Status report on the Monte Carlo models actually available for hadron therapy calculations

Envision-WP6 Report n.1
The present report is the result of the first year of work carried on, inside the ENVISION Project, by the Working Package 6, which addresses the topic of Monte Carlo simulation of in vivo dosimetry in hadrontherapy with light ions. Such a report represents a unique document attempting to evaluate, in a comparative way, the present status of some of the most important Monte Carlo codes (GEANT4/GATE, FLUKA, MCNPX) adopted by the scientific community working in hadrontherapy. WP6 could achieve these results since it benefits from the participations of groups with important experience in the field and directly involved in the development of the codes.

The main purpose of this report is to describe the physics content of such codes and compare the relevant results which characterize the reliability of these packages in hadrontherapy and related imaging activities. We have reviewed the physical models available to describe the interactions of interest in hadrontherapy, including cross-section tables. To characterize the reliability of the physics models implemented in the three Monte Carlo codes considered in this project, we have searched for:

- cross section data,
- data useful for dosimetry (Bragg Peak measurements essentially),
- data on \( \beta^+ \) emitter production,
- data on prompt gamma ray emission,
- data on charged particle emission.

Published materials have been used when available. Eventually we have collected recommendations for the setting and practical use of the reviewed codes, pointing out the main direction of development.

From the analysis of the collected results, it emerges that the amount of experimental data necessary to validate the models, as far as ion interactions are concerned, is still limited. Some differences in the predictions from the considered codes have been found. In most cases (for instance as far as dosimetry is concerned) it is hard, on the basis of the available data, to draw definite conclusions about the superiority of a model with respect to another, but at least the accuracy of the prediction of the different codes has been characterized. In other cases, directions of necessary development clearly emerge, like the case of gamma production from nuclear de-excitation.

Due to the strong connection of some WP6 participants to the development teams, at least in the case of GEANT4 and FLUKA, we expect this work to have a fast impact towards improvements of the codes, so to make them available for the whole interested community.

In conclusion, this report can be used as a reference document for all those involved in Monte Carlo simulations of hadrontherapy experiments. It is also meant to be an evolving document. The present work is also the result coming from the synergical contribution from other Working Packages in ENVISION and from correlated FP7 projects.
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1. Introduction

Monte Carlo codes are now essential tools in hadrontherapy. They can describe the complex physics of hadronic interactions and, in general, all aspects of interaction of radiations with matter. At the same time they are able to consider complex geometries (and interfaces between rather different materials), provide accurate multi-dimensional transport and include fully detailed descriptions of the patient anatomy.

In practice simulation codes are used for the startup and commissioning of new facilities, for beamline modelling and generation of TPS input data, for the validation of analytical TPSs both for physical and biological aspects and for prediction/analysis of in-beam imaging systems.

The modelling of nuclear interactions is however affected by significant uncertainties, since there is no exact and calculable model available. Different phenomenological approaches exist and different codes, with different implementations of physics and tracking, are available to the user.

This report describes the physical models of FLUKA, Geant4 and MCNPX to describe the interactions of interest in hadrontherapy. Evaluation results characterizing the agreement between the data produced by these models and experimental data are provided.

Based on these validation studies, this document includes recommendations regarding the reliability and uncertainties of the physics models available in simulation software appropriate for modelling hadrontherapy experiments.

2. The relevant physics for imaging in hadrontherapy with protons and ions

Interaction models are in general different according to the nature of projectile, energy range and type of relevant reactions. When modelling hadrontherapy experiments we are interested in protons of energy which is typically in the 10 to 250 MeV range, while for ions we consider an interval from 10 to 400 MeV/nucleon.

In these energy ranges the relevant aspects are of different natures. First of all the fundamental mechanism of energy loss and of their fluctuations must be accurate at the level demanded by dosimetry requirements. The dominant physics here concerns electromagnetic interactions, which are generally considered under rather good control from the point of view of model implementation. However it is well known that nuclear physics contributions do play a role at the level of the required sensitivity.

At a further stage we are interested in reaction cross sections (in order to take into account beam attenuation), but also elastic cross sections. Then, entering in the specific field of imaging in proton therapy, we need to obtain a sufficiently reliable description of secondary particle production (p, n, α…). Nuclear physics has to be considered in order to give account of nuclear de-excitation, yield of isotope production (mostly in view of exploitation of positron emission). In the case of nuclear projectiles, also the yield of fragments is important.

It has to be noticed that hadronic interaction models have often limitations and in general it is impossible, for a given single model, to assure a uniform level of quality in the comparison with existing experimental data for all interesting observables. Therefore it is of the utmost importance to compare the performance of different Monte Carlo codes and point out, when applicable, recommendations for their use and directions for further developments.

The codes under consideration in this report mostly follow the approach which is sometimes defined as «microscopic», in the sense that the properties of the interaction are obtained from a description which is, as far as possible, based on the known properties of nuclear constituents and a minimum number of free parameters, to be adjusted by comparison with experimental data. This is recognized, in contrast to other approaches based just on the
parameterization of existing data, as the most powerful approach in terms of prediction and capability of ensuring the expected correlation and conservation laws. The microscopic approach, on the other hand, is often demanding in terms of computational power, and undoubtedly there are cases in which it is not possible to apply it completely. In particular it is unavoidable to make use of databases (tables) collecting fundamental information coming from experiment.

3. The Monte Carlo Models

Three Monte Carlo simulation codes were investigated: FLUKA, Geant4 and MCNPX. The physics models available through these Monte Carlo codes were considered and are listed below.

3.1. FLUKA: Introduction

The FLUKA code [Ferrari05, Battistoni07] is a general purpose Monte Carlo code for the interaction and transport of hadrons, heavy ions, and electromagnetic particles from few keV (or thermal energies for neutrons) to Cosmic Ray energies in whichever material. It is built and maintained with the aim of including the best possible physics models in terms of completeness and precision. In this “microscopic” approach, each step has sound physical bases. Performances are optimized comparing with particle production data at single interaction level. No tuning whatsoever on “integral” data, like calorimeter resolutions, thick target yields etc., is performed. Therefore, final predictions are obtained with minimal free parameters, fixed for all energies and target/projectile combinations. Results in complex cases as well as scaling laws and properties come out naturally from the underlying physics models and the basic conservation laws are fulfilled “a priori”. Moreover, the microscopic approach preserves correlations within interactions and among the shower components and it provides predictions where no experimental data are available. Powerful biasing techniques are available to reduce computing time when required. Descriptions of FLUKA models and extensive benchmarking can be found in the literature (see the web page, http://www.fluka.org). The development and maintenance of FLUKA are performed in the framework of an INFN–CERN agreement. FLUKA has been applied to an extended range of applications spanning from proton and electron accelerator shielding to target design, calorimetry, activation, dosimetry, detector design, Accelerator Driven Systems, cosmic rays, neutrino physics, radiotherapy. 60 different particles plus heavy ions can be transported by the code. The energy range covered for hadron-hadron and hadron-nucleus interaction is from threshold up to 10000 TeV, while electromagnetic and $\mu$ interactions can be dealt with from 1 keV up to 10000 TeV. Nucleus-nucleus interactions are also supported up to 10000 TeV/n, thanks to the interfaces with a modified version of rQMD-2.4 [Sorge89a, Sorge89b, Sorge95] and with Dpmjet-III [Roesler01]. Neutron transport and interactions below 20 MeV and down to thermal energies are treated in the framework of a multi-group approach, with cross section data sets developed for FLUKA starting from standard evaluated databases (mostly ENDF/B-VII, JENDL-3.3 and JEFF-3.1.1).

Transport in arbitrarily complex geometries, including magnetic field, can be accomplished using the FLUKA combinatorial geometry. A suitable voxel geometry module allows modeling properly CT scans or other detailed 3D representations of human beings, typically for dosimetry or therapy planning purposes.

The code has the ability to run either in fully analogue mode, or in biased mode exploiting a
rich variety of variance reduction techniques. FLUKA is jointly developed by the European Laboratory for Particle Physics (CERN) and the Italian National Institute for Nuclear Physics (INFN). The approach adopted in FLUKA for the modelling of hadronic interaction has been described in several papers [Ferrari98, Ballarini03, Ferrari04, Battistoni06].

Hadron-nucleon inelastic collisions are described in terms of resonance production and decay up to a few GeV. At higher energies, a model [Ferrari98] based on the Dual Parton Model (DPM) [Capella94] takes over. The Dual Parton Model is a particular quark/parton string model, and provides reliable results up to several tens of TeV. In DPM, hadron-hadron interactions result in the creation of two or more QCD color strings, from which hadrons have to be generated.

Hadron-nucleus (h-A) interactions as modelled in FLUKA can be schematically described as a sequence of the following steps:

- Glauber-Gribov cascade and high energy collisions
- (Generalized)-IntraNuclear cascade
- Pre-equilibrium emission
- Evaporation/Fragmentation/Fission and final gamma de-excitation

Some of the steps could be missing depending on the projectile energy and identity. Below some details about the implementation of this model of relevance for interactions at energies below 1 GeV are reported. More detailed descriptions can be found in the literature.

3.1.1 The PEANUT Hadron-Nucleus event generator

A basic description of hadronic interactions in FLUKA and of their most recent developments can be found in [Ferrari98, Collazuol00, Battistoni06]. Hadron-nucleon interactions at energies below a few GeV are simulated in FLUKA by the isobar model, through resonance production and decay, and by taking into account elastic, charge, and strangeness exchange. Elementary hadron-hadron collisions at energies above a few GeV are described thanks to an implementation of the Dual Parton Model (DPM) [Capella94], coupled to a hadronization scheme. This model allows a successful description of soft collision processes that cannot be addressed by perturbative QCD. Hadron-hadron collisions are the main building blocks of hadron-nucleus collisions. Multiple collisions of each hadron with the nuclear constituents are taken into account by means of the Glauber-Gribov calculus [Glauber70, Gribov69]. Particular efforts are devoted to the study of nuclear effects on hadron propagation. These are treated by the FLUKA nuclear interaction model called PEANUT [Ferrari94, Fasso95, Ferrari98, Battistoni06]. This model includes a Generalized IntraNuclear Cascade (GINC) with smooth transition to a pre-equilibrium stage performed with standard assumptions on exciton number or excitation energy.

GINC modelling in PEANUT is highly sophisticated. Different nuclear densities are adopted for neutrons and protons, Fermi motion is defined locally including wave packet like uncertainty smearing, the curvature of particle trajectories due to the nuclear potential is taken into account, binding energies are obtained from mass tables and updated after each particle emission, energy-momentum conservation including the recoil of the residual nucleus is ensured. Quantum effects are explicitly included: Pauli blocking, formation zone, nucleon anti-
symmetrization, nucleon-nucleon hard-core correlations, coherence length. Nuclear medium effects on the $\Delta$ resonance properties are accounted for when treating pion interactions [Ferrari98, Fasso95] and pion reinteractions in the nucleus.

The GINC step goes on until all nucleons are below a smooth threshold around 50 MeV, and all particles but nucleons (typically pions) have been emitted or absorbed. At the end of the GINC stage a few particles may have been emitted and the input configuration for the pre-equilibrium stage is characterized by the total number of protons and neutrons, by the number of particle-like excitons (nucleons excited above the Fermi level), and of hole-like excitons (holes created in the Fermi sea by the INC interactions), by the nucleus.

The exciton formalism of FLUKA follows that of M. Blann and coworkers [Blann71, Blann72, Blann83, Blann83b], with some modifications:

- Inverse cross sections from systematics;
- Correlation/formation zone/hardcore effects on reinteractions;
- Constrained exciton state densities for the configurations 1p-1h, 2p-1h, 1p-2h, 2p-2h, 3p-1h and 3p-2h;
- Energy dependent form for the single particle density $g_x$;
- Starting values for the position dependent parameters given by the point like ones as obtained out of the GINC stage;
- Angular distributions of emitted particles in the fast particle approximation.

3.1.2 Heavy ion interactions

In FLUKA heavy ion reactions at incident energies below 100 MeV/n are treated through an original event generator coupling the Boltzmann Master Equation (BME) theory with a semi-classical geometrical picture.

The BME theory is intended to describe the pre-equilibrium de-excitation of the composite system created by the fusion of two ions. The thermalization process is supposed to proceed via nucleon–nucleon scatterings and emissions into continuum of single nucleons and clusters produced by nucleon coalescence [Cavinato98]. In this framework, one has to compute the initial distribution in the nucleon momentum space, incorporating the effect of the mean field dominating the approaching stage of the reaction [Brusati95], and then to solve a set of coupled differential equations, the numerical integration of which provides the double differential multiplicity spectra of the emitted particles.

In order to calculate exclusive cross-sections and correlations, and not only inclusive spectra and average quantities, one can assume that the multiplicity of the ejectiles emitted in a suitably short time interval, coincides with their emission probability. This way, a Monte Carlo event generator that simulates the pre-equilibrium phase using as input the results of the BME Cauchy problem, can be developed [Cavinato96, Cavinato01].

As a part of a transport code extensively describing the radiation–matter interaction over realistic and complex geometries, such an event generator is obviously supposed to deal with the nuclear interaction of any projectile–target pair at any incident energy in its application range. However, it requires the angle–energy multiplicity spectra (as a function of time) of all particles emitted through the pre-equilibrium phase, the run-time calculation of which is definitely too time-consuming. Also the run-time access to pre-computed spectra turns out to be impossible, if we consider every projectile–target–energy combination.

Therefore, the problem has been confronted applying the BME theory to the complete fusion of some representative ion pairs at different energies, carrying out a proper parameterization
of the resultant ejectile total multiplicities and spectra, and creating a database of the obtained parameters. In order to treat systems not included in the computed database, a general dependence of the total multiplicity of pre-equilibrium particles and of the weight of each channel (the ejectiles range from neutron to alpha) has been identified as a function of the system reduced mass, the experimental binding energies of considered ejectiles, and the composite nucleus charge. For the parameters of angular distribution and energy spectra, those of the closest pre-processed system are taken, assuming as proximity criterion the projectile–target mass asymmetry value. This allows simulating the pre-equilibrium emissions for any complete fusion event generating a system the properties of which (reduced mass, ejectile binding energies, charge, asymmetry...) lie inside the domain covered by the available database. The complete fusion probability is evaluated as a function of the incident energy and the mass and atomic numbers of the interacting nuclei [Wilcke80].

For more peripheral collisions, the impact parameter $b$ is chosen according to the differential expression of the reaction cross-section $d\sigma_R/ db$, improved upon the formula proposed by P.J. Karol [Cerutti05]. In this approach, a three body picture of the reaction quite naturally follows, envisaging the production of projectile-like and target-like nuclei, and a middle system preferentially excited, the mass number of which is obtained integrating the projectile's and target's Fermi densities over their overlapping region. The thermalization of the hot third fragment can be performed according to the BME recipe discussed above, since it can be seen as the product of the fusion between well-defined projectile and target fractions. The occurrence of break-up–fusion events, implying two equilibrated nuclei at the stage before the final evaporation / fission / Fermi break-up phase (which in FLUKA is handled by the same module independently of the previous nuclear interaction nature), is considered as well, on the basis of the incident energy and ion masses. At high impact parameters, this reaction mechanism smoothly develops into a single nucleon transfer.

For the intermediate energy range, roughly between 100 MeV/n and 5 GeV/n, the Quantum Molecular Dynamics (QMD) formalism represents a viable solution. FLUKA makes use of an adapted version of a Relativistic QMD code originally developed in Frankfurt, namely rQMD-2.4 [Sorge89a, Sorge89b, Sorge95]. It describes the two interacting nuclei in their initial state as Fermi gases, following the propagation of each nucleon inside the potential generated by the others, and considering the occurrence of two nucleon close collisions possibly giving rise to nucleon-nucleon elastic scattering or particle production. In the original code the final state of this cascade was not identifying nucleon clusters and was affected by serious energy non-conservation issues at the bombarding energies of interest for therapy and space radiation applications. Therefore, the original version of the code has been reworked and now projectile- and target-like residues are reconstructed by gathering the spectator nucleons. Their excitation energies are computed as mostly due to the holes left by the hit nucleons. Moreover, the exact energy balance is assured taking into account the experimental binding energies of nuclei (as for all other models used in FLUKA).

A more accurate description can in principle be provided by a better identification of these residues, including nucleons below a suitable energy threshold in the nucleus frame, and by the calculation of their thermalization. For this purposes, the native rQMD code has been improved in order to forbid the interactions between nucleons belonging to the same nucleus and to determine the number of excitons and the respective excitation energy, in view of a future interface to the PEANUT pre-equilibrium module of FLUKA. After the cascade stage of the interaction, like for BME, the excited pre-fragments are passed to the evaporation/fragmentation models of FLUKA (see next section) which emit low energy
nucleons and fragments in the pre-fragment centre-of-mass. It is important to note that evaporation fragments emitted by projectile-like pre-fragments are typically the most energetic particles following nucleus-nucleus interactions at the energies of interest for therapy. The final $\gamma$ de-excitation is performed when particle emission is no longer energetically possible.

At energies larger than 5 GeV/n, FLUKA makes use of the DPMJET-3 code [Roesler01], again coupled with the FLUKA native evaporation/fragmentation and de-excitation models. No details will be given in this report because the energy range where nucleus-nucleus interactions are treated by DPMJET-3 is well beyond the one of interest for hadrontherapy.

3.1.3 Evaporation, fragmentation and fission

At the end of the fast reaction stages the residual nucleus, or the fragments in a nucleus-nucleus reaction, are supposed to be left in an equilibrium state, in which the excitation energy $U$ is shared by a large number of nucleons. Such equilibrated compound nucleus is supposed to be characterized by its mass, charge and excitation energy with no further memory of the steps which led to its formation. In FLUKA, the excitation energy is dissipated through evaporation in competition with fission, followed by gamma-ray emission. For light nuclei ($A<16$) the evaporation-fission stage is replaced by Fermi break-up.

3.1.4 Evaporation

The FLUKA treatment of evaporation is based on the Weisskopf-Ewing formulation, where the evaporation probability for a particle of type $j$, mass $m_j$, spin $S_j$ and kinetic energy $E$ is given by:

$$R_j(E) \, dE = \frac{(2S_j + 1)m_j}{\pi \hbar^2 S_j} \rho_{\text{inv}} \sigma_{\text{inv}} \left(\frac{U_f}{U_i}\right)^n \frac{E}{U} \, dE$$

where $\rho$ is the nuclear level density for the initial (i) and final (f) nucleus, $U$ is the excitation energy and $\sigma_{\text{inv}}$ is the cross section for the inverse process.

Integration of this probability over the emitted particle energy range provides the total width for evaporation of the particle of type $j$.

The nuclear level density is calculated according to $\rho(U) = \xi e^{-\frac{1}{2}(U-\Delta S)}$, $\Delta$ being the pairing gap in the nucleus considered. The level density parameter $\alpha$ possesses a dependence on $A$ and $Z$, due to shell and deformation effects, and a dependence on excitation energy. Both effects are accounted for, according to the latest IAEA RIPL recommendations. The pairing energies are consistent with the adopted level density parameters. Evaporation Q values are calculated from mass tables that include experimentally determined masses and evaluated ones up to $A=330$.

The calculation of total widths and the sampling of emission energies are performed with exact integrations, supported by rejections when necessary, without the usual approximations.

The inverse cross sections, originally based on the Dostrovsky formulation, have been improved to account for sub-barrier emission:

$$\sigma_{\text{inv}} = (R + \lambda)^2 \frac{\hbar}{2E} \omega \ln \left[ 1 + e^{-\frac{2\pi \Lambda}{\omega}} \right]$$
with parameters chosen in order to reproduce experimental data. An example of the results is in Figure 1.

\textbf{Figure 1.} Comparison PEANUT-ENDF Excitation function for $\alpha$ particle production by neutrons on Si. Symbols: PEANUT results, lines from ENDF compilation. Note that in standard FLUKA simulations PEANUT is NOT used for neutrons below 20 MeV, where the multigroup treatment is at work.

One of the most important developments in the FLUKA evaporation model is the inclusion of heavy fragment emission, with the same formalism as evaporation. Fragments up to $A=24$ can be emitted, either on the ground state or on excited states, for a total of about 600 ejectiles. This fragmentation mechanism is essential in order to correctly reproduce the experimental distributions of residual nuclei, as for instance in Figure 2.
3.1.5 Fission

Fission is simulated in competition with evaporation. The fission probability is calculated as:

$$P_{\text{Fiss}} = \frac{1}{2 \pi \hbar} \int_{B_{\text{Fiss}}}^{E_i} \frac{\rho_{\text{Fiss}}(U_i - B_{\text{Fiss}} - E)}{\rho_i(U_i)} dE$$

Where the fission barrier $B_{\text{Fiss}}$ is calculated following the most recent suggestions by Myers and Swiatecki [Myers99], and the level density enhancement at the saddle point has a dependence on the excitation energy in agreement with theoretical and experimental findings.

3.1.6 Fermi Break-up

For light nuclei, the evaporation models are less sound, because a) already moderate excitation energies can represent a substantial fraction of the (total) binding energy of such nuclei, b) the level structure of such nuclei is usually highly specific and level spacings can be comparable with the excitation energy, c) the mass of the "evaporated" fragment can be comparable or even larger than the mass of the residual nucleus.

Other de-excitation mechanisms are more suitable for these light residual nuclei. A possible choice is the so called Fermi Break-up model, where the excited nucleus is supposed to disassemble into two or more fragments, with branching given by phase space considerations.

In the FLUKA implementation of Fermi break-up [Ferrari96a] all combinations formed by less than six fragments have been considered. All particle stable states with $A < 16$ are included, plus the particle unstable levels with sizeable $\gamma$ decay branching ratios and a few known particle unstable isotopes, like $^8\text{Be}$. Once the final state configuration has been selected, the kinematical quantities of each fragment are chosen according to n-body phase space distribution.
3.1.7 Gamma de-excitation

The evaporation stage ends when the nuclear excitation energy becomes lower than all separation energies for nucleons and fragments. This residual excitation energy is then dissipated through emission of photons [Ferrari96b]. Photon emission during the pre-equilibrium and evaporation stages, in competition with particle emission, can be activated on option.

Gamma de-excitation proceeds through a cascade of consecutive photon emissions, until the ground state is reached. This cascade can be assumed to be statistical as long as the excitation energy is high enough to allow the definition of a continuous nuclear density. Under this assumption, the \( \gamma \)-ray emission probability is again similar to those for evaporation and fission:

\[
F(E_\gamma) \, dE_\gamma = \frac{\rho(E_\gamma)}{\rho(E_\gamma)} \sum L \, f(E_\gamma, L) \, dE_\gamma,
\]

where \( L \) is the multipolarity of the \( \gamma \) transition. A simple assumption for the strength functions \( f(E_\gamma, L) \) can be derived from single-particle estimates: \( f(E_\gamma, L) = c_L E_\gamma^{2L+1} \), where \( E_\gamma^{2L+1} \) is the energy dependence for multipolarity \( L \). For the \( c_L \) coefficients we adopted the Weisskopf single particle estimates. The \( F_L(A) \) factors have been included to partially account for the many effects that induce deviations from the single particle estimates. They are rough \( A \) dependent averages of hindrance and enhancement factors available in literature. Only E1, M1, and E2 transitions have been considered. The last steps of the \( \gamma \) cascade consist of transitions between discrete levels, either known experimentally or estimated from a rotational-like assumption.

3.2. Geant4 9.4

Geant4 is a toolkit for the simulation of the passage of particles through matter. Its areas of application include high energy, nuclear and accelerator physics, as well as studies in medical and space science. The two main reference papers for Geant4 are published in Nuclear Instruments and Methods in Physics Research A 506 (2003) 250-303, and IEEE Transactions on Nuclear Science 53 No. 1 (2006) 270-278. Geant4 is a worldwide collaboration of scientists and software engineers whose goal is to develop, maintain and provide support for the Geant4 toolkit. The direction of the collaboration is handled by a steering board. It is the task of the oversight board to ensure that sufficient resources are made available to the collaboration in order for it to function efficiently. Considering medical applications, the Geant4 modular physics list consists of 5 modules each addressing a type of interactions:

(a) Electromagnetic
(b) Elastic scattering
(c) Inelastic processes for protons
(d) Inelastic processes for heavier ions
(e) Inelastic processes for neutrons.

### 3.2.1 Electromagnetic models

Electromagnetic processes are used to simulate the electromagnetic interactions of particles with matter. In Geant4, three models are available for electromagnetic processes:
- Standard processes, effective for 1 keV to 100 TeV energies,
- Low energy processes, effective for 250 eV to 100 GeV energies,
- Penelope processes, effective for 250 eV to 1 GeV energies.

They are all applicable to clinical proton or heavy ion beams.

The standard electromagnetic package provides a variety of models based on an analytical approach to describe the interactions of electrons, positrons, photons and charged hadrons in the energy range between 1 keV and 100 TeV. The models assume that the atomic electrons are quasi-free (i.e., their binding energy is neglected except for photoelectric effect) while the atomic nucleus is fixed (i.e., the recoil momentum is neglected). The standard package is mainly appropriate for the high-energy physics domain.

The low-energy electromagnetic model is based on a data driven approach. It takes advantage of libraries (EPDL97, EEDL, EADL) that provide data for the calculation of the cross-sections and for the sampling of the final state when modelling photon and electron interactions with matter. The current implementation of low-energy electron and photon processes can be used down to 250 eV. The low-energy package models the ionization by hadrons and ions. It considers different models depending on the energy range and the particle charge. In the high-energy domain (>2 MeV) the Bethe-Bloch formula is applied, while in the low-energy domain (<1 keV for protons) the free electron model is used. In the intermediate energy range, parameterized models based on experimental data from the Ziegler and ICRU review are implemented. Corrections due to the molecular structure of materials and the effect of the nuclear stopping power are included. In the 7.0 version of Geant4 and followings, the parameterization used in the standard electromagnetic model is improved in the 0.1–10 MeV interval, which results in an improved accuracy over the low-energy implementation.

The Penelope models have been specifically developed for Monte-Carlo simulations and great care has been given to the low-energy description. These processes are the Geant4 implementation of the physics models developed for the PENELOPE code (PENetration and Energy LOss of Positrons and Electrons), version 2001. They combine numerical databases with analytical cross-section models. In particular, they include low-energy and atomic effects (e.g. Doppler broadening, shell effects).

Considering hadrontherapy applications, the G4EMStandardPhysics_option3 is the recommended physics list. In this list, a number of parameters can be tuned. Below is a list of the most common adjustable parameters in the Geant4-based simulation toolkit GATE.
- Range cut:

- The **SetCutInRegion** option is used to set the threshold below which no secondary particle will be generated. This threshold can be defined as a distance or as an energy. Production thresholds are defined for a geometrical region. In GATE, the default value is set to 1.0 mm.

  Example: /gate/physics/Gamma/SetCutInRegion world 1 mm

- Step size:

- The **setMaxStepSizeInRegion** option is used to limit the maximum size of the step. Similar to the production threshold, the step limiter is defined for a geometrical region.

  Example: /gate/physics/SetMaxStepSizeInRegion cible 0.1 mm

- The **setStepFunction** can alternatively be used to reach a compromise between calculation time and accurate simulation. With this option, the step size is limited by preventing the stopping range of the considered particle from decreasing by more than a value [Ratio] during the step (\([\text{Ratio}]=\Delta \text{Range}/\text{Range}\)). A lower limit on the step size is moreover introduced (FinalRange). By default for electron, [Ratio] = 0.2 and [Final range] = 0.1 mm.

  Example: /gate/physics/processes/ElectronIonisation/setStepFunction e+ 0.2 0.1 mm

- Pre-calculated table binning:

- The **setDEDXBinning** and **setLambdaBinning** options are used to set the number of bins of the dE/dx table and of the mean free path table respectively. By default, the values are set to 84 for a 0.1 keV to 100 TeV table range.

  Example: /gate/physics/setEMin 0.1 keV
  /gate/physics/setEMax 1 GeV
  /gate/physics/setDEDXBinning 140
  /gate/physics/setLambdaBinning 140

### 3.2.2 Hadronic models

The Geant4 implementation of nuclear interactions results in a collection of extendible models and cross-section datasets that the user can select from and combine in order to build his own hadronic physics list.

- Elastic scattering

Two processes, the HadronElastic and the UHadronElastic processes, are available in Geant4. The HadronElastic process has a default dataset (G4HadronElasticDataset) and six models: G4LElastic, G4NeutronHPElastic, G4NeutronHPorLElastic, G4ElasticHadrNucleusHE, G4LEpp and G4LEnp. The alternative process, which corresponds to a mix of the models of the first process, is supposed to be more accurate. For this process, there is only one model and a main dataset (G4HadronElasticDataset). Another dataset for low energy neutrons is also available (G4NeutronHPElasticData).
Inelastic scattering

In Geant4, fusion, inelastic scattering and fragmentation are included in the inelastic process type. Inelastic processes are modelled based on three main steps:

- Intra-nuclear cascade: the incident particle interacts strongly with the target and produces secondary particles,
- Preequilibrium (thermalization process): the excited target nucleus switches into equilibrated state by emitting excitons and light nuclei,
- De-excitation: the equilibrated nuclear residue evaporates into nucleons/light nuclei or breaks-up into several fragments.

For the simulation of the intra-nuclear cascade phase in the energy region of the present application, Geant4 provides five models: the low-energy parameterized model (LHEP), the Bertini Cascade Model, the Binary Cascade Model, the QMD model and the Precompound model. The pre-equilibrium phase of the reaction is using models that are automatically called by the intra-nuclear cascade models once the energy of the particles in the cascade has reached a lower limit. There are two pre-equilibrium models in Geant4. The first (referred to as the “pre-compound model”) is called by the binary cascade model and the other (referred to as the “pre-equilibrium model”) is used internally by the Bertini cascade model. The cascade, pre-equilibrium state and equilibrium state models are briefly described below.

Cascade models:

The binary cascade model combines a Quantum Molecular Dynamics (QMD) component and a classical cascade component to simulate the inelastic scattering of protons, neutrons and light ions off nuclei for projectile energies between approximately 80 MeV/n and 10 GeV/n. The interaction of the projectile-target system is modelled as a number of binary inelastic collisions between two nucleons, one belonging to the target nucleus and the other being the projectile (if a proton or a neutron) or a component of the projectile (if the projectile is an ion). Secondary particles produced in these reactions can further interact in one-on-one collisions with remaining nucleons in the target, thus creating an intra-nuclear cascade. When the low-energy validity limit of the binary cascade model is reached, the state of the residual nuclear system is registered as the initial state of the pre-compound nucleus model, which is subsequently called.

The Geant4 implementation of the Bertini cascade model is based on the intra-nuclear cascade (INC) model originally proposed by Serber [Serber47]. In addition to the implementation of the INC itself, the model includes a model for equilibrium decay that differs from the pre-compound nucleus model called by the binary cascade model. For the present application, the validity range of the Bertini cascade model is the same as for the binary cascade model (however, only protons and neutrons can be considered as primary particles). In comparison to the binary cascade model, the Bertini implementation introduces a number of simplifications: less accurate description of the target in terms of discontinuous nuclear density distributions and potentials, absence of Coulomb barrier simulation, entirely classical calculation of scattering and disregard of nucleon momenta in the calculation of reaction cross-sections.

The low-energy parameterized model has its origin in the GHEISHA package of GEANT3,
which has been re-engineered into C++ for Geant4. The model, valid from few hundred MeV to 20 GeV, is based on the principle of the intranuclear cascade. Only the first hadron-nucleus interaction is simulated in detail: other interactions in the nucleus are simulated by generating additional hadrons, simply treated as secondary particles that can themselves generate their own intranuclear cascade. This model was designed for fast simulations as it conserves energy and momentum only on average and not on an event-by-event basis. It can therefore be expected that the Binary and Bertini cascade models provide a more accurate description of the cascade development than the low-energy parameterized models.

The G4QMD model is an integration of the JQMD code [Niita95] as a native Geant4 hadronic model, including the Geant4 scattering and decay library and some additional developments. Compared to the rQMD model used in FLUKA, which is based on an approach using Poincaré-invariant Hamilton dynamics, the JQMD is not fully Lorentz invariant. Total nucleus-nucleus reactions cross-sections were derived by Tripathi, Tripathi Light and Shen parametrizations which come from empirical and parameterized formula based on theoretical models. They cover interaction energies from 10 MeV/n to 10 GeV/n. The de-excitation of fragments is described by several models. Evaporation from excited nuclei is handled by default by the Weisskopf-Erwing model (with emission channels \( Z \leq 2, A \leq 4 \)) together with fission and gamma-deexcitation.

► Pre-equilibrium models:

The pre-compound model of Geant4 (G4PreCompoundModel) applies to incoming particle energies below 100 MeV and is a theory-driven model based on Griffin's semi-classical description of composite nucleus decay [Griffin66]. It can be used as an independent model of inelastic scattering or as an interface between the binary cascade model and the equilibrium decay model, i.e., it provides a transition from the excited nucleus state to the equilibrium state after the cascade stage of the inelastic interaction. In this model, the nucleus is viewed as a collection of 'exciton' states, where 'exciton' denotes a particle (or hole) in a state other than the ground state. The number of excitons in the nucleus thus defines the nuclear state. Formally, these states are derived as the eigenstates of a Hamiltonian in an energy interval dE if we assume that the nucleus is at a given excitation energy E. Transitions are allowed between these states, with the restriction that the number of excitons will change by 0 or \( \pm 2 \) (in order to avoid transitions corresponding to matrix elements that vanish identically). Thus, starting with a composite nucleus after the cascade process has terminated, the model simulates a number of successive two-body interactions, which eventually lead to a fully equilibrated residual nucleus. The equilibrated nucleus is then treated by G4ExcitationHandler until its complete de-excitation. Apart from decay by exciton-exciton interactions, the equilibration model also simulates the emission of particles into the continuum as a competing channel to exciton-decay. Six emission channels are implemented. For each channel, the decay rate is calculated and the kinetic energy of the emitted particle is sampled. There are two types of fragments: G4VPreCompoundNucleon (implementing commonalities between G4PreCompoundProton and G4PreCompoundNeutron) and G4VPre-CompoundIon, which simulates the emission of more complex fragments (the latter being assumed to be created by a nucleon ‘condensation’ process). When all transitions are equiprobable, and thus the number of excitons in the system is constant, the nucleus has reached statistical equilibrium and the simulation calls the equilibrium models for further de-excitation.
Equilibrium models:

At the end of the thermalization process, the nucleus is defined by its mass, charge and excitation energy. If the excitation energy exceeds the separation energy, further particles can be emitted. The equilibrium models of Geant4 describe the emission of photons, nucleons and light fragments from this residual state. The decay of the nuclear system is treated by G4ExcitationHandler, which distributes individual fragments to the models that perform the actual break-up of the nucleus (based on the range of model applicability) and return a list of particles and nuclear fragments without excitation energies. G4ExcitationHandler manages five de-excitation models: G4VEvaporation, G4VFission, G4VFermiBreakUp, G4VMultiFragmentation and G4VPhotonEvaporation. All these models have recently undergone several significant improvements and debugging.

Neutron particular case

The interactions of neutrons at low energies are split into four parts: radiative capture, elastic scattering, fission and inelastic scattering as separate processes. Each process has standard models and datasets like other particles. In addition, some “high precision” models and datasets are provided for low-energy interactions. The high precision neutron models depend on an evaluated neutron data library (G4NDL) for cross sections, angular distributions and final state information.

Figure 3 summarizes all the electromagnetic and hadronic models available in Geant4. The ranges of energy where they are effective are reminded.
Table 1 summarizes the hadronic physics processes, models and datasets that can be employed in Geant4 simulations of hadrontherapy experiments.

<table>
<thead>
<tr>
<th>Hadronic process</th>
<th>Particles</th>
<th>Geant4 processes</th>
<th>Geant4 models</th>
<th>Geant4 datasets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>G4HadronElastic</td>
<td></td>
<td>G4NeutronHPElasticData</td>
</tr>
<tr>
<td>Inelastic process for ions</td>
<td>GenericIon</td>
<td>G4IonInelasticProcess</td>
<td>G4QMDReaction G4BinaryLightIonReaction</td>
<td>G4TripathiCrossSection G4IonsKoxCrossSection G4IonsShenCrossSection G4TripathiLightCrossSection</td>
</tr>
<tr>
<td></td>
<td>Deuteron</td>
<td>G4DeuteronInelasticProcess</td>
<td>G4QMDReaction G4BinaryLightIonReaction G4LEDeuteronInelastic</td>
<td>G4HadronInelasticDataSet G4TripathiLightCrossSection</td>
</tr>
<tr>
<td></td>
<td>Triton</td>
<td>G4TritonInelasticProcess</td>
<td>G4QMDReaction G4BinaryLightIonReaction G4LETritonInelastic</td>
<td>G4HadronInelasticDataSet G4TripathiLightCrossSection</td>
</tr>
<tr>
<td></td>
<td>Alpha</td>
<td>G4AlphaInelasticProcess</td>
<td>G4QMDReaction G4BinaryLightIonReaction G4LEAlphaInelastic</td>
<td>G4HadronInelasticDataSet G4TripathiLightCrossSection</td>
</tr>
<tr>
<td>Inelastic process for pions</td>
<td>π⁺, π⁻</td>
<td>G4PionPlusInelasticProcess</td>
<td>G4LEPionMinusInelastic G4PionPlusInelastic G4BerthiniCascade G4BinaryCascade LeadingParticleBias</td>
<td>G4HadronInelasticDataSet G4PInuclearCrossSection</td>
</tr>
<tr>
<td>Radiative capture (neutrons)</td>
<td>Neutron</td>
<td>G4HadronCaptureProcess</td>
<td>G4LCapture G4NeutronHPorCapture</td>
<td>G4HadronCaptureDataSet G4NeutronHPorCaptureData</td>
</tr>
<tr>
<td>Inelastic scattering for neutrons</td>
<td>Neutron</td>
<td>G4NeutronInelasticProcess</td>
<td>G4LENeutronInelastic G4BerthiniCascade G4BinaryCascade G4NeutronHPorLEInelastic LeadingParticleBias</td>
<td>G4HadronInelasticDataSet G4NeutronHPorFissionData</td>
</tr>
</tbody>
</table>

Table 1. Hadronic interactions: processes, models and datasets available in Geant4.
Recommended package

QGSP_BIC_HP, which uses the Binary Cascade model for primary protons and neutrons with energy below \( \sim 10 \text{ GeV} \) and for ions up to few GeV/nucleon, is the recommended package for hadrontherapy. Comparing to the QGSP_BIC physics list, it uses the data-driven high precision neutron package (NeutronHP) to transport neutrons below 20 MeV down to thermal energies. Recent comparisons between simulated and measured charged fragment yields obtained with carbon ion beams show that the QMD model provides better results than the Binary Cascade [Bohlen10].

3.3. Models available in MCNPX

MCNPX (http://mcnpx.lanl.gov) is a Los Alamos 3-D Monte Carlo radiation transport code (superset of MCNP) capable of tracking 34 particle types (nucleons and light ions) and 2000+ heavy ions at nearly all energies (for the low kinetic energy cut off of the transported particles see table 4-1 of [MCNPX08]). MCNPX stands for MCNP eXtended. It is a superset of MCNP4C3 [Bries00] and MCNPX2.3.0 and has many capabilities beyond these constituent codes. These capability extensions enhance physics, sources, tallies, graphics, and infrastructure. It uses standard evaluated data libraries mixed with physics models where libraries are not available. MCNPX is in FORTTRAN90, supported on all UNIX, Linux and PC platforms, and can be multi-processed with PVM or MPI.

As with MCNP, MCNPX uses nuclear data tables to transport neutrons, photons, and electrons. Unlike MCNP, MCNPX also uses (1) nuclear data tables to transport protons; (2) physics models to transport 30 additional particle types (deuterons, tritons, alphas, pions, muons, etc.); and (3) physics models to transport neutrons and protons when no tabular data are available or when the data are above the energy range (e.g. 150 MeV for protons) where the data tables end. MCNPX can mix and match data tables and physics models throughout a problem.

The proton transport physics includes energy straggling, multiple Coulomb scattering, elastic and inelastic scattering, and non-elastic nuclear interactions. The essential elements of the physics content of MCNPX are listed here below:

- Seamless transport of 34-particle types at nearly all energies by mixing and matching of nuclear data table and model physics;
- Heavy-ion (Z>2) transport for all 2000+ ions;
- CEM03, LAQGSM, and INCL4/ABLA physics models in addition to older FLUKA, Bertini, HETC, and Isabel models;
- Burnup / depletion with full integration of CINDER90;
- Delayed neutrons and gammas from CINDER90 radioactive decay products from data libraries and/or physics models;
- Muon capture interactions;
- Fission multiplicity;
- Light-ion recoil;
- Charged ions from neutron capture;
- Inline generation of double differential cross sections and residuals;
- Photon Doppler broadening (from MCNP5);
- Improved S(α,β) physics.
The collision energy-loss model (maximum kinetic energy transfer model) leads to stopping powers in a closer ICRU [ICRU94, MCNPX02] compliance. The energy loss straggling is implemented and described producing improved results in range calculations when selected. A variable of physics card controls selection of straggling model based on the Vavilov1 theory. When the variable is not amended, calculations are performed in the continuous slowing down approximation. The multiple coulomb scattering is also implemented and relies on Rossi’s theory, assuming a Gaussian distribution of angular deflections [Her05, MCNPX02]. In MCNPX, neglecting the small spatial proton displacements makes an additional approximation. Contrary to energy-loss straggling, there is no free parameter to turn off multiple Coulomb scattering.

The nuclear reaction models (contained in MCNPX to transport particles) can be separated into an intra-nuclear cascade stage, a pre-equilibrium stage and an equilibrium stage. In each stage secondary particles are created.

MCNPX offers options based on the Bertini [Bert63,Bert69] and ISABEL models taken from the LAHET Code System [Prael89], the Cascade-Exciton Model (CEM) package [Mash74,Mash01], which has been specially adapted for the MCNPX work, and the INCL4 model [Cugnon97a].

The Bertini model is incorporated into MCNPX through the LAHET implementation of the HETC Monte Carlo code developed at Oak Ridge National Laboratory [Hetc77]. ISABEL is derived from the VEGAS INC code [Chen68]. It has the capability of treating nucleus-nucleus interactions as well as particle-nucleus interactions (although this capability has not been yet fully tested in LAHET or MCNP). It allows for interactions between particles both of which are excited above the Fermi sea. The nuclear density is represented by up to 16 density steps, rather than the three of the Bertini INC. It also allows antiproton annihilation, with emission of kaons and pions. As presently implemented, only projectiles with \(A \leq 4\) are allowed, and antiproton annihilation is not functional. The upper incident energy limit is 1 GeV per nucleon. Running time is generally 5-10 times greater per collision than with the Bertini model. For further information on the use of the Bertini/Isabel models in MCNPX we refer to [MCNPX02, MCNPX05, MCNPX08].

For a description of the multistage pre-equilibrium models (MPM) we refer to [Prael88].

The residual compound nucleus resulting from the intra-nuclear cascade stage undergoes a pre-equilibrium stage before it enters the equilibrium stage [MCNPX02]. In the equilibrium stage three de-excitation channels compete: First, fragmentation of light excited nuclei described by the Fermi breakup model [Brenn81], second, evaporation of particles described by the EVAP model [Dresd81], and third, fission reactions described by the RAL-fission model [Atch80] or the optional ORNL fission model [Barn81]. The residual nuclei that result after a multiple loop of equilibrium de-excitation undergo a final stage of gamma-deexitation with the PHT model [Prael89].

The Cascade-Excitation Model (CEM) of nuclear interactions has been implemented in MCNPX as the nuclear reaction model for nuclei and pion induced reactions up to few GeV of kinetic energy.

As in the LAHET code models of MCNPX, the nuclear interactions in the CEM code are modelled using an intra-nuclear cascade, pre-equilibrium and equilibrium stage. The CEM
The CEM code employs the standard Dubna ICM-model [Barash72], as the intra-nuclear cascade model, and a modified exciton model (MEM) [Gud75, Mash74] for the preequilibrium stage and the evaporation channel of the equilibrium stage [Gud83]. It is optimized for incident nucleon and pion particles with kinetic energies up to 5 GeV and for target materials consisting of carbon and heavier elements.

The CEM code calculates nuclear reactions induced by nucleons, pions, and photons. It assumes that the reactions occur generally in three stages. The first stage is the INC, in which primary particles can be re-scattered and produce secondary particles several times prior to absorption by, or escape from the nucleus. When the cascade stage of a reaction is completed, CEM uses the coalescence model to “create” high-energy d, t, \(^3\)He, and \(^4\)He by final-state interactions among emitted cascade nucleons, already outside of the target. The emission of the cascade particles determines the particle-hole configuration, \(Z, A\), and the excitation energy that is the starting point for the second, preequilibrium stage of the reaction. The subsequent relaxation of the nuclear excitation is treated in terms of an improved version of the modified exciton model of preequilibrium decay followed by the equilibrium evaporation/fission stage of the reaction. Generally, all four components may contribute to experimentally measured particle spectra and other distributions. When the residual nuclei after the INC have atomic numbers with \(A < 13\), CEM uses the Fermi breakup model at any stage of a reaction.

Further information on the CEM model can be found in [Mash06, Mash08a, Mash08b]. According to the developers, the CEM model should be used for proton simulations [Waters10].

Information on the IntraNuclear Cascade Liege – Cugnon (INCL4) model can be found in [Cugnon97a, Cugnon97b, Boud02].

Moreover MCNPX contains an early version of the FLUKA code to handle high energy interactions. The FLUKA high-energy code consists of the Dual Parton Model event generators HADEV and NUCEVT [Ranft85] for hadron-hadron and hadron-nucleus collisions as implemented in the form of EVENTQ in the FLUKA-87 hadron cascade code [Aarnio86, Aarnio87].

For transport of particles in the low energy range (e.g. < 150 MeV for protons) tabulated cross section data are used because according to the developers [Water2010] the models are at lower energies much less accurate than tabulated data sets. Transport of protons below 150 MeV is performed using the LA150H evaluated cross-section libraries files. The minimum energy of the LA150 proton evaluations ranges from 1 keV to 3 MeV (for the different simulated secondary particles) [Chad99, appendix G of MCNPX08].

The organization of the proton libraries is very different than the traditional neutron libraries of MCNP(X). The proton libraries contain total (MT 1), non-elastic (MT 2), and elastic (MT 3) cross sections that can be plotted directly. MT 5 contains reaction cross section data and double-differential energy-angle distributions for emitted neutrons, protons, deuterons, and alphas, and angle-integrated spectra for gammas and stable residual nuclei. At the moment MCNPX (version 2.7C) is not transporting and scoring tallies for positrons emitted during nuclear interactions.

\(^1\) At the moment MCNPX (version 2.7C) is not transporting and scoring tallies for positrons emitted during nuclear interactions.
used to produce the cross sections for particle emission. If the users wants to see a particular particle cross section, then he/she must choose the particle number (1=neutrons, 2=photons, 9=protons, etc). Multiply this times 1000 and add the reaction number. So 9005 will be protons produced from MT5 (reaction cross sections). These spectra are inclusive, meaning the code does not distinguish the particular nuclear interaction that produces them. The proton library evaluators went the MT5 route because putting in all the individual cross sections for all reactions was getting too complex [Waters10].

In the following two pages, total and MT5 cross sections and particle production cross sections for incident protons on C-12 and O-16 respectively from the LA150H library are shown.

![Incident proton on C-12](image_url)

Figure 4. Principal cross-section of protons incident on C-12 from LA150H library.
Figure 5. Neutron, deuteron and secondary proton production cross-section of protons incident on C-12 from LA150H library.

Figure 6. Principal cross-section of protons incident on O-16 from LA150H library.
4. Benchmarking with experimental data: results concerning cross sections

This section presents comparisons between measured cross-sections and cross-sections calculated by the nuclear models from FLUKA and Geant4. Details about the comparisons can be found in [Böhlen10].

Figure 8 presents FLUKA and Geant4 reaction cross sections of carbon ions together with experimental data for H, C, and O [Fang00, Kox8, Kox87, Sihver93, Takechi09, Zhang02].
Figure 8. Total nuclear reaction cross sections for carbon ions interacting with hydrogen, carbon and oxygen are shown as predicted by FLUKA and Geant4 together with experimental data [Fang00, Kox8, Kox87, Sihver93, Takechi09, Zhang02]

For carbon and oxygen targets, Geant4 predicts cross-sections that are about 10% higher than the ones predicted by FLUKA for energies above 100 MeV/n. For hydrogen targets, there are notable differences especially for energies below 20 MeV/n [Böhlen2010].

Nuclear reactions that produce charged fragments are of special importance in ion therapy. Compared to the radiation field of the primary ions, secondary fragments lead to an altered spatial dose distribution due to differing ranges and angular distributions of the fragments and to a modification of the linear energy transfer (LET) spectrum that results in a difference of biological effectiveness for the same delivered dose. The total and partial charge-changing cross-sections are basic quantities characterizing charged particle production of ions in matter. The total charge-changing cross-section is defined as:

\[ \sigma_{\text{tcc}} = \sigma_{\text{tot}} - \sigma_{\text{el}} - \sigma_{\text{neutron-removal only}}, \]

where \( \sigma_{\text{tot}} \) is the total reaction cross-section, \( \sigma_{\text{el}} \) is the elastic cross-section and \( \sigma_{\text{neutron-removal only}} \) is the neutron-only removal cross-section. Partial charge-changing cross-sections \( \sigma_{\text{pcc}, Z} \) measure reactions in which a number of protons \( Z \) are removed from the initial fragment with charge \( Z_0 \) to form a fragment with charge \( Z_0 - Z \).

A comparison between experimental data and simulations for carbon ions interacting in water and polycarbonate is shown in Figures 9 and 10 for total and partial charge-changing cross-sections respectively.
At higher energies, nuclear cross-sections are mostly determined by the geometrical extensions of projectile and target nuclei, and for energies below 1 GeV/n pion production is negligible. Consequently, the charge-changing cross-sections remains almost constant for energies between 200 and 500 MeV/n, and this is true for both Monte-Carlo codes. For lower energies, a steady rise is observed. For FLUKA simulations of carbon ions on water, the total (Figure 9) and partial (Figure 10) charge-changing cross-sections for Li agree well within the experimental error. Partial charge-changing cross-sections for B and Be are slightly underestimated. In addition, the presented cross-sections for carbon on polycarbonate are slightly underestimated by the simulations. Geant4 simulations using the G4QMD model are of similar precision. Geant4 simulations using the Binary Cascade Light Ion model (BIC LI) under-estimate experimental total charge-changing cross-sections by roughly 20%. Interestingly, this trend is reversed for partial charge-changing cross-sections that are over-estimated by around 50%.

5. Dosimetry performance: comparison with Bragg Peak data

In ion beam therapy nuclear reactions cause a significant alteration of the radiation field. This results in a loss of primary beam particles and a build-up of secondary lower-charge fragments. Consequently, the dose distribution along the beam path is different from the dose profile resulting from the passage of primary ions in absence of nuclear interactions. In
particular, the secondary lower-charge fragments, having longer ranges than the primary beam, give rise to the characteristic dose tail beyond the Bragg peak. The importance of these effects generally increases as a function of the beam energy (or penetration depth). For example, for a carbon ion beam at 200 MeV/n about 30% of the primary carbon ions undergo nuclear reactions and do not reach the Bragg peak maximum at about 8.6 cm depth in water whereas at 400 MeV/n only the 30% of the primary particles reach the Bragg peak at about 27.5 cm depth in water.

In the next sections, we compare the depth-dose profiles and positions of the Bragg peak obtained using different Monte-Carlo codes. Experimental data are reported as references. Phantoms made of various materials of therapeutic relevance are considered as targets.

5.1 The proton case

Figure 11 compares the Bragg curves of 100, 140, 180 and 227 MeV proton beams in a water target obtained with the Geant4 (Binary Cascade model) and MCNPX simulation tools to experimental data. Experimental data correspond to measurements performed in a scanned beam at the proton therapy center in Essen, Germany (courtesy of IBA).

Figure 11. Simulated (MCNPX and Geant4) proton depth dose curves in water versus measured depth dose curves [courtesy of IBA]. The curves are normalized to obtain the same deposited energy at the entrance of the target.

In table 2 simulated ranges corresponding to Figure 11 are compared to NIST values. They demonstrate a correct agreement between the two simulation codes and the reference NIST
values. The FLUKA values have also been computed using 2 different values for the water ionization potential.

<table>
<thead>
<tr>
<th>Proton energy (MeV)</th>
<th>NIST</th>
<th>MCNPX</th>
<th>Geant4 9.2 (BIC)</th>
<th>FLUKA ($I_{H2O}=75$ eV)</th>
<th>FLUKA ($I_{H2O}=78$ eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.6</td>
<td>7.8</td>
<td>7.6</td>
<td>7.71</td>
<td>7.73</td>
<td>7.80</td>
</tr>
<tr>
<td>140</td>
<td>13.98</td>
<td>13.8</td>
<td>13.86</td>
<td>13.80</td>
<td>13.89</td>
</tr>
<tr>
<td>227.5</td>
<td>32.34</td>
<td>32.0</td>
<td>32.19</td>
<td>32.00</td>
<td>32.13</td>
</tr>
</tbody>
</table>

Table 2. Comparison between proton range values in water ($\rho = 1$ g.cm$^{-3}$) taken from NIST and obtained from MCNPX, Geant4 and FLUKA simulations.

Similarly, table 3 compares the ranges obtained in a PMMA target. The FLUKA calculated ranges are also presented.

<table>
<thead>
<tr>
<th>Proton energy (MeV)</th>
<th>NIST</th>
<th>FLUKA</th>
<th>MCNPX</th>
<th>Geant4 9.2 (BIC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.6</td>
<td>8.01</td>
<td>7.90</td>
<td>7.8</td>
<td>7.77</td>
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<tr>
<td>140</td>
<td>14.45</td>
<td>14.24</td>
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</tr>
<tr>
<td>180.7</td>
<td>22.39</td>
<td>22.13</td>
<td>22.02</td>
<td>22.01</td>
</tr>
<tr>
<td>227.5</td>
<td>33.23</td>
<td>32.83</td>
<td>33.32</td>
<td>32.7</td>
</tr>
</tbody>
</table>

Table 3. Comparison between proton range values in PMMA ($\rho = 1.19$ g.cm$^{-3}$) taken from NIST and obtained from MCNPX, FLUKA and Geant4 simulations.

Figures 12, 13 and 14 summarize the experimental validation performed by different working groups. They show that a good agreement can be obtained between simulation and experiment with each code.

Figure 12. Bragg curve of a 182.66 MeV/n proton beam on water. Black squares [Parodi10] correspond to experimental data (measured at the Heidelberg Ion Beam Therapy Center) while the solid red line represents the FLUKA results. Both the experimental data and the MC results are normalized by the integral of the Bragg curve calculated between the entrance region and the Bragg Peak.
Figure 13. MCNPX simulated depth dose curves are compared to measurements performed in a scanned beam at the proton therapy center in Essen, Germany (courtesy of IBA). The difference between simulation and experiment (normalized to the maximum energy deposition) is also shown (black points).
Figure 14. Comparison between measured and Geant4 simulated depth-dose profiles in water for 98.71 (a) and 227.65 (b) MeV proton beams. The left and right axes correspond respectively to normalized doses and point-to-point errors. This figure shows that the simulations overestimate the dose deposit in the plateau entrance and underestimate the dose deposit in the Bragg peak region [Grevillot10].

The lateral dose spreading accuracy achievable by Monte-Carlo simulation tools is also an important figure of merit. Table 4 [Grevillot10] compares the transverse profile spreading (σ) at 10 cm, 30 cm and 32 cm depth for a 230 MeV proton beam in water obtained using the GEANT4 9.2 Multiple Scattering algorithm, GEANT4 9.2 Single Scattering algorithm, MCNPX, PHITS Monte-Carlo code [Niita06] and an analytical model (Szymanowski). Here we add also the results obtained with FLUKA in the same simulation conditions. GEANT4 beam spreading is significantly lower than in MCNPX, PHITS, Szymanowski’s model and FLUKA, even if it gets close to PHITS results using the SS algorithm. MCNPX shows the wider beam spreading.

<table>
<thead>
<tr>
<th></th>
<th>GEANT4 (MS)</th>
<th>GEANT4 (SS)</th>
<th>MCNPX</th>
<th>PHITS</th>
<th>Szymanowski</th>
<th>FLUKA</th>
</tr>
</thead>
<tbody>
<tr>
<td>σ cm (mm)</td>
<td>3.1</td>
<td>3.2</td>
<td>3.1</td>
<td>3.4</td>
<td>3.2</td>
<td>3.36</td>
</tr>
<tr>
<td>σ30cm (mm)</td>
<td>6.2</td>
<td>6.8</td>
<td>7.3</td>
<td>6.8</td>
<td>7.1</td>
<td>7.24</td>
</tr>
<tr>
<td>σ32cm (mm)</td>
<td>6.9</td>
<td>7.5</td>
<td>8.1</td>
<td>7.5</td>
<td>7.8</td>
<td>8.00</td>
</tr>
</tbody>
</table>

Table 4: Comparison of the transverse profile spreading (σ) at 10 cm, 30 cm and 32 cm depth for a 230 MeV proton beam in water using the GEANT4 9.2 Multiple Scattering algorithm, GEANT4 9.2 Single Scattering algorithm, MCNPX, PHITS, an analytical model (Szymanowski) and FLUKA. The values for GEANT4, MCNPX, PHITS and the Szymanowski model are taken from [Grevillot10], where the uncertainty on the σ values was estimated to 0.15 mm using ROOT.

Figure 15 compares the transverse profiles at 32 cm for the Monte Carlo codes used in Table 4.
Figure 15. Comparison between simulated transverse dose profiles at 32 cm of depth in water for a 230 MeV proton beam. (Geant4, PHITS and MCNPX profiles are taken from [Grevillot10]).

5.2 The carbon ion case

Figure 16 compares in-depth profiles in water corresponding to 270 carbon ion beams obtained with the MCNPX [Shiver98], FLUKA [Sommerer06] and Geant4 (QMD model) simulation codes to experimental data [Shiver98]. In this figure, a shift in range was performed on all the considered data to only compare the in-depth profile shapes.
Figure 16. Comparison of experimental [Sihver98] and FLUKA [Sommerer06], MCNPX [Sihver98] and Geant4 simulated Bragg peak curves for 270 MeV/n carbon ions on water. A shift in range was performed on all the considered data to only compare the in-depth profile shapes. Results were normalized to the same maximum deposited energy.

As illustrated in Figure 16, MCNPX 2.7c was found to underestimate the dose tail beyond the Bragg peak due to fragmentation products. A good agreement is obtained between the FLUKA and Geant4 simulation tools. Figures 17, 18 and 19 summarize the experimental validation performed by each working group.

Figure 17. Bragg curve of a 400 MeV/n carbon beam on water. The points [Haettner06] correspond to the experimental data while the black solid line represents the FLUKA results. The red and blue lines show the contribution from primary carbon ions and from secondary fragments respectively.
6. Predictions and comparison with data useful for therapy applications

To assess the accuracy and precision of the models, we compared:

- integral fragment yields (versus depth)
- angular fragment yields (versus depth)
- double differential yields

6.1 β⁺ emitters

6.1.1 Proton case

Tables 5 and 6 compare respectively the integrated yields of positron-emitting nuclei (per $10^5$ beam particles) produced by 110 MeV and 140 MeV protons in a PMMA box. The experimental and FLUKA values are extracted from [Parodi04]. The MCNPX values are obtained considering the Parodi experimental cross-sections (Appendix 4). They show a good agreement between the simulation codes first and with the experimental results when considering the $^{11}$C production rate.
Experimental results [Parodi04] are compared to Geant4 (Binary Cascade model) simulated values.

<table>
<thead>
<tr>
<th></th>
<th>$^{11}$C</th>
<th>$\Delta^{11}$C</th>
<th>$^{10}$C</th>
<th>$\Delta^{10}$C</th>
<th>$^{15}$O</th>
<th>$\Delta^{15}$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental results</td>
<td>2200±300</td>
<td>90±30</td>
<td>800±150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GATE Geant4 9.4 (BIC model)</td>
<td>1879</td>
<td>-14.6</td>
<td>132</td>
<td>46.7</td>
<td>697</td>
<td>-12.9</td>
</tr>
</tbody>
</table>

Table 5: Integrated yields of positron-emitting nuclei (per $10^5$ particles) produced by 110 MeV protons in a PMMA phantom. Experimental data by [Parodi04] are compared to Geant4 (Binary Cascade model) simulated values.

<table>
<thead>
<tr>
<th></th>
<th>$^{11}$C</th>
<th>$\Delta^{11}$C</th>
<th>$^{10}$C</th>
<th>$\Delta^{10}$C</th>
<th>$^{15}$O</th>
<th>$\Delta^{15}$O</th>
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<tr>
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<td>3400±400</td>
<td>150±30</td>
<td>1230±180</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GATE Geant4 9.4 (BIC)</td>
<td>2708</td>
<td>-20.3</td>
<td>222</td>
<td>48.0</td>
<td>1017</td>
<td>-17.3</td>
</tr>
<tr>
<td>FLUKA [Parodi04]</td>
<td>2670</td>
<td>-21.5</td>
<td>100</td>
<td>-33.3</td>
<td>1230</td>
<td>0</td>
</tr>
<tr>
<td>MCNPX (Parodi Cross Section)</td>
<td>2638</td>
<td>-22.4</td>
<td>-</td>
<td>-</td>
<td>897</td>
<td>-27.1</td>
</tr>
</tbody>
</table>

Table 6: Integrated yields of positron-emitting nuclei (per $10^5$ particles) produced by 140 MeV protons in a PMMA phantom. Experimental data by [Parodi04] are compared to Geant4 (Binary Cascade model, FLUKA [Parodi04] and MCNPX simulated values.

Figure 20 compares the $^{11}$C, $^{15}$O and $^{10}$C production rates as a function of the depth calculated for a 140 MeV proton beam in a PMMA target with Geant4 (version 9.4 using the Binary Cascade model, internal models), FLUKA (internal models) and MCNPX. In the MCNPX simulations the Parodi cross sections are considered. Figure 20 demonstrates a reasonable agreement between the three Monte-Carlo codes.

Figure 20. $^{11}$C, $^{15}$O and $^{10}$C production rates as a function of the depth calculated for a 140 MeV proton beam in a PMMA target with Geant4 (version 9.4 using the Binary Cascade model, internal models), FLUKA (internal models) [Parodi04] and MCNPX.
Figure 21 compares the measured and FLUKA (internal models and experimental cross sections) [Parodi04] and Geant4 (9.4 version, Binary Cascade model) calculated $\beta^+$ activity profiles (mainly resulting from $^{11}$C and $^{15}$O activation) for a monoenergetic 140 MeV proton beam on a PMMA target. It highlights the improvement obtained when using the experimental cross-sections in the FLUKA simulations.

6.1.2 Carbon ion case

Tables 7, 8 and 9 compare the measured integrated values of $\beta^+$ emitter production rates [Parodi04] to the Geant4 and FLUKA simulated values for 212.12, 259.5 and 343.46 MeV/u energies. The FLUKA values are extracted from [Sommerer07]. For the 259.5 MeV/u energy, the POSGEN values [Parodi04] are also shown.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>$^{11}$C</th>
<th>$^{15}$C</th>
<th>$^{11}$C</th>
<th>$^{15}$C</th>
<th>$^{15}$O</th>
<th>$^{15}$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental results [Parodi04]</td>
<td>7932±3000</td>
<td>105052±13000</td>
<td>21167±3000</td>
<td>9300</td>
<td>93000</td>
<td>19000</td>
</tr>
<tr>
<td>GATE Geant4 9.4 (QMD model)</td>
<td>9300</td>
<td>17.2</td>
<td>93000</td>
<td>-11.5</td>
<td>19000</td>
<td>-10.2</td>
</tr>
<tr>
<td>FLUKA [Sommerer07]</td>
<td>6163</td>
<td>-22.3</td>
<td>105326</td>
<td>0.3</td>
<td>27315</td>
<td>29.1</td>
</tr>
</tbody>
</table>

Table 7: Integrated yields of positron-emitting nuclei (per $10^8$ particles) produced by 212.12 MeV/u carbon ions in a PMMA phantom. Experimental data by [Parodi04] are compared to Geant4 (QMD model) and FLUKA [Sommerer07] simulated values.
Experimental results by [Parodi04] are compared to GATE Geant4 (QMD model) and FLUKA [Sommerer07] simulated values.

<table>
<thead>
<tr>
<th></th>
<th>$^{12}$C</th>
<th>$^{10}$C</th>
<th>$^{11}$C</th>
<th>$^{14}$C</th>
<th>$^{15}$O</th>
<th>$^{18}$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental results [Parodi04]</td>
<td>11470±3000</td>
<td>146461±16000</td>
<td>30798±4000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GATE Geant4 9.4 (QMD model)</td>
<td>16000</td>
<td>39.5</td>
<td>136000</td>
<td>-7.1</td>
<td>31000</td>
<td>-0.7</td>
</tr>
<tr>
<td>FLUKA [Sommerer07]</td>
<td>8630</td>
<td>-24.8</td>
<td>146219</td>
<td>-0.2</td>
<td>42496</td>
<td>38.0</td>
</tr>
<tr>
<td>POSGEN (270 MeV/u)</td>
<td>19600</td>
<td>70.9</td>
<td>266000</td>
<td>81.6</td>
<td>100000</td>
<td>222.6</td>
</tr>
</tbody>
</table>

Table 8: Integrated yields of positron-emitting nuclei (per 10$^6$ particles) produced by 259.5 MeV/u carbon ions in a PMMA phantom. Experimental data by [Parodi04] are compared to Geant4 (QMD model), FLUKA [Sommerer07] and POSGEN (270 MeV/u) simulated values.

<table>
<thead>
<tr>
<th></th>
<th>$^{12}$C</th>
<th>$^{10}$C</th>
<th>$^{11}$C</th>
<th>$^{14}$C</th>
<th>$^{15}$O</th>
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<td>15231±3000</td>
<td>198681±24000</td>
<td>50318±4000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GATE Geant4 9.4 (QMD model)</td>
<td>25000</td>
<td>64.1</td>
<td>220000</td>
<td>10.7</td>
<td>56000</td>
<td>11.3</td>
</tr>
<tr>
<td>FLUKA [Sommerer07]</td>
<td>13341</td>
<td>-12.4</td>
<td>213012</td>
<td>7.2</td>
<td>70148</td>
<td>39.4</td>
</tr>
</tbody>
</table>

Table 9: Integrated yields of positron-emitting nuclei (per 10$^6$ particles) produced by 343.46 MeV/u carbon ions in a PMMA phantom. Experimental data by [Parodi04] are compared to Geant4 (QMD model) and FLUKA [Sommerer07] simulated values.

If the integrated $^{11}$C production rates are better recovered with FLUKA (a maximum difference of 7.2 % vs. 11.5 % with Geant4) a better agreement is obtained with Geant4 for the $^{15}$O production (maximum difference of 394 % with FLUKA against 11.3 % with Geant4).

Figure 22 compares the in-depth profiles of the production rates of the main β+ emitters ($^{11}$C, $^{10}$C and $^{15}$O). The experimental data were acquired at the Gesellschaft für Schwerionenforschung in Darmstadt. The FLUKA profiles are extracted from the Sommerer’s thesis [Sommerer07].
Figure 22. Comparison between experimental and FLUKA and Geant4 (9.4 version, QMD model) calculated distributions of $^{11}$C, $^{14}$C and $^{15}$O for a monoenergetic 259.5 MeV/u carbon ion beam on a PMMA target. The FLUKA results were exacted from the Sommerer’s thesis [Sommerer07].

A normalization factor is necessary to recover the integrated values (Tables 7, 8 and 9) from the experimental profiles (Figure 22). The origin of this factor being not still well understood the profiles should only be compared in shape. For the $^{11}$C and the $^{15}$O, the Geant4 simulations seem to better recover the measured shape than FLUKA. Results seem to be quite similar concerning the $^{10}$C production.

6.2 Prompt gamma production

6.2.1 Proton beam

6.2.2 Carbon ion beam

To study the prompt gamma detection for hadrontherapy monitoring, four experiments were carried out by a collaboration between IPNL and INSA research groups: two experiments at the GANIL facility with low energy beams (73 MeV/u $^{13}\text{C}^{6+}$ and 95 MeV/u $^{12}\text{C}^{6+}$) whereas higher energy measurements were performed at GSI (300 MeV/u and 310 MeV/u $^{12}\text{C}^{6+}$) [TestaE08, TestaM10].

Comparisons between simulations and measurements were carried out for each experiment. In all cases, a large discrepancy was observed between the measured and simulated counting rates: the first results obtained with Geant4 (9.1 and 9.2) show that simulations overestimate the detection of prompt gamma-rays by a constant factor of 12.

This is clearly illustrated in Figure 23, which presents measured and simulated spectra of the energy deposited in a NaI(Tl) detector. The discrepancy ranges over the whole energy spectrum beyond 1 MeV (corresponding to the lowest energy threshold used in our experiments). In this Geant4 9.1 version, the Fermi Break-up de-excitation model was not used.

The INSA-IPNL collaboration has initiated a collaboration with Geant4 developers. This collaboration already resulted in 2 improvements:

- The use of the QMD model as the nuclear collision model. This model better reproduces charged particle emission at energies relevant for hadrontherapy [Böhlen10]. However the photon emission yields obtained with the QMD and Binary Cascade models are very similar so that prompt gamma prediction is not really improved by the use of the QMD model.
- The activation of the Fermi Break-up model, which leads to a reduction by a factor 2 of the Geant4 photon emission overestimation.

The improvement obtained with the Fermi Break-up activation can be clearly seen in Figure 24. This figure presents the measured and simulated prompt gamma yields as a function of
the target depth for PMMA irradiation with 95 MeV/u (top) and 310 MeV/u (bottom) $^{12}$C ion beams. Geant4 gamma yield overestimation ranges from a factor of 5 to 6 before the Bragg peak. The insets that correspond to normalised net yields (background subtracted) show that the experimental gamma profile shape is rather well reproduced by simulations for low ion path (GANIL measurements) which is not the case for larger ion path (GSI measurements).

Figure 24. Measured and Geant4 simulated prompt gamma yields as a function of the target depth for PMMA irradiation with 95 MeV/u $^{12}$C (top) and 310 MeV/u $^{12}$C (bottom) ion beams. These yields correspond to events for which an energy deposition larger than 1 MeV (gamma equivalent) occurs. The insets correspond to normalised net yields (background subtracted). The open points correspond to measurements obtained with the collimated scintillator offset with respect to the target. Simulations settings: Geant4 9.3 with QMD (collision model) and the Fermi Break-up activated (de-excitation model).

An extensive study of de-excitation models has been undertaken for more than a year between the IPNL-INSU Lyon-LPC Clermont collaboration and Jose Manuel Quesada from the Geant4 collaboration. Several possible improvements in the physics models have been identified, in particular in the photon evaporation model. Improvements have already been introduced in the latest Geant4 version (version 9.4 released in December 2010), especially the Fermi Break-up for small nuclei ($A \leq 4$) has been included (in the previous Geant4 version, the Fermi Break-up was applied to nuclei with $4 < A < 17$). Light nucleus de-excitation by the Fermi Break-up model is questionable but there is currently no alternative model to describe the de-excitation of highly excited light nuclei. Note that in Geant4 9.4, the Fermi
Break-up model is activated by default when the binary cascade or the QMD models are instantiated.

Figure 25 presents the latest Geant4 results (Geant4 9.4) on prompt gamma emission: prompt gamma yields as a function of the target depth for PMMA irradiation with 95 MeV/u ion beams. Geant4 gamma yield is overestimated by a factor of about 3 at the target entrance but this factor is still about 6 at the Bragg peak location.

As far as FLUKA is concerned, preliminary promising results are already available. However, work is in progress in order to improve and refine the models describing gamma de-excitation (see 3.1.7) and a systematic presentation of the performance of the code will be postponed to the completion of model revision.

A comparison has been also carried out using MCNPX version 2.7.c [Pel10]. Simulations used cross sections whenever available for protons, neutrons, photons and electrons, and physics models with default settings otherwise. Additional particles included in the transport process are heavy ions, alphas, helium-3, tritons and deuterons. The LAQGSM (Los Alamos Quark-Gluon String Model) is used as the default nuclear cascade/evaporation model to handle heavy ion interactions.

Comparisons of the simulations with the measurements in the figures below show a reasonable agreement but accurate quantitative conclusions cannot be drawn yet.

- First of all, measurements include background and radiations scattered in the beam room that were not simulated with MCNPX,
- Second, the simulation statistics is not optimal for measurements at GANIL and quite poor for GSI. To reduce the variance, simulations were based on an ideal geometry with a cylindrical revolution of the real detection system around the beam axis. Results were normalized to match the actual solid angle, but additional scattered events in the ideal geometry cause a small overestimation of the real count rate,
- Third, since MCNPX was found to underestimate the dose tail beyond the Bragg peak due to fragmentation products (see section 5) even without background in the
measurements, we would expect an underestimation of the count rate caused by fragmentation products at corresponding depths.

Figure 26. Depth detection profile for the 95 MeV/u carbon ion beam of GANIL with a 2 MeV energy threshold and a 1.5 ns TOF window.

Figure 27. Depth detection profile for the 310 MeV/u carbon ion beam of GSI with a 2 MeV energy threshold and a 2.0 ns TOF window.

6.3 Charged particle production

The nuclear interactions undergone by an ion beam in a thick target lead to a loss of primary ions and a build-up of secondary fragments. In the work of [Haettner06] the yield of secondary charged fragments was measured at certain depths in the water target. The experimental results are presented as the number of fragments per primary particle versus depth. In this experiment, only fragments with angles smaller than 10° leaving the water target were detected. Due to their wide angular distributions, not all produced hydrogen and helium fragments were detected. For heavier fragments from lithium to boron, the whole angular range was covered and yields are equivalent to the total number of secondaries leaving the
target. Simulations scored particle spectra and angular distributions at different depths in the water volume with small distances so that nearly continuous curves were obtained. Integral fragment yields were obtained excluding particles with angles larger than 10 degrees (see Figure 28). For H and He ions, FLUKA simulations agree within about 10%. There is an underestimation for Li by a maximum of 20% which was not seen in the respective charge-changing cross-section presented earlier. Heavier fragments are predicted mostly within the experimental error. The GEANT4 simulations employing the G4QMD model reproduce the experimental data rather well and mostly within the experimental precision for all ions, except for He, which is under-estimated by a maximum of 20-30%.

Figure 28. Fragment build-up curves in water of a 400 MeV/u carbon beam as a fraction of primary carbon ions N/N_0. Experimental data are shown as points [Haertner06]. Simulations done for FLUKA (solid) and for GEANT4 using the BIC LI (dashed) and the G4QMD (dotted) model are displayed as lines. The dashed vertical line indicates the position of the Bragg peak.

Figure 29 shows the normalized angular yields of fragments at a water-equivalent depth of 25.8 cm just before the Bragg peak. Due to their small solid angle, fragmentation yields of the forward angles contribute only marginally to the integral fragmentation yields. For therapeutic applications, correct predictions of angular fragment distributions are of importance for describing the dose distribution in vicinity and behind the Bragg peak. FLUKA reproduces the overall shape of the angular yields very well. Larger angles are slightly under-estimated and there are some discrepancies in the forward angles, especially for H and Li. For both Geant4 options, fragmentation yields tend to be under-estimated for small angles but over-estimated for larger angles and fragments heavier than helium.
Figure 29. Normalized angular yields of H, He, Li and B at a water-equivalent depth of 25.8 cm for a 400 MeV/u carbon beam in water. Yields are expressed as number of ion fragments per steradian per incident primary carbon ion. The vertical error bars of the measurements show an estimation of the error due to the method of particle identification [Haettner06]. Simulations with FLUKA, GEANT4 BIC LI and GEANT4 G4QMD are shown as lines.

Figure 30 shows the experimental energy spectra of H, He, Li and B at a depth of 25.8 cm and selected angles together with simulations with FLUKA and Geant4. These graphs correspond to the angles which contribute most to the integral fluences (maximum yield in a fixed $\Delta \theta$ at different azimuthal angles). At a depth of 25.8 cm, this is for heavier fragments from Li to B between 1 and 2 degree and for H and He between 2 and 4 degree. It can be seen that the shape of experimental energy distributions is generally well reproduced by hadronic models of both codes for the different fragments at the selected depths. The spectra of Li, Be (not shown) and B simulations are shifted to slightly lower energies compared to the experimental data (for details see [Böhlen10, Haettner06]).
Figure 30. Number of ion fragments per steradian per MeV/u normalized to the number of incident particles $N_0$ versus fragment energy are shown as produced by a 400 MeV/u carbon beam in water. Graphs are for a water-equivalent thickness of 25.8 cm and show H, He, Li and B fragments at selected angles. The vertical error bars of the measurements [Haettner06] show the statistical error. The horizontal error bars show the time resolution. Simulations with FLUKA, GEANT4 BIC LI and GEANT4 G4QMD are shown.

6.4 Neutron production

Neutron production during patient treatment with ions is important for estimating the secondary cancer risk and radioprotection. Figures 31 and 32 show the predictions of double-differential neutron fluences of FLUKA in comparison with experimental data [Kurosawa99].
Figure 31. Neutron fluence for a carbon ion beam impacting on a thick carbon target. Lines are FLUKA simulations. Points are experimental data [Kurosawa99].

Figure 32. Neutron fluence for a carbon ion beam impacting on a thick copper target. Lines are FLUKA simulations. Points are experimental data [Kurosawa99].
Figure 33. Double differential thick target neutron yield for 113 MeV (left) and 68 MeV (right) protons on Carbon. Symbols are experimental data [Meier89, Meigo97], histograms are FLUKA simulations

7. Recommendations for the use of the available MC Codes in therapy and imaging applications

For each code, we will specify here the models to be selected to get the most accurate results as a function of the application. Information about the cuts to be used should also be provided.

7.1 FLUKA

The recommended FLUKA default physics settings for hadron therapy applications (‘HADROTherapy’) have to be activated. This option uses δ-ray production and transport cuts of 100 keV.

The transport of charged particles is performed through an original Multiple Coulomb scattering algorithm, supplemented by an optional single scattering method. The treatment of ionization energy losses is based on a statistical approach alternative to the standard Landau and Vavilov ones that provides a very good reproduction of fluctuations both for restricted and unrestricted energy losses, and which is particularly suitable for Monte Carlo applications. The charged hadron transport step size is set to 2% loss of kinetic energy.

Multiple scattering with inclusion of nuclear form factors is applied also to heavy ion transport. Up-to-date effective charge parameterizations are employed, and straggling of ion energy losses is described with the same algorithm quoted above, in normal first Born approximation with inclusion of charge exchange effects. Recently, higher order corrections (z^3 and z^4 corrections, where z is the projectile charge) have been implemented. The implementation of Mott corrections to the ion-electron scattering formalism is underway: its effects are expected to be minimal for light ions of relevance for therapy, while they should be significant for medium-heavy ion beams used for research. Electrons and positrons are also transported with an original multiple Coulomb scattering algorithm. The lowest transport limit is 1 keV.

Neutrons are transported down to thermal energies. Hadron-hadron, hadron-nucleus and
nucleus-nucleus reactions are treated down to the Coulomb barrier (see the nuclear model section).

The hadron therapy defaults are optimized for the accurate calculation of dose and include therefore, the CPU-time consuming δ-ray production. Since this latter process is purely related to the electromagnetic energy deposition it can be switched off in simulation concerning secondary particle production in thick target experiments and β*-activity production. δ-ray production can be switched off, or its threshold raised, also when the (minimal) build zone at the beam entrance is not of interest, or the dimension of the volumes of interest for energy deposition is of the order of mm or larger. Moreover, in order to achieve accurate results for residual nuclei production as for instance in PET oriented calculations, the evaporation of heavy fragments must be activated using the FLUKA ‘PHYSICS’ card. This, however, is not the default since it brings a heavy CPU burden, and it is not needed for most applications.

Several recent studies have reported comparisons of nuclear Monte Carlo models of FLUKA [Mairani07, Parodi04, Sommerer06, Sommerer07, Böhlen10, Rinaldi10] for proton and ion therapy. They provide evidence that the agreement between predictions of nuclear reaction models and experimental data is encouraging. Further applications and validations can be found in [Mairani07, Parodi07, Parodi09, Sommerer07]. In Figures 34 and 35, comparisons of FLUKA simulations with the data obtained with Multi Layer Faraday Cups of mostly Cu and CH₂ [Gottschalk99, Paganetti03] are presented [Rinaldi11].

![Figure 34. Experiment (symbols) and FLUKA Monte Carlo calculations (histograms) for the CH₂ MLFC described in [Paganetti2003]. The scale is absolute: linear scale (left), where the channels above 47 have been multiplied by 0.04, log scale (right). A total charge integral background of 1.6% has been added to the Monte Carlo simulation.](image-url)
7.2 Geant4

As shown in the present report, two different physics list, detailed in Appendices 2 and 3, have to be used depending on the incident particle.

First, in the proton case, the Geant4 Binary Cascade model has to be activated for the primary protons (Appendix 2). This model, contrary to the default Low-Energy Parameterized model, better describes the production of secondary particles produced in interactions of protons with nuclei. Unlike the QMD model, it ensures a good prediction of the $\beta^+$ emitter production rates with depth. For neutrons, the Binary Cascade model is activated too for high energies (> 14 MeV) for the same reasons. The high precision neutron package (NeutronHP) is used to transport neutrons down to thermal energies.

Considering electromagnetic models, the use of a high binning of the cross-section tables ($\geq 20$ bins/decade) and $0.1$ mm maximum step size and cut are recommended. Such parameterization yields robust and efficient simulations compared to other Monte-Carlo codes [Grevillot10] (see Appendix 1 for more details). The use of the Opt3 (Table 10) options, which have no influence on the results in the considered homogeneous cases [Grevillot10] but which can be useful thanks to the stepping function in heterogeneous and voxelized media like patient CT data, is also recommended.

<table>
<thead>
<tr>
<th>Stepping function - finalRange</th>
<th>e^- / e^+</th>
<th>Proton</th>
<th>Generic Ion</th>
</tr>
</thead>
<tbody>
<tr>
<td>binning (bins/decade)</td>
<td>0.1 mm</td>
<td>0.05 mm</td>
<td>0.02 mm</td>
</tr>
<tr>
<td>stepping algorithm</td>
<td>distanceToBoundary</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 10. Summary of the Geant4 Opt3 parameters.
Hadronic process | Particles | Geant4 processes | Geant4 models | Geant4 datasets | Energy range
--- | --- | --- | --- | --- | ---
Elastic scattering | GenericIon | G4HadronElasticProcess | G4LElastic | G4HadronElasticDataSet | ...
| All other particles | G4UHadronElasticProcess | G4HadronElastic | G4HadronElasticDataSet | ...
Inelastic process for protons | Protons | G4ProtonInelasticProcess | G4BinaryCascade | G4ProtonInelasticCrossSection | 0-20 GeV
Inelastic process for ions | Deuteron | G4DeuteronInelasticProcess | G4LEDeuteronInelastic | G4TripathLightCrossSection | 0-80 MeV
| Triton | G4TritonInelasticProcess | G4LETritonInelastic | G4TripathLightCrossSection | 80 MeV-20 GeV
| Alpha | G4AlphaInelasticProcess | G4LEAlphaInelastic | G4TripathLightCrossSection | 80 MeV-20 GeV
Inelastic process for pions | π⁺, π⁻ | G4PionPlusInelasticProcess | G4LEPionPlusInelastic | G4HadronInelasticDataSet | ...
| Neutron | G4NeutronCaptureProcess | G4NeutronHPCapture | G4NeutronHPCaptureData | 0-20 MeV
| G4Capture | G4NeutronCaptureDataSet | 14 MeV-20 GeV
| Neutron | G4NeutronInelasticProcess | G4NeutronHPInelastic | G4NeutronHPInelasticData | 0-20 MeV
| G4BinaryCascade | G4NeutronHPInelasticDataSet | 14 MeV-20 GeV
| G4LFission | G4HadronFissionDataSet | 14 MeV-20 GeV

Table 11. Overview of the recommended hadronic models and datasets for proton beam simulation.

In the carbon ion case, the same electromagnetic parameters as previously described in the proton case are recommended. It is the same for the primary protons and neutrons for which the Binary Cascade model is recommended too. Concerning the GenericIon, alpha, deuteron and triton, the **QMD model** has to be used. It better reproduces total charge changing cross-sections, β⁺ emitter, prompt gamma and charged particle production rates, as shown in

| Hadronic process | Particles | Geant4 processes | Geant4 models | Geant4 datasets | Energy range
--- | --- | --- | --- | --- | ---
Elastic scattering | GenericIon | G4HadronElasticProcess | G4LElastic | G4HadronElasticDataSet | ...
| All other particles | G4UHadronElasticProcess | G4HadronElastic | G4HadronElasticDataSet | ...
Inelastic process for protons | Protons | G4ProtonInelasticProcess | G4BinaryCascade | G4ProtonInelasticCrossSection | 0-20 GeV
Inelastic process for ions | Deuteron | G4DeuteronInelasticProcess | G4DEUTeronInelastic | G4TripathLightCrossSection | 0-80 MeV
| Triton | G4TritonInelasticProcess | G4TritonInelastic | G4TripathLightCrossSection | 80 MeV-20 GeV
| Alpha | G4AlphaInelasticProcess | G4LEAlphaInelastic | G4TripathLightCrossSection | 80 MeV-20 GeV
Inelastic process for pions | π⁺, π⁻ | G4PionPlusInelasticProcess | G4LEPionPlusInelastic | G4HadronInelasticDataSet | ...
| Neutron | G4NeutronCaptureProcess | G4NeutronHPCapture | G4NeutronHPCaptureData | 0-20 MeV
| G4Capture | G4NeutronCaptureDataSet | 14 MeV-20 GeV
| Neutron | G4NeutronInelasticProcess | G4NeutronHPInelastic | G4NeutronHPInelasticData | 0-20 MeV
| G4BinaryCascade | G4NeutronHPInelasticDataSet | 14 MeV-20 GeV
| G4LFission | G4HadronFissionDataSet | 14 MeV-20 GeV

Table 12. Overview of the recommended hadronic models and datasets for carbon ion beam simulation.
sections 4, 5 and 6.

Tables 11 and 12 summarize all the recommended simulation parameters in the proton and carbon ion cases respectively.

Several recent studies have reported comparisons of nuclear Monte Carlo models of Geant4 for proton and ion therapy [Pshenichnov06, Zacharatou08, Bohlen10, Grevillot10, Zahra10]. All show encouraging comparison results.

8. Goals and guidelines for future developments

As stated in section 2, the physics models of Monte Carlo codes, and in particular those for hadronic interactions, are subject to several uncertainties. Therefore continuous development, refining and benchmark with new experimental data are carried on by developers. The collections of results contained in this report, although demonstrating an impressive amount of positive results, confirm that there are still significant possible improvements. In the following we briefly summarize the main directions of development of relevance for hadron therapy and imaging.

8.1 FLUKA development

a) Continuing the verification of available models against isotope production data at energies of relevance for therapy (positron emitters first of all).
b) Improving the matching of rQMD and BME predictions around 100 MeV/n,
c) Improvements to BME model,
d) Introduction into BME and rQMD of suitable accounting for angular momentum estimation (this is fundamental to manage isomer production),
e) Improvements to the evaporation models (introducing for instance spin/parity considerations). Achieve a better treatment of discrete levels,
f) Improvements to the gamma de-excitation model (again, introducing spin/parity considerations),
g) Improvements to the Fermi break-up formalism,
h) Introduce preequilibrium emission in rQMD model.

8.2 GEANT4 development

a) Completing the verification of available models against isotope production data at energies of relevance for therapy (positron emitters first of all). A validation of the Geant4 hadronic models with complex heterogeneous phantoms [Parodi05] must be performed before modeling patients,
b) Improving the QMD and Binary Cascade models. The internal parameters used in these models should be adjusted for energies considered in medical applications. A discussion has begun with the Geant4 developers,
c) Improvements to the evaporation models.
d) Improvements to the gamma de-excitation model.
References


[ICRU00] International Commission on Radiation Units and Measurements ICRU, Nuclear data for neutron and proton radiotherapy and for radiation protection, Report 63, March 2000


Appendix 1: Geant4 parameter optimization

In the following sections, the influence of the Geant4 parameters and hadronic models on the Bragg peak position and β+ emitter production rates is studied. The proton case and carbon ion case are respectively considered.

1. Proton case

1.1 Influence of GEANT4 parameters (range cut, step size and database binning) on the Bragg Peak position

The version 6.0 of the GATE simulation toolkit associated with the version 9.2 of the GEANT4 software is used here. A 230 MeV mono-energetic proton beam with a circular shape (10 mm diameter) is simulated in a 60x60x60 cm$^3$ water tank. The depth-dose deposits are stored in element volumes (dosels) of 60x60x1 cm$^3$ attached to the water box.

As previously shown by L. Grévillot [Grevillot10] the pre-calculated stopping power table has a great influence on the Bragg peak position. **Recommendation: 20 bins/decade** (Appendix1-Figure 1).

When choosing a sufficient bin number, the range cut and step size parameters have no major impact on the proton range (Appendix1-Figure 2), which is defined, in the proton case, as the position of the 90% maximum dose point in the distal fall-off region of the Bragg Peak. **They should however be set to values equal to or lower than the pixel size (about 0.1 mm)** to accurately calculate the electron dose deposition [Grevillot10].

Appendix1-Figure 1. Influence of the binning parameters (7, 20 or 50 bins/decade) on dose calculation (230 MeV proton beam – water target). The GATE standard radiotherapy package physics list is used.
Appendix1-Figure 2. Influence of the step size value (0.1, 0.5, 1 and 2 mm) on dose computing (230 MeV proton beam – water target). The GATE standard radiotherapy package physics list is used. The range cut is set to 1 mm and the bin number to 20 bins/decade.

1.2 Influence of the ionization potential of water on the Bragg Peak position

As previously reported in [Soltani08], the value of the ionization potential of water is not yet clearly known. Values from 67.2 eV to 85 eV can be found in the literature (Appendix1-Table 1).

<table>
<thead>
<tr>
<th>I(eV)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>75.0 ±3</td>
<td>ICRU Report 37 and 39</td>
</tr>
<tr>
<td>67.2</td>
<td>ICRU Report 73</td>
</tr>
<tr>
<td>79.7</td>
<td>[Bichsel00], based on stooping experiment</td>
</tr>
<tr>
<td>81.8</td>
<td>[Dingfelder98] based on optical absorption</td>
</tr>
<tr>
<td>77</td>
<td>[Krämer00] based on Bragg peak position</td>
</tr>
<tr>
<td>80-85</td>
<td>[Emfietzoglou06] based on optical loss functions</td>
</tr>
<tr>
<td>80.8</td>
<td>[Paul03] based on [Bichsel00] and [Dingfelder98]</td>
</tr>
</tbody>
</table>

Appendix1-Table 1: Survey of the water-<\i> values reported in the literature [Soltani08].

The water-<\i> value is set to 70.9 eV by default in the 6.0 GATE version. However, when testing several water-<\i> values from 70 to 80 eV, we found that a 76.3 eV value yields the 329.4 mm CSDA range given by NIST with the Geant4 9.2 version (http://physics.nist.gov/PhysRefData/Star/Text/PSTAR.html) (Appendix1-Figures 3 and 4). This value is consistent with what was reported in previous studies [Kramer00] and the ICRU recommendations.
Appendix 1-Figure 3. Influence of the ionization potential of water on the proton range (230 MeV proton beam – water target). The GATE standard radiotherapy package physics list is used. The range cut and the step size are set to 1 mm and the bin number to 20 bins/decade.

Appendix 1-Figure 4. Influence of the ionization potential of water on dose calculation (230 MeV proton beam – water target). The GATE standard radiotherapy package physics list is used. The range cut and the step size are set to 1 mm and the bin number to 20 bins/decade.

1.3 Influence of the physics list on the Bragg Peak position

A 110 MeV mono-energetic proton beam with a circular shape (10 mm diameter) in a 30x30x30 cm PMMA box is simulated. Considering the previous recommendations, the pre-calculated table binning is set to 20 bins/decade. The mean excitation potential of the PMMA target is set to 68.5 eV [Pshenichnov06]. These two values will be kept unchanged unless otherwise stated. Eight physics lists listed in Appendix 1-Table 2 are tested.
Consider the proton range values (Appendix1-Table 3), there is no major impact of the physics list on the proton range. In all the tested cases, $77.54 < R_{\text{PMMA}}(110 \text{ MeV}) < 77.97 \text{ mm}$.

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Electromagnetic package</th>
<th>Step size (mm)</th>
<th>Range cut (mm)</th>
<th>Inelastic process for proton</th>
<th>Inelastic process for neutron</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Standard package</td>
<td>1 mm</td>
<td>1 mm</td>
<td>Standard</td>
<td>Precompound model</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0-170 MeV Precompound Model/170 MeV-500 GeV Binary Cascade model)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Standard package – Option 3 parameters-list</td>
<td>1 mm</td>
<td>1 mm</td>
<td>Standard</td>
<td>Precompound model</td>
</tr>
<tr>
<td>3</td>
<td>Low-energy package</td>
<td>1 mm</td>
<td>1 mm</td>
<td>Standard</td>
<td>G4NeutronHPorLEInelastic (E&lt;20 MeV) Precompound model (E&gt;20 MeV)</td>
</tr>
<tr>
<td>4</td>
<td>Standard package – Option 3 parameters-list</td>
<td>1 mm</td>
<td>1 mm</td>
<td>0-20 MeV G4LEProtonInelastic</td>
<td>0-20 MeV G4LENeutronInelastic Precompound Model Precompound Model</td>
</tr>
<tr>
<td>5</td>
<td>Standard package – Option 3 parameters-list</td>
<td>1 mm</td>
<td>1 mm</td>
<td>0-80 MeV Precompound Model 80 MeV-500 GeV Binary Cascade</td>
<td>0-80 MeV Precompound Model 80 MeV-500 GeV Binary Cascade</td>
</tr>
<tr>
<td>6</td>
<td>Standard package – Option 3 parameters-list</td>
<td>1 mm</td>
<td>1 mm</td>
<td>0 MeV-500 GeV Binary Cascade</td>
<td>0 MeV-500 GeV Binary Cascade</td>
</tr>
<tr>
<td>7</td>
<td>Standard package – Option 3 parameters-list</td>
<td>1 mm</td>
<td>1 mm</td>
<td>0 MeV-500 GeV G4QMDReaction</td>
<td>Precompound model</td>
</tr>
<tr>
<td>8</td>
<td>Standard package – Option 3 parameters-list</td>
<td>1 mm</td>
<td>1 mm</td>
<td>0 MeV-500 GeV Binary Cascade</td>
<td>0-20 MeV G4NeutronHPorLEInelastic Precompound Model</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20 MeV-500 GeV Binary Cascade</td>
</tr>
</tbody>
</table>

Appendix1-Table 2: Physics lists tested in our simulations.

1.4 Influence of the Geant4 version (Geant4 9.2 and Geant4 9.4) on the Bragg Peak position

The new version of the GATE simulation toolkit (GATE v6.1) associated with GEANT4 9.4 is used for comparison. A slight difference in the proton range (about 2 mm at 182 MeV) between the two versions is observed.
Appendix 1—Figure 5. Influence of the Geant4 version on the Bragg peak position (182 MeV proton beam – water target). The GATE physics list recommended in the proton case (Appendix 1) is used.

1.5 Influence of the physics list on the $\beta^+$ emitter production rate

As in the previous section, GATE 6.0 (GEANT4 9.2) was first used here to study the impact of the GATE physics list on the $\beta^+$ emitter production rate. A 110 MeV mono-energetic proton beam with a circular shape of 10 mm diameter was simulated in a 30x30x30 cm$^3$ PMMA box. Eight different physics lists (Appendix 1—Table 2) were tested. The choice of the physics list has a great impact on the $\beta^+$ emitter production rate and on the shape of the curve representing the $\beta^+$ emitter production rate as a function of the target depth (Appendix 1—Table 4 and Appendix 1—Figure 6). The Binary Cascade model (Configuration 6 or 8) is recommended for proton beams based on our results.

<table>
<thead>
<tr>
<th>Experimental results [Parodi04]</th>
<th>$^{11}$C</th>
<th>$\Delta^{11}$C (%)</th>
<th>$^{10}$C</th>
<th>$\Delta^{10}$C (%)</th>
<th>$^{15}$O</th>
<th>$\Delta^{15}$O (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Configuration 1</td>
<td>2200 ± 300</td>
<td>90 ± 30</td>
<td>800 ± 150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Configuration 2</td>
<td>862</td>
<td>-60.8</td>
<td>64</td>
<td>-28.9</td>
<td>394</td>
<td>-50.7</td>
</tr>
<tr>
<td>Configuration 3</td>
<td>868</td>
<td>-60.6</td>
<td>63</td>
<td>-30</td>
<td>361</td>
<td>-54.9</td>
</tr>
<tr>
<td>Configuration 4</td>
<td>898</td>
<td>-59.2</td>
<td>59</td>
<td>-34.4</td>
<td>395</td>
<td>-50.6</td>
</tr>
<tr>
<td>Configuration 5</td>
<td>1431</td>
<td>-34.9</td>
<td>78</td>
<td>-13.3</td>
<td>590</td>
<td>-26.3</td>
</tr>
<tr>
<td>Configuration 6</td>
<td>1357</td>
<td>-38.3</td>
<td>100</td>
<td>11.1</td>
<td>569</td>
<td>-28.9</td>
</tr>
<tr>
<td>Configuration 7</td>
<td>1793</td>
<td>-18.5</td>
<td>113</td>
<td>25.56</td>
<td>776</td>
<td>-3.0</td>
</tr>
<tr>
<td>Configuration 8</td>
<td>979</td>
<td>-55.5</td>
<td>78</td>
<td>-13.3</td>
<td>361</td>
<td>-54.9</td>
</tr>
<tr>
<td>Configuration 9</td>
<td>1829</td>
<td>-16.8</td>
<td>119</td>
<td>32.2</td>
<td>854</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Appendix 1—Table 4. Calculated yields of positron-emitting nuclei (per $10^7$ beam particles) produced by 110 MeV protons in the PMMA phantom. Experimental data by [Parodi04] are shown for comparison.
In addition to the physics list, the step size and range cut values were modified for configuration 1, to check that these criteria do not change the $\beta^+$ emitter production rates. The same comparisons were performed with proton beams of 140, 175 and 200 MeV. In each case, the use of the Binary Cascade Model as hadronic model for proton inelastic interaction (configuration 6 or 8) is recommended.

The same conclusions were obtained with the new version of GATE (v6.1). With GATE V6.1 (Geant4 9.4), the Binary Cascade Model is recommended to obtain a correct $\beta^+$ emitter production rate.

2. The carbon ion case

2.1 Influence of the Geant4 version on the Bragg peak position

270 MeV/u and 330 MeV/u carbon-ion beams in a water target (60x10x10 cm$^3$) were simulated with GATE v6.0 and v.6.1. Considering the deposited energies, there is no major impact of the Geant4 version on the carbon ion range.

2.2 Influence of the physics list on the Bragg peak position

A 260 MeV/u mono-energetic carbon-ion beam was simulated in a 60x10x10 cm$^3$ PMMA box. The Binary Cascade and QMD models were considered with GATE v6.1 (Geant4 9.4). Considering the depth-dose deposition, the physics list has no major impact on the carbon ion range (Appendix1-Figure 7). The conclusion seems however to be slightly different for higher energies (>270 MeV/u) for which the QMD model is recommended [Lechner10] (Appendix1-Table 5).
Appendix1-Figure 7. Impact of the physics list (Binary Cascade model or QMD model) on the dose deposition for a 260 MeV/u carbon ion beam in a PMMA target.

Appendix1-Table 5. Full width at half maximum (in mm) corresponding to $^{12}$C Bragg peak in water. Simulation results were produced with an initial energy spread of 0.15%, using either the ion binary cascade (BiC) or the QMD model [Lechner10].

<table>
<thead>
<tr>
<th></th>
<th>195 MeV/u</th>
<th>200 MeV/u</th>
<th>270 MeV/u</th>
<th>400 MeV/u</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment</td>
<td>2.3</td>
<td>2.3</td>
<td>4.1</td>
<td>10.3</td>
</tr>
<tr>
<td>Geant4 (QMD)</td>
<td>2.3</td>
<td>2.4</td>
<td>4.3</td>
<td>10.3</td>
</tr>
<tr>
<td>Geant4 (BiC)</td>
<td>2.3</td>
<td>2.4</td>
<td>4.4</td>
<td>12.5</td>
</tr>
</tbody>
</table>

2.3 Influence of the physics list on the $\beta^+$ emitter production rate

Appendix1-Table 6 compares integrated values of the $\beta^+$ emitter production rates obtained with Geant4 9.4 with the Binary Cascade and QMD models. It confirms the choice of the QMD model in the case of carbon ion simulations.
Appendix1-Table 6. $\beta^+$ emitter production yields in a PMMA target for different incident energies. The Binary Cascade model (BiC) and QMD model were used in the Geant4 9.4 version.

<table>
<thead>
<tr>
<th>212.12 MeV/u</th>
<th>Experiment</th>
<th>BiC</th>
<th>QMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{12}C$</td>
<td>$8 \pm 3 \times 10^{-4}$</td>
<td>$1.5 \times 10^{-2}$</td>
<td>$9.3 \times 10^{-3}$</td>
</tr>
<tr>
<td>$^{13}C$</td>
<td>$10.5 \pm 1.3 \times 10^{-2}$</td>
<td>$11 \times 10^{-2}$</td>
<td>$9.3 \times 10^{-2}$</td>
</tr>
<tr>
<td>$^{16}O$</td>
<td>$2.1 \pm 0.3 \times 10^{-2}$</td>
<td>$2.4 \times 10^{-2}$</td>
<td>$1.9 \times 10^{-2}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>259.5 MeV/u</th>
<th>Experiment</th>
<th>BiC</th>
<th>QMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{12}C$</td>
<td>$1.2 \pm 0.3 \times 10^{-2}$</td>
<td>$2.1 \times 10^{-2}$</td>
<td>$1.6 \times 10^{-2}$</td>
</tr>
<tr>
<td>$^{13}C$</td>
<td>$14.7 \pm 1.6 \times 10^{-2}$</td>
<td>$16 \times 10^{-2}$</td>
<td>$13.6 \times 10^{-2}$</td>
</tr>
<tr>
<td>$^{16}O$</td>
<td>$3.1 \pm 0.4 \times 10^{-2}$</td>
<td>$3.5 \times 10^{-2}$</td>
<td>$3.1 \times 10^{-2}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>343.46 MeV/u</th>
<th>Experiment</th>
<th>BiC</th>
<th>QMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{12}C$</td>
<td>$1.5 \pm 0.3 \times 10^{-2}$</td>
<td>$2.2 \times 10^{-2}$</td>
<td>$2.5 \times 10^{-2}$</td>
</tr>
<tr>
<td>$^{13}C$</td>
<td>$19.9 \pm 2.4 \times 10^{-2}$</td>
<td>$22 \times 10^{-2}$</td>
<td>$22 \times 10^{-2}$</td>
</tr>
<tr>
<td>$^{16}O$</td>
<td>$5 \pm 0.4 \times 10^{-2}$</td>
<td>$5.1 \times 10^{-2}$</td>
<td>$5.6 \times 10^{-2}$</td>
</tr>
</tbody>
</table>
Appendix 2: GEANT4 physics list recommended for the proton beam simulations

#=====================================  
# Electromagnetic processes  
#=====================================  

/gate/physics/addProcess PhotoElectric  
/gate/physics/addProcess Compton  
/gate/physics/addProcess GammaConversion  

/gate/physics/addProcess ElectronIonisation  
/gate/physics/processes/ElectronIonisation/setStepFunction e+ 0.2 0.1 mm  
/gate/physics/processes/ElectronIonisation/setStepFunction e- 0.2 0.1 mm  

/gate/physics/addProcess Bremsstrahlung  
/gate/physics/addProcess PositronAnnihilation  

/gate/physics/addProcess MultipleScattering  
/gate/physics/processes/MultipleScattering/setGeometricalStepLimiterType e- distanceToBoundary  
/gate/physics/processes/MultipleScattering/setGeometricalStepLimiterType e+ distanceToBoundary  

/gate/physics/addProcess HadronIonisation  
/gate/physics/removeProcess HadronIonisation deuteron  
/gate/physics/removeProcess HadronIonisation triton  
/gate/physics/removeProcess HadronIonisation He3  
/gate/physics/removeProcess HadronIonisation alpha  
/gate/physics/removeProcess HadronIonisation GenericIon  
/gate/physics/processes/HadronIonisation/setStepFunction proton 0.2 0.05 mm  
/gate/physics/processes/HadronIonisation/setStepFunction pi+ 0.2 0.05 mm  
/gate/physics/processes/HadronIonisation/setStepFunction pi- 0.2 0.05 mm  

/gate/physics/addProcess IonIonisation  
/gate/physics/processes/IonIonisation/setStepFunction GenericIon 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction alpha 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction deuteron 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction triton 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction He3 0.1 0.02 mm

#=====================================  
# Hadronic processes  
#=====================================  

/gate/physics/addProcess HadronElastic GenericIon  
/gate/physics/processes/HadronElastic/setModel G4LElastic GenericIon  

/gate/physics/addProcess UHadronElastic  
/gate/physics/processes/UHadronElastic/setModel G4HadronElastic  
/gate/physics/processes/UHadronElastic/setDataSet G4HadronElasticDataSet  

/gate/physics/addProcess ProtonInelastic
/gate/physics/processes/ProtonInelastic/setModel G4BinaryCascade
/gate/physics/processes/ProtonInelastic/G4BinaryCascade/setEmin 0 MeV
/gate/physics/processes/ProtonInelastic/G4BinaryCascade/setEmax 500 GeV

/gate/physics/processes/IonInelastic
/gate/physics/processes/IonInelastic/setModel G4BinaryLightIonReaction
/gate/physics/processes/IonInelastic/setModel G4LEDDeuteronInelastic deuteron
/gate/physics/processes/IonInelastic/setModel G4LETritonInelastic triton
/gate/physics/processes/IonInelastic/setModel G4LEAlphaInelastic alpha
/gate/physics/processes/IonInelastic/G4BinaryLightIonReaction/setEmin 80 MeV deuteron
/gate/physics/processes/IonInelastic/G4BinaryLightIonReaction/setEmax 20 GeV deuteron
/gate/physics/processes/IonInelastic/G4BinaryLightIonReaction/setEmin 80 MeV triton
/gate/physics/processes/IonInelastic/G4BinaryLightIonReaction/setEmax 20 GeV triton
/gate/physics/processes/IonInelastic/G4BinaryLightIonReaction/setEmin 80 MeV alpha
/gate/physics/processes/IonInelastic/G4BinaryLightIonReaction/setEmax 20 GeV alpha
/gate/physics/processes/IonInelastic/G4LEDDeuteronInelastic/setEmin 0 MeV deuteron
/gate/physics/processes/IonInelastic/G4LEDDeuteronInelastic/setEmax 80 MeV deuteron
/gate/physics/processes/IonInelastic/G4LETritonInelastic/setEmin 0 MeV triton
/gate/physics/processes/IonInelastic/G4LETritonInelastic/setEmax 80 MeV triton
/gate/physics/processes/IonInelastic/G4LEAlphaInelastic/setEmin 0 MeV alpha
/gate/physics/processes/IonInelastic/G4LEAlphaInelastic/setEmax 80 MeV alpha
/gate/physics/processes/IonInelastic/G4LETritonInelastic/setDataSet G4IonsShenCrossSection GenericIon
/gate/physics/processes/IonInelastic/setDataSet G4TribathiLightCrossSection deuteron
/gate/physics/processes/IonInelastic/setDataSet G4TribathiLightCrossSection triton
/gate/physics/processes/IonInelastic/setDataSet G4TribathiLightCrossSection alpha

/gate/physics/processes/PionPlusInelastic
/gate/physics/processes/PionPlusInelastic/setModel G4LEPionPlusInelastic
/gate/physics/processes/PionMinusInelastic
/gate/physics/processes/PionMinusInelastic/setModel G4LEPionMinusInelastic

/gate/physics/processes/NeutronCapture
/gate/physics/processes/NeutronCapture/setModel G4NeutronHPCapture
/gate/physics/processes/NeutronCapture/G4NeutronHPCapture/setEmin 0 MeV
/gate/physics/processes/NeutronCapture/G4NeutronHPCapture/setEmax 20 MeV
/gate/physics/processes/NeutronCapture/setModel G4LCapture
/gate/physics/processes/NeutronCapture/G4LCapture/setEmin 14 MeV
/gate/physics/processes/NeutronCapture/G4LCapture/setEmax 20 GeV
/gate/physics/processes/NeutronCapture/setDataSet G4NeutronHPCaptureData
/gate/physics/processes/NeutronCapture/setDataSet G4HadronCaptureDataSet

/gate/physics/processes/Fission
/gate/physics/processes/Fission/setModel G4NeutronHPFission
/gate/physics/processes/Fission/G4NeutronHPFission/setEmin 0 MeV
/gate/physics/processes/Fission/G4NeutronHPFission/setEmax 20 MeV
/gate/physics/processes/Fission/setModel G4LFission
/gate/physics/processes/Fission/G4LFission/setEmin 14 MeV
/gate/physics/processes/Fission/G4LFission/setEmax 20 GeV
/gate/physics/processes/Fission/setDataSet G4NeutronHPFissionData
/gate/physics/processes/Fission/setDataSet G4HadronFissionDataSet

/gate/physics/processes/NeutronInelastic
/gate/physics/processes/NeutronInelastic/setModel G4NeutronHPInelastic
/gate/physics/processes/NeutronInelastic/G4NeutronHPInelastic/setEmin 0 MeV
/gate/physics/processes/NeutronInelastic/G4NeutronHPInelastic/setEmax 20 MeV
/gate/physics/processes/NeutronInelastic/setDataSet G4NeutronHPInelasticData neutron
/gate/physics/processes/NeutronInelastic/setModel G4BinaryCascade
/gate/physics/processes/NeutronInelastic/G4BinaryCascade/setEmin 14 MeV
/gate/physics/processes/NeutronInelastic/G4BinaryCascade/setEmax 20 GeV
/gate/physics/processes/NeutronInelastic/setDataSet G4NeutronInelasticCrossSection neutron

/gate/physics/addProcess Decay

#===================================== # Options #=====================================

#===================================== # Options #=====================================

/gate/physics/setEMin 0.1 keV
/gate/physics/setEMax 1 GeV
/gate/physics/setDEDXBinning 140
/gate/physics/setLambdaBinning 140

/gate/physics/Gamma/SetCutInRegion world 1 mm
/gate/physics/Electron/SetCutInRegion world 1 mm
/gate/physics/Positron/SetCutInRegion world 1 mm

/gate/physics/Gamma/SetCutInRegion cible 0.1 mm
/gate/physics/Electron/SetCutInRegion cible 0.1 mm
/gate/physics/Positron/SetCutInRegion cible 0.1 mm

/gate/physics/SetMaxStepSizeInRegion cible 0.1 mm
/#/gate/physics/ActivateStepLimiter e-
/#/gate/physics/ActivateStepLimiter e+
/#/gate/physics/ActivateStepLimiter proton

70
Appendix 3: GEANT4 physics list recommended for the carbon ion beam simulations

#=====================================  
# Electromagnetic processes  
#=====================================  

/gate/physics/addProcess PhotoElectric  
/gate/physics/addProcess Compton  
/gate/physics/addProcess GammaConversion  

/gate/physics/addProcess ElectronIonisation  
/gate/physics/processes/ElectronIonisation/setStepFunction e+ 0.2 0.1 mm  
/gate/physics/processes/ElectronIonisation/setStepFunction e- 0.2 0.1 mm  

/gate/physics/addProcess Bremsstrahlung  
/gate/physics/addProcess PositronAnnihilation  

/gate/physics/addProcess MultipleScattering  
/gate/physics/processes/MultipleScattering/setGeometricalStepLimiterType e- distanceToBoundary  
/gate/physics/processes/MultipleScattering/setGeometricalStepLimiterType e+ distanceToBoundary  

/gate/physics/addProcess HadronIonisation  
/gate/physics/removeProcess HadronIonisation deuter  
/gate/physics/removeProcess HadronIonisation triton  
/gate/physics/removeProcess HadronIonisation He3  
/gate/physics/removeProcess HadronIonisation alpha  
/gate/physics/removeProcess HadronIonisation GenericIon  
/gate/physics/processes/HadronIonisation/setStepFunction proton 0.2 0.05 mm  
/gate/physics/processes/HadronIonisation/setStepFunction pi+ 0.2 0.05 mm  
/gate/physics/processes/HadronIonisation/setStepFunction pi- 0.2 0.05 mm  

/gate/physics/addProcess IonIonisation  
/gate/physics/processes/IonIonisation/setStepFunction GenericIon 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction alpha 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction deuteron 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction triton 0.1 0.02 mm  
/gate/physics/processes/IonIonisation/setStepFunction He3 0.1 0.02 mm  

#=====================================  
# Hadronic processes  
#=====================================  

/gate/physics/addProcess HadronElastic GenericIon  
/gate/physics/processes/HadronElastic/setModel G4LElastic GenericIon  

/gate/physics/addProcess UHadronElastic  
/gate/physics/processes/UHadronElastic/setModel G4HadronElastic  
/gate/physics/processes/UHadronElastic/setDataSet G4HadronElasticDataSet  

/gate/physics/addProcess ProtonInelastic  
/gate/physics/processes/ProtonInelastic/setModel G4BinaryCascade
/gate/physics/processes/ProtonInelastic/G4BinaryCascade/setEmin 0 MeV
/gate/physics/processes/ProtonInelastic/G4BinaryCascade/setEmax 20 GeV
/gate/physics/processes/ProtonInelastic/setDataSet G4ProtonInelasticCrossSection proton

/gate/physics/addProcess IonInelastic
/gate/physics/processes/IonInelastic/setModel G4QMDReaction GenericIon
/gate/physics/processes/IonInelastic/setModel G4QMDReaction alpha
/gate/physics/processes/IonInelastic/setModel G4QMDReaction deuteron
/gate/physics/processes/IonInelastic/setModel G4QMDReaction triton
/gate/physics/processes/IonInelastic/G4QMDReaction/setEmin 0 MeV deuteron
/gate/physics/processes/IonInelastic/G4QMDReaction/setEmax 20 GeV deuteron
/gate/physics/processes/IonInelastic/G4QMDReaction/setEmin 0 MeV alpha
/gate/physics/processes/IonInelastic/G4QMDReaction/setEmax 20 GeV alpha
/gate/physics/processes/IonInelastic/G4QMDReaction/setEmin 0 MeV triton
/gate/physics/processes/IonInelastic/G4QMDReaction/setEmax 20 GeV triton

/gate/physics/addProcess PionPlusInelastic
/gate/physics/processes/PionPlusInelastic/setModel G4LEPionPlusInelastic

/gate/physics/addProcess PionMinusInelastic
/gate/physics/processes/PionMinusInelastic/setModel G4LEPionMinusInelastic

/gate/physics/addProcess NeutronCapture
/gate/physics/processes/NeutronCapture/setModel G4NeutronHCapture
/gate/physics/processes/NeutronCapture/G4NeutronHCapture/setEmin 0 MeV
/gate/physics/processes/NeutronCapture/G4NeutronHCapture/setEmax 20 MeV
/gate/physics/processes/NeutronCapture/setModel G4LCapture
/gate/physics/processes/NeutronCapture/G4LCapture/setEmin 14 MeV
/gate/physics/processes/NeutronCapture/G4LCapture/setEmax 20 GeV
/gate/physics/processes/NeutronCapture/setDataSet G4NeutronHCaptureData
/gate/physics/processes/NeutronCapture/setDataSet G4HadronCaptureDataSet

/gate/physics/addProcess Fission
/gate/physics/processes/Fission/setModel G4NeutronHFission
/gate/physics/processes/Fission/G4NeutronHFission/setEmin 0 MeV
/gate/physics/processes/Fission/G4NeutronHFission/setEmax 20 MeV
/gate/physics/processes/Fission/setModel G4LFission
/gate/physics/processes/Fission/G4LFission/setEmin 14 MeV
/gate/physics/processes/Fission/G4LFission/setEmax 20 GeV
/gate/physics/processes/Fission/setDataSet G4NeutronHFissionData
/gate/physics/processes/Fission/setDataSet G4HadronFissionDataSet

/gate/physics/addProcess NeutronInelastic
/gate/physics/processes/NeutronInelastic/setModel G4NeutronHPInelastic
/gate/physics/processes/NeutronInelastic/G4NeutronHPInelastic/setEmin 0 MeV
/gate/physics/processes/NeutronInelastic/G4NeutronHPInelastic/setEmax 20 MeV
/gate/physics/processes/NeutronInelastic/setDataSet G4NeutronHPInelasticData neutron
/gate/physics/processes/NeutronInelastic/setModel G4BinaryCascade
/gate/physics/processes/NeutronInelastic/G4BinaryCascade/setEmin 14 MeV
/gate/physics/processes/NeutronInelastic/G4BinaryCascade/setEmax 20 GeV
/gate/physics/processes/NeutronInelastic/setDataSet G4NeutronInelasticCrossSection neutron

/gate/physics/addProcess Decay

#=====================================#    Options#=====================================
/gate/physics/setEMin 0.1 keV
/gate/physics/setEMax 1 GeV
/gate/physics/setDEDXBinning 140
/gate/physics/setLambdaBinning 140

/gate/physics/Gamma/SetCutInRegion world 1 mm
/gate/physics/Electron/SetCutInRegion world 1 mm
/gate/physics/Positron/SetCutInRegion world 1 mm

/gate/physics/Gamma/SetCutInRegion cible 0.1 mm
/gate/physics/Electron/SetCutInRegion cible 0.1 mm
/gate/physics/Positron/SetCutInRegion cible 0.1 mm

/gate/physics/SetMaxStepSizeInRegion cible 0.1 mm

/gate/physics/displayCuts
Appendix 4: Details on proton beam MCNPX simulations

References about the use of MCNPX in proton therapy are given for example in [Stank09].

1. Energy deposition

Three methods are available in MCNPX to tally energy deposition: F6 and F8 tallies and the energy deposition mesh tally type 3. For more details we refer to the MCNPX user’s guide [MCNPX08]. In the present work, F6 tally was used to score dose: scores dose on geometrical elements defined as part of the standard problem geometry. For depth dose curves simulation protons together with neutrons, photons, electrons, deuterons, tritons, helium-3 and alpha particles were transported. Energy cut-off for protons was set to 0.1 MeV, energy particles which fall below are deposited locally. The scoring phantom for depth dose curves was a cylinder of 15 cm radius, 35 cm long, subdivided in slabs along the main cylinder axis. The source was assumed to be a point source with a Gaussian energy distribution. \(10^6\) initial particles were used.

2. \(\beta^+\) emitter production

Production rates of \(^{15}\)O and \(^{11}\)C cannot be directly scored in MCNPX. In order to calculate them we used the method also in [Parodi07a] with the FLUKA code where proton fluences scored by MCNPX were multiplied for respectively \(^{16}\)O(p,pn)\(^{15}\)O and \(^{12}\)C(p,pn)\(^{11}\)C cross sections. This method is also described in the code manual (p. 5-110 of [MCNPX08]). The production cross sections for \(^{15}\)O and \(^{11}\)C cannot be taken directly from the proton library of MCNPX because as explained above the MT5 reaction number is inclusive, meaning that it is not possible to distinguish the particular nuclear reactions that constitute MT5.

Three different data sets (figure 1 and 2) were used here to calculate \(^{15}\)O and \(^{11}\)C production rates:
   i. The same set used by Parodi et al. [Parodi02],
   ii. Talys Based Evaluated Nuclear Data Library [TENDL10],
   iii. Set produced from the MCNPX CEM model.

In Appendix4-Figures 1 and 2 we can already note that the production cross section datasets are quite different for both \(^{15}\)O and \(^{11}\)C. The Parodi cross sections is a collection of measured data, TENDL-2010 cross sections are computed by means of TALYS system. The cross sections using the internal MCNPX model might not be complete because as already mentioned above models do not perform well at low energies. The differences among data sets are consistent with literature [Beebe03].
Appendix 4-Figure 1. $^{16}\text{O}(p,pn)^{15}\text{O}$ reaction cross sections taken from [Parodi02], [TENDL10], [ICRU00] and produced by the CEM model of MCNPX.

Appendix 4-Figure 2. $^{12}\text{C}(p,pn)^{11}\text{C}$ reaction cross sections taken from [Parodi02], [TENDL10], [ICRU00] and produced by the CEM model of MCNPX.
In Appendix 4-Figures 3 and 4 production of $^{11}$C and $^{15}$O in (reactions/particle) obtained from the three cross sections data sets described previously are shown.

Appendix 4-Figure 3. $^{11}$C production as a function of the penetration depth calculated for a 140 MeV proton beam in a PMMA target using the three cross section sets described previously.

Appendix 4-Figure 4. $^{15}$O production as a function of the penetration depth calculated for a 140 MeV proton beam in a PMMA target using the three cross section sets described previously.
In Appendix 4-Table 1 the total amount of $^{11}\text{C}$ and $^{15}\text{O}$ produced in nuclear interactions with the volume of PMMA obtained from simulations using the three data sets for a 140 MeV proton beam is depicted and compared to measured and simulated data with FLUKA taken from [Parodi04].

<table>
<thead>
<tr>
<th></th>
<th>$^{11}\text{C}$</th>
<th>$^{15}\text{O}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental results</td>
<td>3400 ± 400</td>
<td>1230 ± 180</td>
</tr>
<tr>
<td>FLUKA results</td>
<td>2670</td>
<td>1230</td>
</tr>
<tr>
<td>Parodi et al cross sections</td>
<td>2638 ± 1</td>
<td>897 ± 0.3</td>
</tr>
<tr>
<td>TENDL cross sections</td>
<td>744 ± 0.5</td>
<td>188 ± 0.1</td>
</tr>
<tr>
<td>CEM internal model cross sections</td>
<td>1206 ± 0.4</td>
<td>721 ± 0.2</td>
</tr>
</tbody>
</table>

Appendix 4-Table 1. Yields of $^{11}\text{C}$ and $^{15}\text{O}$ (per $10^5$ particles) produced by 140 MeV protons in a PMMA volume. Experimental values and FLUKA simulated data [Parodi04] are shown for comparison.

At the moment MCNPX (version 2.7C) is not transporting and scoring tallies for positrons emitted during nuclear interactions. From $^{12}\text{C}(p, pn)^{11}\text{C}$ reaction, positrons with a maximum energy of 0.96 MeV [Beebe03] are created, while for reaction $^{16}\text{O}(p, pn)^{15}\text{O}$ the maximum energy of the positrons is 1.72 MeV. These positron energies correspond to a range of 0.4-0.8 cm in water.
Appendix 5: FLUKA simulations for the prediction of the $\beta^+$ emitter production

Extensive applications of FLUKA to the prediction of $\beta^+$ emitter production for PET monitoring have been already reported in previous works which are briefly recalled in the following.

For proton therapy, in [Parodi04] it was observed that the intrinsic nuclear models of the code were capable to produce $\beta^+$ emitter absolute yields in reasonable agreement with experimental values (Table 6), but failed to correctly reproduce the slope of the spatial pattern of irradiation-induced activity along depth (Figure 20, with Appendix5-Figure 1). Hence this finding prompted a practical work-around strategy of combining the energy-dependent proton fluence with experimental cross-sections for the activation channels of interest, as also in line with the recommendations from [ICRU00] to use experimental cross-sections for PET applications whenever available. The calculation approach described in [Parodi04] provided so far satisfaction agreement between simulations and experimental data for both phantom investigations with mono-energetic and spread-out Bragg peaks (Appendix1-Figure 1) as well as for first clinical studies [Parodi07b].

The approach used for protons is however not recommendable for heavier ions because of the additional contribution of projectile fragmentation to $\beta^+$ emitter production. Therefore, a first validation of the predictions of the FLUKA internal models for $\beta^+$ emitter yields induced by therapeutic carbon and oxygen ion irradiation has been performed in [Sommerer07]. Overall, promising agreement could be obtained between FLUKA simulations and experimental data both in terms of quantitative yield and spatial distributions, as illustrated in Tables 7, 8 and 9 and Appendix5-Figure 1 for carbon ion irradiation of PMMA targets. Nevertheless, this work also highlighted the needs of further model developments for improved results, as currently being undertaken in the framework of the ENVISION project.
Appendix 5-Figure 1. Comparison between measured and simulated activity distributions measured during (left) and after (right) a 260 MeV/u carbon ion irradiation of a PMMA target [Sommerer07]. Simulated results additionally highlight the impact of including the BME models of FLUKA extending nuclear interactions below 100 MeV/u.