A preclinical simulated dataset of S-values and investigation of the impact of rescaled organ masses using the MOBY phantom

Theodora Kostou1, Panagiotis Papadimitroulas1,2, George Loudos3 and George C Kagadis1,4

1 Department of Medical Physics, School of Medicine, University of Patras, Rion, GR 26504, Greece
2 BET Solutions, 116 Alexandras Ave., Athens, GR 11472, Greece
3 Department of Biomedical Engineering, Technological Educational Institute of Athens, Ag. Spyridonos Street, Egaleo GR 12210, Greece
4 Department of Imaging Physics, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

E-mail: gkagad@gmail.com and George.Kagadis@med.upatras.gr

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Abstract
Nuclear medicine and radiation therapy, although well established, are still rapidly evolving, by exploiting animal models, aiming to define precise dosimetry in molecular imaging protocols. The purpose of the present study was to create a dataset based on the MOBY phantom for the calculation of organ-to-organ S-values of commonly used radionuclides. S-values of most crucial organs were calculated using specific biodistributions with a whole-body heterogeneous source. In order to determine the impact of the varying organs’ size on the S-values, and based on the fact that the anatomic properties of the organs are correlated with S-values, dosimetric calculations were performed by simulating the MOBY-version 2 model with different whole-body masses. The GATE Monte Carlo simulation toolkit was used for all simulations. Two mouse models of different body masses were developed to calculate the S-values of eight commonly used radioisotopes in nuclear imaging studies, namely 18F, 68Ga, 131I, 111In, 177Lu, and 99mTc, 90Y and 188Re. The impact of modified mass of the source organs in S-values was investigated with 18F, and 90Y in five different scalings of the source organs. Based on realistic preclinical exams, three mouse models, 22, 28 and 34 g, were used as input in the GATE simulator based on realistic preclinical exams to calculate the S-values of the six radioisotopes used. Whole body activity distributions were used as the source organ. The simulation procedure was validated in terms of extracting individual organ-to-organ S-values, and consequently
in calculating the new $S$-values using a heterogeneous activity distribution as a source. The calculation was validated with $^{18}$F source in a 30 g mouse model. For the generation of the new $S$-values with heterogeneous activity sources, four organs were used for the calculation of a single $S$-value. The absorbed doses per organ were compared with previously published reports. The validation procedure of $^{18}$F indicates discrepancies, ranging from 5.32 to 7.72%. The $S$-values in Gy/(Bq·s), with the corresponding uncertainties of all simulated cases, are given in the developed dataset. The comparison of the dosimetric calculations on the three different phantoms highlights the impact of the mouse model size on the calculated $S$-values. The developed dataset can be used to improve the accuracy of the absorbed dose calculations in small animal dosimetry and depict the crucial impact the mouse size has on $S$-values’ calculation. The generated $S$-values dataset for different radiopharmaceuticals contributes to the estimation of radiation dose to mice in small animal PET and SPECT exams. Finally, the detailed methodology of the procedure is provided.

Keywords: GATE, internal dosimetry, Monte Carlo, MOBY, $S$-values

(Some figures may appear in colour only in the online journal)

1. Introduction

Mice have been extensively used in preclinical research to develop and test new imaging and treatment methods for human diseases (Hanahan 1989, Deroose et al 2007, Tuveson et al 2011). As the use of radiopharmaceuticals in imaging and therapy is increasing, it becomes very important to achieve a higher level of accuracy in internal dosimetry on small animal studies as well. To obtain appropriate preclinical absorbed dose response–effect relationships, the absorbed dose must be determined as accurately as possible. Monte Carlo (MC) simulations combined with computational digital phantoms offer novel tools for absorbed dose calculation and the accurate anatomic description of the relevant species. The MOBY (mouse), and ROBY (rat) phantoms developed by Segars et al (2004) are based on non-uniform rational B spline (NURBS) mathematical models, allowing flexible manipulation of animal organs and body by defining a set of control points on each surface. Models are provided to the user as interactive programs allowing adaptive scaling of one or more selected organs.

Over the years many authors have used several simulation codes and developed human and animal, mathematical, and voxel-based models for dosimetry applications. More specifically, Bitar et al (2007a) simulated mono-energetic photon and electron sources using the MCNP4c2 (MCNP4C2 2001) MC Code. $S$-values were calculated for 16 beta- or beta–gamma emitting radionuclides, and for a large number of source-target combinations for a 30 g mouse. Hindorf et al (2004) studied the parameters that influence the $S$-value calculation in mouse models using geometric shapes, 10 organs were defined in voxel format for the estimation of self-absorbed dose and cross-absorbed dose. According to their study, organ mass and shape, as well as the source–target distance have a noticeable impact on dose estimation. Boutaleb et al (2009) calculated $S$-values with the N-particle MCNPX transport code and produced two three-dimensional (3D) segmented datasets of $S$-values. They compared the results, and assessed the impact of mouse models for preclinical dosimetry on targeted radionuclide therapy. The first dataset was developed using a mouse model created by Bitar et al (2007b), while
the second one originated using the Digimouse model (Dogdas et al 2007), which is based on a 28 g normal nude male mouse.

Absorbed fractions were established by Stabin et al (2006) at discrete energies for electron, and photon sources assumed to be uniformly distributed throughout 10 source and target regions in two realistic voxel-based models of a transgenic mouse and Sprague–Dawley rat, generated by a dedicated small-animal CT scanner. Mohammadi and Kinase evaluated the photon and electron specific absorbed fractions and $S$-values using mouse voxel phantoms and they investigated the effect of voxel size on $S$-values for some beta emitters such as $^{131}$I, $^{153}$Sm, $^{188}$Re and $^{90}$Y (Mohammadi et al 2011). Specific absorbed fractions and $S$-values were also evaluated by them in whole bodies and all organs of a voxel-based frog and rat models as the source was distributed in the whole body or skeleton (Mohammadi et al 2012). Konijnenberg et al also developed a stylized representation of Wistar rats and performed MC calculations to develop dose fractions (DFs) for several radionuclides (Konijnenberg et al 2004). Keenan et al also calculated specific absorbed fractions (SAFs) with internal photon and electron sources for voxel-based versions of scaled MOBY and ROBY models (Keenan 2010).

In another study, absorbed fractions, and $S$-values have been evaluated for preclinical assessments of radiopharmaceuticals using a mouse voxel model (Kinase et al 2011). More recently, Mauxion et al (2013) generated a 30 g mouse phantom based on the realistic hybrid model MOBY (version 1). Dosimetric calculations ($S$-values and specific absorbed fraction) were performed with two MC codes (MCNPX v2.7a and GATE v6.1) for $^{18}$F, demonstrating that the comparison between two ‘similar’ digital mice leads to different $S$-values. Moreover, a number of experiments have been conducted to assess the impact of organ mass variations on absorbed dose (Mauxion et al 2013). Xie et al already assessed variations in dosimetric characteristics as a function of total-body mass for several PET probes (Xie et al 2013).

In the current study, the major goal was to create a dataset based on realistic simulations of the dosimetric data with high accuracy, in terms of: (a) physics modeling using Geant4, and (b) mouse anatomy modeling using 4D-MOBY. The mouse models used in our study were created by the MOBY interactive scaling program developed by Segars et al (2004). The MOBY mouse model is based on a high-resolution 3D magnetic resonance microscopy (MRM) dataset for the formation of the organ/body surfaces. Using this tool, we produced voxel-based mouse models of varying masses to represent small animals commonly used in preclinical molecular imaging research. Commonly used radiopharmaceuticals were tested to create a large dataset of several organ-to-organ $S$-values in two different mouse sizes, often used in preclinical studies. A new methodology was validated and applied in order to calculate $S$-values from whole-body activity biodistributions as source organ for 6 commonly used radiopharmaceuticals, and three mouse models of different sizes (22, 28, 34 g). Furthermore, we extended the dosimetric calculations in order to investigate the impact level of the organ’s size on the $S$-value calculation by changing the size of specific organs for two different isotopes ($^{18}$F and $^{90}$Y).

2. Methods

2.1. The MOBY mouse computational phantom

The computational whole-body 4D MOBY mouse phantom combines the realism of a voxelized phantom with the flexibility of a mathematical phantom, based on NURBS (Segars et al 2004). The organ shapes are modeled with NURBS surfaces, widely used in 3D computer graphics to accurately describe complex 3D surfaces, providing the scientific community with a realistic model of the 3D mouse anatomy. This computational mouse phantom was used
in all simulations in the present study. The phantom’s accompanying software generates 3D voxelized representations of the mouse anatomy at any user-defined resolution, which can be used as an attenuation and/or emission map in the GATE MC platform (Branco et al 2011). The phantom raw data generated by the MOBY software were transformed into interfile format (uint16).

2.1.1 MOBY models used in S-values calculation using whole-body biodistributions. In order to study the extraction of S-values using specific radiotracer biodistributions, activity maps from literature biodistribution studies were inserted in MOBY (table 1).

Three different mouse models based on MOBY were used, representing typically used mice in preclinical research; 22, 28, and 34 g, respectively, taking as output the 3D dose maps. The three different body masses were produced by modifying all the scaling parameters at 0.9, 0.955 and 1.0, respectively, of their baseline values in the interactive program file. The organ masses for each model are presented in table 2.

All three mouse models were exported in voxelized format in a $70 \times 70 \times 220$ matrix with a 0.5 mm cubic voxel size. The resulting organs and body masses were calculated by multiplying each organ volume with its corresponding density.

2.1.2 MOBY models used in organ-to-organ S-values calculation. In order to be independent of the applied radiopharmaceuticals specific biodistributions, organ-to-organ S-values were extracted for 8 isotopes ($^{18}$F, $^{68}$Ga, $^{131}$I, $^{111}$In, $^{177}$Lu, $^{99m}$Tc, $^{90}$Y and $^{188}$Re) using 2 mouse models (28 and 34 g, respectively). The organ masses are reported in table 2. Densities and material compositions used in this dataset are defined in the International Commission on
Radiological Protection (ICRP 2002). For the applied simulations, particle histories are \( \sim 10^8 \), resulting in relative statistical uncertainties lower than 2% for all the extracted organ-to-organ \( S \)-values.

2.2. GATE Monte Carlo toolkit

This study was conducted on GATE v6.1, which has been extended for radiotherapy and dosimetry applications (Jan et al 2004, Jan et al 2011, Sarrut et al 2014). The model used for simulating physical processes is the ‘Standard’ one of Geant4 v9.4 (GEANT4 2010). GATE’s default model describes electron and photon interactions at energies ranging from 1 keV to 100 TeV. All the appropriate electromagnetic physical processes (photoelectric effect, Compton, Bremsstrahlung, positron-electron annihilation) were included in the performed simulations. The Rayleigh process was simulated using the Penelope model (Salvat et al 2011), which is the only available option in the current release of Geant4. No energy cuts or variance reduction techniques (VRTs) were applied in the physical processes to speed-up the simulations, as it wasn’t on our aim to study parameters that would increase the statistical precision with the VRTs. Instead, we used the GATElab grid to reach as realistic results as possible (in terms of statistics). Voxel-based mouse geometry was implemented with the ‘CompressedMatrix’ option while the deposited energy was scored at the voxel level of the phantom with ‘DoseActor \( E_{dep} \)’. Statistical uncertainties were calculated using ‘Uncertainty\( E_{dep} \) DoseActor’. The size of DoseActor matched the phantom’s matrix. All simulations were carried out in the GateLab grid with 500 Central Processing Units (CPUs) used in parallel mode for each simulation (Camarasu-Pop et al 2013). We extracted the deposited energy of each organ using Matlab and Statistics Toolbox Release 2014a (The MathWorks Inc. Natick, MA, USA).

2.3. Internal dosimetry/absorbed dose

The MIRD schema (Bolch 2009) for internal dosimetry was used in the current study to calculate \( S \)-values and absorbed doses. The mean absorbed dose is given by:

\[
D(r_T, T_D) = \sum_n \int_0^{T_D} A(r_S, t) S(r_T \leftrightarrow r_S) dt ,
\]

where \( A(r_S, t) \) is the cumulative activity in source tissue \( r_S \) over dose integration period \( T_D \).

| Organ  | Mass (g) 22 | Mass (g) 28 | Mass (g) 34 |
|--------|-------------|-------------|-------------|
| Lung   | 0.122       | 0.142       | 0.159       |
| Liver  | 1.787       | 2.160       | 2.385       |
| Kidneys| 0.330       | 0.391       | 0.451       |
| Brain  | 0.573       | 0.674       | 0.679       |
| Marrow | 0.819       | 1.049       | 1.295       |
| Thyroid| 0.015       | 0.015       | 0.019       |
| Total mass | 22         | 28          | 34          |
The $S$-value is defined as the product of the emitted energy per disintegration and the absorbed fraction for the given combination of source and target regions, for the type of radiation emitted, divided by the mass of the target region (equation (3)).

$$S(r_T \leftarrow r_S) = \sum_{n} n_i E_i \varphi_{r_S \leftarrow r_T},$$  \hspace{1cm} (3)

where $n_i$, $E_i$, and $\varphi_{r_S \leftarrow r_T}$ are the number of nuclear transitions per nuclear transformation, the energy per radiation, and the absorbed fraction, respectively.

2.4. Validation of $S$-values calculations

The validation of $S$-value calculation was established in two different steps. Initially, the verification of extracted $S$-values was performed in accordance to the 30 g mouse model reported by Keenan et al (2010). We modified the original MOBY (version 2) model by inserting a $^{18}$F source in several organs to extract $S$-values for a variety of source-to-target organ combinations. Densities and material compositions were defined for air, lungs, bones, and soft tissues, based on the study of Cristy and Eckerman (1987), so as to be directly comparable to the work of Keenan et al (2010). The phantom was generated as a 3D rectangular matrix of $45 \times 45 \times 162$ voxels with a voxel size of $0.625 \times 0.625 \times 0.625$ mm$^3$ in full exhale respiratory phase. The organ masses used for $S$-values calculations matched to those in the study of Keenan’s et al with discrepancies lower than 0.74%. However, the rest of the organs within the mouse model reached larger mass differences of ~30% (table 3).

As shown in table 3, large differences in the organ masses are presented for brain, heart, lungs, intestines and skeleton because of the different MOBY versions (e.g. not being allowed to control the volume of these organs in MOBY version 2). The validation procedure was applied to four basic organs (kidneys, spleen, pancreas, and liver) that the two mouse models had similar organ masses with differences lower than 1%. Table 4 presents the qualitative differences between the two MOBY phantom versions for some anatomical and functional characteristics.

Secondly, we validated the procedure of extracting $S$-values in different organs using heterogeneous source distributions, as shown in table 1. We executed a single simulation, with different activities in four separate organs calculating the $S$-value and the absorbed dose in these four target organs. In this simulation we took into account the self-absorbed dose per organ plus the absorbed dose from the other three organs, respectively. Consequently, we used Keenan et al’s (2010) extracted $S$-values to calculate the absorbed dose on these four single organ-targets, using the four corresponding $S$-values of the organ-sources.

More specifically, absorbed doses for $^{18}$F were calculated simulating a 30 g whole-body mouse that had a heterogeneous source distribution with activity in kidneys, spleen, pancreas, and liver. The deposited energy was calculated in these four target organs using a 3D dose map while the $S$-value for each organ was extracted with the aid of equation (3). For validation purposes, we inserted the same activity (as in our simulation) in the $S$-values reported in
Kennan’s study and we summed the absorbed dose of every one of the four $S$-values with the same target. The absorbed doses results were compared to the absorbed doses resulting from our simulated extracted $S$-values.

The validation of this procedure was extended using two of our mouse models (28 and 34 g) and calculating the absorbed doses in four organs with the two methods: (a) using organ-to-organ $S$-values and summing the absorbed doses, and (b) using the $S$-values extracted from heterogeneous sources with these four organs having activity in one simulation.

3. Results

3.1. Radionuclide $S$-values

Calculated $S$-values for all the studies with specific biodistributions (heterogeneous sources) of six radiotracers and for the three mouse models are presented in the appendix (tables A1(a) and (b)), accompanied by their respective statistical uncertainties, as they were calculated in GATE. 3D dose maps were created as output for each study. The dosimetric results were compared for the three different mouse models for the same radiopharmaceutical each time. Small,
but noticeable, differences are observed between the three models, demonstrating that their differing size has an effect. More specifically, the S-values demonstrated differences between 0.41%–50.00% for the 22, 28 and 34 g mouse models. The smallest difference (0.41%) was reached in 111In-DTPA for brain examination for a 15.04% mass difference, while the biggest one (50%) was observed in the 99Tc-HMPAO for thyroid examination for a 0.52% mass difference.

S-values with homogenous sources for various combinations of source and target organs for 28 and 34 g mouse models are presented in the appendix (tables A2(a)–(h)). Each table displays the calculated S-values of all organs for one radiotracer. The statistical uncertainty of all the S-values results was kept lower than 2%.

### 3.2. Validation of S-values calculation

Calculated S-values for several source and target organs are compared in table 5, showing good agreement. Calculations were obtained using MOBY (version 2) in GATE (this study), and values published by Keenan et al (2010). All statistical uncertainties were kept below 2% for all studied organs. We extracted our model by modifying the organs of interest in order to have the same volume and organ mass (in g). However, due to the different mouse anatomy of the two models, there are organs that had larger variations (i.e. lungs 31%, intestine 29%, and heart 30%), meaning there is no available way of modifying their masses and having total body mass equal to 30 g. The self-absorbed S-values results seem to be in good agreement with differences varying between 5–8%. In general, the cross-organ S-values reported differences ranging from 0.5–20%, while larger differences were reported in the cross organ S-values between the kidneys and liver with differences ranging 20–32%. The exported differences are considered reasonable and may be attributed to the fact that the impact of the stomach content and the large difference in the intestine masses should be taken into account for specific organs. Such differences were previously reported in the literature and attributed to the interposition of such organs (Mauxion et al 2013).

In order to quantify the effect of the organ mass on the extracted S-values an extra study was carried out to investigate the impact of rescaled organ masses on S-values, which is reported in section 3.3.

| Target organ | Model       | Organ mass (g) | S-values (Gy/Bq·s) | Source organ |
|--------------|-------------|----------------|-------------------|--------------|
|              |             |                | Kidneys          |              |
| Kidneys      | Current study | 0.376          | 8.93E–11         | 1.20E–12     |
|              | Keenan et al | 0.374          | 9.68E–11         | 1.26E–12     |
|              | Difference  | 0.534          | –7.74            | –4.79        |
| Spleen       | Current study | 0.137          | 1.24E–12         | 2.34E–10     |
|              | Keenan et al | 0.136          | 1.25E–12         | 2.56E–10     |
|              | Difference  | 0.735          | –0.44            | –8.59        |
| Pancreas     | Current study | 0.376          | 2.52E–12         | 4.17E–12     |
|              | Keenan et al | 0.378          | 2.34E–12         | 3.61E–12     |
|              | Difference  | –0.476         | 7.84             | 15.53        |
| Liver        | Current study | 2.147          | 5.60E–13         | 1.95E–13     |
|              | Keenan et al | 2.150          | 4.22E–13         | 2.31E–13     |
|              | Difference  | –0.102         | 32.70            | –15.74       |

Table 5. S-values for 18F using MOBY in the current study and the respective S-values from the Keenan et al study. Differences of self-absorbed S-values are highlighted in bold.
The validation procedure results for S-value calculation with heterogeneous sources and S-values extracted using organ-to-organ (source-to-target) are presented in table 6. Table 6 presents S-values (Gy/Bq·s) and absorbed doses (mGy) for the 30 g mouse model using our extracted S-values with a heterogeneous activity distribution within the body. The third column contains the absorbed doses results from the S-value extracted for each individual organ, taking into account a single organ source. The absorbed dose was calculated multiplying each S-value with the administered activity used in our simulation, taking into account the activity of all four of the sources. Lastly, the comparison of the absorbed doses in mGy resulted from the calculated S-values, and from Keenan’s S-values for heterogeneous and homogenous sources, respectively, is presented in percentage difference. The difference of the organ masses is already reported in table 5. The differences between the two approaches (our study and Keenan’s et al study) are in the range of 5–8%, which is acceptable according to the variations of the S-values reported in table 5.

The procedure of extracting S-values using heterogeneous sources, with several organsources in a single simulation was further validated using two of our mouse models (28 and 34 g). Thus, we compared the absorbed doses in (mGy) resulting from four identical S-values (organ-to-organ) with the absorbed doses resulting from the S-value of a heterogeneous source (four source organs in one simulation). The dose results are presented in tables 7 and 8 for the 28 and 34 g mouse models, respectively.

### Table 6. Comparison of absorbed doses (mGy) for the 30 g mouse model, extracted from the heterogeneous biodistribution S-values (our study), and from organ-to-organ S-values in Keenan’s et al study (taking into account as source: kidneys, spleen, pancreas and liver).

| Target organ | Mass (g) | Activity/organ (Bq) | Absorbed dose (mGy) heterogeneous source distribution S-values (our S-values) | Absorbed dose (mGy) Keenan et al (2010) S-values | Difference % |
|--------------|---------|---------------------|-------------------------------------------------|-----------------------------------------------|-------------|
| Kidneys      | 0.37    | 1150                | 7.24                                            | 7.65                                          | −5.32       |
| Spleen       | 0.13    | 3466                | 51.40                                           | 55.55                                         | −7.47       |
| Pancreas     | 0.37    | 1178                | 7.66                                            | 8.31                                          | −7.72       |
| Liver        | 2.14    | 11920               | 12.68                                           | 13.6                                          | −6.71       |

### Table 7. S-values (Gy/Bq-s), and absorbed doses (mGy) for the 28 g mouse model, extracted from the heterogeneous biodistribution using the primaries emitted from all the sources.

| Target organ | Mass (g) | Activity/organ (MBq) | Absorbed dose (mGy) heterogeneous source distribution | Absorbed dose (mGy) from combined organ-to-organ S-values | Difference % |
|--------------|---------|----------------------|-------------------------------------------------------|----------------------------------------------------------|-------------|
| Liver        | 2.16    | 80.28                | 1.36                                                  | 1.36                                                     | 0.15        |
| Lungs        | 0.14    | 9.81                 | 1.13                                                  | 1.16                                                     | 2.50        |
| Kidneys      | 0.20    | 67.74                | 10.94                                                 | 10.90                                                    | 0.38        |
| Spleen       | 0.14    | 6.02                 | 1.44                                                  | 1.44                                                     | 0.07        |

#### 3.3. Investigation of S-values with rescaled organ masses

In order to investigate the impact of different organ masses on the calculated S-values we used a 28 g mouse model for two isotopes, $^{18}$F and $^{90}$Y. A group of simulations were executed...
rescaling one organ every time, which was set as the organ-source. We studied the effect on three separate organs (liver, kidney, spleen) and extracted the S-values for each individual case. The S-values for each of the 3 organs were calculated for five different source-organ masses. Figures 1(a)–(c) and 2(a)–(c) present the S-value differentiation for rescaled liver, kidney, and spleen as a source every time for 18F and 90Y, respectively. The mass details of the studied organs are gathered in table 9. For the organ rescaling the parameters ‘vol_liver’, ‘vol_rkidney, vol_lkidney’ and ‘vol_spleen’ were modified in the interactive program so as to keep the rest of the organ masses constant.

Figures 1 and 2 give a clear indication that the rescaling of a source organ affects the self-organ calculated S-values for 18F and 90Y. In Figure 3 we depict the differences in self-absorbed S-values due to organ-source mass scaling for the two isotopes. In order to present comparable results, we have normalized the extracted S-values to the maximum for each organ, as well as the masses of the different organs. In the case of 18F, when rescaling liver and spleen sources we notice that the effect on the target organs S-values is not big. More specifically, rescaling the liver has a maximum difference of 19% in the kidney’s (target) and 12% in the spleen’s (target) calculated S-values, while rescaling the spleen has a maximum difference of 29% in the kidney’s (target) and 0.9% in the liver’s (target) calculated S-values. In contrast there is a high variation in the S-values of the liver and spleen (as targets) when the kidneys act as the

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**Table 8.** S-values (Gy/Bq·s), and absorbed doses (mGy) for the 34 g mouse model, extracted from the heterogeneous biodistribution using the primaries emitted from all the sources.

| Target organ | Mass (g) | Activity/organ | Absorbed dose (mGy) from heterogeneous source distribution | Absorbed dose (mGy) from combined organ-to-organ S-values | Difference % |
|--------------|---------|----------------|-------------------------------------------------|-------------------------------------------------|-------------|
| Liver        | 2.49    | 73.15          | 1.08                                           | 1.08                                            | 0.28        |
| Lungs        | 0.16    | 8.64           | 0.90                                           | 0.92                                            | 2.28        |
| Kidneys      | 0.45    | 61.36          | 4.49                                           | 4.48                                            | 0.22        |
| Spleen       | 0.16    | 5.41           | 1.15                                           | 1.14                                            | 0.44        |

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Figure 1. Trend of S-values in three organs (liver, kidneys, spleen) when scaling; (a) the liver’s mass, (b) the kidneys’ mass, and (c) the spleen’s mass for 18F.

Figure 2. Trend of S-values in three organs (liver, kidneys, spleen) when scaling; (a) the liver’s mass, (b) the kidneys’ mass, and (c) the spleen’s mass for 90Y.
source. That could explain the high differences that were noticed in the validation procedure between liver and kidneys (table 5). For the $^{90}$Y study, liver rescaling has a maximum difference of 19% in the kidney’s (target), and 84% in the spleen’s (target) calculated $S$-values, while spleen rescaling has a maximum difference of 64% in the kidney’s (target), and 21% in the liver’s (target) calculated $S$-values. The effect on the target organs $S$-values is similar to the one reported for the $^{18}$F when rescaling kidneys.

4. Discussion

GATE MC simulations have the advantage of precise physics modeling based on the Geant4 code, while the MOBY phantom can produce realistic imaging data to serve as a gold standard (Segars et al 2007). Animal dosimetry gains continuously increased interest as molecular imaging is applied in new domains (e.g. nanotechnology, theranostics) as a standard tool for studying the biodistribution of novel biomolecules or molecular mechanisms (Jan et al 2011). The detailed study of all parameters on the applied protocols is required, to assess possible effects on results interpretation. The current trend is toward repeated studies in small animals and minimization of injected dose, thus dosimetry needs to be as accurate as possible. The choice of the radionuclide used or radiopharmaceutical can lead to significant differences and the standardization of a methodology for in silico dose assessment can provide an accurate estimation when designing in vivo protocols.

In the current study three MOBY mouse models were used; 22, 28 and 34 g respectively, based on real preclinical specific biodistributions to calculate the $S$-values of six radiotracers ($^{18}$F-FDG, $^{68}$Ga-RGD, Free-$^{131}$I, $^{177}$Lu-TETULOMAB, $^{111}$In-DTPA, and $^{99m}$Tc-HMPAO). Whole body activity distributions were used as the source organ. Calculated $S$-values’ differences were observed for 22 and 28 g mouse models, as well as 28 and 34 g mouse models, respectively. More specifically, for $^{18}$F, a difference of 2.08% was observed between the 22 and 28 g mouse models for the brain, while for the 28 and 34 g mice a 16.96% difference was reached for the same organ. Moreover, in the $^{68}$Ga-RGD study the biggest difference (27.28%) was observed for the brain organ on the 22 and 28 g mouse models. For brain, in

| Source organ | Mass (g) |
|--------------|----------|
| Liver        | 1.08     | 1.51     | 2.16     | 2.81     | 3.21     |
| Kidneys      | 0.10     | 0.14     | 0.20     | 0.26     | 0.30     |
| Spleen       | 0.07     | 0.09     | 0.13     | 0.18     | 0.20     |

Figure 3. Change of self-absorbed $S$-values in three organs (liver, kidneys, spleen) when scaling their masses with (a) $^{18}$F, and (b) $^{90}$Y.
the $^{111}$In-DTPA, an $S$-value difference of 0.41% was observed for mass difference of 15.04%, and 17.09% for mass difference of 0.69%. For $^{177}$Lu discrepancies of 3.68% and 6.9% were reached for 0.52% and 18.65% thyroid mass differences. The biggest difference (50%) was reached in the $^{99}$Tc-HMPAO examination for a 0.52% thyroid mass difference. The reported $S$-values calculated differences due to the rescaling of the MOBY model, are in line with previous reported differences that were calculated in organ-to-organ $S$-values for rescaled mouse models (Xie et al 2013).

An extensive validation procedure was applied in order to standardize the extraction of $S$-values using heterogeneous sources. Absorbed doses in several organs were extracted using $S$-values from previous studies and compared to the ones calculated in our study with multiple sources in every simulation. The results showed good agreement with differences of ~10%. Moreover, we compared the two methods (doses from organ-to-organ $S$-values, and doses from $S$-values with multiple sources) using the exact same mouse model (in anatomy and volumetry). The two approaches showed differences lower than 2.5%.

Despite the $S$-values extracted for the provided biodistributions, $S$-values were also extracted for eight individual organs using 8 commonly used radioisotopes. The $S$-values were calculated for two different mice (total body mass 28 and 34 g, respectively).

Taking into account the literature currently available (Larsson et al 2007, Boutaleb et al 2009, Xie et al 2013) those differences are within the acceptable limits. They can be attributed to the comparison of a single modeled mouse (MOBY), with original data derived either from one mouse with a known weight or from an average weight from a mice population. However, it would not be possible to know in advance the exact dimensions of all organs in a real mouse.

In the present study we tried to quantify the impact of the organ rescaled masses on the calculated $S$-values for two isotopes. It is worth noting that there is an absolute correlation on the self-organ $S$-values, when rescaling the organ source, irrespective of the organ and the radioisotope. The effect and the variations on the cross organ $S$-values are not so clear, as it seems that the whole anatomy of the mouse should be taken into account. Large variations are noticed when rescaling the kidneys (source) and the liver (target) $S$-value for both isotopes ($^{18}$F and $^{90}$Y). In this case, rescaling the kidneys’ mass (two organs in different locations), there are differentiations on the target organ $S$-values reaching ~80%. It is expected that the position (anatomy) of each organ and the spectrum of each isotope might also impact the extracted $S$-values and should be further investigated. Furthermore, when rescaling the spleen mass, similar behavior was observed in all three of the target organs for both isotopes. The spleen is smaller organ than the liver, with simpler geometry than the two kidneys, which indicates that the impact of the spleen mass could be more easily correlated with cross organ $S$-values calculation than more complicated organs.

A step forward would be the use of SPECT/CT (or PET/CT) data and the modification of the standard MOBY phantom to match the exact anatomy of a given mouse. In that way, it would be possible to compare the simulated dosimetric data with better accuracy. This is beyond the aims of the current study, but could present a future research path. Our aim was to provide a more general methodology, which can give a good estimation of the expected dose in various organs for a given source. Using a standard database of organ-to-organ $S$-values for several radioisotopes or even with known $S$-values for specific radiopharmaceutical’s distributions (heterogeneous source), each specimen could be categorized on a specific group of mice, according to its anatomical characteristics. Thus, an estimation of the absorbed dose per organ could be derived using the pre-calculated $S$-values from the database. Highest accuracy could be applied and have a full correlation between the $S$-values, and the anatomical features of the
specimen, as there would not be any assumptions of the organ masses (such as categorizing the mouse on a specific wide group).

This is an ongoing study, and we are currently investigating more radiopharmaceuticals in more models, calculating $S$-values considering more organs as emitting sources. The impact of cardiac and respiratory motion in the absorbed dose of specific organs can be also investigated to quantify the effect on the $S$-values calculation, when the size and the position of the organs are modified. The ultimate goal would be the extension of this dataset into a freely available database, which will need to be properly designed and implemented, to set the requirements for including similar data from other contributors.

5. Conclusion

An $S$-value dataset of commonly used radiopharmaceuticals is presented using the MOBY (version 2) digital phantom and the GATE MC toolkit. Small variations in mice anatomy can result in significant differences in dose calculations, which could lead to the assumption that there is no standard model that can be used as a reference for dosimetry studies. More specifically, there could not be a specific mouse model with standardized organs and anatomy to implement dosimetry for murine studies in general. Nevertheless, extracting $S$-values for several organs with a mouse model can be useful if the dependency of the organ mass and absorbed dose is known. In order to assess the dose in a preclinical study, somebody will need information on the mouse anatomy and volumetry information (e.g. microCT information) combined with the $S$-values. Furthermore, a significant need for dosimetric data for small animal nuclear imaging studies is apparent. In the current study, we provide the community with the $S$-values calculated using whole body heterogeneous biodistributions of commonly used radioisotopes in nuclear medicine, after validating this procedure.

Organ-to-organ (source-to-target) $S$-values are also provided for two mouse models with known organ masses and for eight different radioisotopes. The impact of the size model was also investigated, for three source organs that were scaled in five different sizes. According to the scaling of the source organ there is a standard correlation regarding the self-absorbed $S$-values, while rather high variations resulted on the target-organs $S$-values. According to the present study it is clear that accurate definition of the organ mass is a crucial parameter for murine dosimetry. Thus microCT data seem to be necessary in order to have accurate volumetric details of each organ. Furthermore, it is also clear that the whole anatomy of the mouse has an effect on the extraction of $S$-values, which reaches 10%. This could also be the reason that in the case of rescaling the kidneys, which are in two locations within the body, there is no correlation between the target $S$-values. Next step of this study would be to extensively correlate the calculation of the $S$-values with the mass of several organs, the specified anatomy, and the used radioisotope (energy spectrum), so as to reach more accurate dosimetry data for any kind of mice.

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## Appendix

### Table A1.
(a) $S$-values (Gy/Bq-s) for whole body source for $^{18}$F-FDG, $^{68}$Ga-RGD and $^{111}$In-DTPA for the 22, 28, and the 34 g mouse models—relative statistical uncertainties are given in parentheses ($\pm$%). (b) $S$-values (Gy/Bq-s) for whole body source for $^{177}$Lu-TETULOMAB, $^{99m}$Tc-HMPAO and $^{131}$I for the 22, 28, and the 34 g mouse models—relative statistical uncertainties are given in parentheses ($\pm$%).

| TARGET | $^{18}$F-FDG | $^{68}$Ga-RGD | $^{111}$In-DTPA |
|--------|--------------|---------------|-----------------|
|        | 22 g | 28 g | 34 g | 22 g | 28 g | 34 g | 22 g | 28 g | 34 g |
| Lung   | 2.29E – 12 | 2.00E – 12 | 1.69E – 12 | 3.59E – 12 | 3.18E – 12 | 2.72E – 12 | 1.11E – 12 | 9.51E – 13 | 8.24E – 13 |
|        | (3.5) | (4.19) | (3.76) | (2.79) | (0.87) | (0.78) | (4.08) | (4.47) | (4.50) |
| Liver  | 2.23E – 12 | 1.94E – 12 | 1.71E – 12 | 1.30E – 11 | 1.18E – 11 | 1.06E – 11 | 4.03E – 12 | 3.35E – 13 | 3.04E – 12 |
|        | (3.00) | (3.69) | (3.2) | (1.29) | (0.41) | (0.36) | (1.79) | (1.98) | (1.98) |
| Kidney | 8.54E – 12 | 7.40E – 12 | 6.18E – 12 | 1.36E – 11 | 1.23E – 11 | 1.05E – 11 | 4.18E – 12 | 3.46E – 12 | 2.99E – 12 |
|        | (1.58) | (1.94) | (1.69) | (1.29) | (0.41) | (0.36) | (1.81) | (2.01) | (2.03) |
| Brain  | 2.43E – 12 | 2.38E – 12 | 1.98E – 12 | 3.96E – 13 | 2.88E – 13 | 2.32E – 13 | 9.21E – 14 | 9.18E – 14 | 7.64E – 14 |
|        | (2.78) | (3.42) | (3.01) | (7.87) | (3.15) | (2.77) | (11.1) | (11.90) | (12.06) |
| Marrow | 7.95E – 13 | 6.81E – 13 | 5.71E – 13 | 1.57E – 12 | 1.36E – 12 | 1.10E – 12 | 3.43E – 13 | 2.23E – 13 | 2.38E – 13 |
|        | (5.78) | (7.8) | (6.32) | (4.42) | (1.65) | (1.34) | (6.89) | (7.79) | (7.91) |
| Thyroid| 4.95E – 13 | 4.35E – 13 | 3.58E – 13 | 1.30E – 12 | 1.23E – 12 | 1.01E – 12 | 1.92E – 13 | 1.61E – 13 | 1.42E – 13 |
|        | (6.9) | (9.03) | (7.35) | (4.25) | (1.19) | (1.19) | (7.9) | (8.68) | (8.72) |

| TARGET | $^{177}$Lu-TETULOMAB | $^{99m}$Tc-HMPAO | $^{131}$I |
|--------|----------------------|------------------|---------|
|        | 22 g | 28 g | 34 g | 22 g | 28 g | 34 g | 22 g | 28 g | 34 g |
| Lung   | 4.39E – 12 | 3.71E – 12 | 3.18E – 12 | 4.66E – 12 | 3.86E – 12 | 2.69E – 12 | 7.32E – 13 | 6.47E – 13 | 5.54E – 13 |
|        | (1.42) | (1.75) | (1.57) | (2.14) | (3.01) | (0.58) | (5.29) | (4.19) | (4.01) |
| Liver  | 8.78E – 12 | 7.34E – 12 | 6.63E – 12 | 6.90E – 12 | 5.66E – 13 | 4.33E – 13 | 9.79E – 13 | 8.69E – 13 | 7.62E – 13 |
|        | (0.75) | (0.95) | (0.83) | (4.56) | (5.47) | (1.03) | (5.22) | (4.10) | (3.93) |
| Kidney | 5.79E – 12 | 4.83E – 12 | 4.16E – 12 | 2.52E – 12 | 2.05E – 12 | 1.47E – 12 | 8.92E – 13 | 8.03E – 13 | 6.75E – 13 |
|        | (0.96) | (1.21) | (1.05) | (2.42) | (2.83) | (0.57) | (4.00) | (3.15) | (3.03) |
| Brain  | 4.91E – 14 | 5.36E – 14 | 4.31E – 14 | 6.02E – 13 | 5.88E – 13 | 4.14E – 13 | 3.49E – 13 | 3.10E – 13 | 2.81E – 13 |
|        | (10.59) | (11.25) | (9.9) | (4.52) | (5.25) | (1.07) | (6.63) | (5.33) | (4.98) |
| Marrow | 1.46E – 13 | 1.26E – 13 | 1.15E – 13 | 3.56E – 13 | 2.89E – 13 | 2.08E – 13 | 5.65E – 13 | 4.47E – 13 | 3.40E – 13 |
|        | (8.51) | (10.9) | (8.47) | (7.55) | (8.9) | (1.7) | (7.66) | (6.22) | (5.96) |
| Thyroid| 1.92E – 14 | 1.85E – 14 | 1.72E – 14 | 6.22E – 14 | 4.69E – 14 | 3.13E – 14 | 7.86E – 10 | 6.87E – 10 | 5.91E – 13 |
|        | (9.20) | (10.45) | (8.87) | (9.13) | (9.25) | (2.63) | (0.13) | (0.10) | (0.10) |
Table A2. S-values for several source and target organs for $^{18}$F, $^{68}$Ga, $^{131}$I, $^{111}$In, $^{177}$Lu, $^{99m}$Tc, $^{90}$Y and $^{188}$Re for the 28 g and the 34 g mouse models.

(a) $^{18}$F S-values (Gy/Bq·s)

| Source-organ | 28 g | Heart | Liver | Lung | Kidneys | Spleen | Testses | Brain | Thyroid |
|--------------|------|-------|-------|------|---------|--------|---------|-------|---------|
| Heart        | 28 g | 1.22E−10 | 2.7E−13 | 2.02E−12 | 3.49E−14 | 4.27E−14 | 6.94E−15 | 3.05E−14 | 8.45E−14 |
| Liver        | 34 g | 9.60E−11 | 2.84E−13 | 1.72E−12 | 3.27E−14 | 3.98E−14 | 6.67E−15 | 2.90E−14 | 8.08E−14 |
| Lung         | 28 g | 7.49E−13 | 1.62E−11 | 1.20E−12 | 5.94E−13 | 1.96E−13 | 2.97E−14 | 4.42E−14 | 8.57E−14 |
| Kidneys      | 34 g | 7.46E−13 | 1.42E−11 | 1.05E−12 | 5.16E−13 | 1.79E−13 | 2.70E−14 | 4.04E−14 | 7.87E−14 |
| Spleen       | 28 g | 4.00E−12 | 1.07E−12 | 1.08E−10 | 1.04E−13 | 1.10E−13 | 1.62E−14 | 8.85E−14 | 2.33E−13 |
| Testes       | 34 g | 4.90E−12 | 9.51E−13 | 9.79E−11 | 9.59E−14 | 1.00E−13 | 1.49E−14 | 8.06E−14 | 2.14E−13 |
| Brain        | 28 g | 1.91E−13 | 1.20E−12 | 2.34E−13 | 1.59E−10 | 2.45E−12 | 1.07E−13 | 5.05E−14 | 7.82E−14 |
| Thyroid      | 34 g | 1.98E−14 | 5.39E−13 | 1.10E−13 | 7.22E−11 | 1.04E−12 | 5.05E−14 | 2.37E−14 | 3.64E−14 |

(b) $^{68}$Ga S-values (Gy/Bq·s)

| Source-organ | 28 g | Heart | Liver | Lung | Kidneys | Spleen | Testses | Brain | Thyroid |
|--------------|------|-------|-------|------|---------|--------|---------|-------|---------|
| Heart        | 28 g | 1.73E−10 | 1.67E−12 | 8.82E−12 | 3.38E−14 | 3.77E−14 | 6.65E−15 | 2.86E−14 | 8.30E−14 |
| Liver        | 34 g | 1.41E−10 | 1.55E−12 | 7.62E−12 | 3.19E−14 | 3.62E−14 | 6.16E−15 | 2.70E−14 | 7.83E−14 |
### 68Ga S-values (Gy/Bq·s)

| Target     | model | Heart         | Liver          | Lung          | Kidneys       | Spleen        | Testes        | Brain         | Thyroid       |
|------------|-------|---------------|----------------|---------------|---------------|---------------|---------------|---------------|---------------|
| Liver      | 28 g  | 4.50E−12      | 3.63E−11       | 5.63E−12      | 2.90E−12      | 1.85E−13      | 2.81E−14      | 4.11E−14      | 8.29E−14      |
|            | 34 g  | 4.08E−12      | 3.20E−11       | 4.90E−12      | 2.48E−12      | 1.69E−13      | 2.56E−14      | 3.78E−14      | 7.63E−14      |
| Lung       | 28 g  | 2.14E−11      | 5.04E−12       | 1.19E−10      | 1.01E−13      | 9.91E−14      | 1.56E−14      | 8.28E−14      | 2.67E−13      |
|            | 34 g  | 1.80E−11      | 4.39E−12       | 1.08E−10      | 9.26E−14      | 9.27E−15      | 1.40E−14      | 7.64E−14      | 2.34E−13      |
| Kidneys    | 28 g  | 1.87E−13      | 5.90E−12       | 2.30E−13      | 3.00E−10      | 1.95E−11      | 1.01E−13      | 4.74E−14      | 7.51E−14      |
|            | 34 g  | 8.77E−14      | 2.59E−12       | 1.07E−13      | 1.38E−10      | 8.27E−12      | 4.79E−14      | 2.23E−14      | 3.54E−14      |
| Spleen     | 28 g  | 1.18E−13      | 2.08E−09       | 1.26E−13      | 1.00E−11      | 3.71E−10      | 4.01E−14      | 2.69E−14      | 4.33E−14      |
|            | 34 g  | 1.07E−13      | 1.88E−13       | 1.15E−13      | 8.28E−12      | 3.36E−10      | 3.61E−14      | 2.51E−14      | 3.95E−14      |
| Testes     | 28 g  | 1.92E−14      | 2.97E−14       | 1.82E−14      | 5.38E−14      | 3.66E−14      | 1.55E−10      | 7.24E−15      | 1.04E−14      |
|            | 34 g  | 1.74E−14      | 2.72E−14       | 1.67E−14      | 4.90E−14      | 3.40E−14      | 1.39E−10      | 6.60E−15      | 9.38E−15      |
| Brain      | 28 g  | 8.48E−14      | 4.46E−14       | 9.97E−14      | 2.50E−14      | 2.49E−14      | 7.23E−15      | 1.23E−10      | 1.27E−12      |
|            | 34 g  | 7.51E−14      | 3.96E−14       | 8.83E−14      | 2.22E−14      | 2.27E−14      | 6.38E−15      | 1.06E−10      | 1.02E−12      |
| Thyroid    | 28 g  | 2.39E−13      | 8.66E−14       | 3.20E−13      | 3.89E−14      | 3.90E−14      | 1.02E−14      | 1.28E−12      | 1.96E−09      |
|            | 34 g  | 2.19E−13      | 8.02E−14       | 2.81E−13      | 3.51E−14      | 3.66E−14      | 9.32E−15      | 1.06E−12      | 1.72E−09      |

### 131I S-values (Gy/Bq·s)

| Target     | model | Heart         | Liver          | Lung          | Kidneys       | Spleen        | Testes        | Brain         | Thyroid       |
|------------|-------|---------------|----------------|---------------|---------------|---------------|---------------|---------------|---------------|
| Heart      | 28 g  | 1.11E−10      | 1.34E−13       | 1.40E−12      | 1.33E−14      | 1.60E−14      | 2.57E−15      | 1.14E−14      | 3.24E−14      |
|            | 34 g  | 8.73E−11      | 1.44E−13       | 1.18E−12      | 1.23E−14      | 1.51E−14      | 2.38E−15      | 1.08E−14      | 3.04E−14      |
| Liver      | 28 g  | 3.64E−13      | 1.38E−11       | 7.49E−13      | 3.25E−13      | 7.47E−14      | 1.11E−14      | 1.65E−14      | 3.23E−14      |
|            | 34 g  | 3.80E−13      | 1.20E−11       | 6.54E−13      | 2.79E−13      | 6.80E−14      | 1.01E−14      | 1.51E−14      | 2.96E−14      |
Table A2. (Continued)

(c) 
$^{131}I$ S-values (Gy/Bq s)

| Source-organ | Target | model | Heart  | Liver  | Lung   | Kidneys | Spleen | Testes | Brain  | Thyroid |
|--------------|--------|-------|--------|--------|--------|---------|--------|--------|--------|---------|
| Lung         | 28 g   | 3.41E-12 | 6.73E-13 | 1.05E-10 | 3.94E-14 | 4.17E-14 | 6.18E-15 | 3.37E-14 | 8.86E-14 |
|              | 34 g   | 2.80E-12 | 5.89E-13 | 9.49E-11 | 3.65E-14 | 3.82E-14 | 5.55E-15 | 3.04E-14 | 8.15E-14 |
| Kidneys      | 28 g   | 7.21E-14 | 6.61E-13 | 8.85E-14 | 1.39E-10 | 1.28E-12 | 4.04E-14 | 1.89E-14 | 2.92E-14 |
|              | 34 g   | 3.39E-14 | 2.91E-13 | 4.16E-14 | 6.28E-11 | 5.25E-13 | 1.89E-14 | 8.86E-15 | 1.36E-14 |
| Spleen       | 28 g   | 4.61E-14 | 7.78E-14 | 4.80E-14 | 6.59E-13 | 1.95E-10 | 1.58E-14 | 1.07E-14 | 1.69E-14 |
|              | 34 g   | 4.18E-14 | 7.09E-14 | 4.41E-14 | 5.24E-13 | 1.72E-10 | 1.42E-14 | 9.82E-15 | 1.55E-14 |
| Testes       | 28 g   | 7.38E-15 | 1.17E-14 | 7.16E-15 | 2.11E-14 | 1.57E-14 | 7.01E-11 | 2.88E-15 | 3.98E-15 |
|              | 34 g   | 6.66E-15 | 1.06E-14 | 6.43E-15 | 1.92E-14 | 1.44E-14 | 6.22E-11 | 2.51E-15 | 3.60E-15 |
| Brain        | 28 g   | 3.29E-14 | 1.73E-14 | 3.87E-14 | 9.79E-15 | 1.07E-14 | 2.85E-15 | 4.91E-11 | 1.85E-13 |
|              | 34 g   | 2.89E-14 | 1.53E-14 | 3.42E-14 | 8.56E-15 | 9.53E-15 | 2.47E-15 | 4.18E-11 | 1.66E-13 |
| Thyroid      | 28 g   | 9.05E-14 | 3.40E-14 | 1.01E-13 | 1.45E-14 | 1.66E-14 | 3.96E-15 | 1.83E-13 | 1.51E-09 |
|              | 34 g   | 8.40E-14 | 3.12E-14 | 9.48E-14 | 1.36E-14 | 1.53E-15 | 3.53E-15 | 1.73E-13 | 1.26E-09 |

(d) 
$^{111}$In S-values (Gy/Bq s)

| Source-organ | Target | model | Heart  | Liver  | Lung   | Kidneys | Spleen | Testes | Brain  | Thyroid |
|--------------|--------|-------|--------|--------|--------|---------|--------|--------|--------|---------|
| Heart        | 28 g   | 4.60E-11 | 2.15E-13 | 1.20E-12 | 2.89E-14 | 3.5E-14 | 5.60E-15 | 2.51E-14 | 7.01E-14 |
|              | 34 g   | 3.65E-11 | 2.14E-13 | 1.03E-12 | 2.70E-14 | 3.31E-14 | 5.15E-15 | 2.38E-14 | 6.67E-14 |
| Liver        | 28 g   | 5.83E-13 | 7.13E-12 | 7.74E-13 | 4.26E-13 | 1.63E-13 | 2.44E-14 | 3.61E-14 | 7.06E-14 |
|              | 34 g   | 5.60E-13 | 6.26E-12 | 6.89E-13 | 3.74E-13 | 1.48E-13 | 2.21E-14 | 3.31E-14 | 6.48E-14 |
| Lung         | 28 g   | 2.93E-12 | 6.99E-13 | 3.78E-11 | 8.65E-14 | 9.08E-14 | 1.34E-14 | 7.28E-14 | 1.94E-13 |
|              | 34 g   | 2.44E-12 | 6.21E-13 | 3.41E-11 | 7.92E-14 | 8.36E-14 | 1.19E-14 | 6.72E-14 | 1.77E-13 |
| Target | model | Heart | Liver | Lung | Kidneys | Spleen | Testes | Brain | Thyroid |
|--------|-------|-------|-------|------|---------|--------|--------|-------|---------|
| Kidneys | 28 g  | 1.58E−13 | 8.64E−13 | 1.93E−13 | 6.62E−11 | 1.86E−12 | 8.83E−14 | 4.10E−14 | 6.34E−14 |
|         | 34 g  | 7.44E−14 | 3.91E−13 | 9.07E−14 | 3.01E−11 | 8.10E−13 | 4.15E−14 | 1.92E−14 | 2.96E−14 |
| Spleen  | 28 g  | 1.00E−13 | 1.70E−13 | 1.04E−13 | 9.61E−13 | 8.95E−11 | 3.41E−14 | 2.33E−14 | 3.70E−14 |
|         | 34 g  | 9.09E−14 | 1.55E−13 | 9.59E−14 | 8.11E−13 | 7.97E−11 | 3.11E−14 | 2.11E−14 | 3.36E−14 |
| Testes  | 28 g  | 1.59E−14 | 2.58E−14 | 1.56E−14 | 4.57E−14 | 3.46E−14 | 3.36E−11 | 6.11E−15 | 8.54E−15 |
|         | 34 g  | 1.45E−14 | 2.32E−14 | 1.38E−14 | 4.17E−14 | 3.14E−14 | 3.00E−11 | 5.62E−15 | 7.81E−15 |
| Brain   | 28 g  | 7.17E−14 | 3.80E−14 | 8.47E−14 | 2.13E−14 | 2.33E−14 | 6.17E−15 | 2.45E−11 | 4.05E−13 |
|         | 34 g  | 6.32E−14 | 3.35E−14 | 7.49E−14 | 1.86E−14 | 2.06E−14 | 5.33E−15 | 2.10E−11 | 3.63E−13 |
| Thyroid | 28 g  | 2.00E−13 | 7.50E−14 | 2.23E−13 | 3.37E−14 | 3.60E−14 | 8.26E−15 | 4.03E−13 | 6.08E−10 |
|         | 34 g  | 1.84E−13 | 6.71E−14 | 2.04E−13 | 2.92E−14 | 3.36E−14 | 7.62E−15 | 3.74E−13 | 5.18E−10 |

**Table A2.** Continued

| Target | model | Heart | Liver | Lung | Kidneys | Spleen | Testes | Brain | Thyroid |
|--------|-------|-------|-------|------|---------|--------|--------|-------|---------|
| Heart  | 28 g  | 1.01E−10 | 5.75E−14 | 7.90E−13 | 5.00E−15 | 6.17E−15 | 9.24E−16 | 4.31E−15 | 1.23E−14 |
|         | 34 g  | 7.84E−11 | 6.50E−14 | 6.68E−13 | 4.71E−15 | 5.74E−15 | 8.79E−16 | 4.11E−15 | 1.16E−14 |
| Liver  | 28 g  | 1.55E−13 | 1.12E−11 | 4.05E−13 | 1.55E−13 | 2.84E−14 | 4.13E−15 | 6.12E−15 | 1.23E−14 |
|         | 34 g  | 1.70E−13 | 9.82E−12 | 3.51E−13 | 1.32E−13 | 2.60E−14 | 3.77E−15 | 5.62E−15 | 1.13E−14 |
| Lung   | 28 g  | 1.92E−12 | 3.64E−13 | 1.06E−10 | 1.50E−14 | 1.58E−14 | 2.21E−15 | 1.26E−14 | 3.41E−14 |
|         | 34 g  | 1.57E−12 | 3.16E−13 | 9.60E−11 | 1.37E−14 | 1.45E−14 | 1.99E−15 | 1.15E−14 | 3.14E−14 |
| Kidneys | 28 g  | 2.74E−14 | 3.16E−13 | 3.37E−14 | 1.16E−10 | 5.78E−13 | 1.51E−14 | 6.77E−15 | 1.08E−14 |
|         | 34 g  | 1.29E−14 | 1.38E−13 | 1.59E−14 | 5.24E−11 | 2.30E−13 | 7.15E−15 | 3.17E−15 | 5.10E−15 |
Table A2. (Continued)

(e) \(^{177}\text{Lu}\) S-values (Gy/Bq·s)

| Source-organ | Heart | Liver | Lung | Kidneys | Spleen | Testes | Brain | Thyroid |
|--------------|-------|-------|------|---------|--------|--------|-------|---------|
| Spleen       | 28 g  | 1.73E − 14 | 2.97E − 14 | 1.81E − 14 | 2.97E − 14 | 1.65E − 10 | 5.79E − 15 | 3.57E − 15 | 6.34E − 15 |
|              | 34 g  | 1.57E − 14 | 2.71E − 14 | 1.66E − 14 | 2.30E − 13 | 1.46E − 10 | 5.22E − 15 | 3.55E − 15 | 5.74E − 15 |
| Testes       | 28 g  | 2.67E − 15 | 4.33E − 15 | 2.55E − 15 | 7.90E − 15 | 5.85E − 15 | 5.87E − 11 | 9.28E − 16 | 1.37E − 15 |
|              | 34 g  | 2.40E − 15 | 3.96E − 15 | 2.32E − 15 | 7.22E − 15 | 5.34E − 15 | 5.19E − 11 | 8.37E − 16 | 1.22E − 15 |
| Brain        | 28 g  | 1.23E − 14 | 6.44E − 15 | 1.45E − 14 | 3.52E − 15 | 3.87E − 15 | 9.24E − 16 | 4.05E − 11 | 7.07E − 14 |
|              | 34 g  | 1.09E − 14 | 5.70E − 15 | 1.28E − 14 | 3.07E − 15 | 3.40E − 15 | 8.07E − 16 | 3.44E − 11 | 6.34E − 14 |
| Thyroid      | 28 g  | 3.49E − 14 | 1.28E − 14 | 3.91E − 14 | 5.59E − 15 | 6.36E − 15 | 1.28E − 15 | 7.04E − 14 | 1.36E − 09 |
|              | 34 g  | 3.20E − 14 | 1.17E − 14 | 3.60E − 14 | 4.99E − 15 | 5.79E − 15 | 1.30E − 15 | 6.54E − 14 | 1.13E − 09 |

(f) \(^{99}\text{mTc}\) S-values (Gy/Bq·s)

| Source-organ | Heart | Liver | Lung | Kidneys | Spleen | Testes | Brain | Thyroid |
|--------------|-------|-------|------|---------|--------|--------|-------|---------|
| Heart        | 28 g  | 7.04E − 11 | 2.85E − 14 | 3.32E − 13 | 3.71E − 15 | 4.59E − 15 | 6.90E − 16 | 3.18E − 15 | 9.17E − 15 |
|              | 34 g  | 5.43E − 11 | 3.11E − 14 | 2.82E − 13 | 3.52E − 15 | 4.26E − 15 | 6.40E − 16 | 3.04E − 15 | 8.74E − 15 |
| Liver        | 28 g  | 7.74E − 14 | 7.29E − 12 | 1.82E − 13 | 7.09E − 14 | 2.11E − 14 | 3.05E − 15 | 4.53E − 15 | 9.13E − 15 |
|              | 34 g  | 8.19E − 14 | 6.34E − 12 | 1.59E − 13 | 6.11E − 14 | 1.93E − 14 | 2.78E − 15 | 4.17E − 15 | 8.41E − 15 |
| Lung         | 28 g  | 8.09E − 13 | 1.65E − 13 | 8.23E − 11 | 1.12E − 14 | 1.17E − 14 | 1.65E − 15 | 9.40E − 15 | 2.53E − 14 |
|              | 34 g  | 6.70E − 13 | 1.43E − 13 | 7.39E − 11 | 1.02E − 14 | 1.08E − 14 | 1.48E − 15 | 8.75E − 15 | 2.33E − 14 |
| Kidneys      | 28 g  | 2.04E − 14 | 1.43E − 13 | 2.50E − 14 | 7.60E − 11 | 2.73E − 13 | 1.12E − 14 | 4.99E − 15 | 7.96E − 15 |
|              | 34 g  | 9.63E − 15 | 6.40E − 14 | 1.18E − 14 | 3.42E − 11 | 1.13E − 13 | 5.28E − 15 | 2.36E − 15 | 3.76E − 15 |
| Spleen       | 28 g  | 1.29E − 14 | 2.19E − 14 | 1.35E − 14 | 1.40E − 13 | 1.09E − 10 | 4.32E − 15 | 2.78E − 15 | 4.64E − 15 |
|              | 34 g  | 1.17E − 14 | 2.01E − 14 | 1.24E − 14 | 1.13E − 13 | 9.63E − 11 | 3.97E − 15 | 2.60E − 15 | 4.26E − 15 |
Table A2. (Continued)

| Source-organ | Testes | Brain | Thyroid |
|--------------|--------|-------|---------|
| Testes 28 g  | 1.98E – 15 | 3.21E – 15 | 1.88E – 15 |
| 34 g         | 1.79E – 15 | 2.93E – 15 | 1.74E – 15 |
| Brain 28 g   | 9.17E – 15 | 4.79E – 15 | 1.08E – 14 |
| 34 g         | 8.10E – 15 | 4.22E – 15 | 9.56E – 15 |
| Thyroid 28 g | 2.61E – 14 | 9.71E – 15 | 2.91E – 14 |
| 34 g         | 2.24E – 14 | 8.82E – 15 | 2.66E – 14 |

99mTc S-values (Gy/Bq·s) Target model Heart Liver Lung Kidneys Spleen Testes Brain Thyroid

| Target | model | Heart | Liver | Lung | Kidneys | Spleen | Testes | Brain | Thyroid |
|--------|-------|-------|-------|------|---------|--------|--------|-------|---------|
| Testes | 28 g  | 1.98E – 15 | 3.21E – 15 | 1.88E – 15 | 4.34E – 15 | 3.84E – 11 | 6.76E – 16 | 9.79E – 16 |
| 34 g   |       | 1.79E – 15 | 2.93E – 15 | 1.74E – 15 | 3.94E – 15 | 3.39E – 11 | 6.06E – 16 | 9.11E – 16 |
| Brain  | 28 g  | 9.17E – 15 | 4.79E – 15 | 1.08E – 14 | 2.60E – 15 | 2.87E – 15 | 6.73E – 16 | 2.62E – 11 |
| 34 g   |       | 8.10E – 15 | 4.22E – 15 | 9.56E – 15 | 2.27E – 15 | 2.52E – 15 | 5.88E – 16 | 2.22E – 11 |
| Thyroid| 28 g  | 2.61E – 14 | 9.71E – 15 | 2.91E – 14 | 4.13E – 15 | 4.58E – 15 | 9.88E – 16 | 5.18E – 14 |
| 34 g   |       | 2.24E – 14 | 8.82E – 15 | 2.66E – 14 | 3.78E – 15 | 4.32E – 15 | 9.10E – 16 | 4.83E – 14 |

(g) 99mTc S-values (Gy/Bq·s) Source-organ

| Source-organ | Heart | Liver | Lung | Kidneys | Spleen | Testes | Brain | Thyroid |
|--------------|-------|-------|------|---------|--------|--------|-------|---------|
| Testes 28 g  | 1.98E – 15 | 3.21E – 15 | 1.88E – 15 | 4.34E – 15 | 3.84E – 11 | 6.76E – 16 | 9.79E – 16 |
| 34 g         | 1.79E – 15 | 2.93E – 15 | 1.74E – 15 | 3.94E – 15 | 3.39E – 11 | 6.06E – 16 | 9.11E – 16 |
| Brain 28 g   | 9.17E – 15 | 4.79E – 15 | 1.08E – 14 | 2.60E – 15 | 2.87E – 15 | 6.73E – 16 | 2.62E – 11 |
| 34 g         | 8.10E – 15 | 4.22E – 15 | 9.56E – 15 | 2.27E – 15 | 2.52E – 15 | 5.88E – 16 | 2.22E – 11 |
| Thyroid 28 g | 2.61E – 14 | 9.71E – 15 | 2.91E – 14 | 4.13E – 15 | 4.58E – 15 | 9.88E – 16 | 5.18E – 14 |
| 34 g         | 2.24E – 14 | 8.82E – 15 | 2.66E – 14 | 3.78E – 15 | 4.32E – 15 | 9.10E – 16 | 4.83E – 14 | 7.74E – 10 |

(Continued)
### Table A2. (Continued)

#### (g) $^{90}$Y $S$-values (Gy/Bq·s)

| Target      | model | Heart   | Liver   | Lung    | Kidneys | Spleen | Testes | Brain   | Thyroid |
|-------------|-------|---------|---------|---------|---------|--------|--------|---------|---------|
| Brain       | 28 g  | 3.96E−16| 1.87E−16| 6.55E−16| 1.03E−16| 1.08E−16| 2.66E−17| 1.55E−10| 2.15E−12|
|             | 34 g  | 3.41E−16| 1.77E−16| 5.05E−16| 9.15E−17| 1.01E−16| 1.83E−17| 1.34E−10| 1.66E−12|
| Thyroid     | 28 g  | 1.31E−14| 4.32E−16| 2.82E−13| 1.87E−16| 1.65E−16| 3.89E−17| 2.16E−12| 2.22E−09|
|             | 34 g  | 8.93E−15| 3.89E−16| 1.98E−13| 1.51E−16| 1.43E−16| 2.20E−17| 1.73E−12| 1.95E−09|

#### (h) $^{188}$Re $S$-values (Gy/Bq·s)

| Target      | model | Heart   | Liver   | Lung    | Kidneys | Spleen | Testes | Brain   | Thyroid |
|-------------|-------|---------|---------|---------|---------|--------|--------|---------|---------|
| Heart       | 28 g  | 2.05E−10| 1.81E−12| 9.87E−12| 1.87E−15| 2.34E−15| 3.73E−16| 1.63E−15| 5.33E−15|
|             | 34 g  | 1.66E−10| 1.68E−12| 8.53E−12| 1.77E−15| 2.17E−15| 3.56E−16| 1.53E−15| 4.85E−15|
| Liver       | 28 g  | 4.88E−12| 4.15E−11| 6.17E−12| 3.98E−12| 2.71E−14| 1.57E−15| 2.33E−15| 4.58E−15|
|             | 34 g  | 4.41E−12| 3.66E−11| 5.35E−12| 2.62E−12| 1.95E−14| 1.42E−15| 2.14E−15| 4.20E−15|
| Lung        | 28 g  | 2.40E−11| 5.53E−12| 1.45E−10| 3.47E−15| 9.83E−15| 8.50E−16| 4.73E−15| 9.03E−14|
|             | 34 g  | 2.01E−11| 4.79E−12| 1.32E−10| 2.64E−15| 7.86E−15| 8.05E−16| 4.35E−15| 6.52E−14|
| Kidneys     | 28 g  | 1.02E−14| 6.29E−12| 1.46E−14| 3.62E−10| 2.19E−11| 5.68E−15| 2.63E−15| 4.05E−15|
|             | 34 g  | 4.83E−15| 2.74E−12| 6.47E−15| 1.59E−10| 9.21E−12| 2.68E−15| 1.22E−15| 1.92E−15|
| Spleen      | 28 g  | 6.57E−15| 2.85E−14| 1.17E−14| 1.52E−11| 4.31E−10| 2.23E−15| 1.48E−15| 2.42E−15|
|             | 34 g  | 5.99E−15| 2.04E−14| 9.59E−15| 9.27E−12| 3.89E−10| 2.00E−15| 1.46E−15| 2.17E−15|
| Testes      | 28 g  | 1.02E−15| 1.69E−15| 1.01E−15| 2.85E−16| 2.50E−15| 1.78E−10| 3.90E−16| 5.08E−16|
|             | 34 g  | 9.22E−16| 1.47E−15| 9.00E−16| 2.72E−16| 2.03E−15| 1.60E−10| 3.27E−16| 5.02E−16|
| Brain       | 28 g  | 4.66E−15| 2.47E−15| 5.50E−15| 1.03E−16| 1.55E−15| 3.95E−16| 1.42E−10| 1.17E−12|
|             | 34 g  | 4.09E−15| 2.13E−15| 4.85E−15| 1.18E−16| 1.29E−15| 3.37E−16| 1.22E−10| 8.95E−13|
| Thyroid     | 28 g  | 1.49E−14| 4.87E−15| 1.16E−09| 1.99E−15| 2.36E−15| 6.13E−16| 1.18E−12| 2.34E−09|
|             | 34 g  | 1.32E−14| 4.56E−15| 8.38E−10| 9.87E−16| 2.06E−15| 4.29E−16| 9.36E−13| 2.04E−09|
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