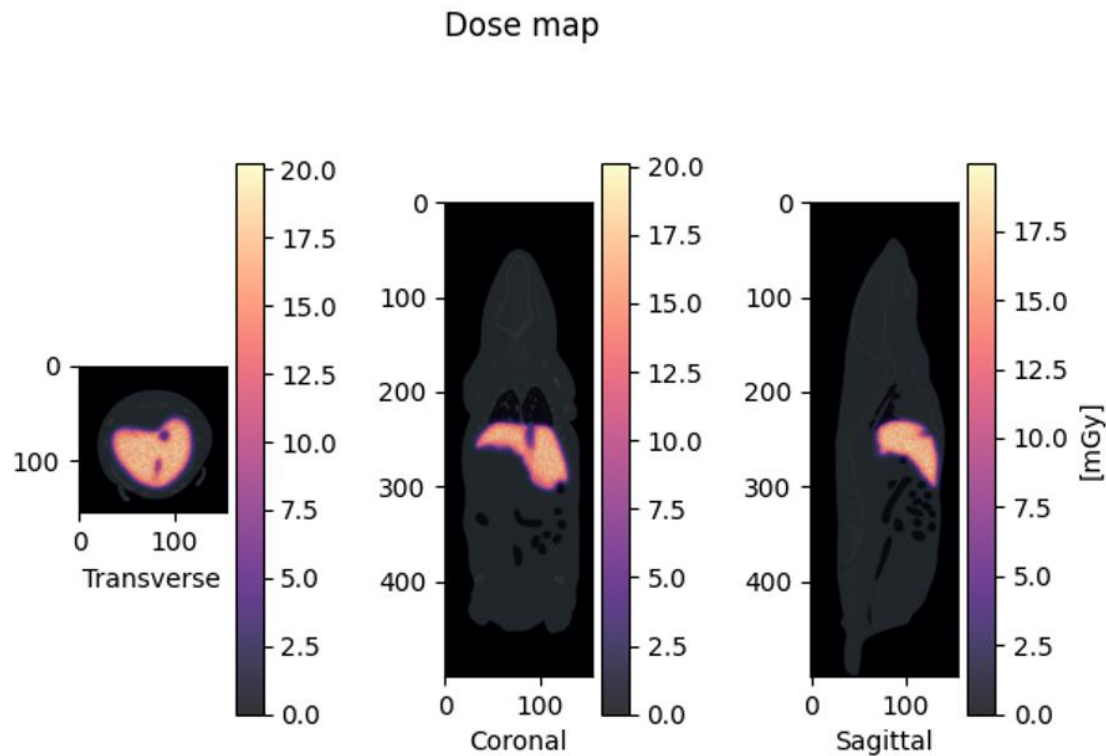
Geant4 Simulation

- Geant4 is a **Montecarlo** simulation code in C++ developed by CERN to model interactions of radiation with matter.
- The Attenuation and Activity maps are imported and 10^7 events of an **Ag-111** decaying in the **source organ** are generated. The MOBY phantom is made a sensitive detector.
- The output files:
 - **dose histograms** of a 3d matrix of voxels containing the deposited energy;
 - **TTree** of a list of **individual dose hits** for each event and its voxel coordinates.



Geant4 Simulation

- The dose histograms' values are converted from MeV/g in Gy and normalized.
- -> Absorbed Dose Maps



S-values

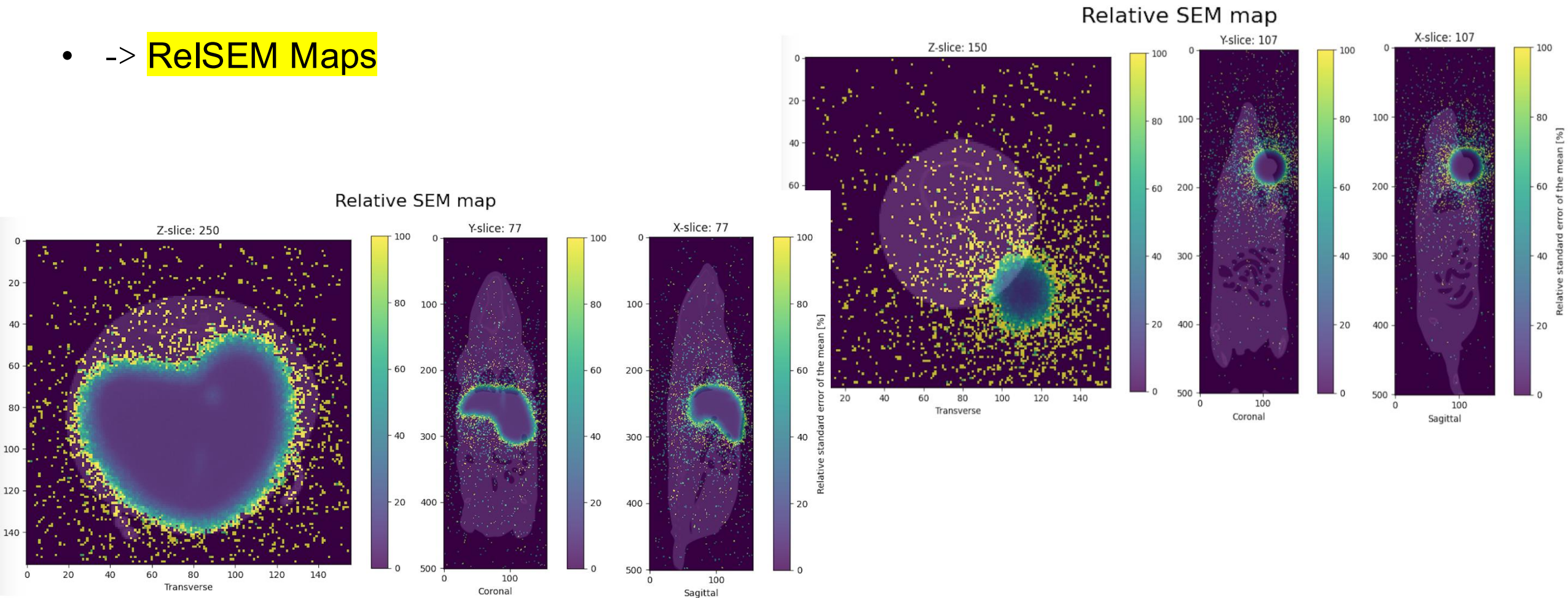
- The **S-values** are calculated as the dose rate per unit of activity [Gy/(Bq*s)].

TARGET ORGAN	SOURCE ORGAN									
	kidney	liver	lungs	muscle	pancreas	spleen	testes	thyroid	tumor	
brain	1.1278e-15	1.6161e-15	3.3433e-13	4.6852e-13	1.2973e-15	1.2734e-15	3.1745e-16	2.4354e-14	3.7624e-15	15 g
heart	4.8130e-15	2.4131e-12	1.2275e-11	1.2370e-12	6.7414e-15	6.9400e-15	1.0559e-15	1.0184e-14	1.4654e-14	
kidney	2.3500e-10	1.9736e-12	5.2169e-15	1.0642e-12	1.2714e-11	8.2023e-12	2.6072e-15	1.5094e-15	2.3546e-15	
liver	2.6493e-12	4.8887e-11	2.7147e-12	6.1927e-13	2.8457e-12	9.6948e-15	1.5378e-15	3.6507e-15	6.5364e-15	
lungs	5.1095e-15	1.6072e-12	1.1372e-10	9.9518e-13	5.7789e-15	5.5772e-15	9.6573e-16	1.3965e-11	1.7974e-13	
pancreas	1.2591e-11	3.1726e-12	6.7776e-15	7.1334e-13	1.9232e-10	2.9298e-11	2.3188e-15	2.0859e-15	3.1176e-15	
spleen	4.0254e-12	1.0393e-14	6.4750e-15	1.4001e-12	1.6294e-11	6.6383e-10	2.0883e-15	1.6729e-15	2.4329e-15	
testes	2.9306e-15	1.6369e-15	8.6304e-16	1.5803e-12	2.6585e-15	2.6036e-15	2.4019e-10	5.4219e-16	7.8362e-16	
thyroid	1.8985e-15	3.9618e-15	1.5979e-11	2.5257e-12	3.6616e-15	1.3269e-15	5.4956e-16	3.7387e-09	1.2033e-14	
tumor	2.5870e-15	7.1295e-15	2.4498e-13	1.4862e-12	2.9159e-15	2.5076e-15	6.0918e-16	1.2713e-14	5.6413e-10	
TARGET ORGAN	SOURCE ORGAN									
	kidney	liver	lungs	muscle	pancreas	spleen	testes	thyroid	tumor	
brain	6.8390e-16	1.1320e-15	1.4653e-13	2.1790e-13	7.7108e-16	7.6143e-16	2.2695e-16	1.1296e-14	4.3413e-15	25 g
heart	2.9806e-15	1.0417e-12	6.4297e-12	6.7167e-13	5.1832e-15	3.7506e-15	5.8384e-16	7.1653e-15	7.0510e-15	
kidney	1.4589e-10	9.7280e-13	3.5204e-15	5.4430e-13	6.5206e-12	3.5353e-12	1.8196e-15	1.2734e-15	1.3149e-15	
liver	1.3031e-12	2.9414e-11	1.3959e-12	3.1798e-13	1.4002e-12	6.6591e-15	9.9380e-16	2.6401e-15	8.7533e-15	
lungs	3.5823e-15	8.4400e-13	7.2072e-11	5.0976e-13	4.3034e-15	4.0213e-15	5.9635e-16	7.8285e-12	8.7533e-15	
pancreas	6.4599e-12	1.5824e-12	4.2837e-15	3.8462e-13	1.2087e-10	1.5314e-11	1.8276e-15	1.5145e-15	1.4426e-15	
spleen	1.7206e-12	6.2893e-15	3.4725e-15	7.4382e-13	8.6725e-12	4.2531e-10	1.6503e-15	1.4252e-15	1.3227e-15	
testes	1.9985e-15	1.1854e-15	6.5327e-16	8.0651e-13	1.7414e-15	1.4539e-15	1.4952e-10	3.3368e-16	3.6061e-16	
thyroid	2.0339e-15	2.6737e-15	9.7902e-12	1.3441e-12	1.2425e-15	9.2486e-16	3.0875e-16	2.5094e-09	1.9894e-14	
tumor	9.8807e-16	1.5824e-15	9.5314e-15	1.3736e-12	1.5665e-15	1.3966e-15	2.9190e-16	2.1380e-14	5.6459e-10	

ReISEM

- The information on the total dose deposited in each voxel for each event is used to calculate the Relative Standard Error of the Mean (ReISEM).

- > **ReISEM Maps**



S-values' Uncertainties

- For each source – target couple, the activity map of the target is used as a mask to calculate the relSEM on the S-value.
- *Expectation*: the uncertainty of a specific source organ S-values is bigger for a smaller and more distant target organ.
- However, the increased *stochastic variance* of the energy deposited in closer organs has to be considered.
- → Increase the statistics and decrease the number of voxels.
- → For now, associate the relSEM calculated for a **source-source** organs couple to all the S-values with that source.

	15 g	20 g	25 g
Blood	2.32 %	2.67 %	2.85 %
Bone	10.95 %	8.16 %	8.68 %
Brain	2.27 %	2.62 %	2.83 %
Heart	1.81 %	2.09 %	2.24 %
Kidney	2.42 %	2.84 %	3.06 %
Liver	5.27 %	6.26 %	6.77 %
Lungs	3.50 %	4.09 %	4.39 %
Muscle	17.86 %	21.21 %	22.94 %
Pancreas	2.69 %	3.15 %	3.38 %
Spleen	1.44 %	1.68 %	1.80 %
Testes	2.40 %	2.82 %	3.03 %
Thyroid	0.61 %	0.69 %	0.74 %
Tumor	1.56 %	1.56 %	1.56 %

Dose Rate Calculation

- The mean absorbed dose rates $D'(r_T, T_D)$ are estimated through the MIRD equation, where we use:

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

- this study's S-values dataset;
- **Injected activity per mass data** from an Ag-111 biodistribution experiment carried out by the ISOLPHARM group in March 2024 at the CAPIR laboratory in Catania.

TARGET ORGAN	Average Injected Activity per Grams (%/g)	Rel. Err.
Blood	0.034	0.294
Bone	0.040	0.152
Brain	0.435	0.287
Heart	0.090	0.318
Kidney	0.385	0.300
Liver	0.770	0.285
Lungs	1.200	0.293
Pancreas	0.040	0.161
Spleen	0.320	0.340

Dose Rate Calculation

15 g Mouse

TARGET ORGAN	DOSE (Gy/s)	Relative Error
Brain	3.37×10^{-7}	0.283
Heart	1.20×10^{-7}	0.184
Kidney	1.63×10^{-7}	0.271
Liver	3.76×10^{-7}	0.278
Lungs	4.37×10^{-7}	0.281
Pancreas	4.94×10^{-8}	0.154
Spleen	1.07×10^{-7}	0.328
Testes	2.09×10^{-11}	0.174
Thyroid	5.95×10^{-8}	0.288

20 g Mouse

TARGET ORGAN	DOSE (Gy/s)	Relative Error
Brain	3.59×10^{-7}	0.196
Heart	1.18×10^{-7}	0.132
Kidney	1.68×10^{-7}	0.191
Liver	3.79×10^{-7}	0.197
Lungs	4.52×10^{-7}	0.200
Pancreas	3.22×10^{-8}	0.141
Spleen	1.13×10^{-7}	0.230
Testes	2.12×10^{-11}	0.120
Thyroid	6.18×10^{-8}	0.204

25 g Mouse

TARGET ORGAN	DOSE (Gy/s)	Relative Error
Brain	3.69×10^{-7}	0.166
Heart	1.19×10^{-7}	0.113
Kidney	1.70×10^{-7}	0.162
Liver	3.80×10^{-7}	0.168
Lungs	4.55×10^{-7}	0.170
Pancreas	4.36×10^{-8}	0.0864
Spleen	1.16×10^{-7}	0.195
Testes	2.20×10^{-11}	0.109
Thyroid	6.04×10^{-8}	0.174

Conclusions and Future Prospectives

- We developed a comprehensive **S-value dataset** for Ag-111 in 3 mice (15, 20, 25 g) using voxel-based MOBY phantoms and Geant4 simulations.
- The S-values dataset was employed to calculate the **mean absorbed dose rates** for key organs.
- Mouse size and organ dimensions significantly impact S-values.
- The developed S-values dataset will improve the accuracy of absorbed dose calculations in preclinical studies.
- The observed dependency of uncertainties on distance was likely due to stochastic variance inherent in Montecarlo simulations.
- Future work:
 - Improve the number of events/simulations to achieve a more physically accurate dataset;
 - Decrease the number of voxels in the MOBY phantoms to agevolate the computing.

