Università degli Studi di Padova

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M.Sc. Degree in Physics

Research Activity report

Internal dosimetry calculations of innovative radiopharmaceuticals using GEANT4 on mice phantoms generated with MOBY

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1 Aims of the experiment

The aims of the activity were

- computing S-values regarding organ-organ effects with $64Cu$ and validate them with the article Xie [2];
- computing S-values regarding biodistribution-organ using Catania's measurements [1];
- computing S-values regarding organ-organ effects with $47Sc$;
- computing S-values regarding biodistribution-organ using Mueller's biodistribution of 2014 (anche qua biblio figa)

2 Introduction

2.1 Introduction

The last few decades have witnessed a revolution in the understanding of the intersection between the coordination chemistry of metallic radionuclides and nuclear medicine applications, opening new frontiers for cancer imaging and therapy. In order to develop new treatments for human diseases, in vivo small animal imaging assays are used, especially mice. To provide in vivo functional imaging and track molecular processes in small animals, radiotracer techniques using positron emission tomography (**PET**) or Single Photon Emission Computed Tomography (**SPECT**) are commonly exploited.

In particular, **PET** has the advantage that each animal can be studied repeatedly: the cavy receives significant levels of radioactivity that result in radiation doses that can change gene expression, tumour characteristics and, in some cases, death.

2.2 MOBY and GEANT4

In this work, it has been used

- **MOBY (v. 2.0)**, a 4-dimensional whole-body mouse model, to produce 4 voxel-based mouse models of different body masses and sizes.

  In order to get different mass values for the mice, the generation parameters have been modified in order to rescale organ sizes and weights.

  To set the different source organ, the activity of the interested one has been set to 1, while the others have been set to 0; for the biodistribution, the activity per voxel has been computed for each organ and inserted in the MOBY generation file.

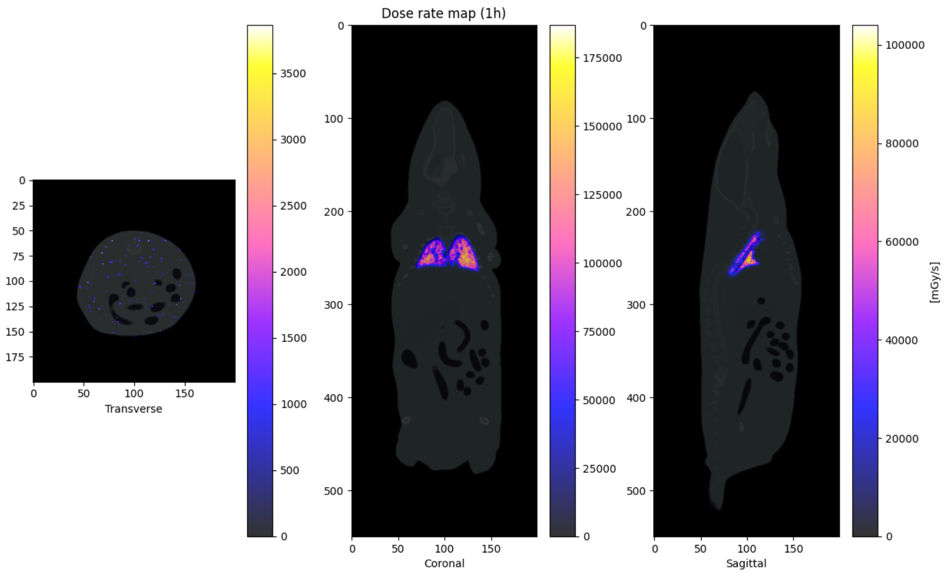

Figure 1: example of phantom, lungs as source of radiation

- **GEANT4 (v. 10.7.0)**, a software for the Montecarlo simulation of the passage of particles through matter, to compute S-values for 16 organs from the positron emitting radionuclides ^{64}Cu and ^{47}Sc. Gammas were considered in the S-value calculations for both the organ-organ results and the biodistribution-organ ones.

In addition, the absorbed dose for some representative radiotracers was assessed using the biodistribution data taken from Catania measurements or l'altra che non ricordo.

2.3 ^{64}Cu

DA PARAFRASARE

Among the variety of medically relevant transition metals, copper draws great interest from the nuclear medicine community as it possesses an attractive combination of isotopes ideal for both diagnostic and therapeutic, i.e., theranostic, applications.

In particular, ^{64}Cu ($t_{1/2} = 12.7h$) possesses a rare emission profile which combines β^+ ($E_{\beta+,max}$ =655keV,$I_{\beta+}$ =18%),β^- ($E_{\beta-,max}$ =573keV,$I_{\beta+}$ =39%,) and electron capture emissions (I_{EC} = 43%).

The relatively low β^+-energy and the resulting annihilation photons produce high-quality images.
Moreover, its relatively long half-life can enable positron emission tomography (**PET**) imaging at later time points than lots of other radioisotopes.

Although its decay profile would make ^{64}Cu a dual diagnostic and therapeutic radionuclide, the high positron branching ratio precludes the latter use.

However, ^{64}Cu retains the potential for theranostic applications when paired with the pure β^{-} emitter ^{67}Cu ($t_{1/2}$ = 61.9 h, $E_{\beta^{-},max}$ = 141 keV, $I_{\beta+}$ = 100%).

2.4 ^{47}Sc

^{47}Sc is an interesting radionuclide for PET imaging and radiotherapy treatments because of its favorable decay characteristics ($t_{1/2} = 3.35d$;$E_{\beta-}$ = 162 keV; E_{γ} = 159 keV) for therapeutic application and for SPECT imaging.

In vitro, ^{47}Sc-folate demonstrated effective reduction of folate receptor-positive ovarian tumor cell viability; moreover, it may have potential for clinical translation and be of particular interest in tandem with ^{44}Sc or ^{43}Sc as a diagnostic match, enabling the realization of radiotheragnostics in future.

3 Computing S-values organ-organ for ^{64}Cu

First of all, it has been considered the effect of a single source organ on itself and other target organs.

In particular, as sources it has been considered

- kidneys
- spleen
- testicles
- brain
- thyroid
- heart
- liver
- lungs
- pancreas
- skin
- bladder
- stomach
- celebral cortex
- vas deferens
- small intestine
- large intestine

while for the targets

- lungs
- heart
- kidneys
- liver
- pancreas
- spleen
- intestine (all together, small and large)
- brain

3.1 21 g mouse model

	lungs	heart	kidneys	liver	pancreas	spleen	intestine	brain
kidney	9.91 e-05	2.25 e-05	7.81 e-02	3.42 e-04	1.53 e-03	3.07 e-04	3.37 e-04	6.26 e-06
spleen	4.53 e-05	2.37 e-05	6.52 e-04	5.22 e-05	4.34 e-03	2.45 e-01	4.65 e-05	6.11 e-06
testicles	2.07 e-05	4.11 e-06	1.29 e-05	7.79 e-06	1.11 e-05	8.53 e-06	3.01 e-05	1.09 e-06
brain	1.09 e-05	3.08 e-05	7.90 e-06	1.18 e-05	6.90 e-06	7.80 e-06	4.88 e-06	2.92 e-02
thyroid	2.85 e-05	6.07 e-05	1.23 e-05	2.44 e-05	1.01 e-05	1.86 e-05	8.41 e-06	1.20 e-04
heart	1.36 e-03	2.44 e-01	2.34 e-05	4.12 e-04	3.72 e-05	2.79 e-05	1.99 e-05	1.99 e-05
liver	3.18 e-04	2.33 e-04	2.62 e-04	1.49 e-02	4.21 e-04	4.86 e-05	1.80 e-04	8.82 e-06
lung	3.71 e-02	8.19 e-03	3.47 e-05	1.17 e-03	3.77 e-05	2.50 e-05	2.18 e-05	2.62 e-05
pancreas	1.70 e-04	3.92 e-05	1.58 e-03	3.44 e-04	6.85 e-02	1.70 e-03	9.54 e-04	5.51 e-06
skin	2.01 e-05	1.50 e-05	1.53 e-05	2.00 e-05	3.82 e-05	1.12 e-04	2.53 e-05	3.73 e-05
bladder	5.58 e-05	8.16 e-06	2.85 e-05	1.30 e-05	2.32 e-05	1.43 e-05	7.33 e-05	2.53 e-05
stomach	2.13 e-04	4.05 e-05	1.48 e-04	7.76 e-04	6.04 e-03	4.85 e-03	1.59 e-04	1.03 e-05
celebral cortex	1.24 e-05	1.97 e-05	5.45 e-06	1.00 e-05	6.02 e-06	7.11 e-06	4.32 e-06	5.12 e-02
vas deferens	3.79 e-05	3.68 e-06	2.19 e-05	1.11 e-05	1.92 e-05	1.37 e-05	5.27 e-05	3.83 e-06
small intestine	6.00 e-03	2.24 e-05	1.27 e-04	1.37 e-04	4.98 e-04	3.82 e-05	1.47 e-02	5.52 e-06
large intestine	6.23 e-03	1.14 e-05	2.83 e-04	5.27 e-05	4.02 e-04	6.49 e-05	1.28 e-02	4.69 e-06

Table 1: S-values organ-organ. Organs on the top are **targets**, organs on the left are the **sources**.

3.2 25 g mouse model

	lungs	heart	kidneys	liver	pancreas	spleen	intestine	brain
kidney	9.16 e-05	2.14 e-05	6.62 e-02	2.71 e-04	1.25 e-03	2.48 e-04	2.79 e-04	5.22 e-06
spleen	4.16 e-05	3.04 e-05	5.04 e-04	4.74 e-05	3.47 e-03	2.10 e-01	4.23 e-05	6.64 e-06
testicular	1.71 e-05	4.08 e-06	1.59 e-05	6.62 e-06	1.32 e-05	1.19 e-05	2.51 e-05	1.90 e-06
brain	1.11 e-05	1.49 e-05	4.65 e-06	1.05 e-05	5.74 e-06	8.52 e-06	4.06 e-06	2.46 e-02
thyroid	2.66 e-05	6.82 e-05	8.25 e-06	2.10 e-05	9.82 e-06	1.03 e-05	7.31 e-06	1.06 e-04
heart	1.08 e-03	2.10 e-01	2.26 e-05	3.28 e-04	3.25 e-05	2.90 e-05	1.69 e-05	1.84 e-05
liver	2.55 e-04	1.94 e-04	2.16 e-04	1.26 e-02	3.45 e-04	4.13 e-05	1.52 e-04	9.82 e-06
lung	3.08 e-02	6.55 e-03	2.86 e-05	9.47 e-04	3.51 e-05	2.72 e-05	1.72 e-05	2.25 e-05
pancreas	1.57 e-04	3.45 e-05	1.29 e-03	2.84 e-04	5.83 e-02	1.38 e-03	7.84 e-04	6.73 e-06
skin	1.70 e-05	1.63 e-05	1.64 e-05	1.65 e-05	3.14 e-05	8.85 e-05	2.14 e-05	2.58 e-05
bladder	4.36 e-05	7.44 e-06	2.26 e-05	1.12 e-05	2.00 e-05	1.42 e-05	6.35 e-05	2.81 e-05
stomach	1.76 e-04	4.84 e-05	1.25 e-04	6.33 e-04	4.93 e-03	3.94 e-03	1.36 e-04	9.24 e-06
celebral cortex	8.06 e-06	9.12 e-06	6.45 e-06	9.67 e-06	7.12 e-06	4.75 e-06	3.80 e-06	4.40 e-02
vas deferens	3.40 e-05	3.61 e-06	1.95 e-05	1.01 e-05	1.78 e-05	1.37 e-05	4.75 e-05	2.03 e-06
small intestine	5.26 e-03	1.81 e-05	1.09 e-04	1.15 e-04	4.09 e-04	4.31 e-05	1.28 e-02	3.42 e-06
large intestine	5.28 e-03	1.48 e-05	2.44 e-04	4.83 e-05	3.28 e-04	5.63 e-05	1.13 e-02	3.73 e-06

Table 2: S-values organ-organ. Organs on the top are **targets**, organs on the left are the **sources**.

3.3 30 g mouse model

to modify

	lungs	heart	kidneys	liver	pancreas	spleen	intestine	brain
kidney	9.16 e-05	2.14 e-05	6.62 e-02	2.71 e-04	1.25 e-03	2.48 e-04	2.79 e-04	5.22 e-06
spleen	4.16 e-05	3.04 e-05	5.04 e-04	4.74 e-05	3.47 e-03	2.10 e-01	4.23 e-05	6.64 e-06
testicular	1.71 e-05	4.08 e-06	1.59 e-05	6.62 e-06	1.32 e-05	1.19 e-05	2.51 e-05	1.90 e-06
brain	1.11 e-05	1.49 e-05	4.65 e-06	1.05 e-05	5.74 e-06	8.52 e-06	4.06 e-06	2.46 e-02
thyroid	2.66 e-05	6.82 e-05	8.25 e-06	2.10 e-05	9.82 e-06	1.03 e-05	7.31 e-06	1.06 e-04
heart	1.08 e-03	2.10 e-01	2.26 e-05	3.28 e-04	3.25 e-05	2.90 e-05	1.69 e-05	1.84 e-05
liver	2.55 e-04	1.94 e-04	2.16 e-04	1.26 e-02	3.45 e-04	4.13 e-05	1.52 e-04	9.82 e-06
lung	3.08 e-02	6.55 e-03	2.86 e-05	9.47 e-04	3.51 e-05	2.72 e-05	1-72 e-05	2.25 e-05
pancreas	1.57 e-04	3.45 e-05	1.29 e-03	2.84 e-04	5.83 e-02	1.38 e-03	7.84 e-04	6.73 e-06
skin	1.70 e-05	1.63 e-05	1.64 e-05	1.65 e-05	3.14 e-05	8.85 e-05	2.14 e-05	2.58 e-05
bladder	4.36 e-05	7.44 e-06	2.26 e-05	1.12 e-05	2.00 e-05	1.42 e-05	6.35 e-05	2.81 e-05
stomach	1.76 e-04	4.84 e-05	1.25 e-04	6.33 e-04	4.93 e-03	3.94 e-03	1.36 e-04	9.24 e-06
celebral cortex	8.06 e-06	9.12 e-06	6.45 e-06	9.67 e-06	7.12 e-06	4.75 e-06	3.80 e-06	4.40 e-02
vas deferens	3.40 e-05	3.61 e-06	1.95 e-05	1.01 e-05	1.78 e-05	1.37 e-05	4.75 e-05	2.03 e-06
small intestine	5.26 e-03	1.81 e-05	1.09 e-04	1.15 e-04	4.09 e-04	4.31 e-05	1.28 e-02	3.42 e-06
large intestine	5.28 e-03	1.48 e-05	2.44 e-04	4.83 e-05	3.28 e-04	5.63 e-05	1.13 e-02	3.73 e-06

Table 3: S-values organ-organ. Organs on the top are **targets**, organs on the left are the **sources**.

3.4 35 g mouse model

to modify

	lungs	heart	kidneys	liver	pancreas	spleen	intestine	brain
kidney	9.16 e-05	2.14 e-05	6.62 e-02	2.71 e-04	1.25 e-03	2.48 e-04	2.79 e-04	5.22 e-06
spleen	4.16 e-05	3.04 e-05	5.04 e-04	4.74 e-05	3.47 e-03	2.10 e-01	4.23 e-05	6.64 e-06
testicular	1.71 e-05	4.08 e-06	1.59 e-05	6.62 e-06	1.32 e-05	1.19 e-05	2.51 e-05	1.90 e-06
brain	1.11 e-05	1.49 e-05	4.65 e-06	1.05 e-05	5.74 e-06	8.52 e-06	4.06 e-06	2.46 e-02
thyroid	2.66 e-05	6.82 e-05	8.25 e-06	2.10 e-05	9.82 e-06	1.03 e-05	7.31 e-06	1.06 e-04
heart	1.08 e-03	2.10 e-01	2.26 e-05	3.28 e-04	3.25 e-05	2.90 e-05	1.69 e-05	1.84 e-05
liver	2.55 e-04	1.94 e-04	2.16 e-04	1.26 e-02	3.45 e-04	4.13 e-05	1.52 e-04	9.82 e-06
lung	3.08 e-02	6.55 e-03	2.86 e-05	9.47 e-04	3.51 e-05	2.72 e-05	1-72 e-05	2.25 e-05
pancreas	1.57 e-04	3.45 e-05	1.29 e-03	2.84 e-04	5.83 e-02	1.38 e-03	7.84 e-04	6.73 e-06
skin	1.70 e-05	1.63 e-05	1.64 e-05	1.65 e-05	3.14 e-05	8.85 e-05	2.14 e-05	2.58 e-05
bladder	4.36 e-05	7.44 e-06	2.26 e-05	1.12 e-05	2.00 e-05	1.42 e-05	6.35 e-05	2.81 e-05
stomach	1.76 e-04	4.84 e-05	1.25 e-04	6.33 e-04	4.93 e-03	3.94 e-03	1.36 e-04	9.24 e-06
celebral cortex	8.06 e-06	9.12 e-06	6.45 e-06	9.67 e-06	7.12 e-06	4.75 e-06	3.80 e-06	4.40 e-02
vas deferens	3.40 e-05	3.61 e-06	1.95 e-05	1.01 e-05	1.78 e-05	1.37 e-05	4.75 e-05	2.03 e-06
small intestine	5.26 e-03	1.81 e-05	1.09 e-04	1.15 e-04	4.09 e-04	4.31 e-05	1.28 e-02	3.42 e-06
large intestine	5.28 e-03	1.48 e-05	2.44 e-04	4.83 e-05	3.28 e-04	5.63 e-05	1.13 e-02	3.73 e-06

Table 4: S-values organ-organ. Organs on the top are **targets**, organs on the left are the **sources**.

4 Considerations

We can observe a difference (max 1 odg) in many results respect to the reference article, probably due to the fact that the latter used Moby v.1 for the phantom generation, and MCNPX for the Montecarlo simulations, while we used Moby v.2 and GEANT4.

Indeed, most of the results are coherent between the two.

5 Conclusions

6 Appendix

References

[1] Tosato M.; Verona M.; Favaretto C.; Pometti M.; Zanoni G.; Scopelliti F.; Cammarata F.P.; Morselli L.; Talip Z.; van der Meulen N.P.; et al. "Chelation of Theranostic Copper Radioisotopes with S-Rich Macrocycles: From Radiolabelling of Copper-64 to In Vivo Investigation." In: *Molecules* (2022).

[2] Tianwu Xie and Habib Zaidi. "Monte Carlo-based evaluation of S-values in mouse models for positron-emitting radionuclides." In: *Phys. Med. Biol* (2013), pp. 169–183.