Integration of SimSET photon history generator in GATE for efficient Monte Carlo simulations of pinhole SPECT

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The authors developed and validated an efficient Monte Carlo simulation (MCS) workflow to facilitate small animal pinhole SPECT imaging research. This workflow seamlessly integrates two existing MCS tools: simulation system for emission tomography (SimSET) and GEANT4 application for emission tomography (GATE). Specifically, we retained the strength of GATE in describing complex collimator/detector configurations to meet the anticipated needs for studying advanced pinhole collimation (e.g., multipinhole) geometry, while inserting the fast SimSET photon history generator (PHG) to circumvent the relatively slow GEANT4 MCS code used by GATE in simulating photon interactions inside voxelized phantoms. For validation, data generated from this new SimSET-GATE workflow were compared with those from GATE-only simulations as well as experimental measurements obtained using a commercial small animal pinhole SPECT system. Our results showed excellent agreement (e.g., in system point response functions and energy spectra) between SimSET-GATE and GATE-only simulations, and, more importantly, a significant computational speedup (up to ~ 10 -fold) provided by the new workflow. Satisfactory agreement between MCS results and experimental data were also observed. In conclusion, the authors have successfully integrated SimSET photon history generator in GATE for fast and realistic pinhole SPECT simulations, which can facilitate research in, for example, the development and application of quantitative pinhole and multipinhole SPECT for small animal imaging. This integrated simulation tool can also be adapted for studying other preclinical and clinical SPECT techniques. © 2008 American Institute of Physics. [DOI: [10.1118/1.2940159](https://doi.org/10.1118/1.2940159)]

Key words: Monte Carlo simulation, SimSET, GATE, SPECT

I. INTRODUCTION

The well-recognized importance of small animal molecular imaging techniques, such as PET and SPECT, has hastened the development of specialized small animal imaging systems, corresponding image reconstruction and correction methods, as well as the optimization of data acquisition and processing protocols.^{1,2} This will inevitably lead to an increasing demand for establishing a fast, realistic, and versatile Monte Carlo simulation (MCS) workflow for molecular imaging.³ It is particularly evident in the research and development of small animal pinhole SPECT,^{4,5} where new or complex system configurations are often the main interest, for example.^{6–11}

There exist a number of general MCS software packages and specialized MCS methods for PET and SPECT imaging research.¹² However, it may be desirable to combine the

strengths of two different MCS tools to meet the requirements of a certain MCS task.^{13–15} For small animal pinhole SPECT, two MCS packages—simulation system for emission tomography (SimSET)¹⁶ and GEANT4 application for emission tomography (GATE)¹⁷—are of particular interest. SimSET, a specialized package optimized for PET/SPECT simulation, employs several importance-sampling techniques,^{12,15,16} and is therefore very efficient for simulating photon interactions and transport inside a voxelized phantom. However, it is difficult within SimSET to model a complex imaging system configuration involving unconventional collimation or acquisition geometry. In comparison, GATE provides intuitive, versatile, and convenient modeling of system geometry through its user-friendly interface. Built upon GEANT4, GATE also provides many useful features, such as simulating decaying radioactive sources, however, GEANT4 is designed for general-purpose MCS and relatively

FIG. 1. Implementation flow chart of SimSET/GATE integration for fast Monte Carlo simulations using voxelized phantom input.

slow in simulating photon interactions and transport inside voxelized phantoms. Previously, a combined SimSET and GATE MCS has been applied to clinical PET.¹⁴ Even though such a method may sacrifice the ability provided by GATE-only simulations to simulate decaying radioactive sources, the potential computational speedup can be very desirable in tasks requiring the generation of near-noise-free data, such as imaging system design and initial validation of reconstruction algorithms. Bearing this tradeoff in mind, to meet the anticipated MCS needs for studying advanced pinhole collimation (e.g., multipinhole) geometry and associated quantitative imaging methods, in this work, we developed and validated an improved MCS workflow by seamlessly integrating the SimSET and GATE MCS codes.

Specifically, we retained the strength of GATE in intuitive implementation of complex system configurations as well as comprehensive simulations for the collimator/detector component, but inserted the fast SimSET photon history generator (PHG) to circumvent the relatively slow GEANT4 (Ref. 26) code used by GATE in simulating photon interactions and transport inside a voxelized phantom. The logistical and technical aspects of the integration will be detailed in the material and methods section. Also in the same section, the design of simulation and experimental studies for validating the accuracy and efficacy of the new integrated workflow were discussed. Outcome of these studies were shown in the results section, which is followed by discussions and conclusions.

II. MATERIAL AND METHODS

II.A. Implementation of the SimSET-GATE integration

The logistics, as introduced previously, is to utilize SimSET, in particular, the PHG component, to simulate the photon interactions within a voxelized phantom, and then, feed the generated photon events to GATE for subsequent simulations of the photon interactions at the collimator and detec-

tor level. At the time of this development, the version of SimSET/PHG we used is 2.6, and GATE version is 2.2.0.

The integration flow chart is shown in Fig. 1. This workflow requires no modification for SimSET/PHG, however, additional coding is needed to allow GATE to recognize and properly handle the SimSET/PHG generated photon events, which are recorded in a history file. The structure of the history file is described in SimSET documentation,²⁷ and a description was also presented in Ref. 13. In short, the information recorded in the history file includes the spatial coordinates (x, y, z) and directional vector (u, v, w) of every photon that intercepts the surface of the target cylinder defined in PHG, as well as the scatter and energy information of the photon. To simplify the subsequent integration with GATE, variance reduction techniques available in SimSET are not used in generating the photon history.

In order to let GATE read in and properly handle the SimSET/PHG photon history, we modified the `GateSourceVoxelTestReader` method in the `GateSourceVoxellized` class of the GATE MCS code. This modification aligned the two spatial coordinates systems used by SimSET and GATE, and inserted photons from SimSET/PHG, which already have predefined position and momentum (in the form of directional vectors), to replace the random particle generations in a voxelized phantom originally performed by GATE/GEANT4. Specifically, after the modification, if a “history file” source is defined during GATE simulation parameter setup, the method `GateSourceVoxellized::GeneratePrimaries (G4Event* event)` in the GATE code will not perform its original functions—instead it will read in information from the history file and then produce particles based on the recorded SimSET/PHG information. This SimSET-originated photon will then interact and transport through the collimator and detector to complete the MCS workflow. Each photon recorded in the SimSET history file is read in only once by GATE to avoid noise correlations. A new history file will be generated using SimSET/PHG when needed, for example, in simulating projection data at a new angular view after the SPECT camera/detector rotates.

II.B. Validation of integrated SimSET-GATE MCS workflow

In the new integrated MCS workflow, the final simulation data are obtained through GATE, which has been validated extensively, e.g., Refs. 18–20. Therefore, for validation of our approach, we first compared the results generated from the new workflow with those obtained from GATE-only simulations through the voxelized phantom and the same system configurations, focusing on agreement between two sets of simulated data and improvements in execution time. If good agreement in simulated data is observed, the efficacy of the new workflow will be demonstrated through the speedup in execution time. Next, the simulation data were compared with the actual experimental data obtained from a commercial small animal pinhole SPECT system (X-SPECT,

FIG. 2. Illustration of (a) point source location and (b) sphere/cylinder phantom configuration used in simulation studies.

Gamma Medica-Ideas, Inc., Northridge, CA) using phantom studies, to demonstrate the accuracy of the MCS workflow in simulating an in-field system.

To make the above two validation steps coherent, the system configurations used in all MCS studies were based on the X-SPECT system installed at the Johns Hopkins Small Animal Imaging Facility. Simple point source and sphere source phantoms were used for comparing MCS and experimental studies, while the mouse whole-body (MOBY) voxelized phantom²¹ was also used in comparing SimSET-GATE and GATE-only simulations. Detailed specifications of the X-SPECT system include the use of discretized NaI crystals (82*82 pixels with a 1.5 mm pitch and 6 mm thickness, 12.5% energy resolution at 140 keV) and a low energy pinhole collimator (1 mm diameter knife-edge aperture made of tungsten and 9 cm pinhole aperture to detector distance). An 8 mm thick backcompartment for the detector was modeled by using a single glass layer. The detector is also enclosed by 5 mm thick lead shielding. All studies were based on imaging of Tc-99m with a 20% energy window centered at 140 keV for data collection. For experimental studies, the point sources were prepared by soaking a resin bead in a Tc-99m solution. For both SimSET/PHG and GATE, photoelectric effects and coherent/Compton scatter were included in the simulations. X-ray production cut was set to 20 keV in GATE, whereas it is not modeled in SimSET/PHG. In this particular study, no dead-time effects were modeled, and photons with an energy lower than 20 keV were not tracked.

The following aspects were compared in detail after planar projection data were obtained from both MCS and experimental studies:

- (1) System sensitivity in detecting Tc-99m point sources at various locations. A Tc-99m point source (~ 0.4 mm in size) with known activity of ~ 180 μ Ci was placed at a different location each time within the field-of-view (FOV) of the pinhole SPECT system. The simulated and measured system photon detection sensitivities at the same location, both on- and off-pinhole axis, were then compared. Specifically, to compare on-axis sensitivity, the point source was placed in air on the central axis [the solid line in Fig. 2(a)] of the pinhole collimator, with a

FIG. 3. Sample sagittal slices of the MOBY phantom (both radiotracer distribution and attenuation map) used in simulation studies.

distance of 1.5, 2, 2.5, 3.5, and 4.5 cm from center of the pinhole aperture, respectively. The detected photon counts in the planar projection data of the single point source were normalized by the known activity of the point source as well as the acquisition time to generate system sensitivity at that particular location within the FOV. Theoretically, the resulting on-axis sensitivity at different distances is expected to follow an inverse square law. In order to compare the off-axis (angular-dependent) sensitivity, projection data were acquired by stepping the same point source in air through the field-of-view of the pinhole collimator along the bottom dashed line shown in Fig. 2(a), which is perpendicular to the central axis and has a fixed distance of 1.5 cm from the pinhole aperture.

- (2) Image profiles and full width at half maximums (FWHMs) obtained from the point source projection data. The profiles through the center of the simulated and measured point source projections in the above studies were plotted. These profiles, as well as the FWHM values calculated from them through Gaussian fitting, were used for comparison.
- (3) Energy spectra. To obtain the energy spectra, we placed a sphere source (3.27 mm in diameter, filled with ~ 100 μ Ci Tc-99m) on the central axis of a water-filled cylindrical phantom (28 mm in diameter, 22 mm in height, and at 25 mm from the aperture) for both simulations and experiments. The center of the sphere source was 12.5 mm away from the bottom of the cylindrical phantom as shown in Fig. 2(b). The energy spectra were extracted from both MCS data and the list-mode data acquired using X-SPECT for comparison.

II.C. Demonstration of efficacy and versatility of the new SimSET-GATE MCS workflow

The voxelized MOBY phantom were used to compare the time needed by SimSET-GATE and GATE-only simulations to generate pinhole SPECT projection data at the same noise level (~ 17000 detected photons) under the same system configuration and acquisition parameters. The radiotracer distribution in the MOBY phantom emulated a typical Tc-99m labeled Annexin-V uptake in ApoE mice²² (Fig. 3). Next, to demonstrate the versatility and flexibility of GATE retained by the new workflow, we extended the above single pinhole

FIG. 4. Measured and simulated (from both SimSET-GATE and GATE) system sensitivity obtained from placing a Tc-99m point source (a) along the axis of the pinhole collimator and at different distances from the pinhole aperture, (b) at 1.5 cm from the pinhole aperture and at different off-axis positions.

SPECT system configuration to simulate projection data acquired from the multipinhole collimator described in Ref. 23.

III. RESULTS

III.A. Validation of the integrated SimSET-GATE MCS workflow

III.A.1. System sensitivity in detecting Tc-99m point sources at various locations

The results from on-axis Tc-99m point source studies are shown in Fig. 4(a), where the sensitivity was plotted as a function of distance from the pinhole. Similarly, the results from off-axis point source studies are shown in Fig. 4(b). Good agreement was observed between the two MCS methods as well as between MCS and experimental studies.

III.A.2. Image profiles and FWHMs obtained from point source projection data

Image profiles through the center of simulated and measured point source projection images are shown in Fig. 5 after being rescaled back to the object plane using the magnification factor. The FWHMs obtained from these profiles are listed in Table I. We found good agreement in both the profiles and the FWHM values, where discrepancies between the simulation and experimental measurement less than $100\ \mu\text{m}$ were observed.

III.A.3. Energy spectra

The simulated and measured energy spectra are shown in Fig. 6, where the comparisons of scatter data are also shown in the bottom plot with a rescaled Y axis. While observing

FIG. 5. Image profiles (rescaled back to the object plane) across the radial direction and through the center of measured and simulated (both SimSET-GATE and GATE) point response functions for a Tc-99m point source at (a) 1.5 cm away from the pinhole aperture and on-axis, (b) 3.5 cm away from the pinhole aperture and on-axis, (c) 1.5 cm away from the pinhole aperture and 23.2° off-axis, and (d) 3.5 cm away from the pinhole aperture and 23.2° off-axis.

TABLE I. Comparison of FWHMs (rescaled back to object plane) in measured and simulated point response functions generated from Tc-99m point sources placed at two different distances from the pinhole aperture and at an on-axis and an off-axis location, respectively.

Source-collimator distance (cm)	On-axis Tc-99m point source			23.2° off-axis Tc-99m point source		
	Experiment	Simulation		Experiment	Simulation	
	FWHM (mm)	SimSET-GATE FWHM (mm)	GATE-only FWHM (mm)	FWHM (mm)	SimSET-GATE FWHM (mm)	GATE-only FWHM (mm)
1.5	1.17	1.15	1.16	1.09	1.08	1.06
3.5	1.26	1.29	1.23	1.42	1.35	1.33

overall good agreement between the simulated and experimental data, some discrepancies are present, in particular, for the range between 60 and 110 keV. The detected scatter photons from the cylindrical phantom represented 17.9% and 18.2% of the total detected photons in SimSET-GATE and GATE-only simulations, respectively.

III.B. Efficacy and versatility of the new workflow

By using a single cluster node (RedHat Linux, AMD Athlon® MP 2200 CPU, 1 GB RAM), we found the time required to generate one pinhole projection view (with ~ 17000 detected photons) using the voxelized MOBY phantom was ~ 5.2 h for SimSET-GATE and ~ 50.1 h for GATE-only simulations, respectively. Increasing the number of projection views will increase the time roughly proportionally for both methods. Therefore, for simulating voxelized phantoms, ~ 10 times of speedup was achieved using the new SimSET-GATE workflow. Furthermore, the new workflow retained the strength of GATE in setting up and extending new system configurations. In Fig. 7, we show the

projection images of the MOBY phantom simulated using a single- and a four-pinhole collimator, respectively. The time required to simulate 225 million photon events at one projection angle are ~ 5.2 and ~ 5.36 h for the above single- and multipinhole collimation, respectively.

IV. DISCUSSION

The GATE MCS code uses GEANT4 as the underlying engine for simulating interactions and transport between photons and matter, therefore, possesses the advantages of GEANT4 in terms of having well-validated physics models. Its powerful visualization capability and intuitive user interface facilitate sophisticated geometry descriptions, which is very desirable for the research and development of complex system configuration like those in small animal pinhole SPECT. However, simulating voxelized phantoms using the current GEANT4 is very slow. In comparison, SimSET is efficient for simulating photon interactions and transport through the voxelized phantom, but provides only a limited number of collimator designs (e.g., parallel, fan, and cone beam collimators) for SPECT, without convenient visualization and user interface for setting up complex system and collimation geometries. Also, SimSET handles photon transport in the collimator without modeling the Monte Carlo process, but rather with analytical implementations of the geometric transfer functions, such as those presented in Ref. 24. To achieve accurate descriptions of the physical process in collimator/detector, particularly for new system configurations and/or simulations involving medium- and high-energy photons, while maintaining the efficient simulation within the voxelized phantom, we implemented the integrated SimSET-GATE MCS workflow. With realistic phantoms, such as MOBY, as input, one can achieve fast and accurate

FIG. 6. Comparison of energy spectra from experimental measured, and SimSET-GATE and GATE Monte Carlo simulation results.

FIG. 7. An example of fast, realistic, and versatile simulations enabled by the new SimSET-GATE workflow: projection images obtained from small animal pinhole SPECT system, and MOBY phantom using 1 (left) and 4 (right) pinholes, with magnification factors 3.6 and 2.6, respectively.

simulations encompassing all aspects of the imaging system, such as, phantom, collimator, and detector.

Our integration of SimSET with GATE to generate a new MCS workflow has been validated by comparison to experimental data and simulated data from GATE. Furthermore, the integrated code is faster, as shown above. Good agreement of simulated data between two MCS workflows was evident in all aspects of the studies, i.e., system sensitivity, image profiles, and energy spectra. In particular, from Fig. 6, the good agreement between the SimSET/PHG and GATE energy spectra contributed from photons scattered inside the phantom validated the integration of the SimSET/PHG and GATE MCS codes for simulating the photon interactions and transport through the phantom, but before the collimator-detector system. The overall good agreement between experimental and simulated data suggests that both SimSET-GATE and GATE MCS workflows are able to accurately simulate the X-SPECT system. The discrepancies observed in energy spectra may be attributed to the inaccurate modeling of the detector's nonuniform energy resolution²⁵ across the entire photon energy range in the simulation.

The speedup achieved with the current implementation of the integrated SimSET and GATE MCS codes can be potentially further improved. For example, to simplify the interface between SimSET/PHG photon history and GATE, we opted to disable the variance reduction techniques in SimSET. A more sophisticated interface combined with careful validation may allow the use of the variance reduction method in some cases to achieve further performance gain. Also, in the current implementation, the GATE components will be executed after SimSET/PHG produced the entire photon history. A pipeline approach might be feasible to allow the GATE code to read in SimSET/PHG generated photons in real time for further performance gain.

It is also possible for the new SimSET-GATE workflow to simulate the photon interactions and transport in all directions within the phantom only once, results of which can be used for all subsequent projection views. The use of the same photon history file for multiple projection views may introduce noise correlation; however, for simulations intended to generate low noise data, these correlations should have little effect on the results. Under this condition, an even greater speedup can be obtained for SPECT simulations requiring generations of multiple projection views. Following this approach, a quick comparison showed that SimSET-GATE and GATE-only require ~ 12 and ~ 227 h, respectively, for simulating four projection views of the voxelized MOBY phantom, which translated into ~ 19 times of difference in speed, as compared to the ten times speedup observed previously using the approach of generating a new photon history file for each of the four projection views.

Combined with the capability of performing fast simulations, the sophisticated yet intuitive geometry description and visualization provided by GATE becomes even more relevant for small animal SPECT research, which often involves new and complex collimator design and detector geometries. For example, multipinhole collimation has generated lots of research interests recently.^{7,9,10} Our

demonstration of the multipinhole simulation showed that the proposed SimSET-GATE workflow can be useful for studies on optimizations of multipinhole collimator designs, data acquisitions methods, and image reconstructions and correction techniques.

V. CONCLUSION

We have successfully developed and implemented a MCS workflow for fast, realistic, and versatile small animal pinhole SPECT simulations by integrating the SimSET photon history generator in GATE MCS codes. This development should be of interest to a wide range of small animal molecular imaging researchers. Also, by adapting the integrated MCS workflow to other imaging configurations, including small animal PET and clinical SPECT and PET, it can be extended to a wide range of applications in clinical and biomedical research studies. (The implementation described herein will be available to the research community as open source software.)

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