Comparison of internal dose estimates obtained using organ-level, voxel S value, and Monte Carlo techniques

Joshua Grimes
Department of Physics and Astronomy, University of British Columbia, Vancouver V5Z 1L8, Canada

Anna Celler
Department of Radiology, University of British Columbia, Vancouver V5Z 1L8, Canada

(Received 23 November 2013; revised 16 July 2014; accepted for publication 27 July 2014; published 14 August 2014)

Purpose: The authors’ objective was to compare internal dose estimates obtained using the Organ Level Dose Assessment with Exponential Modeling (OLINDA/EXM) software, the voxel S value technique, and Monte Carlo simulation. Monte Carlo dose estimates were used as the reference standard to assess the impact of patient-specific anatomy on the final dose estimate.

Methods: Six patients injected with $^{99m}$Tc-hydrazinonicotinamide-Tyr$^3$-octreotide were included in this study. A hybrid planar/SPECT imaging protocol was used to estimate $^{99m}$Tc time-integrated activity coefficients (TIACs) for kidneys, liver, spleen, and tumors. Additionally, TIACs were predicted for $^{131}$I, $^{177}$Lu, and $^{90}$Y assuming the same biological half-lives as the $^{99m}$Tc labeled tracer. The TIACs were used as input for OLINDA/EXM for organ-level dose calculation and voxel level dosimetry was performed using the voxel S value method and Monte Carlo simulation. Dose estimates for $^{99m}$Tc, $^{131}$I, $^{177}$Lu, and $^{90}$Y distributions were evaluated by comparing (i) organ-level S values corresponding to each method, (ii) total tumor and organ doses, (iii) differences in right and left kidney doses, and (iv) voxelized dose distributions calculated by Monte Carlo and the voxel S value technique.

Results: The S values for all investigated radionuclides used by OLINDA/EXM and the corresponding patient-specific S values calculated by Monte Carlo agreed within 2.3% on average for self-irradiation, and differed by as much as 105% for cross-organ irradiation. Total organ doses calculated by OLINDA/EXM and the voxel S value technique agreed with Monte Carlo results within approximately $\pm7\%$. Differences between right and left kidney doses determined by Monte Carlo were as high as 73%. Comparison of the Monte Carlo and voxel S value dose distributions showed that each method produced similar dose volume histograms with a minimum dose covering 90% of the volume (D90) agreeing within $\pm3\%$, on average.

Conclusions: Several aspects of OLINDA/EXM dose calculation were compared with patient-specific dose estimates obtained using Monte Carlo. Differences in patient anatomy led to large differences in cross-organ doses. However, total organ doses were still in good agreement since most of the deposited dose is due to self-irradiation. Comparison of voxelized doses calculated by Monte Carlo and the voxel S value technique showed that the 3D dose distributions produced by the respective methods are nearly identical. © 2014 American Association of Physicists in Medicine.

Key words: Internal dose calculation, Monte Carlo, voxel S values, OLINDA/EXM

1. INTRODUCTION

Absorbed dose calculations for internal radionuclides are used to assess the stochastic risks associated with diagnostic applications of nuclear medicine as well as the deterministic risks to normal tissues associated with therapeutic nuclear medicine; less commonly, such calculations are also used to assess efficacy (i.e., target-tissue dose) for radionuclide therapy. These dose calculations are performed, at least for diagnostic applications, using the methodology developed by the Medical Internal Radiation Dose (MIRD) committee. The general MIRD equation used for calculating the dose to target organs is

$$D(r_T) = \sum S(r_T \leftarrow r_S),$$

where $\bar{A}(r_S)$ is the time-integrated activity (total number of decays integrated over a specified time period) of the source and $S(r_T \leftarrow r_S)$ is the dose deposited in target $r_T$ per unit of cumulated activity in source $r_S$ (often referred to as a S value). The time-integrated activity $\bar{A}(r_S)$ is often normalized by the administered activity to form the time-integrated activity coefficient (TIAC). S values are defined using Eq. (2),

$$S(r_T \leftarrow r_S) = \sum \frac{n_i E_i \varphi_i(r_T \leftarrow r_S)}{m_T},$$

where $m_T$ is the mass of the target, $n_i$ and $E_i$ are the frequency and energy of each radiation type $i$, and $\varphi_i(r_T \leftarrow r_S)$ is the absorbed fraction of energy emitted from the source that is deposited in the target for each radiation type emitted by the radionuclide of interest.
The elements of Eqs. (1) and (2) can be categorized into three major components of dose calculation. These components are (i) information about the biodistribution of activity, which is provided by the time-integrated activity $\tilde{A}(r_S)$ in all source regions, (ii) physical properties of the radionuclide ($n_i$ and $E_i$), and (iii) a dose estimation method that combines information about the activity distribution and the radionuclide properties to calculate the absorbed dose distribution.

In this work, three dose calculation methods that vary in complexity and in the accuracy of the dose estimates that they produce have been evaluated for four different source radionuclides: $^{99m}$Tc, $^{131}$I, $^{177}$Lu, and $^{90}$Y. Doses calculated using the Organ Level Internal Dose Assessment with Exponential Modeling (OLINDA/EXM) software and the voxel S value technique are compared to the results from Monte Carlo simulation, which was considered a reference standard for the purposes of this study. These comparisons were performed in order to investigate the advantages and disadvantages of each method and to study the accuracy of organ-level dose calculations based on reference phantoms.

1. Organ-level dose calculation with OLINDA/EXM

OLINDA/EXM is one of the most widely used programs for organ-level dose calculations. Using OLINDA/EXM, the user inputs organ TIACs and the program calculates the resulting mean absorbed dose for each organ. These doses are estimated using organ-level S values $S$ (organ$_{r}$ $\leftarrow$ organ$_{s}$) pre-calculated by Monte Carlo simulation in standard phantoms representing the average male or female. In these simulations, activity is assumed to be uniformly distributed in source organs and the dose is assumed to be uniformly deposited throughout each target organ.

Clearly, the S values based on standard phantoms are not patient-specific. OLINDA/EXM can make first-order adjustments for patient-specific organ masses if these are known, but not for the shapes and relative positions of organs, which can, of course, also vary from patient to patient. To correct for patient-specific organ masses for alpha and beta emissions, the dose scales linearly with the mass. For photon emissions, the absorbed fraction scales with the cube root of the mass for self-irradiation and directly with the mass for cross-irradiation.

Tumor doses are approximated by OLINDA/EXM using precalculated absorbed fractions to spheres of different sizes filled with uniform activity. These spheres are treated as isolated objects, so cross-dose to or from other tumors or organs is not accounted for.

1.1. Voxel S values

The voxel S value approach considers activity distributions at the voxel level and calculates the corresponding voxelized dose distribution. This method uses lookup tables of absorbed dose fractions in an array of target voxels due to radiation emitted from a single source voxel. These voxel S value $S$ (voxel$_{r}$ $\leftarrow$ voxel$_{s}$) lookup tables are precalculated by Monte Carlo simulation and are radionuclide-, voxel size-, and tissue-specific. Free databases of voxel S values for selected radionuclides and voxel sizes have also recently become available.

Dose calculation with voxel S values is performed by convolving the precalculated table of voxel doses per unit of accumulated activity in a source voxel with the patient-specific accumulated activity distribution. In a volume of $N$ source voxels, the dose to each target voxel is calculated using

$$D(\text{voxel}_{r}) = \sum_{S=0}^{N-1} \tilde{A}(\text{voxel}_{s}) S(\text{voxel}_{r} \leftarrow \text{voxel}_{s}).$$

The drawback of the voxel S value technique is that the lookup tables are calculated for a source material of uniform density and tissue inhomogeneities are not accounted for. However, the advantage of using the voxel S value approach is that it makes 3D dose calculations simple and fast. Furthermore, the assumption of uniform tissue density when voxelized dose distributions are calculated within organs or tumors is a reasonable approximation for many areas in the body.

1.2. Monte Carlo simulation

Monte Carlo techniques use the known physics of photon and particle interactions with matter to simulate radiation transport. Reconstructed SPECT images provide quantitative information about the activity distribution and radioactive emissions can be simulated and propagated through a computerized patient model to determine the resulting 3D dose distribution. The computerized model can be constructed based on a CT image set of the patient, and the method is thus able to take into account patient-specific source and target organ geometries and tissue inhomogeneities.

Monte Carlo simulation is the most robust method for dose estimation, but its use may be quite complicated and it requires very long computation times. Example Monte Carlo codes commonly used for radiotherapy and nuclear medicine applications include the electron gamma shower (EGS) code, MCNP, PENELOPE, and the GEANT code. The EGS code is considered to be a reference standard for clinical radiation dosimetry applications. The latest EGS version, EGSnrc, is accompanied by the user code, DOSXYZnrc, which facilitates calculation of dose distributions in a rectangular voxel phantom.

2. METHODS

2.1. Patient studies

A total of 6 patients (3 males and 3 females) injected with 800–1000 MBq of $^{99m}$Tc-hydrazinonicotinamide-Tyr$^3$-octreotide were included in this study. For each patient, a series of 3–4 whole body planar scans were acquired over a period of 24 h following injection. In addition, a single SPECT/CT scan was acquired approximately 3 h after injection. Further details regarding these patient studies have previously been described.
2.B. SPECT reconstruction

The SPECT images were reconstructed with our quantitative qSPECT method using the iterative ordered-subsets expectation maximization algorithm. These reconstructions included resolution recovery, CT-based attenuation, and analytic scatter corrections. Six iterations and ten subsets were used. A calibration experiment was performed in order to determine the sensitivity factor (in units of counts/minute/kBq) to be used to convert the reconstructed count rate to activity. This calibration experiment was performed using a planar acquisition of a point source of known activity (determined by a dose calibrator), placed in air about 20 cm from the surface of each of the two detectors. In previous work, we have shown that accurate activity estimates with errors less than 5% can be achieved using this in air planar calibration method along with our reconstruction technique.

2.C. Calculation of TIACs

All data were processed and analyzed with the MATLAB-based internal dosimetry package, JADA. A hybrid planar/SPECT approach was employed to plot and integrate time-activity curves for all tumors and each organ with a perceptibly greater activity concentration than that in the surrounding background tissue, which were the kidneys, liver, and spleen. To use the hybrid planar/SPECT approach, counts obtained from the planar scans for each investigated region were plotted versus time. Next, each image-derived tumor or organ time-activity curve was fit to a monoexponential function. Each such curve was then scaled to pass through the corresponding activity determined from the SPECT image (\(A_{\text{SPECT}}\)) at the time of the SPECT acquisition (\(t_{\text{SPECT}}\)). The fitted exponential curves were integrated to find the cumulated activity (\(\bar{A}\)) of the \(^{99m}\text{Tc}\) in each source region

\[
\bar{A} = A_{\text{SPECT}} \frac{e^{\lambda_{\text{SPECT}}}}{\lambda_{\text{eff}}} ,
\]

where \(\lambda_{\text{eff}}\) is the effective elimination constant obtained from the exponential fit.

The \(^{99m}\text{Tc}\) TIACs needed for organ-level dose calculation were determined by dividing the cumulated activities by the injected activity (\(A_{\text{inj}}/A_{\text{inj}}\)). Additionally, predicted TIACs were calculated for \(^{131}\text{I}\), \(^{177}\text{Lu}\), and \(^{90}\text{Y}\) assuming a pharmaceutical labeled with these radionuclides would follow the same time-dependent biodistribution as the \(^{99m}\text{Tc}\) labeled tracer. A summary of the half-lives and emissions for each of the radionuclides investigated in this study is included in Table I.

2.D. Absorbed dose calculation

2.D.1. Organ-level dosimetry

Mean organ doses to each segmented organ from the \(^{99m}\text{Tc}\) injection and the predicted organ doses from \(^{131}\text{I}\), \(^{177}\text{Lu}\), and \(^{90}\text{Y}\) injection were calculated using OLINDA/EXM. The mean dose calculated for each organ included contributions from the self-dose as well as the cross-dose from other segmented regions. The OLINDA/EXM sphere model was used to calculate the dose to tumors.

2.D.2. Voxel level dosimetry

The voxel S value method and Monte Carlo simulation were used to calculate 3D dose rate distributions as well as mean and total doses for tumors and organs. For voxel S value dose calculation, the voxel S values were precalculated using the EGSnrc user-code DOSXYZnrc Monte Carlo program. The relevant parameter settings for creation of the voxel S values were \(^{99m}\text{Tc}\) histories originating from a single source voxel with dimensions of 4.42 mm on edge at the center of a \(215 \times 215 \times 215\) voxel grid inside a soft tissue equivalent medium. The size of this voxel array was large enough so that cross-dose could be calculated between all ROIs using the voxel S value method. The large number of histories used for this Monte Carlo simulation allowed us to achieve low statistical error for the voxel S value lookup table.

For Monte Carlo dose calculation, the total number of histories simulated per source voxel was 100,000 photons and 100,000 electrons sampled from each radionuclide’s emission spectrum. Patient-specific SPECT and CT images were used as input for these Monte Carlo simulations. The total number of voxels simulated from the liver, kidneys, and spleen of each patient was on the order of \(10^4\) voxels, so that an approximate total of \(10^8\) histories were simulated for each patient. The EGSnrc input parameter, ECUT, which is the electron cutoff energy (sum of rest mass and kinetic energy) for which a history is terminated and energy is deposited in the current voxel, was set at 0.561 MeV for the \(^{99m}\text{Tc}\) simulation, 0.591 MeV for the \(^{177}\text{Lu}\) simulation, 0.611 MeV for the \(^{131}\text{I}\) simulation, and 0.711 MeV for the \(^{90}\text{Y}\) simulation. These ECUT values were selected after extensive investigation into what ECUT values could be used to reduce the simulation time without a substantial loss of accuracy in the resulting dose distribution (larger ECUT requires less simulation time).

The 3D dose rate distributions calculated by Monte Carlo simulation and the voxel S value technique were multiplied by the factor \(\exp(\lambda_{\text{eff}} \cdot t_{\text{SPECT}})/\lambda_{\text{eff}}\) in order to convert them to 3D dose distributions. Similar to the organ level
calculations, these dose distributions included self-dose as well as the cross-doses from all organs with considerable uptake. Only patients with entire organs (kidneys, liver, and spleen) visible in a single SPECT field of view were included in this analysis. For each source organ, a separate dose distribution in the volume enclosing all target regions was calculated so that a set of S values could be determined. These S values were found by dividing the mean dose to each target region \( r_T \) by the cumulated activity in source region \( r_S \).

\[
S(r_T \leftarrow r_S) = \frac{D(r_T \leftarrow r_S)}{A(r_S)}.
\]  

(5)

For example, the cross-organ S value for activity in the spleen irradiating the liver, \( S(\text{liver} \leftarrow \text{spleen}) \), was calculated as the mean dose to the liver, calculated by Monte Carlo (or voxel S values) using the spleen as a source organ, divided by the cumulated activity in the spleen.

The total dose to each target was also determined by summing the dose distributions calculated for each source organ. After the Monte Carlo and voxel S value calculations were performed for the \(^{99m}\text{Tc} \) activity distribution, these calculations were repeated using sources of \(^{131}\text{I} \), \(^{177}\text{Lu} \), and \(^{90}\text{Y} \).

2.E. Evaluation of dose estimation methods

The \(^{99m}\text{Tc} \), \(^{131}\text{I} \), \(^{177}\text{Lu} \), and \(^{90}\text{Y} \) dose estimates obtained using each of the three methods were evaluated by:

1. Comparing the organ-level S values corresponding to each method.
2. Comparing the total tumor and organ doses calculated by each method.
3. Investigating the difference in right and left kidney doses from the Monte Carlo simulation.
4. Comparing the Monte Carlo and voxel S value dose distributions voxel-by-voxel.

In each assessment, the Monte Carlo dose distributions were assumed to be the reference standard that the two other methods were compared to.

2.E.1. Comparison of reference and patient-specific S values at the organ-level

The values of \( S(r_T \leftarrow r_S) \) based on the reference phantoms used by OLINDA/EXM, \( S(r_T \leftarrow r_S)_{\text{OLINDA}} \), were compared to the S values calculated by Monte Carlo simulation, \( S(r_T \leftarrow r_S)_{\text{MC}} \), using patient-specific CT images. This assessment was done by finding the percentage difference between the two S values for each source and target region pair. The OLINDA/EXM S values were mass corrected using patient-specific organ masses. The percentage difference \( \Delta S_{\text{OLINDA}}(r_T \leftarrow r_S) \) for each S value array element was calculated as follows:

\[
\Delta S_{\text{OLINDA}}(r_T \leftarrow r_S) = \frac{(S(r_T \leftarrow r_S)_{\text{OLINDA}} - S(r_T \leftarrow r_S)_{\text{MC}})}{S(r_T \leftarrow r_S)_{\text{MC}}} \times 100\%.
\]  

(6)

Since three regions were investigated (kidneys, liver, and spleen), this comparison yielded a \( 3 \times 3 \) array of percentage differences for each patient, which were then used to find the average, standard deviation, minimum and maximum percentage difference for each array element over the entire patient population.

Similarly, the organ-level S values calculated from the voxel S value method, \( S(r_T \leftarrow r_S)_{\text{VSV}} \), were compared to the Monte Carlo determined S values to find

\[
\Delta S_{\text{VSV}}(r_T \leftarrow r_S) = \frac{(S(r_T \leftarrow r_S)_{\text{VSV}} - S(r_T \leftarrow r_S)_{\text{MC}})}{S(r_T \leftarrow r_S)_{\text{MC}}} \times 100\%. \]  

(7)

2.E.2. Total dose assessment

The mean organ and tumor doses calculated using Monte Carlo were compared to the organ and tumor doses calculated using OLINDA/EXM and voxel S values by finding the percentage difference between doses estimated by each of these methods. To compare normal organ doses, the evaluated doses included contributions from self- and cross-organ irradiation. Tumor doses calculated by OLINDA/EXM using the sphere model, which considers self-dose only, were compared to both Monte Carlo self-dose calculations and to Monte Carlo total dose (self-plus cross-dose) calculations.

The Monte Carlo results were analyzed further to determine the percentage of total dose that was due to cross-organ irradiation. In addition, the assumption by OLINDA/EXM that electrons are fully absorbed by source organs was tested by assessing the percentage of the total dose that was due to cross-organ irradiation from electron emissions.

2.E.3. Paired organ analysis

The Monte Carlo dose calculation was used to assess the dose to the right and left kidney separately in order to investigate potential limitations of the assumption made by OLINDA/EXM that paired organs each receive equal dose. The percentage difference between right and left kidney doses \( \Delta K \) was found using:

\[
\Delta K = 100\% \times \frac{\text{R.Kidney dose} - \text{L.Kidney dose}}{\text{Average kidney dose}}.
\]  

(8)

2.E.4. Monte Carlo and voxel S value voxel-by-voxel comparison

The 3D dose distributions calculated by Monte Carlo simulation and the voxel S value method were compared visually by plotting cumulative dose volume histograms (DVHs). In addition, a voxel-by-voxel analysis was carried out to determine the average (±standard deviation) percentage difference between corresponding voxels in the two 3D dose distributions calculated for each patient.

3. RESULTS

The cumulated \(^{99m}\text{Tc} \) activity concentrations for each of the investigated source organs and tumors are summarized in Table II. The highest cumulated organ activity concentration
was most commonly found in the spleen, followed by the kidneys and then the liver. The largest variation in source region concentration was found in tumors, where the cumulated tumor activity concentration in patient 4 was four times greater than in patient 2. There were tumors in three of the patients included in this study. In patient 2, there was a 23 ml paraganglioma located paravertebral at the Th10-11 level; in patient 3, there was a 95 ml neuroendocrine tumor in the pancreas; and in patient 4, there was a 76 ml neuroendocrine tumor in the small bowel.

### 3.A. Comparison of organ-level S values

When the S values used by OLINDA/EXM for each source and target region pair and the corresponding S values calculated using Monte Carlo simulation were compared using Eq. (3), there was generally a good agreement in S values for self-irradiation, but a very poor agreement in S values using Eq. (3), there was generally a good agreement in S values calculated using Monte Carlo simulation were compared between the voxel S value and Monte Carlo doses was 11% or less. There was not good agreement between the liver and spleen where the average values of $\Delta S_{SVS}(\text{Liver} \leftarrow \text{Spleen})$ ranged from 14% with $^{131}\text{I}$ to 31% with $^{99m}\text{Tc}$. Differences in patient specific-anatomy leading to the large discrepancies between OLINDA/EXM and Monte Carlo generated S values can be explained by visualizing the anatomy of two example patients displayed in Fig. 1. The corresponding S value comparisons for these two patients are listed in Tables VII–IX for $^{99m}\text{Tc}$, $^{131}\text{I}$ and $^{177}\text{Lu}$, respectively.

### 3.B. Total organ and tumor dose assessment

There was good agreement between the total organ doses calculated by OLINDA/EXM and the mean doses calculated by Monte Carlo simulation (Fig. 2), regardless of the radionuclide used. The worst agreement was found in the spleen of patient 1 (using $^{177}\text{Lu}$), where the percentage difference between OLINDA/EXM and Monte Carlo doses was $-6.2\%$. Similarly, total doses calculated using the voxel S value method were in good agreement with the Monte Carlo results. In this case, the worst agreement was found in the liver of patient 6 (using $^{99m}\text{Tc}$), where the percentage difference between the voxel S value and Monte Carlo doses was 7.4%.

### Table II. Cumulated $^{99m}\text{Tc}$ activity concentrations in organs, tumors and remainder of the body

| Patient | L. kidney | R. kidney | Liver | Spleen | Tumor | Remainder of the body |
|---------|-----------|-----------|-------|--------|-------|-----------------------|
| 1       | 0.62      | 1.07      | 0.37  | 1.58   | ...   | 0.07                  |
| 2       | 1.33      | 1.34      | 0.41  | 1.08   | 0.71   | 0.07                  |
| 3       | 0.86      | 0.91      | 0.56  | 2.42   | 1.40   | 0.06                  |
| 4       | 0.63      | 0.63      | 0.42  | 1.21   | 2.84   | 0.06                  |
| 5       | 1.26      | 1.18      | 0.53  | 2.12   | ...   | 0.06                  |
| 6       | 0.98      | 1.04      | 0.31  | 1.76   | ...   | 0.05                  |

### Table III. Summary of percentage differences between the $^{99m}\text{Tc}$ patient-specific S values calculated using Monte Carlo and the corresponding S values used by OLINDA/EXM and those calculated using voxel S values for each source and target region pair.

| Source        | Target       | Kidneys       | Liver         | Spleen       |
|---------------|--------------|---------------|---------------|--------------|
| Kidneys       | $\Delta S_{OLINDA}(r_7 \leftarrow r_5)$ | 0.2 ± 1.3 (−1.9–2.1) | −21 ± 24 (−51–10) | 25 ± 49 (−38–105) |
|               | $\Delta S_{SVS}(r_7 \leftarrow r_5)$  | 0.5 ± 1.1 (−1.5–1.8) | 11 ± 5 (4.7–17) | 10 ± 5 (4.6–17) |
| Liver         | $\Delta S_{OLINDA}(r_7 \leftarrow r_5)$ | −23 ± 23 (−43–14) | 2.3 ± 2.2 (−0.4–4.7) | −31 ± 27 (−72–10) |
|               | $\Delta S_{SVS}(r_7 \leftarrow r_5)$  | 11 ± 5 (3.3–16) | 3.8 ± 1.3 (1.6–4.9) | 28 ± 11 (9.5–37) |
| Spleen        | $\Delta S_{OLINDA}(r_7 \leftarrow r_5)$ | −0.9 ± 34 (−47–38) | −45 ± 23 (−68 to −7) | 1.1 ± 2.1 (−2.5–3.8) |
|               | $\Delta S_{SVS}(r_7 \leftarrow r_5)$  | 11 ± 5 (4.6–17) | 31 ± 13 (11–43) | 0.7 ± 1.8 (−2.2–2.5) |

Note: Data are mean ± standard deviation; the range is provided in parentheses.
TABLE IV. Summary of percentage differences between the $^{131}$I patient-specific S values calculated using Monte Carlo and the corresponding S values used by OLINDA/EXM and those calculated using voxel S values for each source and target region pair.

| Source | Target | Kidneys | Liver | Spleen |
|--------|--------|---------|-------|--------|
| Kidneys | ΔSOLINDA($r_T \leftarrow r_S$) | $-1.3 \pm 1.3$ ($-3.7$ to $-0.3$) | $-25 \pm 26$ ($-57$ to $-12$) | $19 \pm 50$ ($-46$ to $97$) |
| | ΔSVSV($r_T \leftarrow r_S$) | $-0.2 \pm 1.5$ ($-2.9$ to $-1.4$) | $5.4 \pm 2.3$ ($1.9$ to $-7.7$) | $3.4 \pm 3.1$ ($-0.2$ to $7.1$) |
| Liver | ΔSOLINDA($r_T \leftarrow r_S$) | $-30 \pm 28$ ($-55$ to $-12$) | $-0.3 \pm 1.6$ ($-2.3$ to $-1.3$) | $-32 \pm 25$ ($-72$ to $3.2$) |
| | ΔSVSV($r_T \leftarrow r_S$) | $4.6 \pm 2.1$ ($1.8$ to $-7.4$) | $1.6 \pm 1.3$ ($-0.3$ to $-2.5$) | $14 \pm 5$ ($4.6$ to $18$) |
| Spleen | ΔSOLINDA($r_T \leftarrow r_S$) | $1.0 \pm 4.0$ ($-58$ to $37$) | $-47 \pm 20$ ($-70$ to $-15$) | $-1.8 \pm 2.2$ ($-5.6$ to $0.3$) |
| | ΔSVSV($r_T \leftarrow r_S$) | $4.7 \pm 2.1$ ($1.7$ to $-7.8$) | $15 \pm 6$ ($4.3$ to $-19$) | $-0.6 \pm 2.3$ ($-4.5$ to $1.8$) |

Note: Data are mean ± standard deviation; the range is provided in parentheses.

TABLE V. Summary of percentage differences between the $^{177}$Lu patient-specific S values calculated using Monte Carlo and the corresponding S values used by OLINDA/EXM and those calculated using voxel S values for each source and target region pair.

| Source | Target | Kidneys | Liver | Spleen |
|--------|--------|---------|-------|--------|
| Kidneys | ΔSOLINDA($r_T \leftarrow r_S$) | $-1.3 \pm 1.4$ ($-3.9$ to $-0.2$) | $-30 \pm 31$ ($-76$ to $95$) | $16 \pm 54$ ($-55$ to $100$) |
| | ΔSVSV($r_T \leftarrow r_S$) | $-0.3 \pm 1.6$ ($-3.2$ to $-1.5$) | $9.0 \pm 4.2$ ($3.8$ to $14$) | $7.1 \pm 5.8$ ($0.5$ to $14$) |
| Liver | ΔSOLINDA($r_T \leftarrow r_S$) | $-40 \pm 35$ ($-83$ to $10$) | $0.1 \pm 1.7$ ($-2.2$ to $-1.6$) | $-33 \pm 27$ ($-73$ to $7.1$) |
| | ΔSVSV($r_T \leftarrow r_S$) | $6.8 \pm 4.6$ ($2.5$ to $-12$) | $1.3 \pm 1.6$ ($-1.0$ to $-2.5$) | $24 \pm 10$ ($8.7$ to $32$) |
| Spleen | ΔSOLINDA($r_T \leftarrow r_S$) | $-1.9 \pm 42$ ($-62$ to $35$) | $-46 \pm 22$ ($-70$ to $-11$) | $-2.1 \pm 2.4$ ($-6.1$ to $-0.2$) |
| | ΔSVSV($r_T \leftarrow r_S$) | $9.0 \pm 3.9$ ($3.4$ to $14$) | $28 \pm 11$ ($9.7$ to $38$) | $-0.8 \pm 2.7$ ($-5.3$ to $2.0$) |

Note: Data are mean ± standard deviation; the range is provided in parentheses.

TABLE VI. Summary of percentage differences between the $^{90}$Y patient-specific S values calculated using Monte Carlo and the corresponding S values used by OLINDA/EXM and those calculated using voxel S values for each source and target region pair. S values for cross-organ irradiation are excluded since there is negligible cross-dose between organs with $^{90}$Y.

| Source | Target | Kidneys | Liver | Spleen |
|--------|--------|---------|-------|--------|
| Kidneys | ΔSOLINDA($r_T \leftarrow r_S$) | $2.9 \pm 3.0$ ($-2.0$ to $-5.5$) | ... | ... |
| | ΔSVSV($r_T \leftarrow r_S$) | $-0.2 \pm 1.4$ ($-2.7$ to $-1.2$) | ... | ... |
| Liver | ΔSOLINDA($r_T \leftarrow r_S$) | ... | $4.6 \pm 2.1$ ($1.8$ to $-7.3$) | ... |
| | ΔSVSV($r_T \leftarrow r_S$) | ... | $1.6 \pm 1.6$ ($-0.6$ to $-3.1$) | ... |
| Spleen | ΔSOLINDA($r_T \leftarrow r_S$) | ... | ... | $-0.7 \pm 2.5$ ($-4.2$ to $-2.7$) |
| | ΔSVSV($r_T \leftarrow r_S$) | ... | ... | $-0.3 \pm 2.9$ ($-4.3$ to $-1.8$) |

Note: Data are mean ± standard deviation; the range is provided in parentheses.
in OLINDA/EXM, the average percentage differences between these doses were $-0.9\% \pm 5.1\%$, $-3.5\% \pm 4.7\%$, $-3.5\% \pm 5.1\%$, and $-0.8\% \pm 3.9\%$ for $^{99m}\text{Tc}$, $^{131}\text{I}$, $^{177}\text{Lu}$, and $^{90}\text{Y}$, respectively. When total doses, including self-plus cross-dose contributions calculated by Monte Carlo were considered, these differences became $-8.8\% \pm 11.1\%$, $-6.0\% \pm 5.4\%$, $-3.8\% \pm 5.2\%$, and $-0.8\% \pm 3.9\%$ for $^{99m}\text{Tc}$, $^{131}\text{I}$, $^{177}\text{Lu}$, and $^{90}\text{Y}$, respectively. The average percentage differences between the Monte Carlo and voxel S value derived tumor doses were $1.1\% \pm 1.9\%$, $-1.1\% \pm 4.0\%$, $-1.5\% \pm 4.6\%$, and $-0.4\% \pm 3.1\%$ for $^{99m}\text{Tc}$, $^{131}\text{I}$, $^{177}\text{Lu}$, and $^{90}\text{Y}$, respectively.

Analysis of the cross-organ irradiation data from Monte Carlo simulation revealed that cross-organ doses made the greatest contribution to total dose calculated for $^{99m}\text{Tc}$ distributions and the least contribution for $^{90}\text{Y}$ distributions (Fig. 3). For example, cross-organ irradiation with $^{99m}\text{Tc}$ contributed as much as 20% to the total organ dose (in the left kidney of patient 6), whereas the largest contribution to total organ dose from $^{90}\text{Y}$ cross-organ irradiation was 1.3% (also in the left kidney of patient 6). Electron emissions were found to contribute less than 0.05% to cross-organ doses in most cases. In situations where two organs were in close contact (e.g., the left kidney and the spleen or the right kidney and the liver), the beta cross-dose contribution was around 0.5% for $^{131}\text{I}$ and around 1% for $^{90}\text{Y}$.

For tumors, cross-organ irradiation contributed as little as 0% (with $^{90}\text{Y}$ in patients 3 and 4) and as much as 16.2% (with $^{99m}\text{Tc}$ in patient 2) to the total tumor dose.

### 3.C. Right and left kidney doses

Results from the comparison of right and left kidney doses, calculated by Monte Carlo simulation, are reported in Table X. For $^{99m}\text{Tc}$, the doses deposited in the right and left kidneys agreed within 7.3% in four out of six patients. Two extreme cases where there was a relatively large difference between individual kidney doses were observed for patients 1 and 6 (Fig. 4).

There was generally a poor agreement between kidney doses calculated with $^{131}\text{I}$, $^{177}\text{Lu}$, and $^{90}\text{Y}$ activities. This was due to a combination of the long physical half-lives of these radionuclides and differences in the washout rates between the two kidneys (demonstrated by the differences in biological half-lives listed in Table X for the right and left kidneys).

### 3.D. Monte Carlo and voxel S value comparison

The dose distributions calculated with the voxel S value method closely matched the dose distributions obtained with Monte Carlo simulation. To illustrate the similarity between the calculated dose distributions, an example comparison of the cumulative DVHs determined by the two methods is shown in Fig. 1. Coronal view of maximum intensity projections for patient 2 (a) and patient 4 (b) illustrating differences in patient-specific anatomy and relative uptake of $^{99m}\text{Tc}$-HYNIC-TOC in the kidneys, liver, and spleen.

---

**Table VII.** Percentage differences between $^{99m}\text{Tc}$ patient-specific S values calculated by Monte Carlo simulation and the corresponding reference S values used by OLINDA/EXM and those calculated using voxel S values for patients 2 and 4.

| Patient 2 | Patient 4 |
|-----------|-----------|
| $^{99m}\text{Tc}$ | Kidneys | Liver | Spleen | Kidneys | Liver | Spleen |
| $\Delta SO Linda (r_T \leftarrow r_S)$ | -0.04 | -41.9 | -38.1 | -0.3 | -0.9 | 105 |
| $\Delta S_{VSV} (r_T \leftarrow r_S)$ | 1.8 | 16.9 | 7.0 | 0.3 | 13.6 | 16.8 |
| $^{131}\text{I}$ | Kidneys | Liver | Spleen | Kidneys | Liver | Spleen |
| $\Delta SO Linda (r_T \leftarrow r_S)$ | -43.0 | 4.7 | -71.7 | 14.0 | 1.0 | 10.3 |
| $\Delta S_{VSV} (r_T \leftarrow r_S)$ | 15.6 | 4.8 | 29.2 | 12.5 | 3.1 | 37.0 |
| $^{177}\text{Lu}$ | Kidneys | Liver | Spleen | Kidneys | Liver | Spleen |
| $\Delta SO Linda (r_T \leftarrow r_S)$ | -32.5 | -67.0 | 0.6 | 37.5 | -35.3 | 2.3 |
| $\Delta S_{VSV} (r_T \leftarrow r_S)$ | 11.7 | 34.5 | -0.01 | 17.5 | 40.9 | 2.3 |

---

**Table VIII.** Percentage differences between $^{131}\text{I}$ patient-specific S values calculated by Monte Carlo simulation and the corresponding reference S values used by OLINDA/EXM and those calculated using voxel S values for patients 2 and 4.

| Patient 2 | Patient 4 |
|-----------|-----------|
| $^{131}\text{I}$ | Kidneys | Liver | Spleen | Kidneys | Liver | Spleen |
| $\Delta SO Linda (r_T \leftarrow r_S)$ | -0.6 | -46.1 | -46.1 | -1.4 | -3.0 | 97.2 |
| $\Delta S_{VSV} (r_T \leftarrow r_S)$ | 1.4 | 7.7 | -0.2 | -0.4 | 6.2 | 7.1 |
| $^{90}\text{Y}$ | Kidneys | Liver | Spleen | Kidneys | Liver | Spleen |
| $\Delta SO Linda (r_T \leftarrow r_S)$ | -48.1 | 0.8 | -71.7 | 11.5 | -2.2 | 3.2 |
| $\Delta S_{VSV} (r_T \leftarrow r_S)$ | 5.1 | 2.3 | 14.2 | 6.1 | 0.06 | 17.5 |
| $^{99m}\text{Tc}$ | Kidneys | Liver | Spleen | Kidneys | Liver | Spleen |
| $\Delta SO Linda (r_T \leftarrow r_S)$ | -37.8 | -68.0 | -2.4 | 33.8 | -40.6 | -0.3 |
| $\Delta S_{VSV} (r_T \leftarrow r_S)$ | 4.8 | 15.5 | -1.5 | 7.8 | 19.0 | 0.9 |
TABLE IX. Percentage differences between $^{177}$Lu patient-specific S values calculated by Monte Carlo simulation and the corresponding reference S values used by OLINDA/EXM and those calculated using voxel S values for patients 2 and 4.

|                      | Patient 2 | Patient 4 |
|----------------------|-----------|-----------|
| $^{177}$Lu           |           |           |
| Kidneys              |           |           |
| $\Delta$SOLINDA($r_T \leftarrow r_S$) | -0.3      | -1.3      |
| $\Delta$SVSV($r_T \leftarrow r_S$)  | 1.5       | 0.5       |
| Liver                |           |           |
| $\Delta$SOLINDA($r_T \leftarrow r_S$) | -53.9     | 10.2      |
| $\Delta$SVSV($r_T \leftarrow r_S$)  | 12.0      | 10.1      |
| Spleen               |           |           |
| $\Delta$SOLINDA($r_T \leftarrow r_S$) | -44.9     | 35.0      |
| $\Delta$SVSV($r_T \leftarrow r_S$)  | 10.1      | 14.3      |

presented in Fig. 5. On average, the D90s (minimum dose covering 90% of the volume) agreed within 2.8% ± 2.9%, 1.4% ± 2.1%, 2.3% ± 2.4%, 2.2% ± 2.9% for $^{99m}$Tc, $^{131}$I, $^{177}$Lu, and $^{90}$Y, respectively. When the dose distributions were analyzed voxel-by-voxel, the largest percentage difference between corresponding voxels averaged over all voxels in the target organs of a single patient was 6.1% ± 6.6% in patient 6 with $^{99m}$Tc.

4. DISCUSSION

In general, good agreement was found between total organ doses calculated using OLINDA/EXM, Voxel S-values, and Monte Carlo for all analyzed isotopes. However, more detailed analysis of these results clearly indicates that patient anatomy had a large impact on cross-organ S values. For example, the value of $\Delta S_{OLINDA}$(Kidneys $\leftarrow$ Spleen) was -38% for patient 2 and 105% for patient 4 when using $^{99m}$Tc (Table VII). As illustrated in Fig. 1, the spleen is found closer to the left kidney in patient 2 than it is in patient 4 leading to the relative differences observed in this S value comparison. Similar results were reported by Divoli et al., who compared $^{131}$I S values used by OLINDA/EXM to patient-specific values calculated by the MCNPX2.5.0 Monte Carlo code. They reported percentage differences between OLINDA/EXM and patient-specific S values ranging from -51% to 84%.

The cross-organ S values calculated using voxel S values and Monte Carlo simulation were in good agreement between the liver and kidneys and between the spleen and kidneys since the volume enclosing each of these pairs of regions is
a relatively uniform tissue medium. However, there was poor agreement in the cross-organ S values between the liver and spleen, where the voxel S value technique overestimated the Monte Carlo calculation by about 30% on average for $^{99m}$Tc and $^{177}$Lu, and by about 15% on average for $^{131}$I. This overestimation was caused by radiation attenuated in the spine lying partly between the spleen and liver, which was properly handled by Monte Carlo simulation, but was not accounted for by the voxel S value calculation where a uniform soft tissue medium was assumed. The overestimation was not as severe for $^{131}$I due to the higher energy gammas (364 keV) it emits compared to the other two radionuclides.

Despite the disagreements in cross-organ S values, the total mean organ doses calculated by each technique remained in reasonable agreement (Fig. 2). This was due to the fact that the self-organ S values were in good agreement (Tables III–VI) and the self-dose accounted for the majority of the dose to each organ containing activity (Fig. 3). The errors in organ cross-dose calculated by OLINDA/EXM may become more relevant in organs with no specific uptake of the radiopharmaceutical; however, this was not investigated as a part of this study.

Cross-organ contributions were greater with $^{131}$I than with $^{177}$Lu. This can be attributed to the higher intensity (82\%) of

![Figure 3](image_url)

**FIG. 3.** Average percent contributions of self- and cross-doses to the total organ and tumor doses, calculated by Monte Carlo simulation with $^{99m}$Tc (a), $^{131}$I (b), $^{177}$Lu (c), and $^{90}$Y (d). Note that the x-axis begins at 80%.

---

**TABLE X.** Percentage difference between right and left kidney doses $\Delta K$ calculated by Monte Carlo for four radionuclides with corresponding biological half-lives in each patient.

| Patient | $^{99m}$Tc | $^{131}$I | $^{177}$Lu | $^{90}$Y | $T_{\text{hot}}$ (h) |
|---------|----------|----------|----------|----------|---------------------|
|         | $\Delta K$ | $\Delta K$ | $\Delta K$ | $\Delta K$ | R. kidney | L. kidney |
| 1       | 44.6     | 37.2     | 37.8     | 42.0     | 30.8     | 37.0     |
| 2       | 2.3      | 10.1     | 10.4     | 6.5      | 38.0     | 33.3     |
| 3       | 7.3      | 13.7     | 14.2     | 11.2     | 31.2     | 28.4     |
| 4       | 2.6      | 3.5      | 3.2      | 1.9      | 36.0     | 35.0     |
| 5       | −2.1     | 73.0     | 68.9     | 50.8     | 194.7    | 47.9     |
| 6       | −19.3    | −47.2    | −46.5    | −37.7    | 35.0     | 56.3     |
| Mean ± SD | 6 ± 21 | 15 ± 40 | 15 ± 38 | 12 ± 32 | 61.0 ± 65.6 | 39.7 ± 10.4 |
model underestimated the total tumor dose by 12%, 10%, and 5% using $^{131}$I, $^{177}$Lu, and $^{90}$Y, respectively. These differences between sphere model and total tumor dose are less than those previously reported by Johnson and Colby$^{22}$ and by Howard et al.$^{23}$ In the study by Johnson et al., 35 tumors ranging in radius from 1.0 to 2.0 cm were simulated and neglecting cross-dose contributions was found to underestimate tumor doses by 10%–25%.$^{22}$ In the study by Howard et al., 57 tumors in a wide range of sizes from 2 to 423 ml were evaluated and use of the sphere model was found to underestimate total tumor dose by up to 31%.$^{23}$ Conversely, Divoli et al. investigated tumors only 7 g in size and found the differences between the sphere model and Monte Carlo total tumor dose calculations to be less than 5%.$^{21}$ The present study only included three tumors, which ranged in volume from 23 to 95 ml. These tumors were larger than the tumors studied by Divoli et al. and by Johnson et al. and they fell inside the range of tumor volumes studied by Howard et al. The likely reasons that cross-dose contributions played a relatively small factor in the total tumor doses of the present study are that these tumors were isolated from other areas with high activity concentration and two of the three tumors (patients 3 and 4) had high cumulated activity concentrations compared to the other source organs (Table II).

In the paired organ analysis, it is interesting to note the influence of the different physical half-lives of the investigated radionuclides. For the shorter lived radionuclide, $^{99m}$Tc, differences in right and left kidney doses were caused by differences in the total activity uptake [Fig. 4(a)] and proximity to highly radioactive organs [Fig. 4(b)], whereas for the longer lived radionuclides, $^{131}$I, $^{177}$Lu, and $^{90}$Y differences in left and right kidney doses were also heavily influenced by differences in the rates of washout from these organs. For example, in patient 2, the right and left kidney doses agreed within 2.3% for $^{99m}$Tc, but a difference of 4.7 h in the biological half-lives of each kidney raised the percent difference to 10% for $^{131}$I and $^{177}$Lu.

Finally, 3D dose distributions calculated by the voxel S value method in approximately 1 h were found to produce very similar dose distributions to those calculated by Monte Carlo simulation, which took 30 h or more. The use of the fast Hartley transform could be used to substantially decrease the computation time of the voxel S value calculation.$^{24}$

### 5. CONCLUSIONS

Several aspects of OLINDA/EXM dose calculations (which are based on reference phantoms representing the average patient) were tested by comparing them with patientspecific Monte Carlo dose estimates. Although anatomy can differ considerably between patients, organ doses calculated by OLINDA/EXM were found to be in good agreement with Monte Carlo mean dose estimates. Furthermore, the sphere model used by OLINDA/EXM agreed reasonably well with Monte Carlo dose estimates with therapeutic agents ($^{131}$I, $^{177}$Lu, and $^{90}$Y) even with cross organ irradiation. The treatment of paired organs by OLINDA/EXM was found to be inaccurate in several cases where the dose to the right and
left kidneys differed by up to 73%. Furthermore, the lack of voxelized dose information is a major limitation of organ-level calculations since nonuniform dose distributions may have important clinical implications. Although Monte Carlo simulation may not currently be feasible for routine patient dose calculations, voxel S values have been shown to produce nearly equivalent 3D dose distributions.

ACKNOWLEDGMENTS

The authors greatly acknowledge the financial support of a four-year doctoral fellowship from the University of British Columbia.

[1] Author to whom correspondence should be addressed. Electronic mail: grimes.joshua@mayo.edu

[2] R. Loevinger, T. F. Budinger, and E. E. Watson, MIRD Primer for Absorbed Dose Calculations (Society of Nuclear Medicine, New York, NY, 1991).

[3] W. E. Bolch, K. F. Eckerman, G. Sgouros, and S. R. Thomas, “MIRD pamphlet No. 21: A generalized schema for radiopharmaceutical dosimetry—standardization of nomenclature,” J. Nucl. Med. 50, 477–484 (2009).

[4] M. G. Stabin, R. B. Sparks, and E. Crowe, “OLINDA/EXM: The second-generation personal computer software for internal dose assessment in nuclear medicine,” J. Nucl. Med. 46, 1023–1027 (2005).

[5] W. E. Bolch, L. G. Bouchet, J. S. Robertson, B. W. Wessels, J. A. Siegel, R. W. Howell, A. K. Erdi, B. Aydogan, S. Costes, and E. E. Watson, in collaboration with the MIRD Committee. Society of Nuclear Medicine: E. E. Watson (Chair), J. S. Robertson (Task Group Leader), W. E. Bolch, A. B. Brill, N. D. Charkes, D. R. Fisher, M. T. Hays, R. W. Howell, J. A. Siegel, S. R. Thomas, and B. W. Wessels, “MIRD pamphlet No. 17: The dosimetry of nonuniform activity distributions—Radionuclide S values at the voxel level,” J. Nucl. Med. 40, 11S-36S (1999).

[6] A. Dieudonne, R. F. Hobbs, W. E. Bolch, G. Sgouros, and I. Gardin, “Fine-resolution voxel S values for constructing absorbed dose distributions at variable voxel size,” J. Nucl. Med. 51, 1600–1607 (2010).

[7] M. Pacilio, N. Lanconelli, S. Lo Meo, M. Betti, L. Montani, L. A. Torres Aroche, and M. A. Coca Perez, “Differences among Monte Carlo codes in the calculations of voxel S values for radionuclide targeted therapy and analysis of their impact on absorbed dose evaluations,” Med. Phys. 36, 1543–1552 (2009).

[8] N. Lanconelli, M. Pacilio, S. Lo Meo, F. Botta, A. Di Dia, A. T. Aroche, M. A. Perez, and M. Cremonesi, “A free database of radionuclide voxel S values for the dosimetry of nonuniform activity distributions,” Phys. Med. Biol. 57, 517–533 (2012).

[9] D. W. O. Rogers, “Low energy electron transport with EGS,” Nucl. Instrum. Meth. 227, 535–548 (1984).

[10] J. S. Hendricks and J. F. Briesmeister, “Recent MCNP developments,” IEEE Trans. Nucl. Sci. 39, 1035–1040 (1992).

[11] H. Yoriyaz, M. G. Stabin, and A. dos Santos, “Monte Carlo MCNP-4B-based absorbed dose distribution estimates for patient-specific dosimetry,” J. Nucl. Med. 42, 662–669 (2001).

[12] J. Sempau, E. Acosta, J. Baro, J. M. Fernandez-Varea, and F. Salvat, “An algorithm for Monte Carlo simulation of coupled electron-photon transport,” Nucl. Instrum. Meth. B 132, 377–390 (1997).

[13] M. G. Pia, “The Geant4 Toolkit: Simulation capabilities and application results,” Nucl. Phys. B 125, 60–68 (2003).

[14] L. Strigari, E. Menghi, M. D’Andrea, and M. Benassi, “Monte Carlo dose voxel kernel calculations of beta-emitting and auger-emitting radionuclides for internal dosimetry: A comparison between EGSnrcMP and EGS4,” Med. Phys. 33, 3383–3389 (2006).

[15] J. Grimes, A. Celler, B. Birkenfeld, S. Schcherbinin, M. H. Listewnik, H. Piwowarska-Bińska, R. Mikolajczak, and P. Zorga, “Patient-specific radiation dosimetry of 99mTc-HYNIC-Tyr3-octreotide in neuroendocrine tumors,” J. Nucl. Med. 52, 1474–1481 (2011).

[16] S. Schcherbinin, A. Celler, T. Belhocine, R. Vanderwerf, and A. Driedger, “Accuracy of quantitative reconstructions in SPECT/CT imaging,” Phys. Med. Biol. 53, 4595–4604 (2008).

[17] J. Grimes, C. Uribe, and A. Celler, “JADA: A graphical user interface for comprehensive internal dose assessment in nuclear medicine,” Med. Phys. 40, 072501 (12 pp.) (2013).

[18] A. Divoli, S. Chiavassa, L. Ferrer, J. Barbet, G. D. Flux, and M. Bardies, “Effect of patient morphology on dosimetric calculations for internal irradiation as assessed by comparisons of Monte Carlo versus conventional methodologies,” J. Nucl. Med. 50, 316–323 (2009).

[19] T. K. Johnson and S. B. Colby, “Photon contribution to tumor dose from considerations of 131I radiolabeled antibody uptake in liver, spleen, and whole body,” Med. Phys. 20, 1667–1674 (1993).

[20] D. M. Howard, K. J. Kearfott, S. J. Wilderman, and Y. K. Dewaraja, “Algorithm for Monte Carlo simulation of electron transport. I. EGSnrc, the new EGS4 version,” Med. Phys. 27, 485–498 (2000).

[21] B. Walters and I. Kawrakow, “DOSXYZnrc users manual,” Technical Report No. PIRS-794, RevB, 2005.

[22] L. Strigari, E. Menghi, M. D’Andrea, and M. Benassi, “Monte Carlo dose voxel kernel calculations of beta-emitting and auger-emitting radionuclides for internal dosimetry: A comparison between EGSnrcMP and EGS4,” Med. Phys. 33, 3383–3389 (2006).

[23] J. Grimes, A. Celler, B. Birkenfeld, S. Schcherbinin, M. H. Listewnik, H. Piwowarska-Bińska, R. Mikolajczak, and P. Zorga, “Patient-specific radiation dosimetry of 99mTc-HYNIC-Tyr3-octreotide in neuroendocrine tumors,” J. Nucl. Med. 52, 1474–1481 (2011).

[24] S. Schcherbinin, A. Celler, T. Belhocine, R. Vanderwerf, and A. Driedger, “Accuracy of quantitative reconstructions in SPECT/CT imaging,” Phys. Med. Biol. 53, 4595–4604 (2008).

[25] J. Grimes, C. Uribe, and A. Celler, “JADA: A graphical user interface for comprehensive internal dose assessment in nuclear medicine,” Med. Phys. 40, 072501 (12 pp.) (2013).

[26] A. Divoli, S. Chiavassa, L. Ferrer, J. Barbet, G. D. Flux, and M. Bardies, “Effect of patient morphology on dosimetric calculations for internal irradiation as assessed by comparisons of Monte Carlo versus conventional methodologies,” J. Nucl. Med. 50, 316–323 (2009).

[27] T. K. Johnson and S. B. Colby, “Photon contribution to tumor dose from considerations of 131I radiolabeled antibody uptake in liver, spleen, and whole body,” Med. Phys. 20, 1667–1674 (1993).

[28] D. M. Howard, K. J. Kearfott, S. J. Wilderman, and Y. K. Dewaraja, “Comparison of I-131 radioimmunotherapy tumour dosimetry: Unit density sphere model versus patient-specific Monte Carlo calculations,” Cancer Biother. Radiopharm. 26, 615–621 (2011).

[29] A. K. Erdi, E. D. Yorke, M. H. Loew, Y. E. Erdi, M. Sarfaraz, and B. W. Wessels, “Use of the fast Hartley transform for three-dimensional dose calculation in radionuclide therapy,” Med. Phys. 25, 2226–2233 (1998).