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Target fragmentation in protontherapy

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Summary. — In protontherapy, secondary particles are produced through primary beam interactions with the patients body. The fragments are created in the inelastic interaction of the beam with the target nuclei and have low kinetic energies and/or high atomic numbers as compared to primary protons. Secondary particles produce an altered dose distribution, due to a different range of fragments and have high LET, that lead to an increase of RBE for the same delivered dose. The inclusion of target fragmentation processes is important for the accurate calculation of the treatment plan. In this study, Monte Carlo simulations were employed to estimate the effect of target fragmentation in proton therapy. In particular, the range distribution of secondary particles has been evaluated using the FLUKA code. For the evaluation of the impact of target fragmentation, the fluence of secondary particles has been calculated with simulation at different depths.

1. – Introduction

In the interaction with the biological tissues, protons mainly lose energy by means of electromagnetic Coulomb interactions with electrons. The rate of energy loss per unit mass increases with depth as particles slow down reaching a maximum known as Bragg peak.

In addition, nuclear interactions can take place with the atomic nuclei of the target material. In protontherapy, the projectile energies are in a range between 60 and 250 MeV, so only target fragmentation can occur. Nuclear fragmentation reactions lead to the attenuation of the primary beam flux along the penetration depth and to the build-up of low-Z fragments (up to $Z = 8$). These particles have low kinetic energies (few MeV) and low residual range (10–100 μm): they will deposit all their energy close to their generation point. Fragments have high atomic number compared to the incident beam of protons and are characterized by high LET values that can be expected to be

associated with an enhanced RBE. However, it is not a simple issue to determine the contribution of target fragmentation to the overall dose.

In the proton Bragg curve, the target fragment build-up effect takes place in the first centimeters of the entrance channel [1]. Indeed, from recent studies it emerges that the effect of nuclear interaction, as compared to ionization, is more relevant in the entrance region [2] and this is reflected in an increase of the biological damage (10%) in the entrance channel [3]. Therefore, the effect of target fragmentation is of interest in radiobiology research (especially for $Z > 1$) and in particular relevant for normal tissues in the entrance region. The target fragmentation should be carefully considered when performing dose calculations for proton treatment planning.

Monte Carlo (MC) methods can be exploited to provide information on target fragmentation in proton therapy. They are able to take full account of the mixed ra-

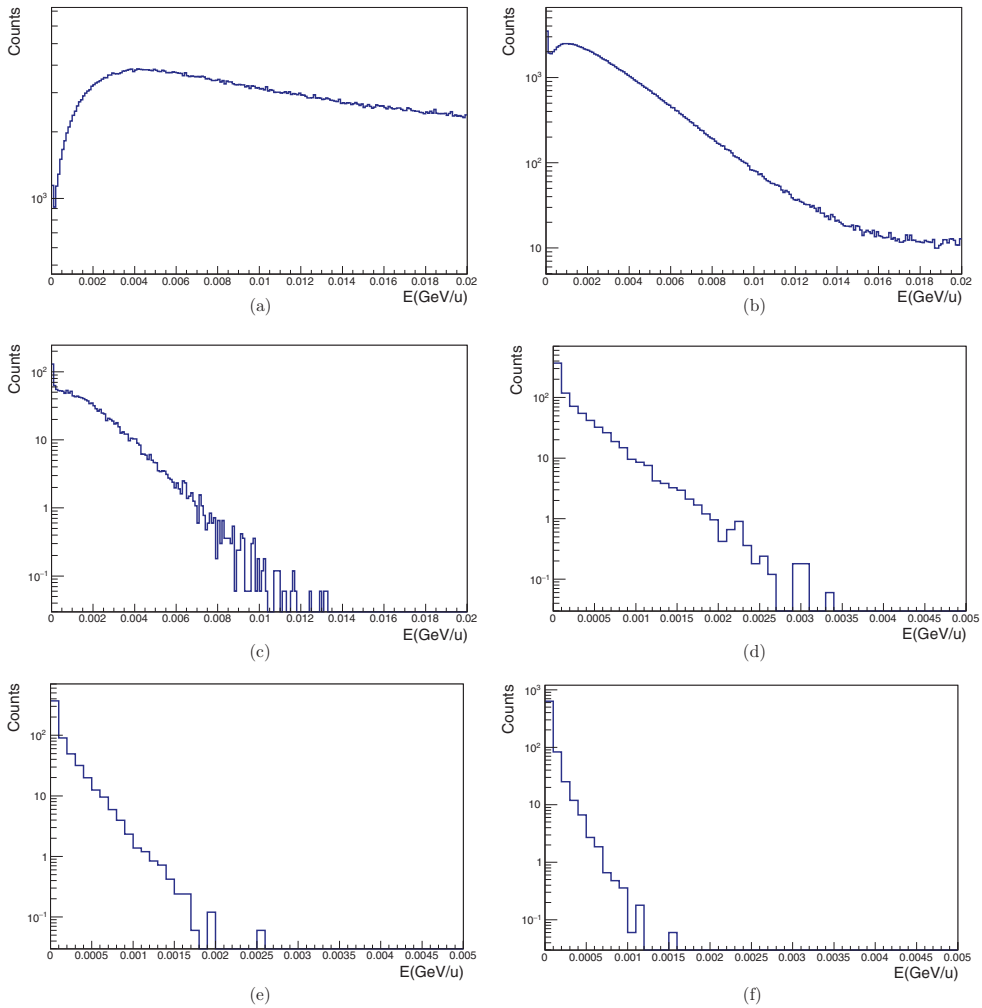

Fig. 1. – Energy distribution of ^{1}H (a), ^{4}He (b), ^{7}Li (c), ^{12}C (d), ^{14}N (e) and ^{15}O (f) produced by a proton beam of 200 MeV in water.

diation fields and provide detailed predictions of particles originating in the nuclear interactions [4].

In this work, the range distributions of fragments induced by a proton beam in water have been evaluated by means of the FLUKA MC code [5, 6], which has been validated with experimental data [1] and is currently used in many hadron therapy centers for verification of the treatment plan (see sect. **2**). For the implementation of the target fragmentation in the Treatment Planning System (TPS), a study of the fragment fluence as a function of depth is also necessary (sect. **3**).

2. – Range of fragments

Target fragments can have high charge, low kinetic energy, small residual range and high biological effectiveness.

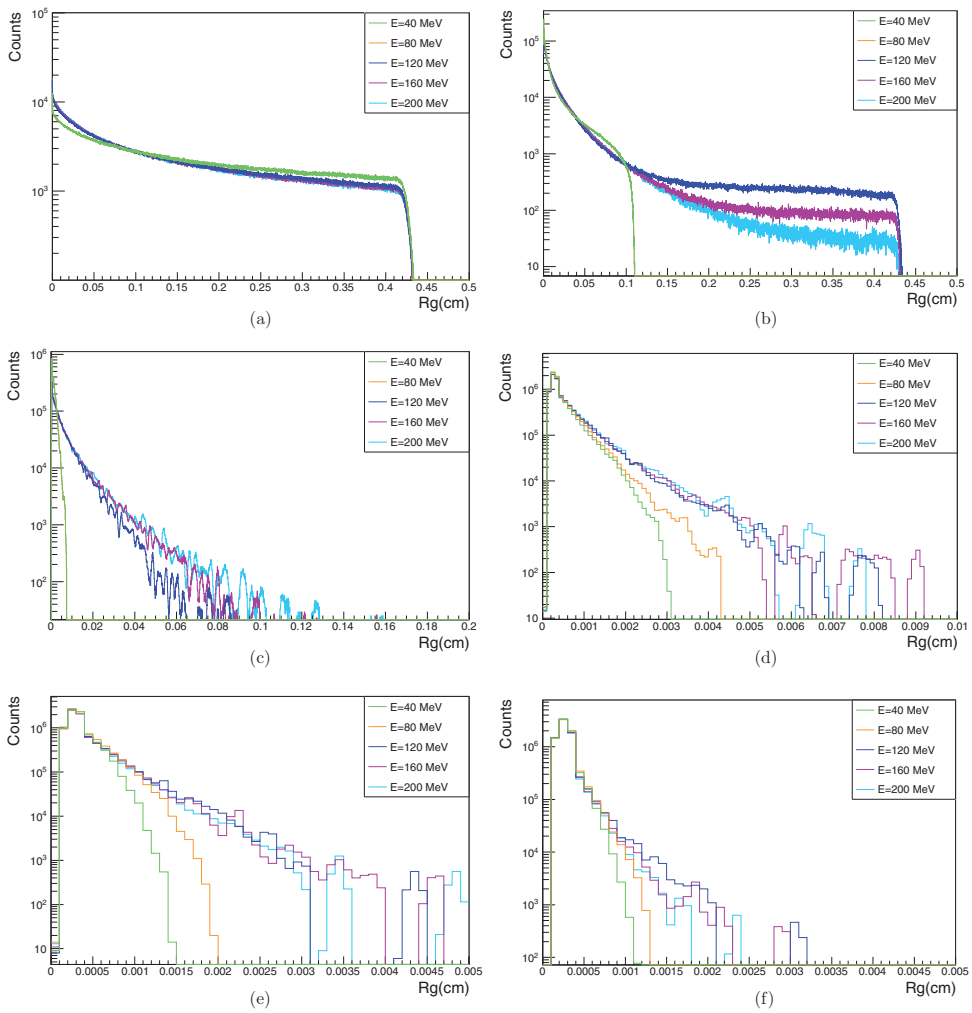

Fig. 2. – Range distribution of ^{1}H (a), ^{4}He (b), ^{7}Li (c), ^{12}C (d), ^{14}N (e) and ^{15}O (f).

A previous study of the fragment range is shown in [2], where a table with mean energies evaluated with the Goldhaber formula and the corresponding fragment residual range are reported. These results are not experimental data, but are average quantities evaluated using an analytical approach.

One step forward is the evaluation of the range distribution of fragments by means of a Monte Carlo code studying the energy and residual range of target fragments produced in water. In this work, the range distribution of fragments has been evaluated with FLUKA in two simulation steps.

The first simulation is performed with proton pencil beams of different energies ($E_p =$ 40, 80, 120, 160, 200 MeV) impinging on a thin water target (1 mm). The energy spectrum of each fragment has been scored. Looking at the results in fig. 1, the energy distributions of fragments are highly asymmetrical and assume values up to 20 MeV/u.

In the second simulation, the primary beams are the fragments with energy distribution given by the result of the previous simulation (fig. 1). The range distribution is obtained scoring the end position of each particle and calculating the projected range as

TABLE I. – *Range of fragments: the mean value of the range distribution produced by a proton of 200 MeV in water evaluated with the FLUKA MC code.*

Fragment	R_p (μm)
^{1}H	1392
^{2}H	2117
^{3}H	1383
^{3}He	465.7
^{4}He	218.3
^{6}He	229.3
^{6}Li	75.7
^{7}Li	74.1
^{7}Be	42.6
^{9}Be	26.1
^{9}B	24.4
^{10}B	14.5
^{11}B	11.2
^{10}C	9.9
^{11}C	8.1
^{12}C	5.9
^{13}N	4.4
^{14}N	4.1
^{15}O	2.8
^{16}O	3.5

the distance between the initial and the final position, using the relation

$$R_p = \sqrt{(x_f - x_i)^2 + (y_f - y_i)^2 + (z_f - z_i)^2}. \tag{1}$$

The projected range R_p is different from the real trajectory, but fragments have low energy, so it can be assumed as a good approximation.

In fig. 2, a selection of range distribution for fragments evaluated with FLUKA is shown. The mean range is in the order of 100–1000 μm for light secondaries, while for heavier fragments is about 3–10 μm.

The mean range obtained from the distribution of each fragment is reported in table I. For heavier fragments, the mean range obtained from the distribution is similar to the value reported in [2], while for low-Z fragments there is a difference between the average range in the analytical formula and the MC evaluation. The Monte Carlo approach, as compared with the analytical approach used in [2], gives a more complete description of the physical processes and the range estimation is therefore more reliable.

In conclusion, the range distributions of the main fragments produced by protons have been analyzed, considering different beam energies. The energy spectra of fragments used as input for the range evaluation is between 0 and 20 MeV/u.

The range of these particles is very small (in the order of 10–100 μm) and only one or a few cells are directly hit. Therefore, target fragments deposit all their energy close to their generation point, so the contribution of target fragmentation is relevant for normal tissues in the entrance region and should be considered by TPS.

3. – Fragment fluences

Another important quantity for the study of target fragmentation and its biological effect in proton therapy is the fragment fluence.

For the inclusion of target fragmentation in the TPS a study of secondaries production in water is performed with FLUKA. One of the aims of the MoVe-IT (Modeling and Verification for Ion beam Treatment planning) project is to explore and implement the biological impact of target fragmentation. In order to include the contribution of target fragmentation and estimate the biological impact of fragments in treatment planning systems, the fragment fluence as a function of atomic number, charge, energy and depth has been studied with FLUKA.

In the simulation setup, the source is a proton beam of 150 MeV impinging on a water phantom. The fluence has been evaluated at different depths in the volume. In fig. 3, a selection of the results of fragment fluences is reported. For the main fragments produced in water at $z = 5, 10, 15$ cm of water, the energy of target fragments is in the range $0 < E < 10$ MeV/u and the energy decreases with increasing depth.

Secondary protons are the main contributors to the target fragments, according to [7], but a significant contribution to the dose distribution is given also by helium fragments [8].

The radiobiological effect of target fragments with $Z > 1$ is almost unexplored. A database for fragments fluence (energy, depth, Z and A) will be created in order to implement the transport of fragments in the TPS. TRiP98, currently used in the MoVe-IT project, is able to properly account for the mixed radiation field in proton therapy for the description of proton beam biological effects. So, it offers the possibility to use different biophysical models for the proton beam biological effect description.

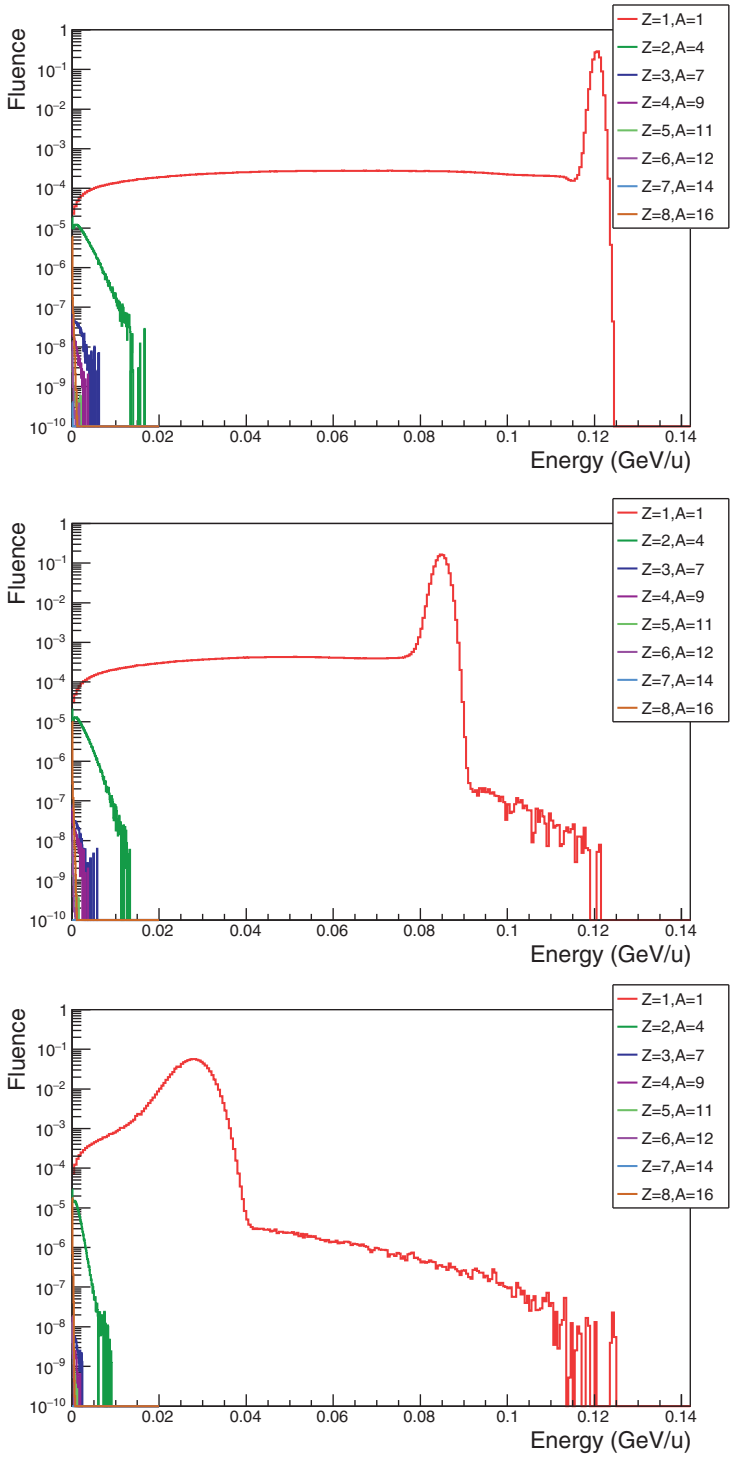

Fig. 3. – Fluence of target fragments ($1 \leq Z \leq 8$, $1 \leq A \leq 16$) induced by 150 MeV protons in water at $z = 5$ (top), 10 (middle), 15 cm (bottom) (Bragg peak at 15.8 cm).

4. – Conclusions

Target fragmentation can be associated with several aspects of potential clinical relevance. Recent studies [2, 9] demonstrated that secondary target fragments contribute to the overall dose deposited in the patient especially in the entrance channel and give a non-negligible dose to normal tissues, potentially causing secondary malignancy formation. Therefore, the effect of target fragmentation must be included in the Treatment Planning System.

In this study, the range distribution of target fragments has been evaluated using the FLUKA MC code. The advantage of the MC approach is due to the complete description of physical processes, giving more reliable results on the fragments range with respect to analytical approaches. From the range study, it emerges that target fragments have atomic number in the range $1 \leq Z \leq 8$ and their energies are in the range of $0 < E < 20\,\mathrm{MeV}/u$, that leads to an increase of RBE. The mean range of fragments obtained by the MC distribution is in the order of 10–100 μm: target fragments deposit all their energy close to their generation point (one or a few cells are directly hit).

The fluence of fragments is also very important and from this study it has been shown to decrease with increasing depth, so the range of fragments is smaller at the end of the depth dose profile. Starting from these preliminary results, the next step is the creation of a fragment database (fluence, energy, Z, A) for the inclusion of target fragmentation in the TPS.

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