Internal dosimetry with the Monte Carlo code GATE: validation using the ICRP/ICRU female reference computational model

Daphnée Villoing\textsuperscript{1,2,3}, Sara Marcatili\textsuperscript{1,2,4}, Marie-Paule Garcia\textsuperscript{1,2} and Manuel Bardies\textsuperscript{1,2}

\textsuperscript{1} Inserm, UMR1037 CRCT, F-31000 Toulouse, France
\textsuperscript{2} Université Toulouse III-Paul Sabatier, UMR1037 CRCT, F-31000 Toulouse, France
E-mail: daphnee.villoing@nih.gov and manuel.bardies@inserm.fr

Received 31 July 2015, revised 28 October 2016
Accepted for publication 8 November 2016
Published 9 February 2017

Abstract
The purpose of this work was to validate GATE-based clinical scale absorbed dose calculations in nuclear medicine dosimetry.

GATE (version 6.2) and MCNPX (version 2.7.a) were used to derive dosimetric parameters (absorbed fractions, specific absorbed fractions and \textit{S}-values) for the reference female computational model proposed by the International Commission on Radiological Protection in ICRP report 110.

Monoenergetic photons and electrons (from 50 keV to 2 MeV) and four isotopes currently used in nuclear medicine (fluorine-18, lutetium-177, iodine-131 and yttrium-90) were investigated.

Absorbed fractions, specific absorbed fractions and \textit{S}-values were generated with GATE and MCNPX for 12 regions of interest in the ICRP 110 female computational model, thereby leading to 144 source/target pair configurations. Relative differences between GATE and MCNPX obtained in specific configurations (self-irradiation or cross-irradiation) are presented. Relative differences in absorbed fractions, specific absorbed fractions or \textit{S}-values are below 10\%, and in most cases less than 5\%. Dosimetric results generated with GATE for the 12 volumes of interest are available as supplemental data.

\textsuperscript{3} Now at Division of Cancer Epidemiology and Genetics, NCI, NIH, Rockville, MD, USA.
\textsuperscript{4} Now at Laboratoire de Physique Subatomique et de Cosmologie, Université Grenoble-Alpes, CNRS/IN2P3, F-38026 Grenoble, France.

Original content from this work may be used under the terms of the Creative Commons Attribution 3.0 licence. Any further distribution of this work must maintain attribution to the author(s) and the title of the work, journal citation and DOI.
GATE can be safely used for radiopharmaceutical dosimetry at the clinical scale. This makes GATE a viable option for Monte Carlo modelling of both imaging and absorbed dose in nuclear medicine.

Keywords: Monte Carlo modelling, internal dosimetry, GATE, MCNPX, voxelized models

Supplementary material for this article is available online

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

1. Introduction

Monte Carlo radiation transport modelling is heavily used in nuclear medicine (Zaidi and Sgouros 2003, Ljungberg et al 2013). In nuclear medicine, specifically, Monte Carlo modelling can be used in a broad range of applications: for example Monte Carlo modelling was used (partially) for the generation of reference S-values in MIRD pamphlet 11 as early as 1975 (Snyder et al 1975) and scintigraphic image modelling has also been investigated for some decades (Ljungberg and Strand 1989). The Monte Carlo codes used in nuclear medicine dosimetry were initially conceived for particle and nuclear physics, and they were later adapted for the low energy regime encountered in nuclear medicine (in the order of eV to MeV). MCNP/MCNPX, EGSnrc, Geant4, Penelope, Fluka (Briesmeister 2000, Kawrakow and Rogers 2003 Salvat et al 2003, Agostinelli et al 2003, Ferrari et al 2005) are examples of generalist Monte Carlo codes that have been proposed in the context of nuclear medicine dosimetry.

Monte Carlo modelling was initially used for reference dosimetry—i.e. absorbed dose calculations for reference models, such as those proposed by the ICRP or the MIRD committee (Snyder et al 1975, Cristy and Eckerman 1987, Stabin et al 1995). Reference dosimetric parameters, such as S-values, were later implemented in dosimetry software like MIRDOSE (Stabin 1996) or OLINDA (Stabin et al 2005). Monte Carlo based patient-specific dosimetry has also been proposed. Moreover, as recent computing model structures have become more realistic, methodological differences in absorbed dose computations have become less and less apparent between model-based and patient-specific (voxel-based) approaches. Monte Carlo is now used in radiopharmaceutical dosimetry, both for model and patient-specific dosimetry.

Contrary to those designed for dosimetry, the majority of Monte Carlo codes used in scintigraphic image modelling have been specifically developed for the purpose (Ljungberg and Strand 1989). One of the reasons is that generalist Monte Carlo codes are too complex and not yet adapted to scintigraphic image modelling specificities (tomography for example, or time dependent phenomena). In addition, specific Monte Carlo codes designed for imaging have been explicitly tuned for the purpose, which represents a major asset in terms of computing speed.

The simulation platform GATE (Santin et al 2003, Jan et al 2004) was publicly released in 2004, initially for nuclear medicine imaging, as a means to conciliate both worlds: GATE is based on the GEANT4 simulation toolkit (Agostinelli et al 2003) and therefore benefits from a very large user’s database that guarantees sustainability and continuous optimisation and debugging. However, GATE has been specifically developed for nuclear medicine needs. In particular, GATE allows the explicit modelling of time-related events such as source or detector movement and source decay kinetics.
Within a few years, GATE has become a widely spread modelling platform in nuclear medicine. The first applications of GATE were in scintigraphic equipment and image modelling for research and development, and several publications present the validation of scintigraphic systems compared to experimental acquisitions, in SPECT (Staelens et al. 2003, Assiè et al. 2005, Autret et al. 2005) or in PET imaging (Lamare et al. 2006, Gonias et al. 2007).

Besides applications in nuclear medicine imaging, new areas of development have been investigated in the past few years, leading to the integration of new classes allowing energy deposition and absorbed dose scoring in the latest versions of GATE (Jan et al. 2011, Sarrut et al. 2014). Dose point kernels and pencil beam kernels generated with GATE v6.0, EGSnrc and MCNP4C were compared for a range of monoenergetic electrons (Maigne et al. 2011). At the clinical scale, Parach and Rajabi (2011) compared GATE v4.0 to MCNP4B using the Zubal voxel phantom (Zubal et al. 1994) for monoenergetic electrons of 935 keV and photons from 10 keV to 1 MeV. Photons’ specific absorbed fractions were also calculated for different energies (Parach et al. 2011) on a voxelized version of the mathematical Snyder phantom (Snyder et al. 1969, 1978) and compared to the published MIRD data (Snyder et al. 1975).

However, no complete dosimetry validation of GATE for clinical applications in nuclear medicine dosimetry has been presented to date.

In this work, the finely segmented ICRP 110 (ICRP 2009) female reference computational model was used in order to validate GATE in a context of internal dosimetry at the clinical scale. A further motivation to select the ICRP 110 computational models is that, even though ICRP 103 recommends using these models for reference absorbed dose calculations, to our knowledge very few $S$-values are publicly available to date. Some specific absorbed fractions were calculated for ICRP 110 models implemented in the dosimetry package OEDIPE (Chiavassa et al. 2005, 2006) using MCNPX (Briesmeister 2000) by Hadid et al. (2010), and compared with EGSnrc (Kawrakow and Rogers 2003) for a number of source-target configurations and monoenergetic photons and electrons. Lamart et al. (2011) and Geng et al. (2015) both focused their work on the thyroid, with iodine-131 but also iodine-125 in Geng’s study. More specifically, Lamart et al. (2016) computed $S$-values for iodine-131 in various source/target combinations with MCNPX; some of them were therefore used as benchmarks in this study.

Here, we compare GATE to the well-established and validated Monte Carlo code MCNPX with various configurations of source location and type of emission.

2. Material and methods

2.1. The ICRP/ICRU female reference computational model

In publication 103 (ICRP 2007), the ICRP promoted using more realistic voxel-based models to update reference dosimetric data. To match the characteristics of the new reference humans (male and female) presented in publication 89 (ICRP 2002, ICRU 1992), voxel adult reference models REX (REference adult male voXel model) and REGINA were derived from existing voxel models GOLEM and LAURA (Zankl and Wittmann 2001, Zankl et al. 2005, 2007). These two voxel-based models were presented in ICRP report 110 (ICRP 2009). They allow for a more realistic definition of human anatomy. In addition, under the assumption that radiopharmaceutical distribution and kinetics can be assessed at that scale, absorbed dose calculations can be performed at the voxel level, thereby allowing for a better assessment of absorbed dose gradients (dose-volume-histograms) within organ or tissues of interest.

We based our comparison on the female reference computational model (as opposed to the male model), due to its better spatial sampling (≈14 million voxels for the female model...
versus ~7 million for the male). From the various data provided in ICRP 110, a 3D raw image, AF.raw, could be obtained. Characteristics are given in table 1.

The 141 tissues or organs, 53 different materials and specific atomic composition described in ICRP publication 110 were taken into account during the computations. Within the 141 tissues, 25 different subregions (table 2), grouped in 12 different organs of interest, were considered for the comparison (table 3).
2.2. Radiation transport modelling

2.2.1. GATE. Simulations were performed with GATE version 6.2, which is based on Monte Carlo code GEANT4 version 9.5.p01. The activity was uniformly distributed in each voxel of a given region of interest with a range option. Compressed matrix navigation (Taschereau and Chatziioannou 2008) was chosen in order to speed up the simulation. GATE standard physics list (option 3) was used for this study at the clinical level and production range cuts were set to 0.1 mm for gamma particles, electrons and positrons. Cubic spline interpolation was applied to continuous energy spectra used in simulations. The deposited energy was scored at the voxel level with the DoseActor $E_{Dep}$, and associated uncertainties were calculated in each ‘dosel’ (scoring voxel) with the DoseActor $\text{Uncertainty}_{E_{Dep}}$. The dosel grid (scoring matrix volume) was defined with the dimensions of the input phantom matrix. GATE was run with a Mersenne Twister random number generator. An in-house ImageJ plugin was developed to obtain energy deposition and associated uncertainties at the organ level, from 3D maps generated as the output of GATE.

2.2.2. MCNPX. The version of MCNPX used here was version 2.7.a. An in-house ImageJ macro was used to transform the voxelized model, provided in a raw format, into MCNPX input format. Standard libraries were used and default energy cuts of 1 keV were set. Tally ‘F8’ was used to score energies in MeV per source particle, in order to directly obtain energy depositions in each region of interest at the organ level. The MCNPX parameter, ESTEP, was adjusted in all simulations in order to insure enough energy steps in each region of interest: at least ten energy steps were ensured in each target organ.

With both code settings, the transport of secondary particles was taken into account.

2.3. Dosimetry calculations

2.3.1. Dosimetric parameters. To compare Monte Carlo codes GATE and MCNPX dosimetry results, different dosimetry parameters were considered, according to the Medical Internal Radiation Dose (MIRD) committee definitions (Loevinger et al 1991).

| Organ/tissue          | IDs           | Mass (g) |
|-----------------------|---------------|----------|
| Adrenals              | 1, 2          | 13.00    |
| Brain                 | 61            | 1300.00  |
| Gall bladder wall     | 70            | 10.24    |
| Gall bladder content  | 71            | 45.75    |
| Heart wall            | 87            | 250.00   |
| Heart content         | 88            | 370.00   |
| Kidneys               | 89, 90, 91, 92, 93, 94 | 275.00   |
| Liver                 | 95            | 1400.00  |
| Lungs                 | 96, 97, 98, 99 | 950.00   |
| Ovaries               | 111, 112      | 11.00    |
| Pancreas              | 113           | 120.00   |
| Spleen                | 127           | 130.00   |
| Thyroid               | 132           | 17.00    |
| Urinary bladder wall  | 137           | 40.00    |
| Urinary bladder content| 138         | 200.00   |
• The absorbed fraction (AF) $\phi(k \leftrightarrow h)$ represents the ratio of the energy $E_0$ emitted in source region $h$ to the energy absorbed $E$ in target region $k$:

$$\phi(k \leftrightarrow h) = \frac{E}{E_0}. \quad (1)$$

• The specific absorbed fraction (SAF) $\Phi(k \leftrightarrow h)$, is the ratio of the absorbed fraction by the mass of the target organ $m_k$:

$$\Phi(k \leftrightarrow h) = \frac{\phi(k \leftrightarrow h)}{m_k}. \quad (2)$$

• The $S$-value ($\text{Gy}(\text{Bq} \cdot \text{s})^{-1}$) is the mean absorbed dose to the target $k$ per unit of cumulated activity in the source region $h$:

$$S(k \leftrightarrow h) = \sum_i \Delta_i \Phi(k \leftrightarrow h). \quad (3)$$

Here $\Delta_i = n_i E_i$ and $E_i$ is the energy emitted for radiation type $i$ with a probability $n_i$.

The relative difference between the results obtained with both codes was calculated by taking MCNPX as the reference, due to its historical precedence. The uncertainty on the relative difference was calculated by the method of propagation (Cramer 1999), which uses the standard deviation of each variable implemented in the calculation.

2.3.2. Self/cross absorbed dose. For both dosimetric parameters, two different situations can be considered. If source and target organs are identical ($r_h = r_k$), self-irradiation in the organ is quantified. If source and target organs are different ($r_h \neq r_k$), cross-irradiation from one organ to another is studied.

Obviously, for self-irradiation, non-penetrating radiation at the scale of the organ/tissue (electrons) are likely to be the major contributor to the absorbed dose delivered. Conversely, photon irradiation is likely to contribute preponderantly to cross-irradiation, with the possible exception of hollow organs such as the gallbladder, heart and urinary bladder, where the content is usually considered as the source and the wall as the target, but for which both photon and electron contributions to the absorbed dose can be important.

It was decided to present the comparison between MCNPX and GATE for nine organs in a context of organ self-irradiation and three hollow organs (gall bladder, heart and urinary bladder) in a context of cross-irradiation. Monte Carlo simulations were run for these 12 different organs of interest (table 3), considering a total of 144 source/target pairs. GATE results are available in supplemental data for these 144 source/target pairs (stacks.iop.org/PMB/62/1885/mmedia). Besides, the calculation was also performed for 25 organs of interest (table 2), thereby generating a database of 625 source/target pairs, available on demand.

2.3.3. Radiation. Absorbed fractions and SAFs were calculated with GATE and MCNPX for monoenergetic photons and electrons of 50 keV, 100 keV, 500 keV, 1 MeV and 2 MeV. The comparison was completed by calculating $S$-values for different radionuclides commonly used in nuclear medicine (diagnostic or therapy), such as fluorine-18, iodine-131, lutetium-177 and yttrium-90. All nuclear data used were taken from ICRP 107 (ICRP 2008). The main physical characteristics of these radionuclides are presented in table 4.

2.3.4. Computing resources. A computing cluster of 20 MacPro (Intel Xeon Westmere 12-core; RAM 16 GB; archiving system 16 TB) providing 480 virtual cores was used to
perform the calculations. An application programming interface (API) Xgrid, developed by Apple, was used to manage parallel computing. Each GATE simulation was launched on one core at a time, whereas MCNPX simulations were launched on 240–480 cores.

### 3. Results and discussions

With MCNPX, 100 million primaries were simulated for radionuclides to obtain adequate associated uncertainties (relative uncertainty <0.5% in case of self-absorption), and 10 million for monoenergetic particles. Parallel computing was performed with MCNPX, each simulation being spread on 240–480 virtual cores of the computing cluster. On average, ∼12 h/CPU were needed for each source organ for lutetium-177 simulations, ∼72 h/CPU for fluorine-18, ∼28 h/CPU for iodine-131 and ∼48 h/CPU for yttrium-90. Between 2 h30/CPU were required for 50 keV monoenergetic photons and 9 h/CPU for 2 MeV monoenergetic photons, and between 1 h30/CPU for 50 keV monoenergetic photons and 12 h/CPU for 2 MeV

![Table 4. Main physical characteristics of $^{18}$F, $^{131}$I, $^{90}$Y, $^{177}$Lu (ICRP 2008).](image-url)
1892

monoe energetic electrons. Finally, the equivalent of 20 d were required to perform the MCNPX calculations on 240 cores of that cluster.

With GATE, 100 million of primaries were systematically simulated to ensure acceptable uncertainties (relative uncertainty < 0.5% in case of self-absorption). Computation times were reduced by launching the 192 different GATE simulations on 192 cores at the same time on our 480 virtual core cluster. About 2h/CPU were required on average for each source organ for lutetium-177 simulations, ~20h/CPU for fluorine-18, ~30h/CPU for iodine-131 and ~30h/CPU for yttrium-90. Between 13h/CPU were required for 50 keV monoenergetic photons and 23h/CPU for 2 MeV monoenergetic photons, and between 1 h30/CPU for 50 keV monoenergetic photons and 13h/CPU for 2 MeV monoenergetic electrons. All in all, 14 d were needed to perform GATE calculations on the cluster.

GATE computation times were found consistent with those listed in Marcatili et al (2015), and MCNPX computation times were in agreement with Hadid et al (2010), taking into account the differences of CPU speed, the range of starting energy (10 keV to 1 MeV for Hadid et al against 50 keV to 2 MeV in this work), and the choice of source organs.

3.1. Comparison between GATE and MCNPX

144 values of deposited energy and absorbed fractions (12 source tissues against 12 target tissues) were computed with each Monte Carlo code, and then converted into 144 specific absorbed fractions (SAFs) or $S$-values, depending on the type of emission (monoenergetic particles or radionuclide emission spectra). The full dataset of GATE results (SAFs or $S$-values) is available in supplemental data, with associated statistical uncertainty.

Relative differences between GATE and MCNPX were computed by taking MCNPX as the reference.

A study on the validity of the reciprocity theorem was conducted both for monoenergetic electrons and photons. This theorem stipulates that for any pair of regions in a uniform isotropic (source activity is assumed uniformly distributed in regions of an infinite, homogeneous material of constant mass density) or uniform scatterless model (source concentration is assumed uniform, i.e. constant, throughout the source regions of a material in which the radiation is absorbed without scatter or buildup), the specific absorbed fraction is independent of which region is designated source and which is designated target, in symbols $\Phi_{1}(r_2 \rightarrow r_1) = \Phi_{2}(r_1 \rightarrow r_2)$ (Loevinger 1969). All source/target couples matching the conditions of application of the reciprocity theorem, that is couples with consistent inter-organ distance, were studied with our results: Kidneys ↔ Lungs, Liver ↔ Spleen, Pancreas ↔ Spleen and Liver ↔ Pancreas.

For photons, a good agreement was found between organ 1 → organ 2 and organ 2 → organ 1 SAFs results for the four source/target couples, with at maximum ∼4.82% of relative difference in the case of low energy photons (50 keV) and mostly less than ± 2% of relative difference between two SAFs; both values were well below Cristy’s tolerance criterion of 10% (Cristy 1983). For electrons, a good agreement was found between organ 1 → organ 2 and organ 2 → organ 1 SAFs results for medium and high energy electrons (500 keV, 1 MeV, 2 MeV), with less than ± 3% of relative difference between two SAFs, therefore below 10%. Higher relative differences, however, were observed for low energy electrons. These differences can be explained by the fact that, in this case, the conditions of the reciprocity theorem are not satisfied due to the short range of low energy electrons, causing a non-uniform distribution of deposited energy in the target organ. Hence, these relative differences are not considered significant.

In the special case of hollow organs, such as the urinary bladder and the gallbladder, no reciprocity can be considered between the content of the organ and the wall. Energy emitted
by a very thin wall (a width of one or two voxels at maximum) surrounding the content organ is inhomogeneously and anisotropically deposited, with most of the energy in the outlying ring of this content organ. As mentioned above, the reciprocity theorem is not valid, and the relative differences cannot be considered significant.

In summary, a reciprocity was observed with our values whenever the conditions of the reciprocity theorem were fulfilled. More information is available in supplemental data.

3.1.1. Monoenergetic electrons. For monoenergetic electrons, self-absorbed fractions were calculated for nine (source = target) volumes of interest. As expected, most values are close to 1 (non-penetrating radiations), especially for low energies and small organs/tissues: for low and medium energy electrons (< 500 keV), almost all emitted energy is absorbed in the source organ: over 99.5% for low energy electrons (50 keV and 100 keV) and over 90% for medium energy electrons (500 keV), due to the ratio of the electron range to the radius of the source organ. For high-energy electrons (> 500 keV), a significant part of the energy is absorbed in neighbouring organs: on average 11.5% for 1 MeV electrons and 22% for 2 MeV electrons.

Relative differences between absorbed fractions are presented in figure 1 for source = target configuration (self-absorption). As can be seen, the relative differences are very small; they are always inferior to 1% and in the range of 0.0 to 0.2% for most organs considered in the study.

Mean values of the relative differences between the codes were $0.02 \pm 0.07\% \sigma$ for 50 keV electrons, $0.02 \pm 0.05\% \sigma$ for 100 keV electrons, $−0.02 \pm 0.06\% \sigma$ for 500 keV electrons, $−0.05 \pm 0.11\% \sigma$ for 1 MeV electrons and $−0.14 \pm 0.21\% \sigma$ for 2 MeV electrons.

The highest relative difference was found for the lungs, with $−0.26 \pm 0.27\% \sigma$ on average for all energies. Uncertainties on the relative differences were inferior or equal to 0.021%.

For cross-irradiation, electron absorbed fractions were calculated for the three source/target configurations. On average for all source/target configurations, the absorbed fraction increased
with energy: 0.08% ± 0.02% σ for 50 keV emissions, 0.28% ± 0.08% σ for 100 keV emissions, 2.91% ± 0.83% σ for 500 keV emissions, 5.58% ± 1.48% σ for 1 MeV emissions and 8.18% ± 3.24% σ for 2 MeV emissions.

Relative differences in SAFs obtained by GATE and MCNPX (taken as the reference) are represented in figure 2. Here again, relative differences between codes are very small; they are usually inferior to 1%, with the exception of low energy electrons for the gallbladder content/wall combination.

In the case of cross-irradiation between organ content and wall, the electron range is usually smaller than the source distance to the walls: most energy is actually absorbed in the source (organ/tissue content); hence the organ wall receives a minimal part of the emitted energy.

The highest relative differences observed between the codes were actually related to small absorbed fractions (AFs) values for low energy electrons.

Comparing low energy electron results, the highest relative differences between the codes were found for gallbladder content to gallbladder wall cross-irradiation. This could be directly related to the limited image spatial resolution: with a typical thickness of 12 mm (ICRP 1975), the gallbladder wall is smaller than the voxel size. As a consequence, the wall is very irregularly represented, and it does not completely enclose the gallbladder content. In addition, the modeling of electron energy-loss straggling varies from one Monte Carlo code to another, with non negligible consequences for dosimetry in small anatomic structures, especially in low resolution models. This effect was also put in evidence by Marcatili et al (2014) who compared the dosimetry of low and high resolution models of the bladder wall. They proved the importance of a multiscale dosimetry in Monte Carlo simulations of small anatomical structures.

In other cross-irradiation configurations (different source/target organs), relative differences may be high due to higher source to target distances, hence very low absorbed fractions.

All uncertainties on relative differences were found inferior or equal to 1.20% for cross-irradiation considerations (0.30% for 100 keV to 2 MeV electrons).
For monoenergetic photons, in the case of auto-absorption (source = target), absorbed fractions are usually low, and decrease with increasing energy for all tissues/organs: 12.54% ± 8.98% $\sigma$ for 50 keV emissions, 7.10% ± 5.27% $\sigma$ for 100 keV emissions, 7.22% ± 4.98% $\sigma$ for 500 keV emissions, 6.48% ± 4.59% $\sigma$ for 1 MeV emissions, and 5.01% ± 3.82% $\sigma$ for 2 MeV emissions.

As expected, the lowest absorbed fractions were found for small organs: 2.37% ± 0.83% $\sigma$ for adrenals, 2.44% ± 0.94% $\sigma$ for ovaries and 3.10% ± 1.37% $\sigma$ for the thyroid, all emitted energies combined, as most of the emitted energy is absorbed outside the source. All relative uncertainties computed for GATE or MCNPX calculations were found inferior to 0.07%.

For self-absorption, relative differences in specific absorbed fractions for monoenergetic photons are presented in figure 3. As can be seen, relative differences between codes are acceptable, always below 7% and usually below 2 to 4%.

Cross irradiation resulted in higher SAFs than self-absorption. On average, lower relative differences were observed between the two codes in that context. Mean relative differences of 3.14% ± 0.50% $\sigma$ were observed between codes for 50 keV monoenergetic photon emissions from organs content to walls, 2.13% ± 0.59% $\sigma$ for 100 keV photons, −0.91% ± 0.79% $\sigma$ for 500 keV photons, 0.13% ± 0.98% $\sigma$ for 1 MeV photons and 1.81% ± 1.34%. All values are represented in figure 4.

In general, the highest relative differences were noticed for very small SAFs, concerning small and long-distance target organs and were found to be below 6%, except for non-significant SAFs.

3.1.2. Monoenergetic photons. For monoenergetic photons, in the case of auto-absorption (source = target), absorbed fractions are usually low, and decrease with increasing energy for all tissues/organs: 12.54% ± 8.98% $\sigma$ for 50 keV emissions, 7.10% ± 5.27% $\sigma$ for 100 keV emissions, 7.22% ± 4.98% $\sigma$ for 500 keV emissions, 6.48% ± 4.59% $\sigma$ for 1 MeV emissions, and 5.01% ± 3.82% $\sigma$ for 2 MeV emissions.

As expected, the lowest absorbed fractions were found for small organs: 2.37% ± 0.83% $\sigma$ for adrenals, 2.44% ± 0.94% $\sigma$ for ovaries and 3.10% ± 1.37% $\sigma$ for the thyroid, all emitted energies combined, as most of the emitted energy is absorbed outside the source. All relative uncertainties computed for GATE or MCNPX calculations were found inferior to 0.07%.

For self-absorption, relative differences in specific absorbed fractions for monoenergetic photons are presented in figure 3. As can be seen, relative differences between codes are acceptable, always below 7% and usually below 2 to 4%.

Cross irradiation resulted in higher SAFs than self-absorption. On average, lower relative differences were observed between the two codes in that context. Mean relative differences of 3.14% ± 0.50% $\sigma$ were observed between codes for 50 keV monoenergetic photon emissions from organs content to walls, 2.13% ± 0.59% $\sigma$ for 100 keV photons, −0.91% ± 0.79% $\sigma$ for 500 keV photons, 0.13% ± 0.98% $\sigma$ for 1 MeV photons and 1.81% ± 1.34%. All values are represented in figure 4.

In general, the highest relative differences were noticed for very small SAFs, concerning small and long-distance target organs and were found to be below 6%, except for non-significant SAFs.

3.1.3. Comparison with Hadid et al. Hadid et al (2010) presented results for the ICRP 110 models, for some source/target pairs, and for monoenergetic particles. It was possible to compare their results with those produced during this experiment in a reduced number of cases, however an interesting point is that both works used MCNPX to compute SAFs (compared with EGSnrc for Hadid et al, and with GATE in this work). Results are presented in tables 5.
**Figure 4.** Relative differences between specific absorbed fractions computed with GATE and MCNPX (taken as reference) for monoenergetic photons emission of 0.05, 0.1, 0.5, 1.0 and 2.0 MeV, for three source organs in a case of cross-irradiation.

**Table 5.** Comparison of our work with data published in Hadid *et al* (2010).

### Electrons

| E(MeV) | Hadid *et al* | This work |
|-------|---------------|-----------|
|       | MCNPX         | EGSnrc    | MCNPX | GATE |
| 0.05  | $2.18 \times 10^{-06}$ | $2.17 \times 10^{-06}$ | $2.45 \times 10^{-06}$ | $1.94 \times 10^{-06}$ |
| 0.10  | $6.11 \times 10^{-06}$ | $6.41 \times 10^{-06}$ | $6.77 \times 10^{-06}$ | $6.26 \times 10^{-06}$ |
| 0.50  | $3.23 \times 10^{-05}$ | $3.22 \times 10^{-05}$ | $3.23 \times 10^{-05}$ | $3.20 \times 10^{-05}$ |
| 1.00  | $6.02 \times 10^{-05}$ | $6.04 \times 10^{-05}$ | $5.98 \times 10^{-05}$ | $5.93 \times 10^{-05}$ |

### Lungs $\rightarrow$ Thyroid SAFs (kg$^{-1}$)

| E(MeV) | Hadid *et al* | This work |
|-------|---------------|-----------|
|       | MCNPX         | EGSnrc    | MCNPX | GATE |
| 0.05  | $1.05 \times 10^{00}$ | $1.05 \times 10^{00}$ | $1.05 \times 10^{00}$ | $1.05 \times 10^{00}$ |
| 0.10  | $1.05 \times 10^{00}$ | $1.05 \times 10^{00}$ | $1.05 \times 10^{00}$ | $1.05 \times 10^{00}$ |
| 0.50  | $9.99 \times 10^{-01}$ | $9.95 \times 10^{-01}$ | $1.02 \times 10^{-00}$ | $1.02 \times 10^{-00}$ |
| 1.00  | $9.42 \times 10^{-01}$ | $9.35 \times 10^{-01}$ | $9.82 \times 10^{-01}$ | $9.82 \times 10^{-01}$ |

### Lungs $\rightarrow$ Lungs SAFs (kg$^{-1}$)

| E(MeV) | Hadid *et al* | This work |
|-------|---------------|-----------|
|       | MCNPX         | EGSnrc    | MCNPX | GATE |
| 0.05  | $8.18 \times 10^{-05}$ | $7.75 \times 10^{-05}$ | $8.01 \times 10^{-05}$ | $8.04 \times 10^{-05}$ |
| 0.10  | $2.69 \times 10^{-04}$ | $2.62 \times 10^{-04}$ | $2.61 \times 10^{-04}$ | $2.57 \times 10^{-04}$ |
| 0.50  | $2.67 \times 10^{-03}$ | $2.65 \times 10^{-03}$ | $2.66 \times 10^{-03}$ | $2.59 \times 10^{-03}$ |
| 1.00  | $5.55 \times 10^{-03}$ | $5.52 \times 10^{-03}$ | $5.54 \times 10^{-03}$ | $5.54 \times 10^{-03}$ |

### Lungs $\rightarrow$ Liver SAFs (kg$^{-1}$)

| E(MeV) | Hadid *et al* | This work |
|-------|---------------|-----------|
|       | MCNPX         | EGSnrc    | MCNPX | GATE |
| 0.05  | $8.18 \times 10^{-05}$ | $7.75 \times 10^{-05}$ | $8.01 \times 10^{-05}$ | $8.04 \times 10^{-05}$ |
| 0.10  | $2.69 \times 10^{-04}$ | $2.62 \times 10^{-04}$ | $2.61 \times 10^{-04}$ | $2.57 \times 10^{-04}$ |
| 0.50  | $2.67 \times 10^{-03}$ | $2.65 \times 10^{-03}$ | $2.66 \times 10^{-03}$ | $2.59 \times 10^{-03}$ |
| 1.00  | $5.55 \times 10^{-03}$ | $5.52 \times 10^{-03}$ | $5.54 \times 10^{-03}$ | $5.54 \times 10^{-03}$ |
and 6. As can be seen, the results are completely in agreement. This is especially true for self-absorption values for electrons (Lungs Lungs /uni2190), but also for all source-target configurations involving electron energies above 500 keV. For photons, excellent agreement was found between all codes, except in self-absorption (Lungs Lungs /uni2190), where variations were higher

Table 6. Comparison of our work with data published in Hadid et al (2010). Photons.

| E(MeV) | Hadid et al MCNPX | Hadid et al EGSnrc | This work MCNPX | This work GATE |
|-------|------------------|-------------------|----------------|--------------|
| 0.05  | 2.51 × 10⁻²      | 2.55 × 10⁻²      | 2.51 × 10⁻²    | 2.46 × 10⁻²  |
| 0.10  | 1.80 × 10⁻²      | 1.81 × 10⁻²      | 1.80 × 10⁻²    | 1.77 × 10⁻²  |
| 0.50  | 1.60 × 10⁻²      | 1.61 × 10⁻²      | 1.61 × 10⁻²    | 1.62 × 10⁻²  |
| 1.00  | 1.47 × 10⁻²      | 1.48 × 10⁻²      | 1.48 × 10⁻²    | 1.50 × 10⁻²  |

Figure 5. Relative differences between S-values computed with GATE and MCNPX (taken as reference) for radionuclides emissions fluorine-18, iodine-131, lutetium-177 and yttrium-90 for nine source organs.
than expected (up to 10%). Additionally, in that case, there seems to be a difference between the values generated using MCNPX by the two teams. This difference may be related to the Oedipe input format. Hadid et al. used MCNPX version 2.6, whereas version 2.7.a was used for this experiment. Still, it is difficult to find a satisfactory explanation for these differences.

### 3.1.4. Radionuclides.

For the different isotopes considered in this study (\(^{18}\text{F}\), \(^{177}\text{Lu}\), \(^{131}\text{I}\) and \(^{90}\text{Y}\)), \(S\)-values were computed for the 12 organs/tissues of interest, thereby providing for 144 source/target pairs for each radionuclide. In the following, nine source = target configurations (self-irradiation) and three source content to source wall configurations (as examples of cross-irradiation) are presented.

For self-irradiation, uncertainties on \(S\)-values were inferior to 0.04%, both with GATE and with MCNPX.

Relative differences in the \(S\)-values obtained with GATE and MCNPX (taken as the reference) are presented in figure 5 for the self-irradiation configuration. Relative differences observed between the two codes are low, on average 0.57% ± 0.21% \(\sigma\) for fluorine-18, 2.52% ± 0.09% \(\sigma\) for lutetium-177, −3.06% ± 2.93% \(\sigma\) for iodine-131 and 2.16% ± 0.98% \(\sigma\) for yttrium-90.

For cross irradiation, relative differences between GATE and MCNPX were more pronounced, depending both on the radionuclide and the source-to-target distance configuration, as represented in figure 6.

In general, very small relative differences were observed for fluorine-18 (0.37% ± 0.66% \(\sigma\)). For lutetium-177, MCNPX \(S\)-values were systematically higher than GATE \(S\)-values, and the average relative difference was 7.19% ± 1.67% \(\sigma\). For iodine-131, MCNPX \(S\)-values were systematically lower than GATE \(S\)-values, and the average relative difference was −3.06% ± 2.93% \(\sigma\). For yttrium-90, no specific conclusion could be drawn from relative differences observed.

When considering low to medium source-to-target distance configurations (with reasonable target organ sizes), relative differences were inferior to 4%. Higher differences were observed for distant source/target pairs and very small target organs. It must be noted that \(S\)-values computed in that context are very small, several orders of magnitude lower than self-absorption \(S\)-values. This means that, even though the codes may yield different results, the dosimetric impact should not be considered as major.

### 3.1.5. Comparison with Lamart et al.

Lamart et al. (2016) published MCNPX v2.7 \(S\)-values for iodine-131 dosimetry with the male and female ICRP 110 models and various source/target combinations, some of which match those considered in this study. \(S\)-values obtained for self-absorption in the two studies and their relative differences, taking Lamart et al. as a reference, are presented in table 7.

Relative differences were small or non existent, and a correlation between source/target organ masses and relative differences between the two studies could be highlighted: as presented in figure 7, relative differences between \(S\)-values follow here a decreasing exponential law, function of organ mass.

This very good agreement with Lamart et al results was a good benchmark of our MCNPX \(S\)-value results.

### 3.1.6. Preliminary conclusion.

The differences observed between GATE and MCNPX are minor. This is especially true for electron absorbed fractions, which is understandable as electrons behave mostly as non-penetrating radiation at that scale. However some variations were observed in certain situations (monoenergetic photons for self-absorption, and for the three emitting radionuclides).
In principle, since the comparison was performed on the same voxelized model for the same material and the same emission spectrum, the sources of variation should be reduced to the implementation of the source definition in each code, and/or to differences in radiation transport algorithms and physics lists (cross sections).

The excellent match between the codes observed for monoenergetic electrons was a motive to focus the following part of the work on the source definition, especially the beta spectrum resampling.

3.2. Influence of the emission spectrum definition

In an attempt to clarify the source of discrepancies between GATE and MCNPX for β-emitters, extra simulations were launched that considered radiation types independently: only monoenergetic electrons and photons were first simulated with both codes, and then only the...
Relative differences obtained between GATE and MCNPX in each of these situations were compared to full spectrum simulation. Some results are presented here as an example for lutetium-177. All uncertainties on $S$-values were inferior to 0.01% for $\beta$ spectrum simulations, 0.05% for monoenergetic particles, and 0.05% for complete emissions ($\beta$ spectrum and monoenergetic photons and electrons), both with GATE and MCNPX.

**Figure 7.** Correlation between $S$-values relative differences and organ masses in case of self-absorption.

**Figure 8.** Relative differences between $S$-values computed with GATE and MCNPX (taken as the reference) for lutetium-177, for the entire emission spectrum, monoenergetic emissions and $\beta$ spectrum alone, for nine source organs.

beta spectrum. Relative differences obtained between GATE and MCNPX in each of these situations were compared to full spectrum simulation. Some results are presented here as an example for lutetium-177. All uncertainties on $S$-values were inferior to 0.01% for $\beta$ spectrum simulations, 0.05% for monoenergetic particles, and 0.05% for complete emissions ($\beta$ spectrum and monoenergetic photons and electrons), both with GATE and MCNPX.
Uncertainties on the relative differences between GATE and MCNPX S-values were inferior to 0.05%.

As can be seen in figure 8, the relative differences are more important for the beta component of the irradiation. In the case of self-absorption, mean relative differences obtained between the two codes were $-0.64\% \pm 0.31\% \sigma$ for monoenergetic emissions, $2.92\% \pm 0.09\% \sigma$ for $\beta$ spectra alone, against $2.53\% \pm 0.09\% \sigma$ for the full emissions as given in section 3.1.3.

This behaviour can also be observed for other isotopes and configurations (data not shown). These results seem to indicate that the way beta spectra were interpolated (internally) in the different codes (as our calculations were based on the same decay dataset) may cause the discrepancies. Still, the variations observed are quite minor.

4. Conclusion

A comparison was performed between GATE and MCNPX dosimetric results for the same geometry (ICRP 110 reference woman computational model), with monoenergetic photons and electrons ranging from 50 keV to 2 MeV, and for four radionuclides commonly used in nuclear medicine, for diagnostics ($^{18}$F) or therapy ($^{177}$Lu, $^{131}$I and $^{90}$Y).

The results obtained were remarkably close, with relative variations less than 10% in all situations, and most relative differences less than 5%, both for monoenergetic electrons or photons. Interestingly, this very good agreement between MCNPX and GATE was observed both for self-absorption (source = target) and cross-irradiation (source $\neq$ target) conditions. The largest relative differences were observed as could be expected for photons in a context of cross-irradiation when sources and targets are distant. However, in that situation S-values are usually very small and contribute marginally to the irradiation.

GATE has been mostly used so far in a context of scintigraphic image modelling. The potential of GATE in the context of dosimetry was presented recently, in nuclear medicine applications but also in external beam radiotherapy, hadron therapy and brachytherapy (Sarrut et al 2014). In our paper, a systematic benchmarking of GATE results (AFs, SAFs or S-values in a geometric context close to the clinics) versus a Monte Carlo code such as MCNPX — established as a reference for absorbed dose calculations by its historical precedence — has been presented.

This is important, as using a single Monte Carlo code for both scintigraphic image modelling and absorbed dose calculations is now a viable option with GATE. This allows setting up global projects in nuclear medicine clinical dosimetry that require both imaging and dosimetry (Garcia et al 2015).

Additional work in establishing a broader database of dosimetric results for the ICRP 110 models is underway. This will consider both male and female models and additional isotopes. It must be stressed that the segmentation of the computing models in 141 different volumes of interest would yield about 20000 possible source/target configurations. We therefore intend to select a number of representative source/target configurations. However, generation of specific dosimetric results for exotic isotopes or special source/target pairs could be easily implemented.

Acknowledgments

This work was partly sponsored by the European Metrology Research Programme (EMRP) as Researcher Grant Contract HLT11-REG2 MetroMRT. The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union. This project has
received funding from the EMPIR programme 15HLT06 MRTDosimetry co-financed by the Participating States and from the European Union’s Horizon 2020 research and innovation programme.

This work was funded partly by a grant on Research proposal in physics, mathematics and engineering sciences applied to cancer research from INSERM (2013–2015) and ANR project tGate N°ANR-14-CE23-0008-05.

Conflicts of interest

The authors claim no conflicts of interest.

References

Agostinelli S et al 2003 Geant4: a simulation toolkit Nucl. Instrum. Methods 506 250–303
Assié K, Gardin I, Véra P and Buvat I 2005 Validation of the Monte Carlo simulator GATE for Indium-111 imaging Phys. Med. Biol. 50 3113–25
Autret D, Bitar A, Ferrer L, Lisbona A and Bardiès M 2005 Monte Carlo modeling of gamma cameras for I-131 imaging in targeted radiotherapy Cancer Biother. Radiopharm. 20 77–84
Briesmeister J F 2000 MCNP: a general Monte N-particle transport code, version 4C Technical Report No LA-12709-M (Los Alamos, NM: Los Alamos National Laboratory)
Chiavassa S, Aubineau-Lanèce I, Bitar A, Lisbona A, Barbet J, Franck D, Jourdain J R and Bardiès M 2006 Validation of a personalized dosimetric evaluation tool (Oedipe) for targeted radiotherapy based on the Monte Carlo MCNPX code Phys. Med. Biol. 51 601–16
Chiavassa S, Bardiès M, Jourdain J R and Franck D 2005 OEDIPE: a personalized dosimetry tool associating voxel-based models with MCNPX Cancer Biother. Radiopharm. 20 325–32
Cramer H 1999 Mathematical Methods of Statistics (Princeton, NJ: Princeton University Press)
Cristy M 1983 Applying the reciprocal dose principle to heterogeneous phantoms: practical experience from Monte Carlo studies Phys. Med. Biol. 28 1289–303
Cristy M and Eckerman K F 1987 A specific absorbed fractions of energy at various ages from internal photon sources: part I Methods ORNL/TM-8381/volume 1 (Oak Ridge, TN: Oak Ridge National Laboratory)
Ferrari A, Sala P R, Fasso A and Ranft J 2005 FLUKA: a multi-particle transport code SLAC Report CERN-2005–10, INFN/TC_05/11, SLAC-R-773
Garcia M P, Villoing D, McKay E, Ferrer L, Cremonesi M, Ferrari M and Bardiès M 2015 TestDose: a nuclear medicine software based on Monte-Carlo modelling for generating gamma camera acquisitions and dosimetry Med. Phys. 42 6885–94
Geng C, Tang X, Qian W, Guan F, Johns J, Yu H, Gong C, Shu D and Chen D 2015 Calculations of S-values and effective dose for the radiiodine carrier and surrounding individuals based on Chinese hybrid reference phantoms using the Monte Carlo technique J. Radiol. Prot. 35 707–17
Gonias P et al 2007 Validation of a GATE model for the simulation of the Siemens biograph 6 PET scanner Nucl. Instrum. Methods Phys. Res. 571 263–6
Hadid L, Desbrée A, Schlattl H, Franck D, Blanchardon E and Zankl M 2010 Application of the ICRP/ICRU reference computational phantoms to internal dosimetry: calculation of specific absorbed fractions of energy for photons and electrons Phys. Med. Biol. 55 3631–41
ICRU 1992 Phantoms and Computational Models in Therapy, Diagnosis and Protection (ICRU Report vol 48) (Bethesda, MD: ICRU)
ICRP 1975 Report on the Task Group on Reference Man (ICRP Publication vol 23) (Oxford: Pergamon)
ICRP 2002 Basic Anatomical and Physiological Data for use in Radiological Protection Reference Values (ICRP Publication vol 89) (Oxford: Pergamon)
ICRP 2007 Recommendations of the Internal Commission on Radiological Protection (ICRP Publication vol 103) (Oxford: Elsevier)
ICRP 2008 Nuclear Decay for Dosimetric Calculations (ICRP Publication vol 107) (Oxford: Elsevier)
ICRP 2009 Adult Reference Computational Phantoms (ICRP Publication vol 110) (Oxford: Elsevier)
Jan S et al 2004 GATE: a simulation toolkit for PET and SPECT Phys. Med. Biol. 49 4543–61
Taschereau R and Chatziioannou A F 2008 Compressed voxels for high-resolution phantom simulations in GATE. *Mol. Imaging Biol.* **10** 40–7

Zaidi H and Sgouros G 2003 *Therapeutic Applications of Monte Carlo Calculations in Nuclear Medicine* (Bristol: IOP Publishing)

Zankl M and Wittmann A 2001 The adult male voxel model Golem segmented from whole-body CT patient data. *Environ. Biophys.* **40** 153–62

Zankl M, Becker J, Fill U and Petoussi-Henss N 2005 GSF male and female adult voxel models representing ICRP reference man—the present status. *Proc. 2005 Topical Meeting. The Monte Carlo Method: Versatility Unbounded in a Dynamic Computing World (Chattanooga, TN)* (La Grange Park, IL: American Nuclear Society) (CD-ROM)

Zankl M, Eckerman K F and Bolch W E 2007 Voxel-based models representing the male and female ICRP reference adult—the skeleton. *Radiat. Prot. Dosim.* **127** 174–86

Zubal I G, Harrell C R, Smith E O, Rattner Z, Gindi G and Hoffer P B 1994 Computerized three-dimensional segmented human anatomy. *Med. Phys.* **21** 299–302