VALIDATION OF GATE MONTE CARLO SIMULATIONS FOR INDIUM 111 IMAGING

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***Abstract*-- Accurate quantification of indium 111 (^{111}In) Single Photon Emission Computed Tomography (SPECT) images is helpful to characterize the distribution of ZEVALIN® labeled with ^{111}In before therapy using ZEVALIN® labeled with yttrium 90, in patients with non-Hodgkin lymphoma. To optimize acquisition and processing protocols, Monte Carlo simulations of ^{111}In SPECT data should be useful. In that context, we studied the validity of the Monte Carlo simulation code GATE for simulations of SPECT acquisitions involving ^{111}In.**

***Methods*: Acquisitions of line sources and of a cylindrical phantom including spheres were performed using a DST-Xli camera equipped with MEHR collimators, together with the corresponding simulations. The simulation model included photon tracking in the camera collimator, NaI crystal, back-compartment, and camera shielding. Energy spectra, spatial resolution, sensitivity values, images and count profiles obtained for real and simulated data were compared.**

***Results*: The simulated and real spectra agreed well for all configurations. The simulated spatial resolutions differed by less than 0.1 mm from the measured values, for line sources in air at 0 to 15 cm from the collimator. In water, the simulated and measured full width at tenth maximum differed by about 10% at 6.6 cm from the collimator. The simulated sensitivity values were within 4.7% ± 3.3% of the experimental values for line sources at 0 to 20 cm from the collimator. The simulation of the cylindrical phantom reproduced well the experimental results.**

***Conclusion*: Provided an appropriate detector model is developed, GATE enables accurate simulation of ^{111}In data.**

I. INTRODUCTION

Radioimmunotherapy is a promising therapeutic approach that necessitates accurate absolute activity quantification. To customize the radioimmunotherapy protocol to each patient, the in vivo distribution of the therapeutic agent could be determined using a SPECT scan of a radiotracer presenting the same biodistribution as the therapeutic agent. For instance, SPECT scans with ZEVALIN® radiolabeled with indium 111 (^{111}In) could be used to study the biodistribution of ZEVALIN® radiolabeled with yttrium 90 (^{90}Y) for the treatment of non-Hodgkin lymphoma. In that context, accurate quantification of SPECT images is required for accurate dose calculations. We are therefore interested in the accurate quantification of ^{111}In SPECT images and are willing to use Monte Carlo simulations to optimize acquisition and processing protocols. Although Monte Carlo simulations involving ^{111}In have already been used [1,2], to our knowledge, validation of SPECT Monte Carlo simulation codes in the context of ^{111}In imaging has not been reported so far. The purpose of this study was thus to validate the Monte Carlo simulation code GATE [3-5] for SPECT ^{111}In imaging.

Manuscript received October 19, 2004. This work was supported by "La Ligue Nationale Contre Le Cancer", France.

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II. MATERIAL AND METHODS

A. Phantoms

Five phantoms were used. The phantom LINE1 consisted of a 6 cm long line source (inner diameter of 1.1 mm) filled with 3.7 MBq of ^{111}In and placed on a 4 cm x 40 cm x 40 cm polystyrene block (density of 100 mg/cm^3) (Fig. 1A). The phantom LINE1w consisted of the same line source placed in a 30 cm x 30 cm x 30 cm water tank at 3.6 cm from the surface of the water. The water tank was placed on the polystyrene block (Fig. 1B).

The phantom LINE2 consisted of a 5 cm long line source (inner diameter of 1.1 mm) filled with 1.3 MBq of ^{111}In and placed on a 4 cm x 40 cm x 40 cm polystyrene block (density of 100 mg/cm^3) (Fig. 1A). The phantom LINE2w consisted of the same line source placed in a 30 cm x 30 cm x 30 cm water tank at 3.6 cm from the surface of the water. The water tank was placed on the polystyrene block (Fig. 1B).

The phantom CYL consisted of a cylindrical phantom (Deluxe Jaszczack Phantom™, 18.6 cm high and 22.25 cm in diameter) including 5 spheres (inner diameters of 33.5, 28, 16, 13.5, 10.5 mm) with activity set to 129.5 kBq/ml. A cold conic bony insert (5.35 cm in diameter at one end and 3.7 cm in diameter at the other end, 4.5 cm long, density of 1.93g/cm^3) was introduced at the centre of the phantom. Background activity was 15.8 kBq/ml. The sphere-to-background activity concentration ratio was 8.2.

B. Data acquisitions

A DST-Xli camera (General Electric) equipped with a Medium Energy High Resolution (MEHR) collimator was used to perform the following acquisitions:

- Planar acquisitions in the 20% windows centered on 171 (W1) and 245 keV (W2) of LINE2 in air, at 0, 5, 10, 15 and 20 cm from the collimator and of LINE2w. About 550 kcounts were recorded in W1+W2 for both acquisitions.

- Planar acquisitions in 32 energy windows from 48 to 282 keV (12 windows of 8 keV from 48 to 144 keV, 7 windows of 6 keV from 144 to 186 keV, 3 windows of 10 keV from 186 to 216 keV, 1 window of 8 keV from 216 to 224 keV, 7 windows of 6 keV from 224 to 266 keV, 2 windows of 8 keV from 266 to 282 keV) of LINE1 (844 kcounts) and of LINE1w (1.13 Mcounts).
- A SPECT acquisition of CYL: 128 projections 128 x 128, pixel size = 4.52 mm, radius of rotation of 25.2 cm in 32 energy windows from 93 to 290 keV (17 windows of 6 keV from 93 to 198 keV, 1 window of 8 keV from 198 to 206 keV, 14 windows of 6 keV from 206 to 290 keV). About 40.8 Mcounts were acquired.
- A 3 min long planar acquisition and a SPECT acquisition with the same acquisition parameters as those of the CYL SPECT acquisition without any activity in the field of view of the detector, for background activity measurement.

The spheres of CYL were filled with a contrast medium (Iopamiron 300, Shering) and a General Electric LightSpeed RT was used to perform a CT acquisition of CYL entirely filled with water with acquisition parameters of 140 kV and 240 mA. Fifty three slices (slice thickness = 5 mm, matrix size 512 x 512, pixel size = 0.68 mm x 0.68 mm) were acquired.

C. *Simulations*

Simulations were performed using GATE [6] based on the GEANT4 toolkit.
The DST-Xli gamma camera was modeled by GATE as a combination of:

- MEHR lead collimator (55 mm thick, 3 mm flat-to-flat distance of the hexagonal holes and 0.6 mm septal thickness),
- 3.8'' thick NaI crystal,
- a back-compartment, accounting for photomultiplier tubes and associated electronics, modeled as a 5 cm layer of a material with a density of 2.2 g/cm^3,
- a head shielding in lead.

This camera model will be called GATE model I (Fig. 1) hereafter. A GATE model II identical to GATE model I but without back-compartment has also been studied.
GATE allows for an accurate Monte Carlo modelling of photon transport in the collimator, the crystal, the back-compartment and the head shielding. To demonstrate the importance of modeling all camera components using the Monte Carlo approach, the DST-Xli gamma camera was also modeled by SimSET [7]. The SimSET model was identical to GATE model I but with an analytical modelling of the MEHR collimator instead of a Monte Carlo modelling.
The energy resolution of the camera was assumed to be 10% at 171 and 245 keV. These values were determined by analyzing the energy spectrum of a point source in air.

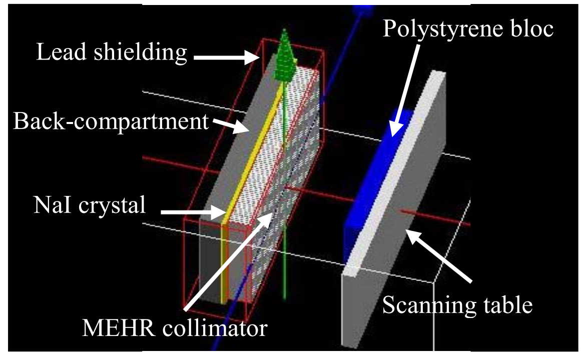

Fig. 1. Gamma camera DST-Xli as modeled by GATE model I.

The line sources and the cylindrical phantom were analytically described to serve as an input for GATE. To model the two emission energies of ^{111}In (171 and 245 keV), two independent simulations were performed and appropriately weighted to account for the respective importance of the 171 and 245 emission rays.
The phantom experiments were simulated, using the very same geometrical configurations as for the real experiments.
For both LINE1 and LINE1w, 500 million counts were simulated at each emission energy. The total number of detected events between 48 and 282 keV was about 121 kcounts for LINE1 and about 225 kcounts for LINE1w.
For both LINE2 and LINE2w, 800 million counts were simulated at each emission energy. The total number of events detected in the two 20% energy windows centered on 171 and 245 keV was about 315 kcounts for LINE2 and about 101 kcounts for LINE2w.
For CYL, 30 billion counts were simulated. About 197 kcounts were detected in the two 20% energy windows centered on 171 and 245 keV.

D. *Assessment of the simulation accuracy*

The consistency between simulated and real data was assessed by considering:

- the energy spectra of events recorded in the whole field of view for LINE1, LINE1w and CYL.
- the spatial resolution, as assessed by the Full Width at Half Maximum (FWHM) and the Full Width at Tenth Maximum (FWTM) for the different source-to-collimator distances for LINE2 and at a 6.6 cm source-to-collimator distance for LINE2w.
- the sensitivity defined as the number of detected events divided by the number of emitted or simulated events, calculated for the LINE2 configuration. Standard deviations of the simulated data were obtained by repeating each simulation five times and those of the experimental data were obtained by considering the 5% error in the dose calibrator.

In addition, the agreement between experimental and simulated data was semi-quantitatively assessed on a reconstructed slice passing through the center of the spheres of the CYL phantom. Simulated and acquired projections corresponding to the two 20% energy windows centered on 171 and 245 keV were obtained by summing the appropriate energy windows among the 32 that were recorded. The projections corresponding to the two photopeaks were then summed and reconstructed using

OSEM (4 subsets, 6 iterations), without any scatter nor attenuation correction. The reconstructed voxel size was 4.52 mm x 4.52 mm x 4.52 mm. An 18 mm thick profile through the 33.5 cm diameter sphere was drawn both on experimental and simulated data.

III. RESULTS AND DISCUSSION

A. Energy spectra

Figure 2 shows the experimental and simulated energy spectra obtained for LINE1, with different simulation models: GATE model I, GATE model II and SimSET model. GATE model I appears as the most appropriate to accurately reproduce the experimental data.

Figure 3 shows the experimental and simulated spectra obtained for LINE1w (Fig. 3A) and CYL (Fig. 3B), using GATE model I. This figure confirms that GATE model I accurately reproduces experimental data in various configurations.

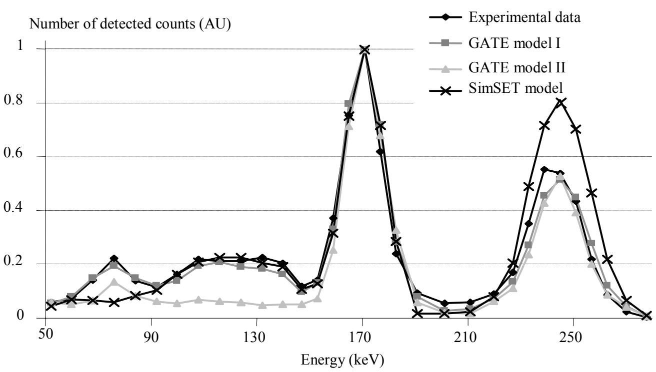

Fig. 2. Experimental and simulated spectra of LINE1 using different simulation models: SimSET model, GATE model I and GATE model II.

Figures 2 and 3 demonstrated a trend towards an underestimation of detected counts from 200 keV and a slight off-set between the experimental and simulated 245 keV photopeaks. This is due to the non-optimal response of the gamma camera over the large energy range that was investigated. Indeed, looking at the location of the photopeaks of ^{99m}Tc (140 keV), ^{111}In (171 and 245 keV) and ^{131}I (364 keV) by performing point source acquisitions in air, we found that the energy at which these photopeaks were detected were 139, 170, 242 and 358 keV respectively. The corresponding percent differences between real and detected photopeak energies were 0.7 %, 0.6 %, 1.2 % and 1.6 %. The energy response of the camera was therefore not perfectly linear while the simulated energy response was. Actually, GATE makes it possible to simulate a non-linear energy response of the detector if this was of any interest.

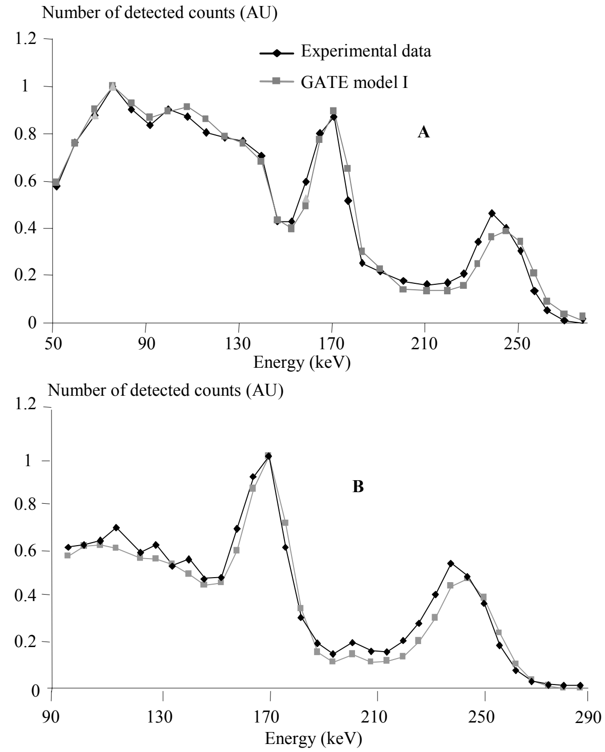

Fig. 3. Acquired and simulated spectra of LINE1w (A) and CYL (B) when using GATE model I.

The agreement between data simulated with GATE model I and real data was made possible thanks to the Monte Carlo simulation of photon transport within the collimator. An analytical model of the collimator response as that available in SimSET was not enough to correctly reproduce the acquired energy spectra. Precise modeling of the back-compartment of the gamma camera was also required to accurately reproduce experimental data. Ignoring the back-compartment as in GATE model II made the simulated data very different from the acquired data. All parameters of the camera model were derived from the known characteristics of the detector, except the material and thickness of the back-compartment which were empirically adjusted based on the agreement between simulated and experimental energy spectra.

B. Spatial resolution

The FWHM and FWTM for the LINE2 configurations are given in Table 1. The FWHM in air were predicted with GATE model I within 1.5%. The LINE2 configuration at 10 cm from the collimator was also simulated using SimSET for comparison purpose. The simulated FWHM with SimSET was 7.9 mm (corresponding to a 15.8% difference compared to the experimental value).

For the LINE2w configuration (line-source-collimator distance = 6.6 cm), the experimental and simulated FWHM were 9.6 and 8.3 mm respectively (corresponding to a 13.5% difference). The experimental and simulated FWTM were 17 mm and 15.1 mm respectively (corresponding to a 11.2% difference).

C. Sensitivity

Figure 4 shows the simulated and measured sensitivity values in air and associated standard deviations for different source-to-collimator distances (LINE2 configurations).

Table 1: FWHM and FWTM in mm for different ^{111}In line source-to-collimator distances obtained from simulations and real experiments for LINE2. Percent differences between simulations and acquisitions (with respect to the acquisition value) are given in parentheses.

	Source-to-collimator distance (mm)	0	50	100	150	200
FWHM	Simulations	5.7 (-1.7%)	7 (0%)	9.6 (1.1%)	11.5 (0%)	14.4 (1.4%)
	Measurements	5.8	7	9.5	11.5	14.2
	Source-to-collimator distance (mm)	0	50	100	150	200
FWTM	Simulations	9.5 (20.3%)	11.8 (-7.8%)	16 (-4.8%)	19.5 (-3%)	24.4 (-1.6%)
	Measurements	7.9	12.8	16.8	20.1	24.8

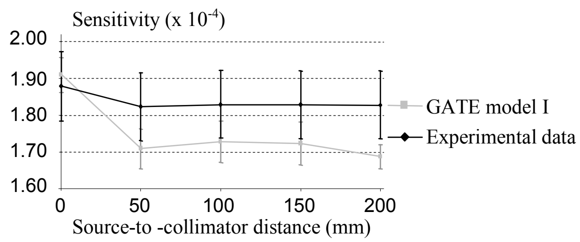

Fig. 4. Sensitivity values for different ^{111}In line source-to-collimator distances obtained from simulations and real experiments in air.

As expected, the sensitivity did not depend on the source-to-collimator distance in the experimental data and in the simulated data. The average percent difference between simulated and experimental sensitivity values was 4.7% ± 3.3%, for source-to-collimator distance between 0 and 20 cm. GATE is thus able to accurately predict the spatial resolution and the sensitivity of the imaging device.

D. Cylindrical phantom

Figure 5 shows a reconstructed slice through the spheres of the CYL phantom and the profiles drawn through the 33.5 cm diameter sphere for the experimental and simulated data.
Despite the lower statistics of the simulated images compared to the experimental images, Figure 5A shows a good agreement between experimental and simulated images. Simulated and experimental profiles drawn through the 33.5 cm diameter sphere agree reasonably well. These results demonstrate the ability of GATE to reproduce realistic phantom data.

E. Computation time

Total computation time for the GATE simulations was about 64 hours CPU for LINE1, 111 hours CPU for LINE2 and 600 hours CPU for CYL on a Pentium 4 - 2 GHz computer.
A drawback of GATE is the computation time. This drawback becomes major when using voxelised geometries. A solution to speed up simulations is to use variance reduction, computer clusters or “gridification” [8]. These different solutions are currently under study in the OpenGATE collaboration (http://www-lphe.epfl.ch/~PET/research/gate).

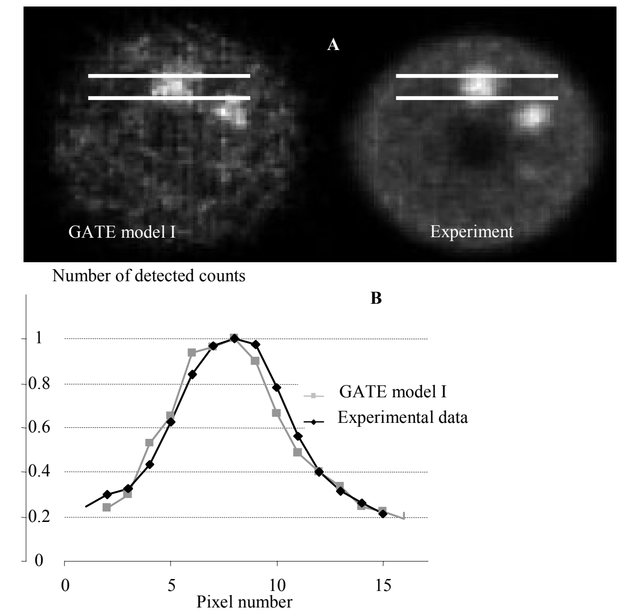

Fig. 5. Reconstructed slices through the spheres of the CYL phantom (a) and profiles (b) taken at the location shown on the images.

IV. Conclusion

With careful modeling of all detector components, including Monte Carlo transport of photons in the collimator, the back-compartment and the shielding of the camera head, GATE enables accurate simulation of ^{111}In SPECT acquisitions in terms of energy spectra, spatial resolution, sensitivity and modeling of complicated source distributions. GATE can thus be used to model realistic ^{111}In SPECT acquisitions.

V. Acknowledgments

This work was supported by “La Ligue Nationale Contre Le Cancer”, France.

VI. References

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