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# TestDose: a SPECT image generator for clinical dosimetry studies

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## ABSTRACT

Patient-specific dosimetry in nuclear medicine relies on activity quantification in volumes of interest from scintigraphic imaging. Clinical dosimetry protocols have to be benchmarked against results computed from test phantoms. The design of an adequate model is a crucial step for the validation of image-based activity quantification. We propose a computing platform to automatically generate simulated SPECT images from a dynamic phantom for arbitrary scintigraphic image protocols. As regards the image generation, we first use the open-source NCAT phantom code to generate an anatomical model and 3D activity maps for different source compartments. This information is used as input for an image simulator and each source is modelled separately. Then, a compartmental model is designed, which describes interactions between different functional compartments. As a result, we can derive time-activity curves for each compartment with sampling time determined from real image acquisition protocols. Finally, to get an image at a given time after radionuclide injection, the resulting projections are aggregated by scaling the compartment contribution using the specific pharmacokinetics and corrupted by Poisson noise. Our platform consists of many software packages, either in-house developments or open-source codes. In particular, an important part of our work has been to integrate the GATE simulator in our platform, in order to generate automatically the command files needed to run a simulation. Furthermore, some developments were added in the GATE code, to optimize the generation of projections with multiple energy windows in a minimum computation time.

**Keywords:** Nuclear Medicine, Monte-Carlo modelling, SPECT imaging

## 1. INTRODUCTION

Molecular Radiotherapy (MRT) is a speciality of nuclear medicine and consists in the use of a vector specific to a cell receptor. This vector is labeled with a radioactive compound to carry the radiation as close as possible to the tumor cell. One of the keys of MRT optimization relies on the personalization of absorbed doses delivered to the patient. Internal dosimetry aims at defining a therapeutic window to find the balance between efficacy of the treatment of tumor cell and toxicity to normal cells. In other words, we want to increase the irradiation exposure on tumour cells and protect surrounding healthy tissue. Many critical steps are involved in the absorbed dose evaluation. First, we need to localize the injected radioactive sources by scintigraphic imaging, both in space and time. And then, varying factors may include quantitative imaging processing, time-activity curve assessment and ends with absorbed dose calculation. Global clinical dosimetry accuracy relies on the accuracy of each of these steps, but currently clinical dosimetry approaches vary from one nuclear medicine service to another, leading to a wide heterogeneity of implemented dosimetry approaches. The ‘DosiTest’ project\* (supported by the French National Institute of Health and Medical Research) represents the first attempt to take into account the various aspects involved in clinical dosimetry protocols. We propose to setup a multicentric clinical dosimetry trial based on Monte-Carlo modelling. By comparing results from multiple centers, we will be able to identify critical steps in a dosimetric study and the final objective is to propose a reference methodology applicable in a clinical context. Our work participates to that project and focuses on scintigraphic image generation. The specificity of our approach is to simulate site-specific scintigraphic images so that each centre can implement its

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\*<http://www.dositest.fr>

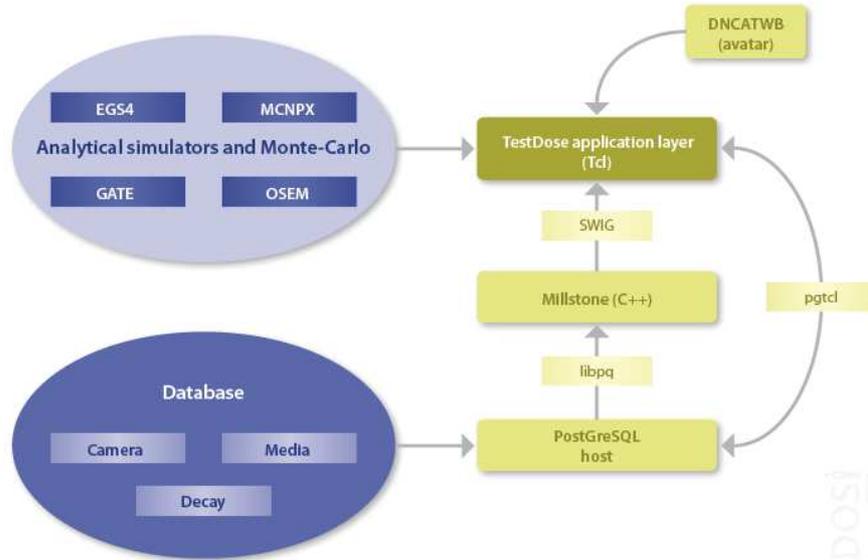


Figure 1. Overall diagram of the software ‘TestDose’.

own dosimetry approach. Basically, differences in clinical imaging protocols come from the diversity of gamma-cameras, temporal sampling, acquisition mode and implemented corrections.

In this paper, we present the application software ‘TestDose’ which is the computing architecture of the ‘DosiTest’ project. It consists in a complete pipeline from model generation to scintigraphic image simulation. In order to allow maximal flexibility, we suggest to use a compartmental model approach.<sup>1,2</sup> The idea is to simulate separately each source compartment. We create a virtual but realistic patient based on the NCAT-WB phantom<sup>3</sup> to generate an anatomical model and 3D activity maps for different source compartments (see section 2.2). Kinetic information for a given radiopharmaceutical are computed from the compartment model (see section 2.3). And then, image generation is performed using the GATE Monte Carlo simulator<sup>4</sup> (see section 3.3). Finally, the results from a feasible study are given in section 3.

## 2. METHODS

### 2.1 TestDose

Our in-house software ‘TestDose’ runs on Macintosh operating system 10.6 (snow leopard) and above. The overall diagram of the software is given in figure 1. It is composed of several packages called in turn by *tcl* scripts of the application layer. Those scripts have access to data stored in a *PostgreSQL* database via an interface layer coded in *C/C++*. Furthermore, image processing methods are implemented in the previous layer, using the ITK library<sup>†</sup>.

Three databases are available and accessed when creating the command files for the simulation of the SPECT images (see section 3.3) : (1) the ‘Camera’ database where model-specific gamma camera information are stored, (2) the ‘Media’ database where a description of the elemental composition of a range of biological materials is given and (3) the ‘Decay’ database where we can find the emission characteristics of the considered radionuclides. The generation of the virtual patient based on the NCAT-WB phantom is performed by the module ‘Avatar’ and can be seen as an input of the application layer. Finally, some analytical and Monte Carlo simulators are combined to the platform, such as OSEM and GATE for image simulation.

<sup>†</sup>Segmentation and Registration Toolkit (<http://www.itk.org>)

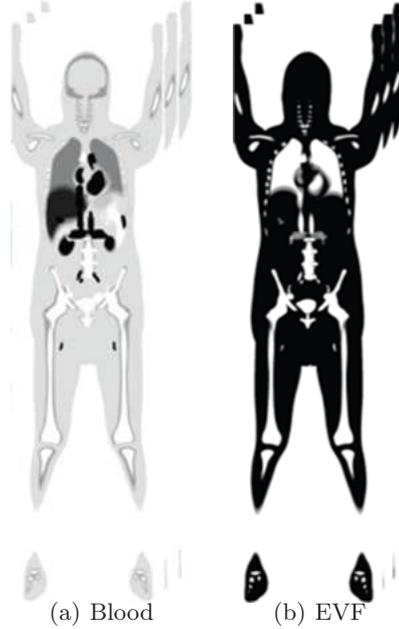


Figure 2. 3D activity maps of the blood and extravascular fluid (EVF) compartments.

## 2.2 Virtual patient generation

The NCAT-WB phantom is a realistic and flexible 4D anthropomorphic model<sup>3</sup> which allows a whole-body modelling of the patient with cardiac and respiratory motions. Furthermore, an interesting feature of this phantom is the possibility to add spherical tumors.

A modification in the original code allows each functional compartment to be represented by a 3D volume where a voxel value is set to its geometry contribution<sup>5</sup> (*e.g.*, a voxel located in the liver may represent 90% of liver and 10% of blood). Those 3D volumes can be seen as activity maps such as illustrated in the figure 2 for the blood and extravascular fluid (EVF) compartments. We can observe the different concentration of both compartments in the human body. As an example, we can notice the high presence of blood in the heart and the non-presence of extravascular fluid, whereas in the soft tissues, the EVF exhibits very high density and the blood much weaker densities. In addition to those activity maps for functional compartments, the program yields separated volumes for each user-defined human body materials (*e.g.*, bones, lungs, etc) giving an anatomical information.

Each volume is stored in our platform database as a BLOB (Binary Large Object) and is accessed in the image simulation module as input data (see paragraph 3.3).

## 2.3 Kinetic evaluation

For a given radiopharmaceutical study, a reference pharmacokinetic is assigned to each volume of interest using the compartmental model approach. A compartmental model is mathematically defined by a system of linear differential equations describing the exchanges between compartments.<sup>1,2</sup> The figure 3 illustrates the exchanges between our compartments of interest. The transfer constants  $k_{i,j}$  between interacting source compartments are then input parameters of our software, as well as the initial injected activity in the blood compartment and elimination rates of the urine at a given time. From those inputs, defining the activity present in a given compartment at any time point of the kinetic study (that can span over days or weeks) is trivial. This allows an easy computation of the total cumulated activity (for the whole study). It is also possible to define the cumulated activity for every source volume during the acquisition time of any ‘virtual’ scintigraphic imaging session.

For each imaging procedure, an activity table is stored in our platform database, that contains cumulated activity in each compartment over acquisition time.

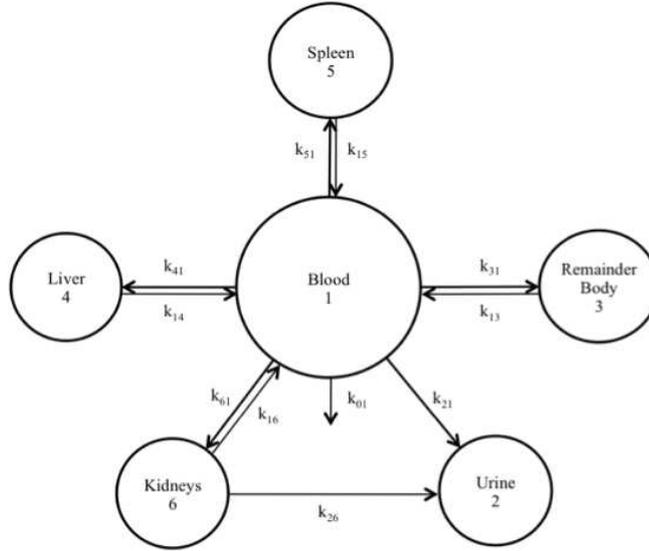


Figure 3. Compartmental model: exchanges between different compartments.

## 2.4 Simulation of SPECT images

Initially, in the ‘TestDose’ software, the simulation process was performed using an analytic code, *osem*.<sup>5</sup> In this work, we propose to integrate the Monte-Carlo simulator, GATE.<sup>4</sup> Indeed, Monte-Carlo simulators are assessed to be more accurate than analytic simulators for radiation propagation in heterogeneous media. However, Monte-Carlo modelling requires huge computation times and intensive computing grids are mandatory to run simulations within a reasonable time.

Many developments were implemented to manage image modelling using GATE: (1) automatic generation of the command files, (2) the process to load the simulated images back into our platform database.

The command file generation consists in finding the relevant information in our platform database via the object links and translating it in the GATE script language. ‘TestDose’ creates as many command files as source compartments and each one is composed of several distinct parts as follows:

1. **Camera geometry and features:** The GATE simulator allows any gamma camera simulation, provided that an accurate description of the system is given.<sup>6,7</sup> Model-specific gamma camera information is stored in the ‘Camera’ database (see figure 1).
2. **Phantom geometry:** The phantom is the aggregation of the voxelized volumes representing the human body materials from the NCAT-WB phantom code (see section 2.2). Moreover, the resulting volume is converted into interfile format.
3. **Physical processes:** This part is similar for any simulation and takes into account Compton and Rayleigh scattering, photoelectric absorption and X-ray whose energy is superior to 50 KeV.
4. **Radioactive source geometry and features:** To define source geometry, we make use of voxelized source volumes, as for phantom geometry. However, source compartments are not aggregated, since we want to simulate each compartment separately. Each volume is converted into interfile format. The emission characteristics of each considered radionuclide is available from the ‘Decay’ database of our platform (see figure 1).
5. **Output files:** Projections are saved in Interfile format. Subtractive scatter correction methods such as the dual- or the triple-energy-window method may be needed in post processing on images. A development was added in the GATE code, to optimize the generation of projections with multiple energy windows in a minimum computation time. This relieves from the need to save an output file in the ROOT format which may be sometimes very voluminous and to process those files *a posteriori*. It is now possible to save images from multiple energy windows into one interfile output without creating ROOT output file. This new development is available for the whole community into the release of GATE v6.2.

Target	Source	Rate constant ( $s^{-1}$ )
EVF	Blood	$1.38 \cdot 10^{-5}$
Blood	EVF	$1.61 \cdot 10^{-6}$
Kidney	Blood	$3.21 \cdot 10^{-6}$
Urine	Kidney	$7.70 \cdot 10^{-4}$
Liver	Liver	$2.40 \cdot 10^{-6}$
Spleen	Spleen	$3.00 \cdot 10^{-6}$

Figure 4. Compartments included in the compartment model and their transfer constants.

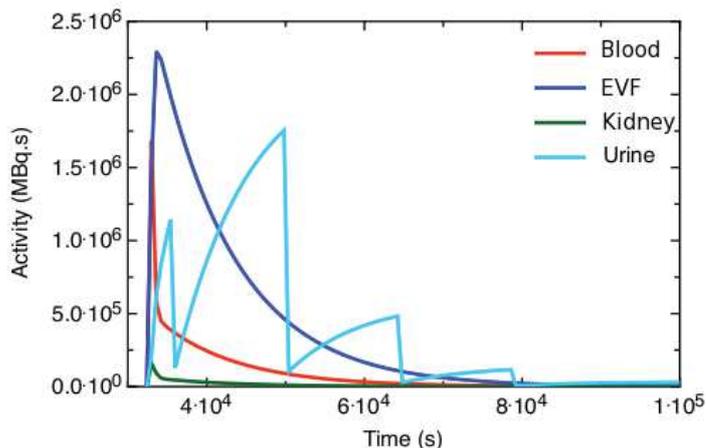


Figure 5. Time Activity Curves: elimination kinetics of the radionuclide in different compartments.

The various command files are exported from ‘TestDose’ and launched on a computer cluster for intensive computing. For a given imaging protocol, this process is not repeated for every imaging session, i.e. only one set of source images is simulated and loaded back into the software database. In order to get an image at each required time-point, ‘TestDose’ scales each pixel in the source image by its corresponding cumulated activity (see section 2.3) and then aggregates the different source images. Finally, the final image is corrupted by Poisson noise to give account of statistical fluctuations that would occur for each imaging session.

### 3. RESULTS

#### 3.1 Input parameters

**Pharmacokinetic data** were designed thanks to a compartment model composed of 6 compartments: blood, hepatic, renal, splenic, urine and extra-vascular fluid (see figure 3). We used whole-body images acquired for a radioimmunotherapy protocol using  $^{131}\text{I}$ -labelled monoclonal antibodies for the treatment medullary thyroid cancer<sup>8</sup> and we derived empirically a compartment model which allows realistic image simulation. We observe in table 4 that 4 compartments interact with each other according to transfer constants whereas hepatic and splenic compartments are isolated (containing respectively 10% and 1.5% of the initial injected activity). The figure 5 shows the corresponding time-activity curves that can be derived for each compartment.

As regards the **geometric model**, we specified the location of spherical tumors into the NCAT phantom (see section 2.2): 3 tumors in the liver (20, 20 and 40 mm diameter), 2 tumors in the right lung (20 and 40 mm diameter) and 1 tumor in the left lung (20 mm diameter). Additionally, 3 materials were used to describe human body densities: bones, lungs and soft tissue. Thus, the NCAT phantom code yielded 15 different voxelized volumes (3 materials, 6 source compartments and 6 tumors).

#### 3.2 Acquisition protocol

At time 0, the injected activity in the blood compartment of the phantom was 2.4 GBq of  $^{131}\text{I}$  to which was added the activities of the other source organs and tumors. Therefore, the total activity at time 0 was 2.7 GBq. Whole-body acquisitions were simulated at day 3, day 4, day 8 and day 10 post-injection. For each imaging session, we used the ‘step and shoot’ acquisition mode to simulate 5 planar acquisitions of 300 seconds each with 2 static heads (anterior and posterior view). Between each acquisition, the heads were translated along the body with a step of 378 mm to mimic the conditions of clinical acquisitions.

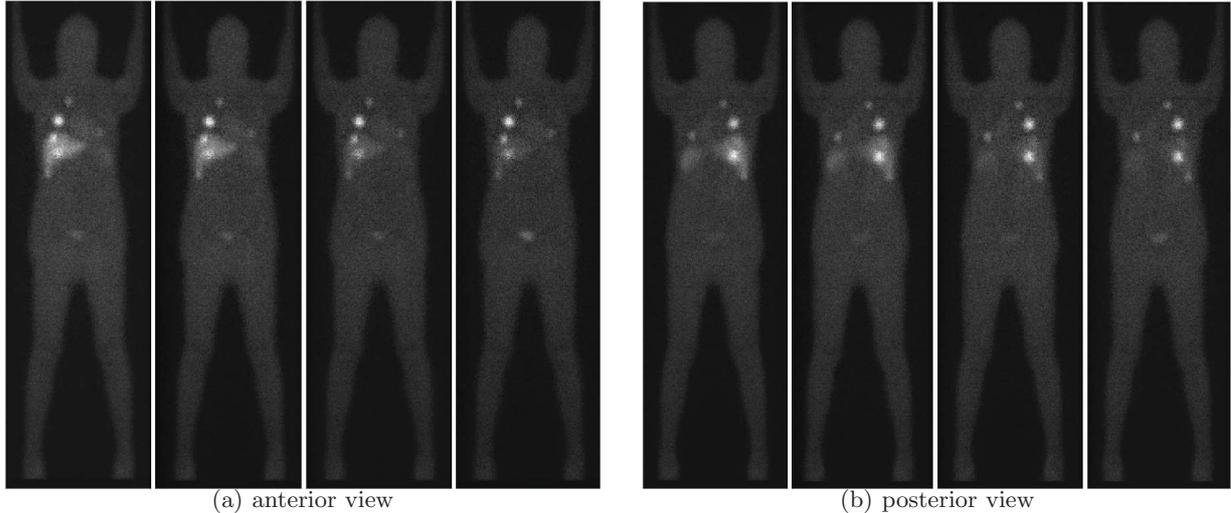


Figure 6. The whole-body images generated with GATE. From left to right: the acquisitions at  $d_3$ ,  $d_4$ ,  $d_8$  and  $d_{10}$ .

### 3.3 Image generation

Planar image simulations were performed with the GATE simulator. We used the GE Millenium-VG camera model already validated in a previous work.<sup>6</sup> Figure 6 shows simulated whole-body images with the anterior and posterior views at different times after injection. Activity variation in the different compartments over time, as defined by the pharmacokinetic model (see section 2.3) can be clearly seen. We carried out Monte-Carlo simulations on a *XGrid* controlled computing grid which is composed of 480 cores. In our software, a task (corresponding to a command file) is defined for a compartment simulation in a specific gantry position and the cumulated activity concentration is set to 10 MBq.s *per cc*. Thus, we split each task in 400 subtasks which were distributed on the cores. 11 days were necessary to complete the whole simulation set. In particular, 86.5% and 8.8% of computation time were dedicated to the extra-vascular fluid and blood compartments, respectively, due to the large number of simulated particles per cc and the volume occupied by those compartments in the human body.

## 4. CONCLUSIONS

We proposed a computing framework to facilitate the generation of adequate scintigraphic images for clinical dosimetry studies. A complete pipeline from model generation to scintigraphic image simulation was designed using the compartment model concept. To achieve this goal, many in-house packages and open-source code were combined, such as a NURBS-based anthropomorphic phantom program NCAT and the GATE simulator. Furthermore, a new development was committed to the GATE code to allow straightforward multiple energy windows modelling. We evaluated our modelling platform on whole-body planar acquisitions performed at various times post injection, with a site-specific camera model. In the near future, more validated camera models will be included in our database and further developments will be made to deal with different acquisition modes (*e.g.*, tomoscintigraphic or dynamic acquisitions).

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