

Developments of the nuclear reaction and fragmentation models in FLUKA for ion collisions at therapeutic energies

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Abstract

Protons and carbon ions have been used for decades in several institutes worldwide for cancer treatments. The treatment planning systems rely on accurate modeling of the nuclear reaction and fragmentation processes that occur inside the patient's tissues. The accuracy of FLUKA in the field of proton and carbon ion therapy has been extensively validated. Helium ions are considered as a viable alternative to protons and carbon ions as they are featured by intermediate physical and biological properties. However, as the interest on helium ions is growing again only recently, and therefore some refinements on the FLUKA physics models for helium ions are still needed, prior to the deployment of FLUKA for helium ion therapy. In this work, nuclear reactions of primary helium ions were investigated in the therapeutic energy range and in elements of interest for hadron therapy (carbon and oxygen). Based on recent experimental measurements performed at the Heidelberg Ion-Beam Therapy center by the Space Radiation physics sub-group of the Biophysics Department at GSI (Germany), the nuclear reaction cross section models implemented in FLUKA were refined. This allowed the achievement of more accurate dose calculations.

1 Background

Ionizing radiation is exploited in radiotherapy to damage malignant cells' DNA and therefore to cause tumor death. In radiotherapy the absorbed dose D is defined as the energy deposited per unit of mass by ionizing radiation and is measured in gray (Gy). The main goal of radiotherapy is to deliver high dose to the tumor, such to completely destroy it, whereas the dose delivered to healthy tissues has to be minimized as much as possible. Unlike photons, the depth-dose profile of light ions is characterized by an initial low plateau and a so called Bragg peak at the end of the particle range. The Bragg peak is due to the increasing energy loss, dE , in the unit path, dx , with decreasing particle velocity, as described by the Bethe-Bloch equation.

As a result of the physical characteristics of ions, especially in the case of deep-seated tumors, hadron therapy offers an improved dose conformation to the tumor and a better sparing of the surrounding healthy tissues in comparison to conventional radiotherapy [1]. Furthermore, carbon ions possess a higher biological effectiveness, which makes them particularly suitable for treating radio-resistant tumors.

Protons and carbon ions have been implemented for radiotherapy treatments for decades worldwide. In addition, helium ions are planned to be used in the near future at the Heidelberg Ion-Beam Therapy center (HIT) in Germany [2, 3]. In comparison to protons, helium ions shows a reduced lateral beam spread. With respect to carbon ions, helium ions have a much lower linear energy transfer and therefore, a less pronounced biological effectiveness, which might be particularly beneficial in the case of pediatric

patients. Nevertheless, in the case of ions heavier than protons, the quality of biological dose calculations in hadron therapy strongly depends on the ability to predict secondary fragments produced as a consequence of non-elastic nuclear reactions that occur in the patient's tissues. The resulting fragments have broader lateral distributions and most have longer paths than the primary particles, as range scales with A/Z^2 . Therefore, they can reach and damage healthy tissues surrounding the tumor. For accurate calculations of the dose and relative biological effectiveness (RBE), the secondary fragments produced, as well as their physical and biological properties, have to be correctly predicted. Commercial treatment planning systems (TPS) used in clinics are supported by Monte Carlo particle transport and interaction codes, which are able to model non-elastic nuclear reactions and fragment production very accurately. For instance, the FLUKA code [4, 5], developed by an INFN-CERN collaboration, is used at HIT (Heidelberg, Germany), MIT (Marburg, Germany) and CNAO (Pavia, Italy) to provide all the basic inputs to the TPS and to validate the TPS's dose calculations, especially in complex scenarios [6]. Our research aims at improving the physics models embedded in FLUKA for helium ions, in order to calculate the dose delivered during radiotherapy treatments more accurately.

2 Method

2.1 Nuclear reaction cross sections in FLUKA

Nucleus-nucleus reaction cross sections are calculated in FLUKA based on a cross-section parametrization, developed by NASA, and whose original expression is [7]:

$$\sigma_R = \pi r_0^2 (A_p^{1/3} + A_t^{1/3} + \delta_E)^2 (1 - R_C B / E_{cm}) X_m \quad (1)$$

where $r_0 = 1.1$ fm, A_p and A_t are the mass number of the projectile and target, respectively, δ_E is an energy dependent parameter which includes the effects of Pauli blocking and transparency, R_C is a Coulomb multiplier, needed to make the formalism for light, medium and heavy systems unique, B is the energy-dependent Coulomb interaction barrier, E_{cm} is the colliding system center of mass energy, X_m is a low-energy multiplier that accounts for the strength of the optical model interaction and differs from the unity only in case of light systems. In [7] δ_E was expressed in terms of a factor D that depends on the density of the colliding system. In particular, for alpha-nucleus collisions, the proposed best values for D was:

$$D_{Tripathi} = 2.77 - 8.0 \cdot 10^{-3} \cdot A_t + 1.8 \cdot 10^{-5} \cdot A_t^2 - \frac{0.8}{1 + e^{\frac{250-E}{75}}} \quad (2)$$

However, to increase the agreement with experimental data at low energies, some refinement in the original Tripathi model is needed. For instance, in [8] the following value for D was proposed:

$$D_{Tripathi}^{optimized} = 2.2 - 8.0 \cdot 10^{-3} \cdot A_t + 1.8 \cdot 10^{-5} \cdot A_t^2 - \frac{0.3}{1 + e^{\frac{120-E}{50}}} \quad (3)$$

Concerning FLUKA, the theoretical expression from [7] was empirically modified [9], based on experimental data available in literature (e.g. [10, 11]). New measurements in the therapeutic energy range [8, 12] have allowed further refinements of the FLUKA model for nuclear reaction cross sections of helium ions in graphite and oxygen, as discussed in section 3.1.

2.2 Dose calculations in FLUKA

Continuous ionizing energy losses of charge particles are modeled in FLUKA based on a continuous slowing down approach on the basis of the Bethe-Bloch equation. However, in addition to the energy loss due to inelastic collisions with atomic electrons, nuclear interactions with material nuclei have to be considered, as they influence the beam fluence, and therefore the dose delivered during radiotherapy treatments. The probability of nuclear interactions are sampled in FLUKA on an event-by-event basis. The probability, P , that a particle travels a path length x without undergoing a nuclear reaction is:

$$P(x) = e^{-\frac{x N_A \rho \sigma_R}{A_t}} \quad (4)$$

where σ_R is the total nuclear reaction cross section. However, in many experiments (e.g. [8, 12]) only mass- and charge-changing cross sections, i.e. variations in the mass number or atomic number of the projectile, could be measured, whereas for dose calculations, the *total* nuclear reaction cross section is needed. The difference between total and mass-changing cross section arises as some primary helium ions may undergo a non-elastic reaction in the target without undergoing fragmentation. The amount of such events was estimated in FLUKA at different energies in the therapeutic energy range (50-250 MeV/u). Based on these results, an energy dependent normalization factor was calculated. Applying the normalization factor to the fragmentation cross sections shown in Figure 1, the total nuclear reaction cross section was obtained. The total cross section values were finally used to calculate the dose delivered from helium ion beams, at different therapeutic initial energies, as a function of depth in water. Experimental data measured at HIT [13] were compared with the FLUKA predictions.

3 Results and Discussion

3.1 Nuclear reaction cross sections in FLUKA

Especially at low energies the lack of experimental data for light and medium systems makes benchmarking of the nuclear reaction models in FLUKA and validation of the FLUKA predictions a challenging task. As example, Figures 1 a) and c) show the fragmentation cross sections for ${}^4\text{He}+{}^{12}\text{C}$ and ${}^4\text{He}+{}^{16}\text{O}$ collisions that were implemented in the FLUKA development version 2017.1. Comparisons with recently acquired experimental data on fragmentation cross sections of ${}^4\text{He}$ on ${}^{12}\text{C}$ [8] showed that a refinement of the fragmentation cross section curve in FLUKA was required in the therapeutic energy range. Subsequent measurements of ${}^4\text{He}$ ion collisions in ${}^{16}\text{O}$ also confirmed those findings [12]. The new fragmentation cross section curves, which have been implemented in the FLUKA development version starting from 2018, are shown in Figure 1 b) and d).

3.2 Dose calculations in FLUKA

Dose calculations were performed using the FLUKA development version 2017.1 (which contains the old cross section curves, shown on the left in Figure 1) and 2018.0 (which contains the new cross section curves, shown on the right in Figure 1). For both versions the normalization factor needed to obtain the total nuclear reaction cross section from the fragmentation cross sections was considered (see section 2.2). As example, table 1 lists the percentage of primary helium ions that, according to predictions of the FLUKA models, interact in the target without breaking up for some representative energy, both for carbon and oxygen targets.

Table 1: Percentage of primary helium ions calculated with FLUKA that interact in the target without breaking up, for 5 initial beam energies in the therapeutic energy range.

Beam energy (MeV/u)	Target material	
	Carbon	Oxygen
50	14.7%	11.0%
100	11.5%	8.0%
150	7.8%	7.6%
200	5.7%	4.9%
250	4.6%	4.2%

Figure 2 shows the dose calculated in water using the FLUKA development versions 2017.1 and 2018.0, for two initial beam energies, 100 and 190 MeV/u. Simulations are compared with experimental data

[13], and the results are normalized to the integrated area under the simulated curves. In the case of the FLUKA development version 2018.0, less primary ions reach the Bragg peak, due to the increased nuclear reaction cross section values, and consequently higher probability that the primary ions undergo a nuclear reaction, in the more recent FLUKA development version (see Figure 1 and Eq. 4). As a result, a stronger degradation of the Bragg peak and therefore a significant improvement on the dose calculation was achieved, especially for more energetic beams. For example, for the cases shown in Figure 2, the maximum difference between experimental and simulated data at the peak was reduced from 3% to 0.5% for the less energetic beam, and from 8% to 1.6% in the more energetic beam.

The residual differences are not a critical issue, as they are mitigated when the so-called spread-out Bragg peak is used in the clinical practice, i.e. hundreds or even thousands of single pencil beams are combined together in order to cover the entire tumor in depth. Consequently, the differences between experiments and simulations, as far as dose calculations are concerned, are sufficiently small with respect to the clinical requirements.

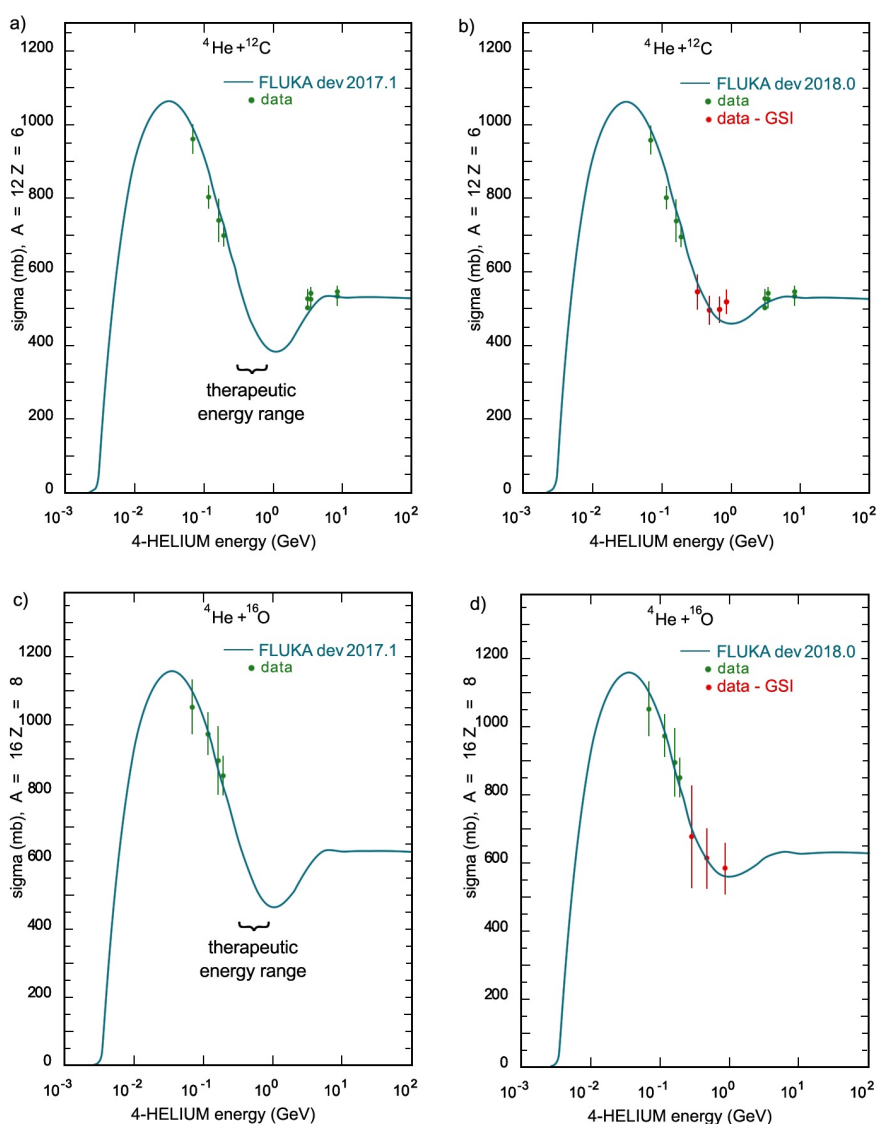


Fig. 1: Fragmentation cross section curves for ${}^4\text{He}+{}^{12}\text{C}$ (top) and ${}^4\text{He}+{}^{16}\text{O}$ (bottom) collisions implemented in the previous FLUKA development version, 2017.1 (left) and in the new FLUKA development version, 2018.0 (right), compared with experimental measurements [8, 10, 11]

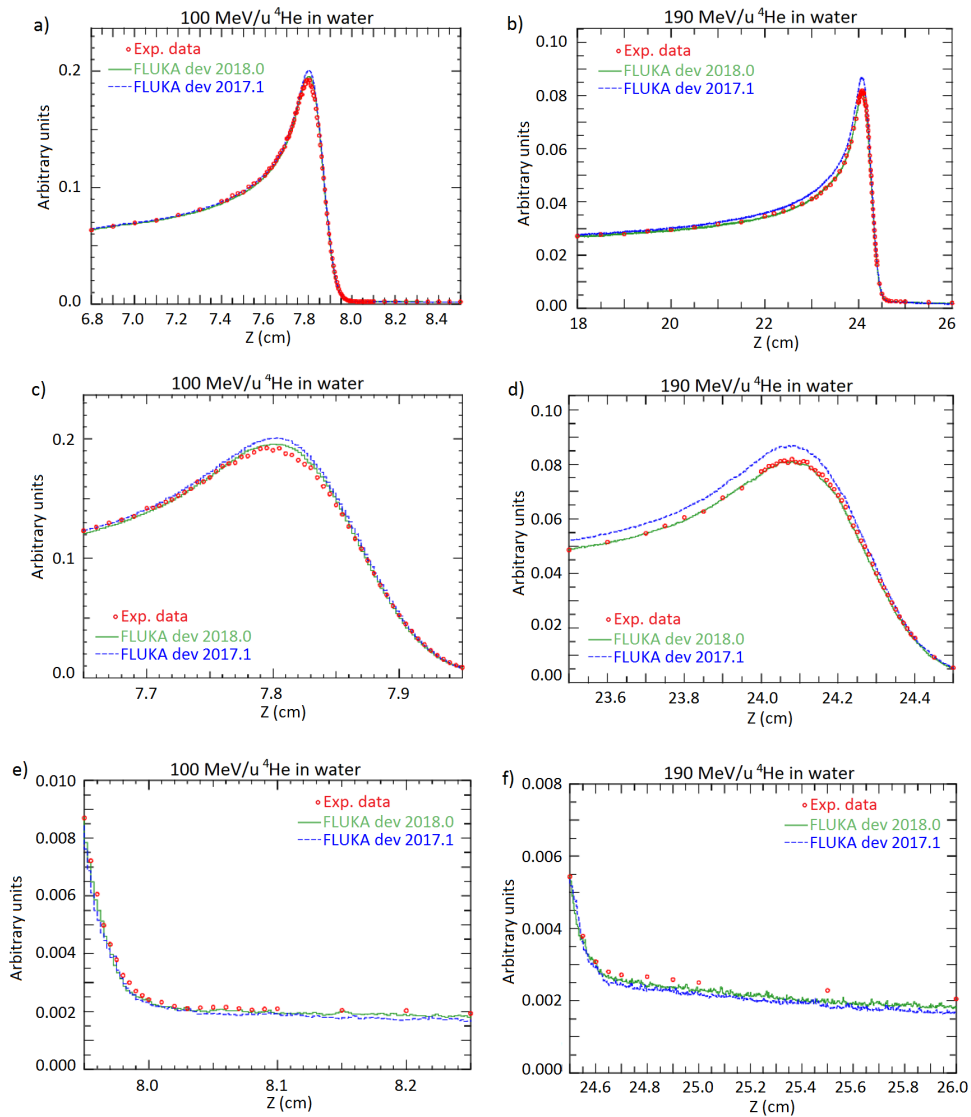


Fig. 2: Experimental dose measurements (*red dots*) [13] acquired with helium ion beams at 100 MeV/u (*left*) and 190 MeV/u (*right*) are compared with FLUKA predictions, using two different development versions, 2017.1 (*dashed, blue line*) and 2018.0 (*solid, green line*). The top row shows a broader range of depth values in water, whereas the middle row and bottom row are, respectively, a zoom of the peak and fragmentation tail.

4 Conclusions and Outlook

In view of the employment of helium ions for radiotherapy at HIT in the close future, refinements and improvements of the physics models embedded in the FLUKA code were required. In this work, the fragmentation cross section curves implemented in FLUKA for ${}^4\text{He}+{}^{12}\text{C}$ and ${}^4\text{He}+{}^{16}\text{O}$ collisions were benchmarked against new experimental data in the therapeutic energy range. The previous models used in the FLUKA development version 2017.1 were adapted such to increase the agreement with experimental measurements (see Figure 1). Validation of the new cross section curves was performed by comparing experimental data and FLUKA simulations of dose delivered in water by helium ion beams. Depth-dose profiles obtained with two initial beam energies, 100 and 190 MeV/u, were investigated and shown in this article as examples (see Figure 2). It was found that using the refined nuclear reaction cross section curve, a better agreement with the experimental data was achieved. Therefore, the new nuclear reaction

cross section parametrization has been implemented in the FLUKA development version starting from 2018. These improvements were needed prior to the clinical use of FLUKA for helium ion therapy. This work can be extended at energies above those used for hadron therapy and for projectile and target materials heavier than carbon. Enhancement of the accuracy of the nuclear reaction cross section models could be beneficial also for other FLUKA applications, like heavy ion collisions and space radiation research.

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