An analytic model to calculate voxel s-values for $^{177}$Lu

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Abstract

Objective. $^{177}$Lu is one of the most employed isotopes in targeted radionuclide therapies and theranostics, and 3D internal dosimetry for such procedures has great importance. Voxel S-Values (VSVs) approach is widely used for this purpose, but VSVs are available for a limited number of voxel dimensions. The aim of this work is to develop an analytic model for the calculation of $^{177}$Lu-VSVs in any cubic voxelized geometry of practical interest. Approach. Monte Carlo (MC) simulations were implemented with the toolkit GAMOS to evaluate VSVs in voxelized geometries of soft tissue from a source of $^{177}$Lu homogeneously distributed in the central voxel. Nine geometric setups, containing 15 × 15 × 15 cubic voxels of sides $l$ ranging from 2 mm to 6 mm, in steps of 0.5 mm, were considered. For each $l$, the VSVs computed as a function of the ‘normalized radius’, $R_n = R/l$ (with $R =$ distance from the center of the source voxel), were fitted with a parametric function. The dependencies of the parameters as a function of $l$ were then fitted with appropriate functions, in order to implement the model for deducing $^{177}$Lu-VSVs for any $l$ within the aforementioned range. Main results. The MC-derived VSVs were satisfactorily compared with literature data for validation, and the VSVs computed with the analytic model agree with the MC ones within 2% for $R_n < 2$ and within 6% for $R_n > 2$. Significance. The proposed model enables the easy and fast calculation, with a simple spreadsheet, of $^{177}$Lu-VSVs in any cubic voxelized geometry of practical interest, avoiding the necessity of implementing ad-hoc MC simulations to estimate VSVs for specific voxel dimensions not available in literature data.

1. Introduction

Lutetium-177 is a $\beta^−$ emitter with favorable nuclear characteristics as a therapeutic radionuclide, including its low energy $\beta^−$ emissions ($E_{\beta^−-max} = 496.8$ keV and ($E_{\beta^−} = 133.64$ keV), its convenient physical half-life of 6.639 days and the low abundance of gamma emissions in its decays, useful for imaging (Kossert et al 2012, Pillai and Knapp 2015). Nuclear medicine therapies with Lutetium-labeled radiopharmaceuticals are expanding since, in addition to the traditional peptide receptor radionuclide therapy (PRRT) of neuroendocrine tumors (NETs) (Kim and Kim 2017, del Olmo-García et al 2022), $^{177}$Lu therapies with prostate specific membrane antigen (PSMA) ligands have been introduced for the treatment of prostate cancer (Emmett et al 2017, Sartor et al 2021) together with other Lutetium-labeled radiopharmaceuticals for the treatment of other diseases and for theranostic uses (Pillai and Knapp 2015, Das and Banerjee 2016).

The internal dosimetry of these therapies is necessary for the prediction of the therapeutic efficacy and for their safety; in this context, three-dimensional dosimetry is useful to estimate both the radiation absorbed doses in the target tissues of the therapy, and in the organs at risk (Berenato et al 2016, Del Prete et al...
The calculation approaches for three-dimensional internal dosimetry are: the convolution of dose point-kernels (DPKs), the convolution of voxel S-factors, also called voxel S-values (VSVs), and the direct Monte Carlo (MC) simulation (Amato et al 2022, Auditore et al 2022). Direct MC is the most accurate one, but requires demanding resources and is currently used only for research (Pistone et al 2021); therefore, DPKs and VSVs are the most widely used for clinical dosimetry (Dewaraja et al 2012). The VSVs convolution approach, introduced and described in detail in the MIRD pamphlet n.17 (Boich et al 1999), has the advantage of not needing CPU-intensive conversion of spherical coordinates to Cartesian ones over the target volumes, differently from DPK convolution (Lee et al 2018). However, the VSVs approach requires tabulated S-values for the examined isotope with the corresponding voxel size of the considered tomographic scans, from which the time-integrated activity matrix for convolution is deduced. In fact, the different SPECT-CT scanners generally reconstruct with matrices of different sizes; for this reason, the available bibliographic resources, such as https://medphys.it/down_voxel.htm, publish VSVs in a number of standard voxel sizes, which by the way is limited. For voxel dimensions not available in the literature, a viable but unpractical solution is to ask for a specific Monte Carlo calculation, to research groups active in the field. Alternatively, Amato et al (2012) proposed a general analytical method for the calculation of VSVs for beta- and gamma-emitting radionuclides. This method, however, is based on the interpolation of parameters in the two-dimensional space of energy of emitted radiation and voxel size. Fernández et al (2013) also tested analytic methods based on the down-sampling of high-resolution VSVs, on VSVs interpolation and/or fits, but did not provide tabular data nor analytic expressions in order to precisely reproduce their results, showing rather that such analytic methodologies are feasible and suggesting to the interested readers to develop them for specific radionuclides in future studies.

The purpose of this work is to introduce a specific analytic model for $^{177}$Lu, to be more accurate than the general method by Amato et al (2012) and which can be straightforwardly implemented in a simple electronic spreadsheet, in order to allow the computation of $^{177}$Lu VSVs in any cubic voxel dimension of practical interest.

2. Materials and methods

2.1. Monte Carlo simulations

We developed Monte Carlo (MC) simulations for the calculation of VSVs for $^{177}$Lu using GAMOS (Arce et al 2008, Arce et al 2014), a GEANT4-based user-friendly framework for medical physics applications (Auditore et al 2019, Amato et al 2020, Pistone et al 2020). GEANT4 (Agostinelli et al 2003, Allison et al 2006, Allison et al 2016) is a simulation toolkit for radiation transport widely used and well validated in many fields of physics, including medical radiation physics and radioprotection, internal dosimetry, and VSVs calculations (Amato and Lizio 2009, Pacilio et al 2009, Amato et al 2013a, 2013b).

In particular, we exploited GAMOS version 6.2.0, relying on GEANT4 version 10.06.p02. A cubic World volume of 50 cm side and made of soft tissue was set. In detail, G4_TISSUE_SOFT_ICRP material, with density 1.03 g cm$^{-3}$ and elemental composition according to the ICRP definition (Geant4 Collaboration 2020) was adopted. Within the World, nine voxelized cubic geometries were considered, each one containing $15 \times 15 \times 15$ voxels and centered in the origin of the reference system, with the following voxel sizes: 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5 and 6 mm. For each $l$, independent simulations were prepared, setting the central voxel as a homogeneous and isotropic source of $^{177}$Lu. The $^{177}$Lu decay was implemented from the data of (Stabin and da Luz 2002), publicly available at http://doseinfo-radar.com, performing a dedicated simulation for each of the three types of primary particles: $\beta$ electrons, monoenergetic (Auger and Conversion) electrons, and X and $\gamma$ photons, and then merging their results by accounting for their relative probabilities. The transport of the emitted radiation was simulated with the G4EMExtendedPhysics Physics List (Gamos Collaboration 2020), and the absorbed dose per event was scored in each of the aforementioned voxels, together with its respective statistical uncertainty in terms of standard deviation of the mean (Chetty et al 2006). These 3D dose outputs were then processed with home-made Python scripts in order to: (i) label each voxel with indices $(i,j,k)$ ranging from $(-7, -7, -7)$ to $(7, 7, 7)$; (ii) convert the doses per event (Gy/event) into S-Values (mGy/Mbq-s); (iii) average the S-Values of the symmetrical voxels with respect to the center of the volume, and calculate the statistical uncertainties; (iv) produce text outputs reporting the S-Values in column as a function of the voxel indices and of the dimensionless normalized radius $R_n$, defined as:

$$R_n = \sqrt{i^2 + j^2 + k^2} = R/l$$

(1)

where $R$ indicates the distance from the center of the central voxel.

For each run, $10^6$ histories were simulated, a number which guaranteed statistical uncertainties below 1% for the final S-Values, in all the voxels and for every $l$ value. The simulations were run on a local workstation provided with Intel(R) Core(TM) i7-10700K @ 3.80 GHz CPUs and 32 GB RAM, and lasted on average 4 h for $\beta$ spectrum runs, 3 h for monoenergetic electrons runs, and 9 h for photons runs.

To validate the correct functioning of the simulations and post-processing procedures, the obtained
S-Values, $S_{MC}(i,j,k)$, were compared with the ones of Lanconelli et al (2012) publicly available at https://medphys.it/down_svoxel.htm, $S_{Lan}(i,j,k)$, in terms of relative percent differences $\kappa(i,j,k)$ (% in each voxel, for the available corresponding $l$ values (3, 4, 5 and 6 mm):

$$\kappa(i, j, k) = 100 \cdot \frac{S_{MC}(i, j, k) - S_{Lan}(i, j, k)}{S_{Lan}(i, j, k)}$$

(2)

The $S_{Lan}(i,j,k)$ had been calculated via direct MC simulation, using the EGSnrc-based DOSXYZnrc code, and were in turn successfully compared with the results of two other MC codes: MCNP4c and PENELOPE (Lanconelli et al 2012).

2.2. Analytic model

The following function was selected to fit the MC-derived S-Values represented as a function of $R_n$, $S_{MC}(R_n)$:

$$S(R_n) = a \cdot \exp(-\exp(b \cdot R_n^c)) + \frac{f}{(R_n^g + 0.02)}$$

(3)

where $a$, $b$, $c$, $f$ and $g$ are the fit parameters for each examined $l$. The first term in the right side of equation (3) is derived by the empirical expression introduced in equation (4) of Amato et al (2012) to model $S(R_n)$ for monoenergetic electrons, and in our work it is aimed at describing the contribution of $\beta$-particles and monoenergetic electrons of $^{177}$Lu decay to the S-Values. The second term of equation (3) is derived by equation (5) of Amato et al (2012) and it is aimed at describing the contribution of the photons of $^{177}$Lu decay to the S-Values.

The five parameters of equation (3) were then fitted as a function of $l$, $a$ and $f$ were fitted with a function of the following type:

$$y(l) = \frac{p_0}{(l^p_1 + p_2)}$$

(4)

with $p_0$, $p_1$ and $p_2$ as fit parameters. $b$, $c$ and $g$ were fitted with a 3rd-order polynomial function:

$$y(l) = q_0 + q_1 l + q_2 l^2 + q_3 l^3$$

(5)

with $q_0$, $q_1$, $q_2$ and $q_3$ as fit parameters.

As it will be clear from the results, a corrective term for the unique $S(1,1,1)$ located at $R_n \approx 1.732$ had to be introduced, $\delta(l)$:

$$S(1, 1, 1, l) = S_{Eq.3}(1, 1, 1, l) + \delta(l)$$

(6)

$\delta(l)$ was obtained by fitting the differences between the MC-derived S-Value, $S_{MC}(1,1,1,l)$, and the S-Value deduced from the fit of equation (3), $S(1,1,1,l)$; a bi-exponential fit function was adopted.

Figure 1. Relative percent differences $\kappa$ (equation (2)) as a function of $R_n$ for the $l$ values available for comparison: 3, 4, 5 and 6 mm.
since it demonstrated to optimally reproduce the trend of the differences as a function of $l$:  

$$
\delta(l) = A_1 \cdot \exp(-l/t_1) + A_2 \cdot \exp(-l/t_2) + \gamma_0
$$  

with $A_1, A_2, t_1, t_2$ and $\gamma_0$ as parameters.

All the fits described in this section were performed with the software QtiPlot\(^5\) 0.9.8.9 using the Nelder-Mead Simplex algorithm.

The analytic model constituted by equations (3)–(5) and including the corrective term for voxel (1,1,1) of equations (6) and (7) was implemented in a simple spreadsheet, enabling the calculation of VSVs for $^{177}$Lu for whatever voxel dimension $l$ between 2 mm and 6 mm.

In order to validate the analytic model, the VSVs calculated through it were first compared with the MC-derived ones for all the $l$ values for which they were simulated (reported in section 2.1). Second, they were compared for three additional $l$ values randomly selected between 2 mm and 3 mm, 3 mm and 5 mm, and 5 mm and 6 mm, to assess the capability of the model of calculating correctly VSVs for small, medium and large voxel sizes of practical interest. For these three $l$ values, namely 2.68 mm, 4.32 mm and 5.35 mm, MC simulations were performed to evaluate S-Values in the same way described in section 2.1, and were compared with the S-Values from the analytic model. All the mentioned comparisons were reported in terms of relative percent differences $\varepsilon(i,j,k)$ (%) defined as follows:
In order to assess how the accuracy of our new analytic model compares with the existing general model by Amato et al (2012), the VSVs calculated according to Amato et al (2012) were also compared in terms of $\varepsilon$ with the MC-derived ones.

Processing a further refinement of the model by replacing the term $\varepsilon_i$ in the equation with $\varepsilon(i, j, k) = 100 \cdot \frac{S(i, j, k) - S_{MC}(i, j, k)}{S_{MC}(i, j, k)}$ (8)

In order to assess how the accuracy of our new analytic model compares with the existing general model by Amato et al (2012), the VSVs calculated according to Amato et al (2012) were also compared in terms of $\varepsilon$ with the MC-derived ones.
As an additional feature of the model, the possibility to apply a density correction to the analytic S-Values following the approach of Dieudonné et al. (2013) and Kim et al. (2022) was included in the spreadsheet implementing the calculation, so that the interested users can adjust the density in the VSVs calculation. The density corrected S-Values, $S_\rho(R_n)$, are calculated as:

Table A2. Values of the fit parameters, $\chi^2$/dof and $R^2$ for the fits of $a$ and $f$ as a function of $l$ with equation (4) of this work.

| Parameter | $p_0$          | $p_1$          | $p_2$          | $\chi^2$/dof | $R^2$ |
|-----------|----------------|----------------|----------------|--------------|-------|
| $a$       | 5.1421E+01     | 2.9307E+00     | 3.2387E-01     | 1.3522E-05   | 1.0000 |
| $f$       | 1.2624E-03     | 1.9576E+00     | $-4.7564E-01$  | 1.0344E-12   | 1.0000 |

Table A3. Values of the fit parameters, $\chi^2$/dof and $R^2$ for the fits of $b$, $c$ and $g$ as a function of $l$ with equation (5) of this work.

| Parameter | $q_0$          | $q_1$          | $q_2$          | $q_3$         | $\chi^2$/dof | $R^2$ |
|-----------|----------------|----------------|----------------|--------------|--------------|-------|
| $b$       | 1.2273E+00     | 1.8829E-01     | $-2.7291E-02$  | 1.5923E-03   | 2.7766E-06   | 1.0000 |
| $c$       | 8.2992E-01     | $-1.4232E-03$  | $-1.9297E-03$  | 1.4504E-04   | 1.3002E-07   | 1.0000 |
| $g$       | 2.2239E+00     | $-1.5055E-01$  | 2.5665E-02     | $-1.4905E-03$| 1.6580E-06   | 1.0000 |

Figure 4. Values (markers) of the parameters $a$, $b$, $c$, $f$ and $g$ of equation (3), as a function of $l$ and respective fits (lines) with equation (4) for $a$ and $f$, with equation (5) for $b$, $c$ and $g$. 

As an additional feature of the model, the possibility to apply a density correction to the analytic S-Values following the approach of Dieudonné et al. (2013) and Kim et al. (2022) was included in the spreadsheet implementing the calculation, so that the interested users can adjust the density in the VSVs calculation. The density corrected S-Values, $S_\rho(R_n)$, are calculated as:

Table A2. Values of the fit parameters, $\chi^2$/dof and $R^2$ for the fits of $a$ and $f$ as a function of $l$ with equation (4) of this work.

| Parameter | $p_0$          | $p_1$          | $p_2$          | $\chi^2$/dof | $R^2$ |
|-----------|----------------|----------------|----------------|--------------|-------|
| $a$       | 5.1421E+01     | 2.9307E+00     | 3.2387E-01     | 1.3522E-05   | 1.0000 |
| $f$       | 1.2624E-03     | 1.9576E+00     | $-4.7564E-01$  | 1.0344E-12   | 1.0000 |

Table A3. Values of the fit parameters, $\chi^2$/dof and $R^2$ for the fits of $b$, $c$ and $g$ as a function of $l$ with equation (5) of this work.

| Parameter | $q_0$          | $q_1$          | $q_2$          | $q_3$         | $\chi^2$/dof | $R^2$ |
|-----------|----------------|----------------|----------------|--------------|--------------|-------|
| $b$       | 1.2273E+00     | 1.8829E-01     | $-2.7291E-02$  | 1.5923E-03   | 2.7766E-06   | 1.0000 |
| $c$       | 8.2992E-01     | $-1.4232E-03$  | $-1.9297E-03$  | 1.4504E-04   | 1.3002E-07   | 1.0000 |
| $g$       | 2.2239E+00     | $-1.5055E-01$  | 2.5665E-02     | $-1.4905E-03$| 1.6580E-06   | 1.0000 |
where $\rho$ is the user-defined density (in g·cm$^{-3}$) and 1.03 g·cm$^{-3}$ is the density of the soft tissue for which the MC VSVs were calculated (section 2.1).

3. Results

3.1. Monte Carlo simulations validation
In figure 1 are reported the relative percent differences $\kappa$ (equation (2)) between the S-Values obtained with the MC simulations performed in this work and the ones by Lanconelli et al (2012), as a function of $R_n$; the highest value of normalized radius is $R_n \approx 8.66$, corresponding to the voxel (5,5,5), since it is the farthest one from the origin in the data selected for the comparison, which used voxel grids of 11 × 11 × 11. All the $\kappa$ values lie within ±2% except for $R_n = 0$, i.e. for $S(0,0,0)$, for which $\kappa \approx +9\%$.

3.2. VSVs from Monte Carlo simulations and analytic model
In figures 2 and 3, the Voxel S-Values, evaluated with the Gamos MC simulations, are plotted as a function of $R_n$ (listed in tabular form in the supplementary data), together with the fits performed using the analytic model function of equation (3); in the bottom panels the relative percent differences $\epsilon(i,j,k)$ (equation (8)) are reported, evaluated for each discrete $R_n$ value of the MC VSVs. The VSVs, fits and $\epsilon$’s for the different voxel dimensions were split into two figures (figure 2 for 2, 3, 4, 5 and 6 mm, figure 3 for 2.5, 3.5, 4.5 and 5.5 mm) for clarity purpose, in order to avoid graphical superpositions of markers and curves. Error bars were omitted since the uncertainties were below 1% for all the data points, even at the farthest distances from the source.

All the fits of the VSVs converged with $R^2 > 0.99$, and the values of the obtained parameters are listed in table A1 of the Annex, and are also represented as a function of $l$ in figure 4. Figure 4 also shows the fits of the mentioned parameters as a function of $l$ with the functions reported in equations (4) and (5), which all converged with $R^2 > 0.99$; the optimized parameters of these fits are reported in tables A2 and A3 of the Annex and were used to build the spreadsheet implementing the analytic model, available in the supplementary data and including the possibility to apply density correction, according to equation (9).

3.3. Validation of the analytic model
Considering the comparison between $S_{MC}$ and $S$ from the analytic model, despite the excellent goodness of the fits, significant discrepancies were found for the single $S(1,1,1)$, with $\epsilon(1,1,1)$ values up to about $-31\%$. 

![Figure 5. Differences between S-Values calculated with Gamos MC simulations and with the fit function of equation (3) for the voxel (1,1,1), and fit $\delta(l)$ as a function of $l$ according to equation (7).](image)

Table A4. Values of the fit parameters, $\chi^2$/dof and $R^2$ for the fit $\delta(l)$ (equation (7)) of the differences $S_{MC}(1,1,1) - S(1,1,1)$ (equation (6)) as a function of $l$.

| $A_1$ | $t_1$ | $A_2$ | $t_2$ | $y_0$ | $\chi^2$/dof | $R^2$ |
|-------|-------|-------|-------|-------|---------------|-------|
| 6.4545e-04 | 7.3882e-01 | 8.2173e-02 | 2.8725e-01 | 8.1909e-07 | 9.2516e-10 | 1.00000 |

Figure 5. Differences between S-Values calculated with GAMOS MC simulations and with the fit function of equation (3) for the voxel (1,1,1), and fit $\delta(l)$ as a function of $l$ according to equation (7).
depending on \( l \), whereas all the other \( \varepsilon(i,j,k) \) remained within ±6%, and within ±2% for \( R_n < 2 \).

Adopting the corrective term introduced in equations (6) and (7), the updated \( \varepsilon(1,1,1) \) values lie well below ±1%, as noticeable in the lower panel of figures 2 and 3, where they are depicted as open markers. The corrective factor \( \delta(l) \) as a function of \( l \) is shown in figure 5, and the fit parameters of \( \delta(l) \) are reported in table A4 of the Annex.

Considering the comparison of MC simulations and analytic model for the three test voxel sizes 2.68 mm, 4.32 mm and 5.35 mm (section 2.2), in figure 6 are reported their \( S_{MC}(R_n) \) and \( S(R_n) \) including the correction term for \( S(1,1,1) \), together with their respective \( \varepsilon(i,j,k) \), lying within −6% and +3% for \( l = 5.35 \) mm and within ±2% for \( l = 2.68 \) mm and 4.32 mm. The MC-derived \( S_{MC}(R_n) \) for these three voxel dimensions are also reported in tabular form in the supplementary data.

4. Discussion

As figures 2 and 3 show, all the MC-derived \(^{177}\text{Lu-}\) VSVs exhibit a similar behavior as a function of \( R_n \) for the different \( l \)’s: (i) an early rapid decrease for \( R_n < 2 \), corresponding to the energy deposition from \( \beta \)'s and monoenergetic electrons; (ii) a smooth knee of the trend at \( R_n \sim 2 \), in correspondence of the maximum range of \(^{177}\text{Lu-} \) \( \beta \)'s in soft tissue (1.7 mm, according to Hosono et al 2018); (iii) a slower decrease for \( R_n > 2 \), corresponding to the contribution of the monoenergetic photons of \(^{177}\text{Lu} \) decay and also to Bremsstrahlung photons produced by interactions of electrons in the medium. The similar trend of all the VSV’s justifies
the use of the function of equation (3) to fit them. This feature in addition translates in a very smooth variation with \( l \) of all the fit parameters, exhibiting monotonically increasing or monotonically decreasing trends, and supporting the reliability of the fitting method over the range of voxel dimensions considered.

Concerning the validation of the MC simulations done through the comparison with the literature data of Lanconelli et al. (2012), it appears largely satisfactory for \( R_n > 0 \), being the relative percent differences \( \kappa \) within 2% for all the \( l \) values available. The larger differences for \( R_n = 0 \), with \( \kappa \approx 9\% \), aside from reasonable discrepancies caused by the use of different simulation software and settings, is most likely due to the fact that in Lanconelli et al. (2012) no mention is made of monoenergetic electrons of \(^{177}\)Lu decay, which probably were neglected in that work. This hypothesis is supported by the fact that we found out that the relative contribution of monoenergetic electrons to the total absorbed dose in the central voxel is of about 10%, which perfectly matches the missing 9% of Lanconelli’s VSVs with respect to ours.

The analytic model developed in this work for the calculation of \(^{177}\)Lu-VSVs was satisfactorily validated comparing its results with MC ones for all the examined voxel dimensions: the relative percent differences \( \varepsilon \) are within ±6%, and by the way these discrepancies are found for \( R_n \) values at the end of the tails of the VSVs, corresponding to the farthest voxels from the source, with the smallest contribution to the total absorbed dose; for \( R_n < 2 \), i.e. within the range of \(^{177}\)Lu \( \beta \)'s, for which a prominent contribution to the absorbed dose is given, \( \varepsilon \)'s are always within ±2%, including \( S(1,1,1) \) after the incorporation of the voxel-specific correction term. These results demonstrated a significantly improved accuracy with respect to the pre-existing analytic model by Amato et al. (2012), whose \( \varepsilon \)'s are within −20% and 0% for \( R_n < 2 \) and between −20% and +40% overall, as shown in figure 7.

In the work of Fernández et al. (2013) it was suggested that analytic models based on the fitting of VSVs for specific radionuclides are feasible and their development is encouraged. In particular, they reported good results using polynomials fitting functions for separate intervals of voxel sizes; however, the order of the polynomials and the fit parameters were not reported in their work. In the present work, a unique function for fitting the entire range of examined voxel sizes is provided (equation (3)), together with the functions for fitting the involved parameters as a function of the voxel size (equations (4) and (5)) plus a corrective term for \( S(1,1,1) \) (equations (6) and (7)). In addition, our results are provided in the Annex in tabular form, and a spreadsheet automatically implementing all the mentioned calculations is provided as Supplementary material.

In view of all the described features, the proposed analytic method shows to be a solid radionuclide-specific calculation tool for \(^{177}\)Lu-VSVs. It enables an accurate, very simple and fast calculation of VSVs, requiring from the user only the input of the desired voxel dimensions in the provided spreadsheet, which instantaneously calculates all the parameters and consequently the VSVs, according to the introduced model. At will, also a desired density for the VSVs estimation can be given as input, to obtain density-corrected VSVs. Apart from the user-friendliness and computation rapidity, a major strength of the model is its capability of enabling the calculation of \(^{177}\)Lu-VSVs for whatever decimal voxel dimension between 2 mm and 6 mm. When dealing with 3D activity images deduced from PET or SPECT matrices with voxel

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**Figure 7.** Relative percent differences \( \varepsilon \) between the VSVs by Amato et al. (2012) and the MC-derived ones of the present work, for all the available voxel dimensions (the model by Amato et al. (2012) was built for voxel sizes larger than 3 mm).
dimensions not exactly matching the standard values commonly found in literature, this model permits to perform VSV’s-based dosimetry avoiding the implementation of ad-hoc MC simulations to calculate the VSV for specific voxel dimensions, while maintaining an high accuracy in the dosimetric calculation.

5. Conclusion

The proposed analytic model allows the easy and fast calculation of VSV’s for 177Lu in any cubic voxel dimension between 2 mm and 6 mm by means of a simple spreadsheet. It ensures VSV’s estimations in agreement with MC ones with ε < 2% for normalized radii within the maximum range of 177Lu β-electrons, and ε < 6% in the farthest voxels from the central one. This approach permits to perform VSV’s-based dosimetry employing any tomographic activity matrix of practical interest, avoiding the need of implementing ad-hoc MC simulations to deduce VSV’s for specific voxel dimensions.

Data availability statement

The data that support the findings of this study are available upon reasonable request from the authors.

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