D 6.2 - Software: upgraded MC simulation tools capable of simulating a complete in-beam ET experiment, from the beam to the detected events.

Dissemination level [PU]

ENVISION
European NoVel Imaging Systems for ION therapy

Project type: FP7 Cooperation: Health - Collaborative Project (CP)
Start date of project: 1st February 2010 Duration: 48 months

WP n° and title: WP 6 - Monte Carlo simulation of in-vivo dosimetry
WP leader: Irène Buvat, Giuseppe Battistoni
Author(s):
Contributor(s):
Deliverable due: 31 January 2012
Report date: 26 February 2012

Dissemination Level

<table>
<thead>
<tr>
<th></th>
<th>Public</th>
<th>PP</th>
<th>RE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP</td>
<td>Restricted to other programme participants (including the Commission Services)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RE</td>
<td>Restricted to a group specified by the consortium (including the Commission Services)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ENVISION -GA n°241851
TABLE OF CONTENTS

| Introduction                                                                 | 3 |
| 1. Upgraded MC simulation tools capable of simulating a complete in-beam ET experiment. | 3 |
| 2. Description of one reference clinical case, including the complete patient model and beam characteristics | 14 |
|                                                                               | 16 |
Introduction

Deliverable 2 consists of:

- Upgraded MC simulation tools capable of simulating a complete in-beam ET experiment.
- Description of one reference clinical case, including the complete patient model and beam characteristics.

1. Upgraded MC simulation tools capable of simulating a complete in-beam ET experiment.

Two tools supporting full modelling of in-beam ET experiments are developed in parallel, in line with the previous expertise of WP6 participants with the Geant4/GATE and FLUKA Monte Carlo simulation tools. Following recent developments, these two tools can now be used for a complete modelling of an hadrontherapy treatment coupled with PET imaging. The most recent features of these 2 tools are now described, as well as the demonstration of the feasibility of using the codes for complete modelling of in-beam PET experiments, as well as the feasibility are now described.

1.1. Using GATE for modelling an in-room PET experiment: from the proton irradiation to the PET scanner modelling

Since 2010, hadronic treatments as well as imaging devices can be modeled with the GATE Monte Carlo simulation tool (http://www.opengatecollaboration.org). This document, written in the framework of the European FP7 ENVISION project (Grant Agreement No. 241851), briefly describes how to simulate an in-room PET experiment with GATE. For that purpose, two examples, based on the irradiation of a homogeneous target by monoenergetic carbon ions (C12) and of a heterogeneous phantom by monoenergetic protons, are described.

Set-up 1: Irradiation of a homogeneous target by carbon ions (C12)

Set-up description

The direct simulation of the whole in-room PET experiment is time-consuming in GATE due to all nuclear fragmentation processes occurring in the phantom. An alternative and flexible option, used in this example, consists in dividing the simulation in two steps:

- The hadrontherapy treatment simulation,
- The imaging simulation.

During the hadrontherapy treatment simulation, the beam as well as the homogeneous target were simulated. The $\beta^+$ emitter maps (C11, C10, O15) were stored using the ProductionAndStoppingActor of GATE. The resulting maps were introduced as input sources in the second imaging simulation.

This splitting in two distinct simulations offers one main advantage: the treatment step can be simulated only once, and many imaging simulations (possibly corresponding to different scanners or acquisition parameters) can then be performed taking the output of the treatment simulation as the input of the imaging simulation.

Hadrontherapy treatment simulation

A perfect line beam (no angular opening) of $10^6$ carbon ions (C12 - 260 AMeV) irradiating a 10×10×60 cm$^3$ PMMA ($\rho = 1.19$ g/cm$^3$, H (0.080541), C (0.599846), O (0.319613), I (Ionization potential) = 74 eV) target placed in air was simulated (Figure 1). Three maps, corresponding to the spatial distributions of the main $\beta^+$ emitters (C11, O15, C10), were stored at the end of this simulation.
D 6.2 - Software: upgraded MC simulation tools capable of simulating a complete in-beam ET experiment, from the beam to the detected events. Dissemination level [PU]

Figure 1. Set-up scheme.

Imaging simulation

A dedicated double-head PET imager (GSI Darmstadt) was simulated in GATE (Figure 2 – Appendix 2). A detailed description of the PET system can be found in (Enghardt et al 2004). The β+ emitter maps were introduced as sources using the following command lines:

```
/gate/source/addSource voxel voxel
/gate/source/voxel/reader/insert image
/gate/source/voxel/imageReader/translator/insert linear
/gate/source/voxel/imageReader/linearTranslator/setScale 5.67e-1 Bq
/gate/source/voxel/imageReader/readFile C11-Stop.dat
/gate/source/voxel/setPosition -300 -50 -50 mm
/gate/source/voxel/gps/particle e+
/gate/source/voxel/gps/energytype Carbon11
/gate/source/voxel/setForcedUnstableFlag true
/gate/source/voxel/setForcedHalfLife 1222.8 s
```

The energy spectra of the β+ emitters (except for C10) as well as their half-lives were taken into account in the simulations. A ROOT output was stored at the end of the simulation.

Figure 2. Simulation of the double-head PET system using GATE.
Results

PET sinograms

The GATE simulation yielded a ROOT output, in which the features of interest of all interactions occurring in the PET system (Singles) were stored. A C++ program was developed to visualize the corresponding PET sinogram (Figure 3). A 250-850 keV energy window was used in Figure 3.

Reconstructed images

Reconstruction algorithms dedicated to the GSI PET system were developed by the HZDR (Helmholtz-Zentrum Dresden-Rossendorf) group (Pönisch et al 2003). These reconstruction algorithms require a binary List Mode Data (LMD) file as input file. A C++ program has therefore been developed to convert GATE outputs (ROOT data – Single Tree) in the appropriate binary format.

Figure 3. PET sinograms resulting from the irradiation of a PMMA target by a monoenergetic carbon ion beam (300 s acquisition duration (left), 3600 s acquisition duration (right)). At the bottom, notations used to plot the sinograms are shown.

Figure 4 and Figure 5 show the reconstructed images obtained from the GATE simulated PET data (3600 s acquisition duration). The Rossendorf FBP (Filtered Back-Projection) and MLEM (Maximum Likelihood Expectation Maximization) algorithms (1, 5 and 10 iterations) were used. A 438.75×151.875×151.875 mm³ (260×90×90 voxels of 1.6875 mm width) reconstruction volume was defined. Attenuation as well as solid angle corrections were applied. In Figure 6, laterally integrated profiles obtained after the reconstruction step (corresponding to the annihilation points) are compared to the profile of decayed beta+ emitters (evaluated from input maps). In this figure, all profiles have been normalized to the maximum value.
D 6.2 - Software: upgraded MC simulation tools capable of simulating a complete in-beam ET experiment, from the beam to the detected events.

Figure 4. Sections of the reconstructed images of the GATE sinogram using the FBP algorithm (3600 s acquisition duration).
D 6.2 - Software: upgraded MC simulation tools capable of simulating a complete in-beam ET experiment, from the beam to the detected events.

Dissemination level [PU]

Figure 5. Sections of the reconstructed images of the GATE sinogram using the MLEM algorithm (1, 5 and 10 iterations – 3600 s acquisition duration).
D 6.2 - Software: upgraded MC simulation tools capable of simulating a complete in-beam ET experiment, from the beam to the detected events.

**Figure 6.** Comparison of laterally integrated profiles obtained after the reconstruction step to the real beta+ emitter profile in depth (GATE simulation – 3600 s acquisition duration). Profiles have been normalized to the maximum activity.

**Set-up 2: Irradiation of a heterogeneous phantom by monoenergetic protons**

**Set-up description**

The same methodology as the one described previously was used to simulate PET images resulting from the irradiation of a heterogeneous phantom by monoenergetic protons.

**Hadrontherapy treatment simulation**

A perfect line beam (no angular opening) of $10^6$ protons irradiating a heterogeneous phantom ($72 \times 77 \times 222$ mm$^3$) placed in air was simulated. The monoenergetic protons (156.06 MeV) were produced by a point source located 20 cm upstream from the entrance of the phantom (Figure 7).

**Figure 7.** Scheme of the simulated set-up.

The simulated heterogeneous phantom (Parodi *et al* 2005) (Figure 8) was made of slabs of organic plastic and tissue substitutes. Characteristics of all materials are described in Tables 1 and 2. In Table 3, the
Conversion of Hounsfield Units (HU) to material chemical compositions and densities used in our simulations is given.

Figure 8. X-ray CT of the heterogeneous phantom. The arrow shows the beam position and direction. Characteristics of all inserts are described in Tables 1 and 2.

Table 1. Composition of the irradiated heterogeneous phantom.

<table>
<thead>
<tr>
<th>Number</th>
<th>Material</th>
<th>Thickness / min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Polyethylene (PE)</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>Bone equivalent</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Polyethylene (PE)</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>Lung equivalent</td>
<td>29</td>
</tr>
<tr>
<td>5</td>
<td>Muscle equivalent</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>Polyethylene (PE)</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>Polymethyl methacrylate (PMMA)</td>
<td>50</td>
</tr>
<tr>
<td>8</td>
<td>Muscle equivalent</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>Polyethylene (PE)</td>
<td>55</td>
</tr>
</tbody>
</table>

Table 2. Composition (fraction by weight) and density of the materials in the heterogeneous phantom.

<table>
<thead>
<tr>
<th>Medium</th>
<th>H</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>Mg</th>
<th>Si</th>
<th>Cl</th>
<th>Ca</th>
<th>ρ</th>
<th>g/cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>14.37</td>
<td>85.63</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>PMMA</td>
<td>8.05</td>
<td>59.99</td>
<td>31.96</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>1.18</td>
<td></td>
</tr>
<tr>
<td>Bone eq.</td>
<td>3.10</td>
<td>31.26</td>
<td>0.99</td>
<td>37.57</td>
<td>−</td>
<td>−</td>
<td>0.05</td>
<td>27.03</td>
<td>1.89</td>
<td></td>
</tr>
<tr>
<td>Muscle eq.</td>
<td>8.41</td>
<td>67.97</td>
<td>2.27</td>
<td>18.87</td>
<td>−</td>
<td>−</td>
<td>0.13</td>
<td>2.35</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Lung eq.</td>
<td>8.36</td>
<td>60.41</td>
<td>1.67</td>
<td>17.33</td>
<td>11.36</td>
<td>0.72</td>
<td>0.15</td>
<td>−</td>
<td>0.30</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Conversion of Hounsfield Units (HU) to material characteristics (density, chemical composition).

<table>
<thead>
<tr>
<th>Material</th>
<th>HU min</th>
<th>HU max</th>
<th>Density (g/cm³)</th>
<th>Chemical composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>-1024</td>
<td>-990</td>
<td>0.00120</td>
<td>N (0.755267), O (0.231781), Ar (0.012827), C (0.000124)</td>
</tr>
</tbody>
</table>
Details about the simulation (physics list, reading of the CT scanner data) can be found in the GATE macro used for the simulation in Appendix 1. Three maps, corresponding to the spatial distributions of the main β⁺ emitters (C11, O15, C10), were stored at the end of this first simulation.

**Imaging simulation**

As for the homogeneous target simulation, the dedicated double-head PET imager (GSI Darmstadt) was simulated in GATE (Figure 2 – Appendix 2).

**Results**

**PET sinograms**

Figure 9 shows the PET sinograms resulting from the irradiation of the heterogeneous phantom by a monoenergetic proton beam. In Figure 4, a 250-850 keV energy window was used.

![PET sinograms](image)

Figure 9. PET sinograms resulting from the irradiation of the heterogeneous phantom by a monoenergetic proton beam (300 s acquisition duration (left), 3600 s acquisition duration (right)).

**Reconstructed images**

Figure 10 and Figure 11 show the reconstructed images obtained from the GATE simulated PET data (300 s acquisition duration). The Rossendorf FBP (Filtered Back-Projection) and MLEM (Maximum Likelihood Expectation Maximization) algorithms (5 iterations) were used. A 438.75×151.875×151.875 mm³ (260×90×90 voxels of 1.6875 mm width) reconstruction volume was defined. Attenuation as well as solid angle corrections were applied. In Figure 12, laterally integrated profiles obtained after the reconstruction step (corresponding to the annihilation points) are compared to the profile of decayed beta⁺ emitters (evaluated from input maps). In this figure, all profiles have been normalized to the maximum value. Further
simulations with a larger number of incident protons will be run in a near future. These simulations will allow us to improve the statistics of the $\beta^+$ emitter maps.

Figure 10. Sections of the reconstructed images of the GATE PET data using the FBP algorithm (300 s acquisition duration).

Figure 11. Sections of the reconstructed images of the GATE PET data using the MLEM algorithm (5 iterations - 300 s acquisition duration).
Conclusions and prospects

In this study, an in-room PET experience has been simulated using GATE. The dedicated double-PET system of GSI has been modelled and the Rossendorf reconstruction algorithms have been used to reconstruct the simulated PET sinograms. These preliminary results confirm the relevance and usefulness of the GATE Monte Carlo simulation tool for study and validation of imaging-based dose monitoring in hadrontherapy. GATE is currently the only open source simulation tool allowing for an integrated modelling of medical imaging and radiation treatment. In addition to the GATE code, we now offer macro examples on the OpenGATE website (http://www.opengatecollaboration.org) to assist users willing to model combined hadrontherapy and imaging experiments. Now that the tool is available, various set-up including patient scans will be simulated and shared with other work packages to help in the understanding and advances in image-based hadrontherapy monitoring.

Practical details to get the deliverable and associated documentation:
OpenGATE website: http://www.opengatecollaboration.org
GATE source code: http://www.opengatecollaboration.org/releasedownload
Documentation and recommendations for GATE users:
http://www.opengatecollaboration.org/Documentation

References

Pönisch F, Enghardt W, Lauckner K 2003 Attenuation and scatter correction for in-beam positron emission tomography monitoring of tumor irradiations with heavy ions Phys Med Biol 48 2419-2436
1.2 Using FLUKA for modelling an in-room PET experiment

1.2.1 Improvement in the code

In 2010 and 2011, several developments have been introduced in the FLUKA code in order to accomplish the needs emerging from the application in hadron therapy and related imaging.

The present released version (fluka2011.2.3) is available for download at the FLUKA site ([http://www.fluka.org](http://www.fluka.org)). The list of the new features which have relevance for ENVISION, and the application to hadron therapy in general are listed below as obtained from the different Release Notes issued in 2010 and 2011. Most of the physics improvements are brand new and still unpublished:

- Stopping power models have been thoroughly reworked, and are now more precise particularly for heavy ions. In particular, the Barkas ($Z^3$), Bloch ($Z^4$), and Mott corrections have been implemented.
- Nuclear stopping power is now calculated and taken into account. It matters only for heavy ions at low energies.
- The lower limit for photon transport has been lowered to 100 eV. Macroscopic surface effects (refraction/reflection) are not treated.
- Nuclear deexcitation by photon emission makes use of an extended database of known levels and transitions. The evaporation stage is also consistent with this database.
- The Boltzmann Master Equation, BME, model for heavy ion interactions at low-medium energies is now included in the distributed version. It can handle all projectiles with $A>=4$ on all targets, with the exception of systems lighter than (alpha, 6Li). BME is invoked for projectile energies lower than 125 MeV/A, however its limit of validity is 150 MeV/A. (The BME is still in a developing phase).
- Geometry transformations: directives allowing roto-translations and expansions for sets of bodies are now available in geometry. They can be applied also to the voxel part and therefore can be used in geometries taken from CT image import.
- A few compounds of dosimetric interest are now available as pre-defined materials.
- An accurate description of the basic physics processes of Compton scattering and positron annihilation in matter requires the consideration of atomic shell structure effects and, in specific, the momentum distributions of the atomic electrons. Two-quanta positron annihilation is a physics process which is of particular importance for applications such as positron emission tomography (PET).

Two algorithms that model Compton scattering and two-quanta positron annihilation at rest while accounting for shell structure effects are proposed. Both models revert to a detailed mechanistic description of the processes and incorporate consistently Doppler broadening and binding effects. Their mechanistic description together with their relatively low level of complexity makes the models particularly suited to be employed by fast sampling methods for Monte Carlo particle transport. Momentum distributions of shell electrons that are required by the models are obtained from parametrized one-electron Compton profiles and in the framework of a free electron gas for conduction electrons. The Compton scattering model uses a very general approach that does not employ any free parameters. In contrast, the complex physics of electron-positron annihilation resulting in acollinear photons is described by a semi-empirical approach. Comparison of the Compton scattering model with simpler modelling approaches illustrates the detailed accounting for shell structure effects. Confrontation of both newly-developed models with experimental data shows a satisfactory agreement. Compton scattering with full account for binding and orbital electron motion is now proposed. Up to now FLUKA included two possibilities for the treatment of Compton scattering:

1) "naive" scattering on free electrons.
2) Compton scattering corrected by an inelastic form factor, $S(q,Z)$. 

ENVISION -GA n°241851
Now a third possibility has been added, where both binding effects and orbital motion of all electronic shells of all elements are accounted for. This is particularly relevant for low energy photons and/or heavy elements.

- The "sophisticated" Compton scattering, including electron binding and Doppler effects is now activated by default for "defaults" CALORIME, PRECISIO, EM-CASCA, or HADROTHE

Demonstration of the feasibility of using FLUKA for extensive in-beam PET experiments modeling

The capability of FLUKA to model the whole imaging process from the incoming ion beam to the detection of the emerging annihilation photons was already demonstrated through extensive simulation of in-beam PET experiments performed at GSI (F. Sommerer et al. Phys. Med. Biol. 54, 2009, 3979). Moreover, capability of FLUKA transport in CT geometries has been already demonstrated for clinical cases (K Parodi et al., Phys. Med. Biol., 52 (12), 2007, p.3369-3387, A. Mairani et al, Nuclear Science Symposium Conference Record NSS ’08. IEEE, 2008) and phantom (M. Chin et al 2011, to be published) cases. Moreover, FLUKA treatment plan re-calculations in the clinical environment are performed at the Heidelberg Ion Beam Therapy Center (Somerer F, Unholtz D, Brons S, et al. "An easy-to-use Monte Carlo framework for ion therapy at the Heidelberg Ion-Beam Therapy Center”. Poster Abstract of the ESTRO Conference 2010, Radiother. Oncol. 2010; 96 (S1): 481, supported by the EU-PARTNER project) and at CNAO (Thesis at Univeristy of Milano, made available in the WP6 Shared Document section of Envision web site).

2. Description of one reference clinical case, including the complete patient model and beam characteristics

In addition we are now delivering a fully documented case of clinical case on the basis of a real case made available by CNAO (Italy).

This case actually consists of:

- all information needed to reproduce the irradiation of a human phantom (Fig. 13), where all CT scans are made available (example in Fig. 14)
- a treatment planning prescription coded in DICOM format, including the definition of Target Volume, Organs at Risk etc.
- the FLUKA geometry to reproduce the actual beam delivery system at CNAO (Fig. 15) (validated by experimental measurement in situ).
- the procedure to read the CT scans in order to produce the voxel geometry for FLUKA (this is based on the use of MATLAB scripts)
- the appropriate source routine to reproduce the actual features of CNAO beam on the basis of the results of the treatment planning calculations.
- At present this case considers just proton treatment since CNAO, at this time, has not completed the commissioning for $^{12}$C.

An example of simulation results is shown in Fig. 16.

The simulation can produce in output spectra (and event by event output) of all possible resulting particles.

This work is described in a Thesis of University of Milano (by A. Panfili), available on the Envision web site in the WP6 Shared Document section
Figure 13: Picture of the anthropomorphic phantom used at CNAO

Figure 14: Geometry of CNAO beam delivery nozzle considered in the simulation

Figure 15: Examples of slices from the available CT scans of the phantom. The map of predicted dose, as resulting from the TPS used at CNAO is superimposed.
D 6.2 - Software: upgraded MC simulation tools capable of simulating a complete in-beam ET experiment, from the beam to the detected events.

Dissemination level [PU]

Figure 16: Example of the comparison between TPS prediction (top left) with FLUKA simulation (top right). Notice that in the simulation also air around the phantom is considered. Bottom panel: comparison of the dose profile along an X slice of above images between TPS (red) and FLUKA simulation (blue).