IL NUOVO CIMENTO Vol. 34 C, N. 1 Gennaio-Febbraio 2011
DOI 10.1393/ncc/i2011-10810-5

Colloquia: IFA 2010

Applications of Monte Carlo methods to special radiotherapeutic techniques

F. Romano(1)(*), G. A. P. Cirrone(1), G. Cuttone(1), F. Di Rosa(1), S. E. Mazzaglia(1), M. G. Sabini(2) and D. Sardina(1)

(1) *INFN, Laboratori Nazionali del Sud - Catania, Italy*
(2) *Department of Imaging, Cannizzaro Hospital - Catania, Italy*

(ricevuto il 26 Luglio 2010; approvato l' 8 Settembre 2010; pubblicato online il 15 Febbraio 2011)

Summary. — Monte Carlo (MC) methods are considered one of the most powerful and precise approaches to study and solve medical physics issues. They, indeed, can be applied in all the situations where to use deterministic algorithms is infeasible or impossible. Surprising improvements in computer technology have promoted a wide diffusion of this technique, giving rise to the born of several Monte Carlo codes, such as the GEANT4 toolkit. In this paper we show some of the applications we developed using GEANT4. In particular, the simulation of two different radiotherapy techniques, such as proton/ion therapy and stereotactic radiosurgery will be discussed. In the first case we show the main features of our last public version of the GEANT4 *Hadrontherapy* program, also discussing the issues related to the nuclear fragmentation. In the second case, we show the procedures followed for the simulation of a Gamma Knife device, in order to validate the Treatment Planning System (TPS) used for the dose computation.

PACS 87.55.K- – Monte Carlo methods.
PACS 87.53.-j – Effects of ionizing radiation on biological systems.
PACS 87.53.Ly – Stereotactic radiosurgery.

1. – Introduction

With the term "*simulation*" we mean the imitation of real things, states of affairs or processes. Monte Carlo (MC) simulations are used in many contexts, including Economics, Finance, Biology, Chemistry and, not last, Physical Sciences. In particular, medical physics applications have gained great benefits using MC methods. The high level of accuracy demanded for cancer treatment with ionizing radiation has led to a high degree of complexity in the techniques used for the dose conformation to the tumour target. For this reason MC codes are today widely used in this field, representing a

(*) E-mail: francesco.romano@lns.infn.it

fundamental tool for the study of dosimetric systems, the reproduction of clinical beam line, the development and test of new kind of detectors and the verification of the Treatment Planning Systems (TPS). All the results presented and discussed in this paper have been obtained with the GEANT4 (*GEometry ANd Tracking*) Monte Carlo toolkit, which is, among several codes today available, one of the most versatile and widespread ones.

GEANT4 is a C++ object oriented toolkit permitting the simulation of particle interactions with matter [1]. It provides advanced functionalities for all the typical domains of detector simulation: geometry and material modeling, description of particle properties, physical processes, tracking, event and run management, user interface and visualization. Initially developed for High Energy Experiments (HEP) simulation, GEANT4 is now widely used also for medical physics application [2]. It allows, indeed, the tracking of any charged and uncharged particle relevant for radio diagnostics and radiation therapy. The possibility to allow geometry changes during a simulation is of particular interest for the medical domain. This significantly facilitates the execution 4D Monte Carlo simulations, where time-dependent information is involved. The applications described in the following sections make use of this kind of features of the toolkit.

Results shown in this paper have been performed with the 9.2 (patch 1) version of GEANT4 [3].

2. – GEANT4 simulations in hadrontherapy

2˙1. *The Hadrontherapy application.* – *Hadrontherapy* is a free and open source application created, regularly maintained and improved by some of the authors of this paper. It has been initially developed for the simulation of the CATANA (Centro di AdroTerapia ed Applivazioni Nucleari Avanzate) beam line of the Laboratori Nazionali del Sud (LNS) of INFN in Catania, where ocular tumours are treated using 62 MeV proton beams accelerated by a Superconducting Cyclotron (CS) [4]. *Hadrontherapy* permits the simulation, via simple macro commands, of a typical beam line for proton/ion therapy including all the necessary transport elements: diffusion and modulation systems for the particles spatial and energy distribution, collimators, transmission detectors as well as detectors for the dose distribution measurements [5]. Since the beginning of its development, *Hadrontherapy* has undergone many changes and its capabilities have grown to such an extent that in 2009 the authors decided to release a specific version separated from the one included in the GEANT4 *Advanced Example*. This full version offers many adds in comparison to the basic one, such as the modularization of the geometry and of the implemented physical models, the possibility to easily calculate stopping powers and ranges for any couple of ion-material combinations, the implementation of specific algorithms for the calculation of the average 3-dimensional LET (Linear Energy Transfer) and a new graphical user interface, based on the QT libraries. Moreover, next versions of the application will include the possibility to use DICOM interfaces in order to take into account the different tissue densities.

Figure 1 shows the *Hadrontherapy* graphic output when LNS proton therapy beam line is simulated. Each beam transport element is exactly reproduced and the simulated primary beam (blue tracks) together with secondary particles produced (green and red tracks) are also shown. The red cubic box (on the right) is the volume where dose, fluence and any useful parameter can be stored.

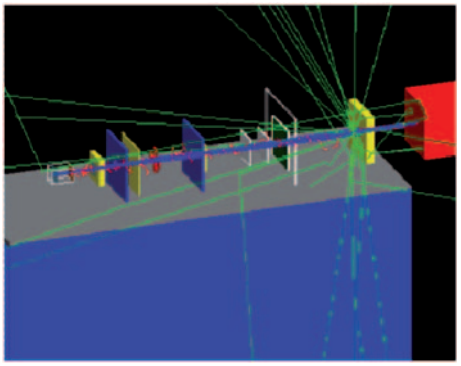

Fig. 1. – Graphic view of the CATANA proton beam line simulated in the *Hadrontherapy* application.

2˙2. *Carbon ion therapy and related studies.* – Besides protons, heavier ions have been also investigated in the past for therapeutic purposes, because of their enhanced biological effects [6]. After many years of studies about the effects of different kind of ions, the scientific community has finally accepted carbon ions as the best compromise between local control of the tumour and negative side effects for healthy tissues. Carbon ion therapy is now performed in Europe and Japan. Many new hadrontherapy centres have been recently built or planned [7]. Carbon ions show a higher spatial conformation, thanks to a smaller lateral scattering and an enhanced biological effect at the end of their path, where the Bragg peak overlaps the tumour target.

On the other hand, the nuclear interactions with the atomic nuclei of the traversed tissues produce charged fragments. This last aspect represents the main drawback coming from the use of carbon ion beams. A *mixed radiation field* is present in the target volume, where both primary and secondary particles travel through the matter with different biological effects. For an accurate calculation of the final biological dose, each single contribution has to be considered and weighted depending on the respective biological efficiency. Monte Carlo simulations represent a powerful tool to reproduce such a complex configuration. Using *Hadrontherapy* we have obtained the depth dose distributions (*i.e.*, Bragg peaks) of carbon ion incident beams inside a PMMA cubic phantom. It has been divided into 4000 slices, 10 μm of thickness, orthogonal to the beam direction, where the total dose is retrieved (fig. 2, left). In order to have reasonable statistical fluctuations (less than 3%) without huge calculation time, a production cut of 0.01 mm and a maxStep of 0.01 mm have been defined as simulation transport parameters. The data obtained by the simulation have been compared with data acquired at INFN-LNS of Catania in order to verify the developed code. An experiment has been performed for this purpose with carbon ions accelerated at 62 AMeV. The dose distributions have been measured with a parallel plate ionization chamber, having an active volume of 0.055 cm^3, polarized with an electric field of 300 V and coupled with a dedicated electrometer. The chamber, placed in a cubic phantom, is able to measure the depth dose distribution with a spatial resolution of 50 μm by means of a motorized system. Figure 2 (right) shows a comparison between experimental and Geant4 Bragg peaks. The good agreement demonstrates the accuracy of the GEANT4 simulation in the dose reconstruction.

For a complete characterization of the clinical beam, dose, fluence, and LET distributions of fragments produced at different depths have to be known. We calculated

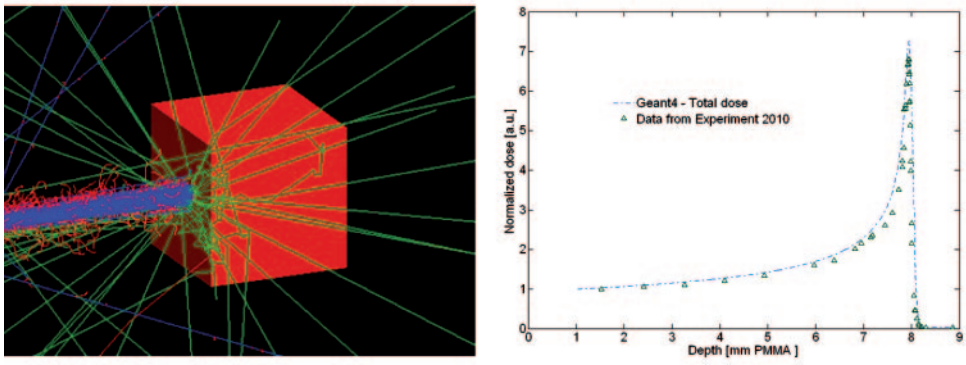

Fig. 2. – Left: cubic phantom used in the simulation to store the released dose at different depths. Right: comparison between experimental and simulated carbon ions Bragg peaks at 62 AMeV on PMMA, normalized at the entrance.

these quantities using the *Hadrontherapy* application, both for primary and secondary particles. In fig. 3 an example of secondary particles contribution on the total dose distribution is shown. It can be distinguished, in semi-logarithmic scale, the dose contribution for each atomic number Z and the sum of the secondary particle contributions, which are responsible of a typical *tail* just after the Bragg peak. As expected, the main contribution in the distal part of the peak is essentially due to α-particles and, partially, also to hydrogen isotopes (p, d, t).

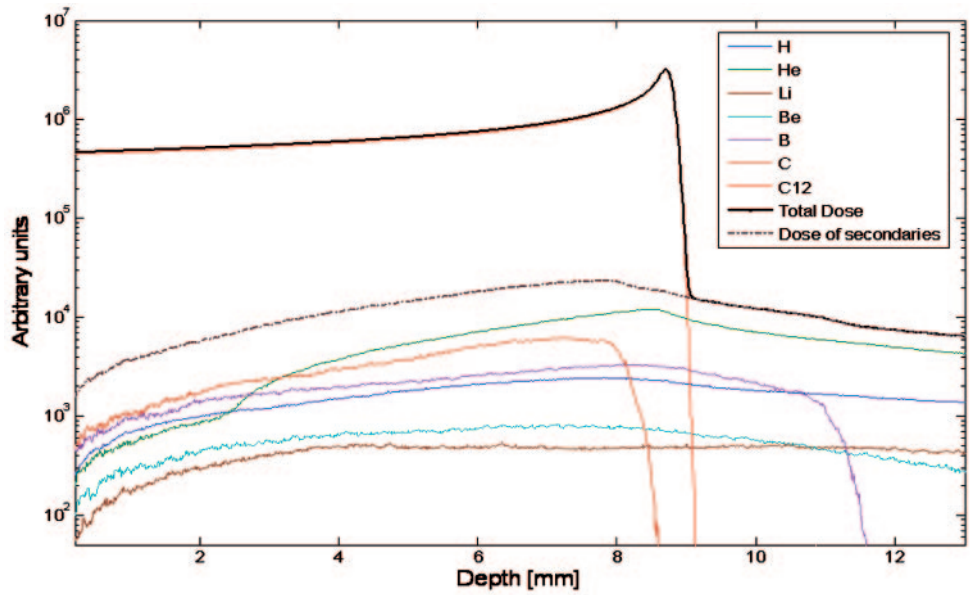

Fig. 3. – (Colour on-line) Total depth dose distribution (Bragg curve, in black) and contributions of charged fragments (coloured lines) in PMMA. Dotted line represents the sum of contributions released by secondary particles.

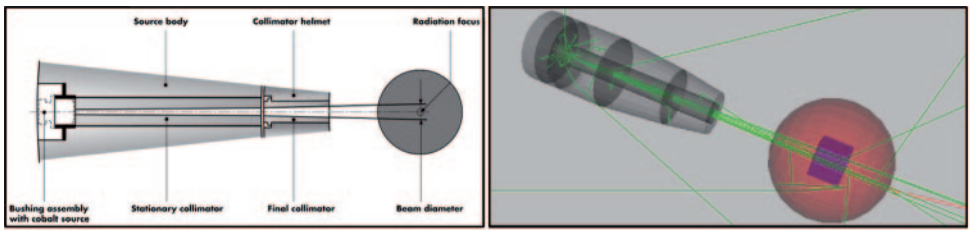

Fig. 4. – (Colour on-line) One of the ^{60}Co sources with the respective collimation system and the spherical phantom. Left: schematic representation of the source and beam channel. Right: visualization of the geometrical elements and trajectories simulated with GEANT4 (photons in green, electrons in red).

3. – GEANT4 simulation of a Gamma Knife device

The *Leksell Gamma Knife* is a radio-surgical device manufactured by *Elekta Instruments Inc.* and used to treat brain disorders, such as benign or malignant tumours, which are often inaccessible to conventional surgery [8]. In Stereotactic Radiosurgery high doses with sharp dose gradients are delivered in a single session in order to minimize undesired effects on critical brain structures adjacent to the target. Since 2005 a Gamma Knife unit (model C) has been installed at Cannizzaro Hospital of Catania and several patients have been treated so far.

Gamma radiation, emitted by 201 ^{60}Co sources arranged in a hemispherical shape, focuses on the isocentre, where the target volume has to be located. The radiation beam is collimated by means of fixed and mobile collimation systems in order to obtain four possible beam diameters at the isocentre: 4, 8, 14 and 18 mm. Using an Automatic Position System it is possible to combine different "shots" to cover complex shapes of tumour. Calculations of the delivered dose are performed by the TPS *Leksell GammaPlan (LGP)* [9]. It includes some approximations related to the gamma-rays energy and the target material in order to compute the prescribed dose in a reasonable time.

We simulated the GammaKnife device installed in Catania for the purpose of verifying the accuracy of the TPS and to check if the simplifications used in its algorithms can affect the planned dose distributions. Similar studies have been already carried out with the Monte Carlo codes EGS4 [10], PENELOPE [11] and MCNP [12], where all the radioactive sources have been fully simulated. Our application has been developed using the GEANT4 toolkit, with original solutions involving time-dependent geometries.

3˙1. *Monte Carlo simulation and comparison with the TPS.* – The Gamma Knife Unit consists of a cast-iron body containing the ^{60}Co sources and the collimation system. Sources are displaced along five parallel rings at the same distance from the isocentre. Depending on the specific ring, sources are located with a different spacing, respectively with an angle of 7.6°, 8°, 9°, 9° and 10°. Photons of 1.17 and 1.33 MeV are emitted and collimated by cylindrical and conical lead elements. A spherical phantom is placed at the isocentre for routinely measurements of dose distributions at different depths.

We have simulated this device considering a different approach respect to the previously mentioned works. Indeed, exploiting the geometrical symmetry of the sources we decided to simulate only one single source (with the respective collimators) rotating the spherical phantom, rather than reproduce 201 sources with a fixed phantom (fig. 4). In such a way, the final dose distribution is due to the integration of the contributions

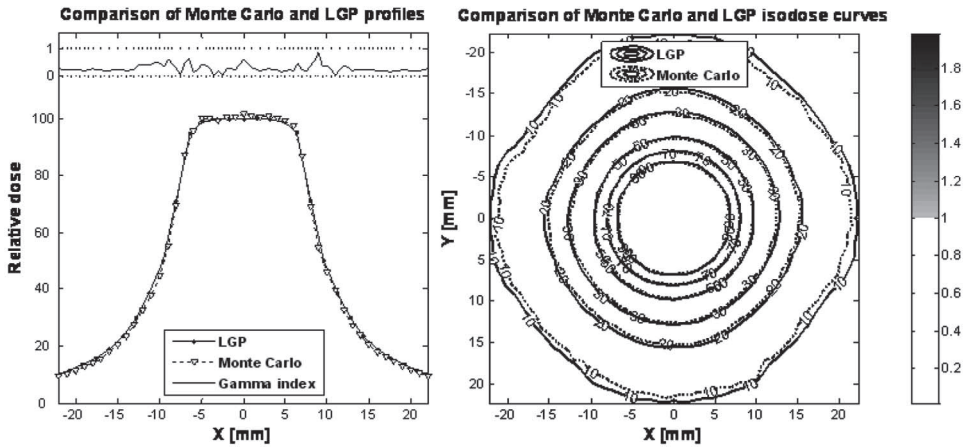

Fig. 5. – (Colour on-line) Comparison between GEANT4 results and LGP predictions in the central plane (axial) of the spherical phantom, for the 14 mm collimator. Left: X profiles and gamma index (line on the top). Right: isodose curves and gamma index (in grey levels).

related to 201 different angular positions. This solution permits a simpler code development and higher flexibility for further modifications of the sources location (depending on the specific Unit model). The absorbed dose in the phantom has been stored using a voxelized geometry similar to the *Hadrontherapy* application (see subsect. **2**˙2), with cubic voxels of 1 mm of side. In order to achieve acceptable statistical fluctuations (less than 3%), a huge number of primary events must been sampled; hence, the simulation has been split into 20 jobs and submitted to a Linux cluster installed at LNS-INFN.

In order to verify the reliability of the Gamma Knife application, a set of experimental measurements has been carried out at Cannizzaro Hospital. *GafChromic films* have been irradiated inside a spherical phantom with all the available collimators. Digital images of the films have been acquired with a transmission scanner and analyzed in one and two dimensions. Experimental and simulated dose distributions have been compared with the GEANT4 results, with a good agreement.

Once the application has been validated, it has been used to study and verify the dose distributions predicted by the LGP, which computes the released dose in a 3D array of $31 \times 31 \times 31$ elements arranged in a cubic shape, considering the phantom entirely composed by water. X-Y profiles and isodose curves respectively of the GEANT4 application and LGP have been superimposed. For a quantitative comparison between the two dose distributions we have used the *gamma index* method, which combines together the "*dose-difference (DD)*" and "*distance-to-agreement (DTA)*" [13]. This method allows to compare point by point two dose distributions and to show their level of agreement according to the acceptance criteria which characterize the specific radiotherapeutic technique. In fig. 5 (left) a comparison between GEANT4 and LGP X profiles is shown for the 14 mm collimator. Points not passing the gamma index test cross the straight line on the top of the graph. In the same figure (right) the isodose curves for both the two distributions are represented; points with an acceptable agreement are visualized in white, while points which do not pass the gamma index test are in grey levels. The comparisons, executed for each available collimator, demonstrate as the dose analytically calculated by LGP is in agreement with the Monte Carlo predictions. Therefore, we can conclude

that LGP compute the dose to be delivered to the tumour target with a good level of accuracy. On the other hand, LGP predictions get worse when different density materials are considered in the dose calculation. The presence of inhomogeneities, indeed, causes uncertainties in the LGP computations because of the approximations included in the algorithm [14].

4. – Conclusions and perspectives

Monte Carlo methods play an important role in medical physics applications, in particular in case of complex methodologies and devices, representing the best approach when also different tissue densities have to be taken into account.

The results presented in this work show how the GEANT4 *Hadrontherapy* application is able to simulate in detail each element of a proton/ion beam, well reproducing the measured depth dose distributions. Moreover, it permits to study the issues related to the carbon ions fragmentation, considering the single contributions of the produced isotopes. These results together with the knowledge of the LET distributions are useful to link radiobiological data with physical ones. On this regard we plan to include new interesting features in the future versions of the application, such as the implementation of a radiobiological model for the evaluation of the biological damage.

The simulation of the Gamma Knife demonstrates how the use of interesting features of GEANT4 allows to reproduce in a simple way also the most complex geometries, even maintaining high level of accuracy. The Gamma Knife application, still in a private version, has been recently proposed and accepted by the GEANT4 international collaboration as a public example; it will be included among the *Advanced Examples* category for the future releases of the toolkit.

The topics discussed in this paper clearly show as the Monte Carlo techniques represent a powerful tool which medical physics community has been more and more widely using.

REFERENCES

[1] Agostinelli G. *et al.*, *Nucl. Instrum. Methods A*, **506** (2004) 250.
[2] Allison J. *et al.*, *IEEE Trans. Nucl. Sci.*, **53** (2006) 270.
[3] The GEANT4 website, `http://geant4.cern.ch`.
[4] Cirrone G. A. P. *et al.*, *IEEE Trans. Nucl. Sci.*, **51** (2004) 860.
[5] Cirrone G. A. P. *et al.*, *IEEE Trans. Nucl. Sci.*, **52** (2005) 262.
[6] Amaldi U. *et al.*, *Riv. Med.*, **14** (2008) 7.
[7] Cuttone G. and Calabretta L., *Riv. Med.*, **14** (2008) 43.
[8] *Elekta, Leksell Gamma Unit - User's Manual* (Elekta Instrument, Stockholm) 2003.
[9] *Elekta, Reference Manual for Leksell GamaPlan* (Elekta Instrument, Stockholm) 2003.
[10] Cheung J. Y. C. *et al.*, *Med. Phys.*, **25** (1998) 1673.
[11] Moskvin V. *et al.*, *Phys. Med. Biol.*, **47** (2002) 1995.
[12] Trnka J. *et al.*, *Med. Phys.*, **34** (2006) 63.
[13] Low D. *et al.*, *Med. Phys.*, **25** (1998) 656.
[14] Romano F. *et al.*, *Proceedings of the 2007 IEEE Nuclear Science Symposium and Medical Imaging Conference, Honolulu, Hawaii, U.S.A., 27 October - 3 November 2007* (2007), p. 2581.