Molecular Imaging of Small Animals PET using Monte Carlo Simulations

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***Abstract* – This work is based on the use of a simulation system dedicated for small animal PET imaging. GATE, a Monte Carlo simulation platform based on the Geant4 libraries, is well suited for modelling microPET systems like the microPET® FOCUS 220 and to implement realistic phantoms, such as the MOBY phantom, and radioactive distribution maps obtained from real exams. We used the validated microPET® FOCUS 220 simulation model, with GATE, to produce real simulated PET mouse exams. Results from simulated real studies of the mouse body using [18F]fluoride and the 2-Deoxy-[18F]fluoro-D-glucose (FDG) imaging protocols are presented. These simulations include the injections of real radioactive doses into the animal and the use of real time frames. We also simulate the respiratory mouse motion during an FDG PET exam using the model proposed in the dynamic MOBY phantom. The qualitative and quantitative results from simulated data are in good agreement with the experimental data.**

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I. INTRODUCTION

The advances in genomic technologies over the last decade have led to an increased interest in vivo small animal imaging, especially with the use of new animal models of diseases. The genetic resemblance between human and mouse allow its use to reproduce many human diseases making this an important and widely research tool [1], [2]. In the field of molecular imaging techniques Positron Emission Tomography (PET) is an extremely powerful tool to examine these models. PET is a non-invasive nuclear medicine technique which provides spatial and temporal distribution of radiotracers allows us to understand physiological, metabolic and molecular processes of the body [3]. Due to some limitations and difficulties associated to the small animal studies in vivo, related the resolution and sensitivity of the scanner, the injected dose in the animal and the image quantification [4], Monte Carlo simulations are an essential tool for assist these developments: in designing new medical imaging devices, optimising data acquisition protocols, developing and assessing of tomographic reconstruction algorithms or evaluating correction methods for improve image quantification [5]. In this study, we used the Geant4 Application for Tomographic Emission (GATE) Monte Carlo platform for modelling the microPET® FOCUS 220 system and for implementing realistic phantoms for small animal imaging [6]. The main goal of this work was to produce realistic simulated exams for the *[^{18}F]fluoride* and the *2-Deoxy-[^{18}F]fluoro-D-glucose* (FDG) radiotracers using the validated microPET® FOCUS 220 system for the GATE platform and real mouse phantoms descriptions. These results are the consequence of the complete installation of this Monte Carlo platform simulation on a cluster computing architecture.

II. MATERIALS AND METHODS

A. Monte Carlo Simulation using GATE

The scanner modelled for this study is the microPET® FOCUS 220, one of the last generation of commercial scanners dedicated to high resolution small animal imaging [7]. The GATE is a generic Monte Carlo simulation platform dedicated to nuclear medicine, based on Geant4 libraries, a well-established code for the simulation of radiation transport. GATE encapsulates the Geant4 libraries to achieve a modular, versatile and scripted simulation toolkit adapted to emission and transmission tomography. The use of GATE facilitates the description of different components necessary for the accurate modelling of a PET or a SPECT system, starting from the geometry up to the creation of a processing chain for the detected events. It allows describing time-dependent phenomena such as detector or patient movements, source decay kinetics, dead tome for coincidence acquisitions including delay coincidences measurement. The complete validation results of the microPET® FOCUS 220 simulation system using GATE is given by the reference [8].

B. Mouse phantoms

We used in this work the MOBY phantom which combines the realism of a voxelized phantom, with the flexibility of a mathematical phantom, based on non-uniform rational B-splines (NURBS) [9].We applied a resampling on the default matrix to reduce the voxel number to 40×40×124 voxels with a voxel unit size of 0.5×0.5×0.5 mm3 (Fig. 1). This method allows the reduction of the computing time resulting from the particle tracking inside the material and volume descriptions.

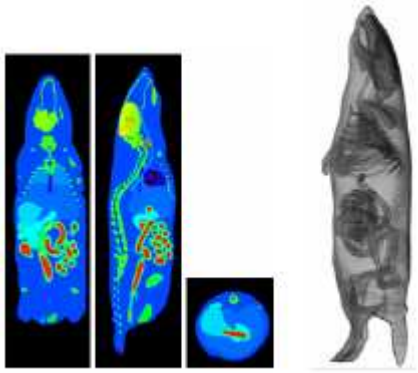

Fig. 1 – Coronal, sagital and transaxial slices correspondent to the emission map (left) and illustration of the attenuation map (right) generated by the MOBY program.

The phantom also includes 4D models of the mouse's cardiac and respiratory motions. We used the respiratory MOBY feature in our simulations. The MOBY respiratory motion was set up to be dependent on two time varying parameters: change in the height of the diaphragm and the amount of chest expansion. We manipulated these parameters to produce a "stress breathing", in order to mimic the respiratory motion in a real PET examination. A set of 10 temporal frames of 0.037 s was generated over a complete respiratory cycle (Fig. 2). On this configuration the diaphragm height was set to 4.2 mm and the expansion of the chest was set to 6.0 mm.

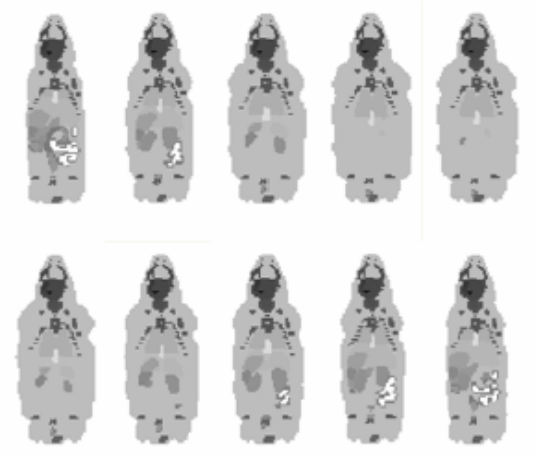

Fig. 2 – Coronal slices corresponding to the breathing motion, over one respiratory cycle. The matrix size was set to 55×55×124 voxels, with a voxel unit of 0.5×0.5×0.5 mm^3.

To generate realistic mouse phantoms, for a dedicated exam, we used a real whole body mouse acquisition, performed at the CEA/SHFJ (Orsay, France). The exam consisted in a classic exam of 400 µCi injected dose of *[^{18}F]fluoride* of 60 minutes acquisition time (20 minutes post injection). In addition, we used a real dynamic whole body mouse FDG exam to generate the emission map phantom. The mouse was injected with an activity of 220 µCi and scanned during 90 minutes.

C. Simulation set-up

The simulations were performed using realistic acquisitions parameters. We used two functional models: the *[^{18}F]fluoride* and the FDG radiotracer models. The *[^{18}F]fluoride* ion is a radioisotope with high affinity to bone structures. The FDG is the most used radiotracer for cancer detection, is an analogue of glucose and is taken up by living cells through the normal glucose pathway. The activity distribution in our simulations was set according to the activity distribution assigned to the different whole body structures for the *[^{18}F]fluoride* and the FDG radiotracers, respectively. The FDG biodistribution is defined by the Time Activity Curves (TACs) (Fig. 3).

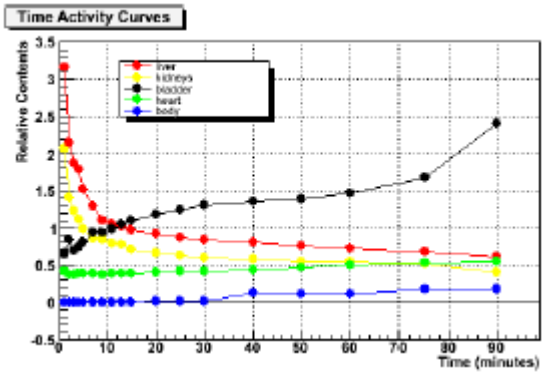

Fig. 3 – TACs used as input in our simulation studies for the FDG functional model.

In both protocols the physical effects like positron range, gamma accolinearity and tissue attenuation are not taken into account to reproduce gold standard results. These gold standard images will define the optimal results that we could obtain with a dedicated scanner and a specific radiotracer. Images were reconstructed using FORE+OSEM2D (16 subsets and 4 iterations).

III RESULTS

A. Simulation studies for the [^{18}F]fluoride and the FDG

We simulated an activity map close to the *[^{18}F]fluoride* distribution at the last acquisition time frame for the phantom generated from the *[^{18}F]fluoride* exam (Fig. 4) and the MOBY phantom (Fig. 5).

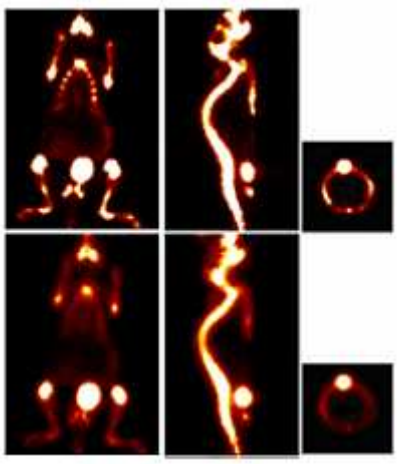

Fig. 4 – Slices of the real (top) and the simulated exam (bottom), after a full simu lation of 9.6×10^9 particles. We simulated 284 µCi in the whole body mouse for 900 s acquisition time. The simulation ran on a cluster of 50 CPUs with a global computing time of 10h36'

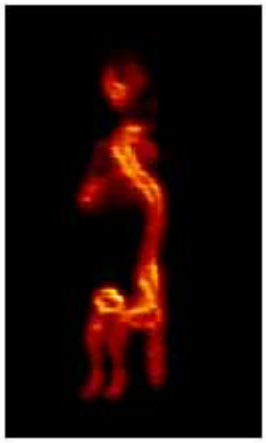

Fig. 5 – Maximum Intensity Projection (MIP) for the MOBY phantom after a full simulation of 4.0×109 particles, which is equivalent 2.21 mCi injected dose with 500 s for the acquisition time. This corresponds to an exam with an activity distribution of 0.5 mCi in the whole body during 30 minutes. The simulation was computed on a cluster of 50 CPUs and took an average of 21h30'.

We defined activity map close to those for the FDG biodistribution both for the MOBY phantom (Fig. 6) and the phantom generated from the real acquisition (Fig. 7).

To validate the accuracy of the simulations quantitative output we compared the real data against the simulated data for the data results illustrated by the Fig. 7. The plot in Fig. 8 shows the relative activity concentration for thesimulation data are in good agreement with the same measurements for the real values.

B. Simulation study for the respiratory motion

We generated an emission dataset using typical values of FDG uptake for each organ at the last acquisition frame, for the non normal tidal breathing of the MOBY phantom previous described. The gold standard simulation were computed on a cluster of 10 CPUs during 24h, corresponding to an acquisition time of 568.5 s at the last frame (900 s) which correspond to a total of 3.5×10^9 particles (Fig. 9).

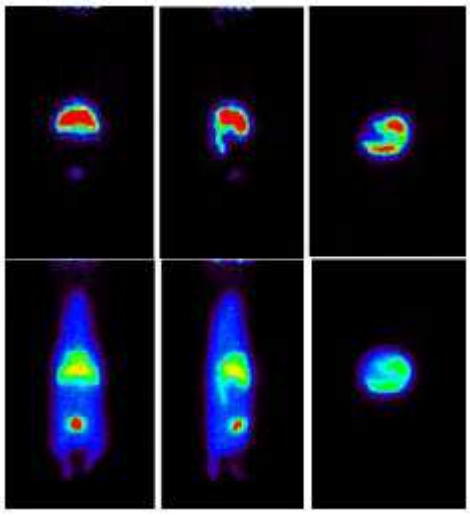

Fig. 6 – Simulated slices for the first (top) and the last frame (bottom) of an FDG exam using the MOBY phantom. For the first frame we simulated 219 µCi for an acquisition time of 60 s which produced 4.9×108 particles, using a cluster of 6 CPUs during a computing time less than 6 h. For the last frame we simulated 131 µCi (4.2×109 tracking particles) for a 15 minutes acquisition time, using 10

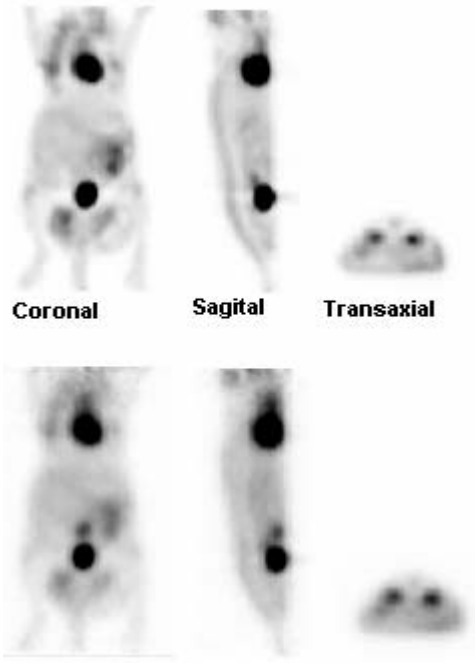

Fig. 7 –Slices of the real (top) and the simulated exam (bottom), after a full simulation of 3.5×109 particles. We simulated an activity of 112 µCi for 15 minutes acquisition time. The simulation ran on a cluster of 10 CPUs with a global computing time of 12h31'.

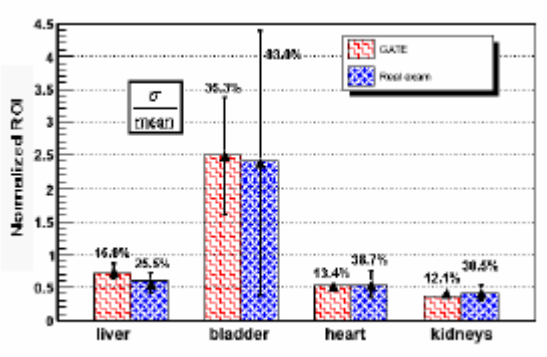

Fig. 8 – Comparison between PET image quantification and the GATE measurements.

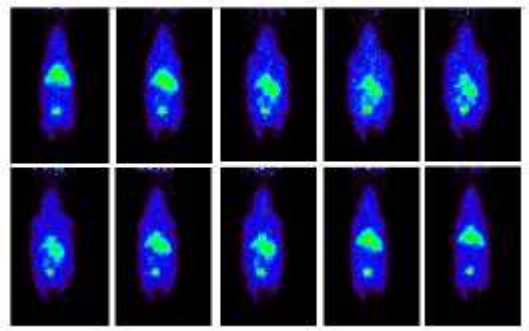

Fig. 9 – Coronal slices corresponding to the simulation of the breathing motion, over one respiratory cycle for a FDG exam at the last time frame.

IV. CONCLUSIONS AND PERSPECTIVES

The results presented shows that GATE is well suited to model the FOCUS system for quantitative analysis and to implement realistic voxelized mouse body phantoms. We have shown that the GATE platform can simulate small animal PET acquisitions under realistic conditions, to improve the quantitative analysis in mouse body studies. We showed a first preliminary approach of Monte Carlo simulation studies for the FDG radiotracer using the MOBY phantom which include respiratory motion. This work is being complemented by accessing the impact of such motion in the detection of lung lesions (including lesion movement as a function of respiratory motion).

In fact, lung motion is expected to introduce additional image blurring which may degrade lesion detection sensitivity. In this context, one of the aims in our work will be to optimize acquisition protocols, image correction procedures and reconstruction methods in these situations. In the near future, realistic dynamic simulations with different radiotracers, as the *3-Deoxy-[^{18}F]fluorothymidine* (FLT), for whole body exams will be done. Biological kinetics using compartmental modeling will be implemented inside the GATE platform.

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