FLUKA simulation of target fragmentation in protontherapy

A. Embriaco[a,*], A. Attili[b], E. V. Bellinzona[c,d], Y. Dong[a,e], L. Grzanka[f], I. Mattei[a], S. Muraro[a], E. Scifoni[d], F. Tommasino[c,d], S. M. Valle[a], G. Battistoni[a,d]

[a] *Istituto Nazionale di Fisica Nucleare, Sezione di Milano, Italy*
[b] *Istituto Nazionale di Fisica Nucleare, Sezione di Roma Tre, Italy*
[c] *Università degli studi di Trento, Italy*
[d] *TIFPA Trento Institute for Fundamental Physics and Application, Italy*
[e] *Università degli studi di Milano, Italy*
[f] *Institute of Nuclear Physics, Kraków, Poland*

Abstract

In protontherapy, secondary particles are created in nuclear interaction of the beam with the target nuclei. The secondary fragments have low kinetic energies and high atomic numbers as compared to primary protons. Secondary particles have high LET and deposit all their energy close to the generation point. For their characteristics, secondary particles can produce an altered dose distribution and lead to an increase of RBE for the same delivered dose. Moreover, target fragmentation processes is relevant mostly in the entrance region, due to higher incident energy, in presence of healthy tissues. The inclusion of target fragmentation processes in the dose calculation of a treatment planning system can be relevant to improve the treatment accuracy and for this reason it is one of the major task of the MoVe IT project.

In this study, Monte Carlo simulations were employed to fully characterize the mixed radiation field generated by target fragmentation in protontherapy. The production cross section and the range of secondary particles has been evaluated by means of the FLUKA code. As a first step to evaluate the biological impact of target fragmentation, the fluence of secondary particles has been calculated at different depths in order to generate an MC database of fragments fluence to be included in TPS and allowing its comparison with conventional beam description.

Keywords: protontherapy, target fragmentation, Monte Carlo simulation

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

*Corresponding author
Email address: alessia.embriaco@mi.infn.it (A. Embriaco)

addition, nuclear interactions can take place with the atomic nuclei of target material. At therapeutic energies of proton beam (60-250 MeV), only target fragmentation can occur.
Target fragmentation can be associated with several aspects of potential clinical relevance. In protontherapy, nuclear interaction produce an attenuation of primary particles along the penetration depth and the build-up of target fragments that covers the first centimeters of the entrance region. Fragments created in inelastic interactions of the beam with the target nuclei have low kinetic energy, high atomic number and high LET as compared to primary protons [1]. These secondary particles alters the dose distribution, due to their different ranges. The range of such fragments is of the order of 10-100 μm and only one or a few cells can be hit [2]. Secondary particles are characterized by high LET values [3] that can be expected to be associated with an enhanced RBE for the corresponding delivered dose [4]. The energy dependence of the nuclear interaction cross section makes target fragmentation relevant mostly in the entrance region [5], leading to a possible increase of the Normal Tissue Complication Probability (NTCP).
Due to high LET of fragments, target fragmentation is of strong interest in radiobiological dose estimation and can be considered in the evaluation of the treatment. Nowadays, target fragmentation is not considered in commercial Treatment Planning Systems (TPSs). The production cross sections of target fragments and their energy spectra is still poorly measured.
In the MoVe IT (Modeling and Verification for Ion beam Treatment planning) project, the effect of target fragmentation will be included in the TPS. The TRiP98 code [6, 7] is able to take into account the the mixed radiation field for the description of biological effects of target fragmentation. In order to implement the transport of fragments in the TPS, a database for fragments fluence will be created.
In this paper Monte Carlo (MC) simulation are performed to evaluate the amount of those target fragments respect to primary protons fluence. The production cross sections of fragments at therapeutic energies have been evaluated by means of the FLUKA MC code. Starting from energy distribution of fragments, the range distribution has been derived. To include the impact of fragmentation in the TPS and estimate the biological effect of fragments, the fluence of target fragments at different depths has been calculated with FLUKA.

2. MoVe IT project

The aim of MoVe IT (Modeling and Verification for Ion beam Treatment planning) project is developing and testing innovative treatment planning models for particle therapy, accounting for a higher complexity of biophysical processes. The main effects that will be explored and implemented in MoVe-IT are: the biological impact of target nuclei fragmentation, relative biological effectiveness (RBE) and intra-tumor heterogeneity.
To implement the transport of fragments in the TPS, a MC database of fragments fluence storing atomic and mass number of each fragments and their energy at different depth is ongoing.
In MoVe-IT, the TPS modelling part is based on the use of TRiP98 (Treatment Planning for Particles) [6, 7]: the first TPS for actively scanned heavy ions developed in the GSI pilot

project on carbon ion therapy. Treatment planning implementation offers the way to test the input models, e.g. fragment fluence, in a macroscopic measurable quantity: the biological dose. Depth dose distribution, nuclear fragments spectra and stopping power data are the input of TPS. The biological effects of target fragmentation can be evaluated as for projectile fragments using the available RBE model, in particular including LEMIV. Considering the contribution of each single fragment produced by a proton in water, the evaluation of total RBE is based on a mixed field approach. The results of RBE evaluation will be imported in TRiP98 Treatment Planning System and test the biological dose differences with respect to the default calculations.

3. FLUKA simulation

MC codes are able to take full account of the mixed radiation fields and provide detailed predictions of particles originating in the nuclear interactions [8]. A Monte Carlo study has been performed with FLUKA [9] code which is often used as a reference in hadrontherapy [10] and has been benchmarked against measured data.
All simulations were performed using the PRECISION defaults card and physics card COALESCE to activate the coalescence mechanism, which is recommended for the study of fragments production in protontherapy. The materials used are the default materials implemented in FLUKA. For the water phantom, we have defined the mean ionization potential as 77 eV using the MAT-PROP card. This value has been suggested by the HIT and CNAO groups, where the simulation with this mean ionization potential is validated with experimental data. The FLUKA simulations were performed with 10^9 simulated particles, in 10 batches of 10^8 histories each.

4. Production Cross Section

The production cross section due to inelastic interaction induced by proton beam in water has been evaluated using FLUKA code. The simulation is performed with proton pencil beams of different initial kinetic energies impinging on a thin water target. The target is a sphere of water with radius of 100 μm. The initial kinetic energies considered are 50, 100, 150, 200 and 250 MeV in order to cover the range of therapeutic energies. The production cross section of each fragment produced by inelastic interaction in water has been scored. FLUKA is able to score the energy distribution by particle type with the USRYIELD card combined with an AUXSCORE card. The AUXSCORE allow to select and distinguish the contribution of different particles. In Fig.1, the energy distribution of main fragments produced by proton beam of 150 and 250 MeV has been reported.

In Table 1, the mean energies of each fragment are reported. From these results, it emerges that heavy fragments have low kinetic energies (few MeV) so they will deposit all their energy close to their generation point.

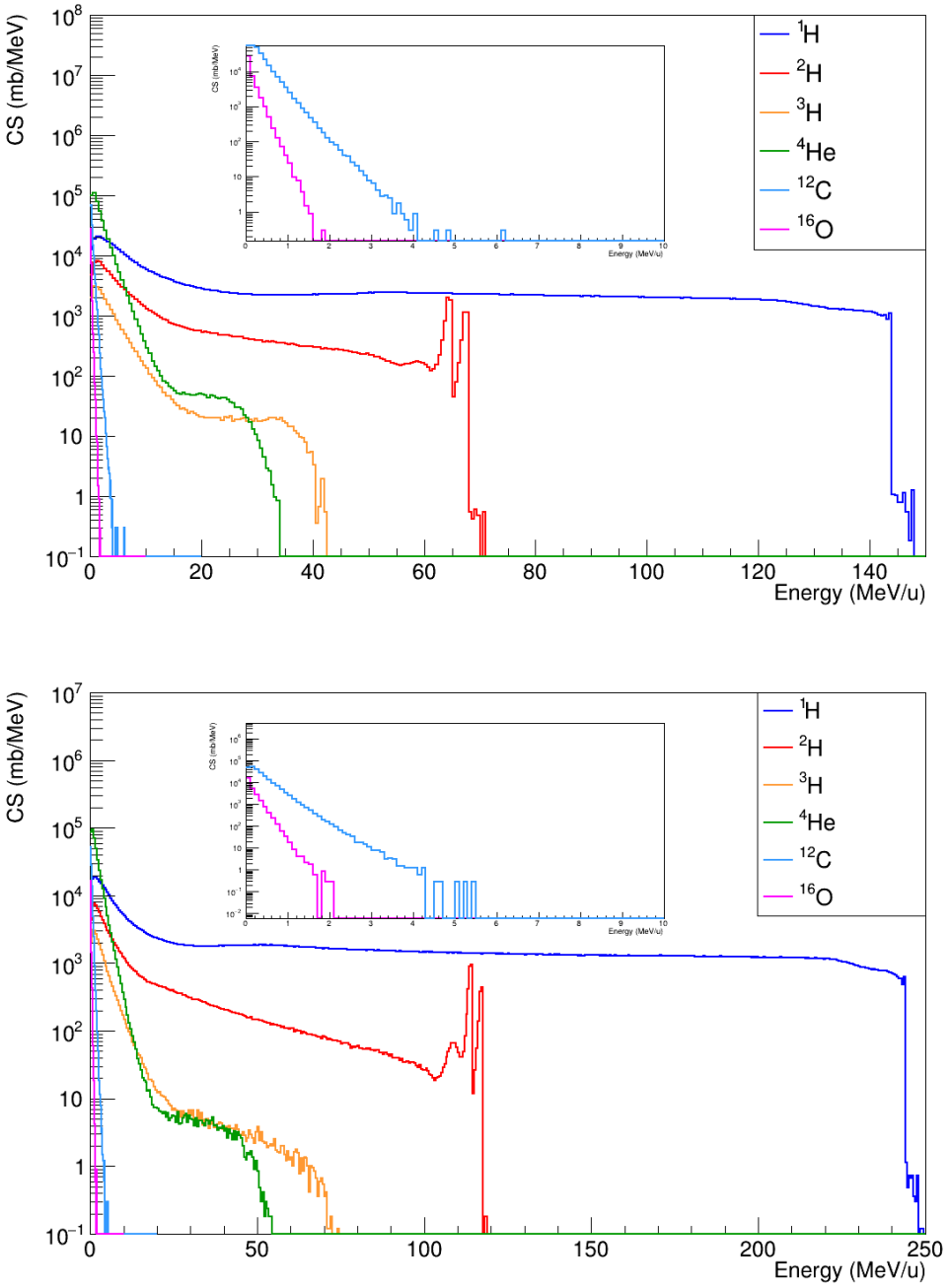


Figure 1: Production cross section (CS) of inelastic interaction induced by proton beam of 150 MeV (top) and 250 MeV (bottom) in water. The plots are in logarithmic scale.

5. Range of Fragments

The range of fragments has been evaluated in two simulation steps. In the first simulation, proton pencil beams of different initial kinetic energies (E_k=40, 80, 120, 160, 200 MeV)

	$E_p = 150MeV$	$E_p = 250MeV$
Fragment	$E_M(MeV/u)$	$E_M(MeV/u)$
^{1}H	48.5	82.8
^{2}H	15.2	17.2
^{3}H	3.9	3.8
^{4}He	1.7	1.7
^{12}C	0.3	0.3
^{16}O	0.1	0.1

Table 1: Mean energy (E_M) of main fragments produced by proton beam of 150 and 250 MeV (E_p) in water evaluated with FLUKA MC code.

impinging on a thin water target has been considered. The target is a plane of 1 mm of depth and the energy distribution of each fragment has been scored. In the second one, the source are the fragments with energy distribution given by the result of the previous simulation (0 < E < 20 MeV/u). For each fragments produced in water, the range distribution is obtained scoring the end position of each particle and calculating the projected range as:

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

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

In Fig.2, the range distribution for fragments produced by proton of 160 MeV in water has been evaluated with FLUKA. The mean range of fragments are reported in Table 2: the range of fragments with $Z < 3$ are very small (in the order of $100 - 1000$ μm) and few cells are directly hit.

Fragment	R_p (μm)
^{1}H	1409
^{2}H	2121
^{3}H	1391
^{4}He	255.8
^{12}C	5.8
^{16}O	3.2

Table 2: Range of fragments: the mean value of range distribution produced by proton of 160 MeV in water evaluated with FLUKA MC code.

For heavier fragments, the mean range obtained from the FLUKA distribution is similar to the value reported in [2], while there is a difference between the average range in the analytical formula and the MC evaluation for low Z fragments. In the simulation, the range has been evaluated starting from the energy spectrum of each secondary particles, while in [2] it has been calculated considering the average energy of fragments obtained with

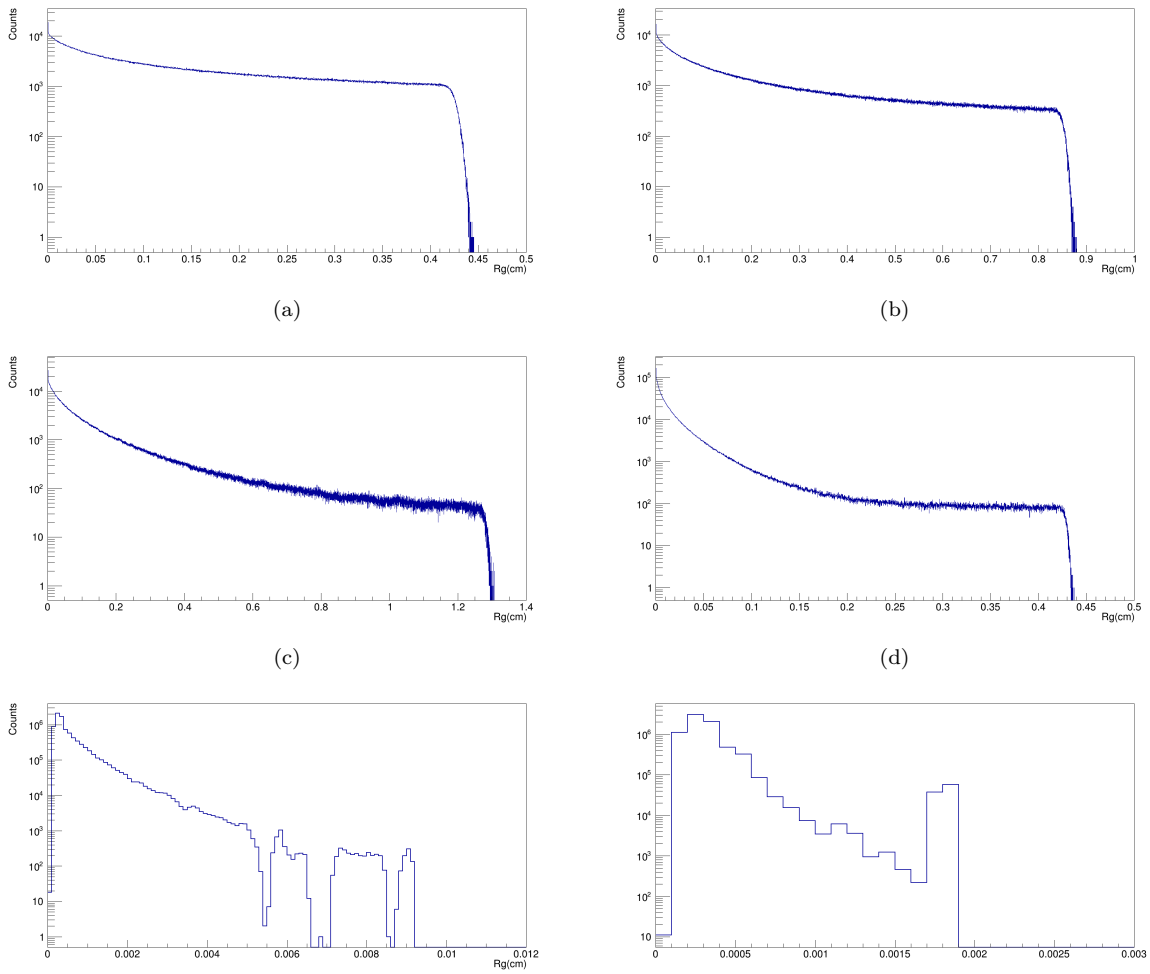
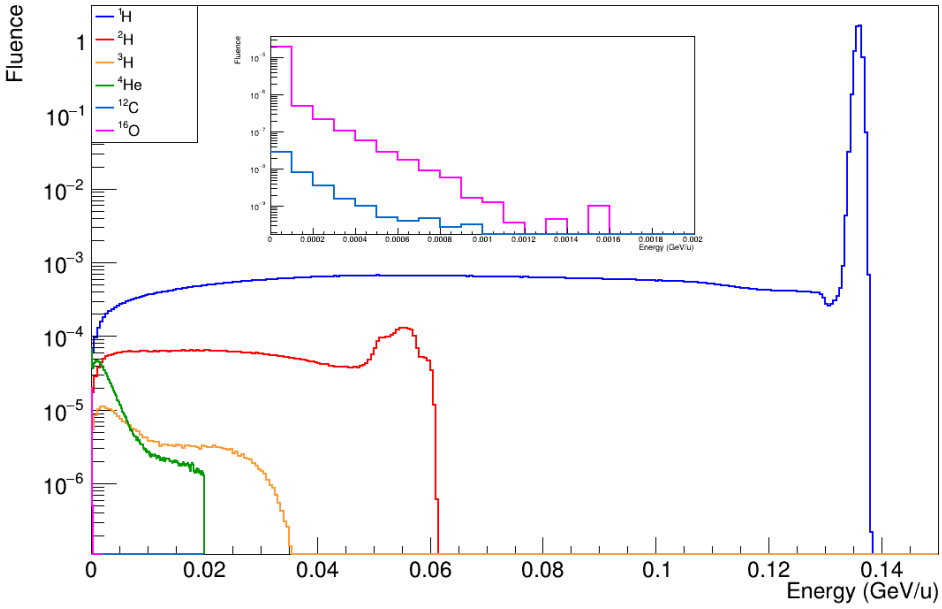
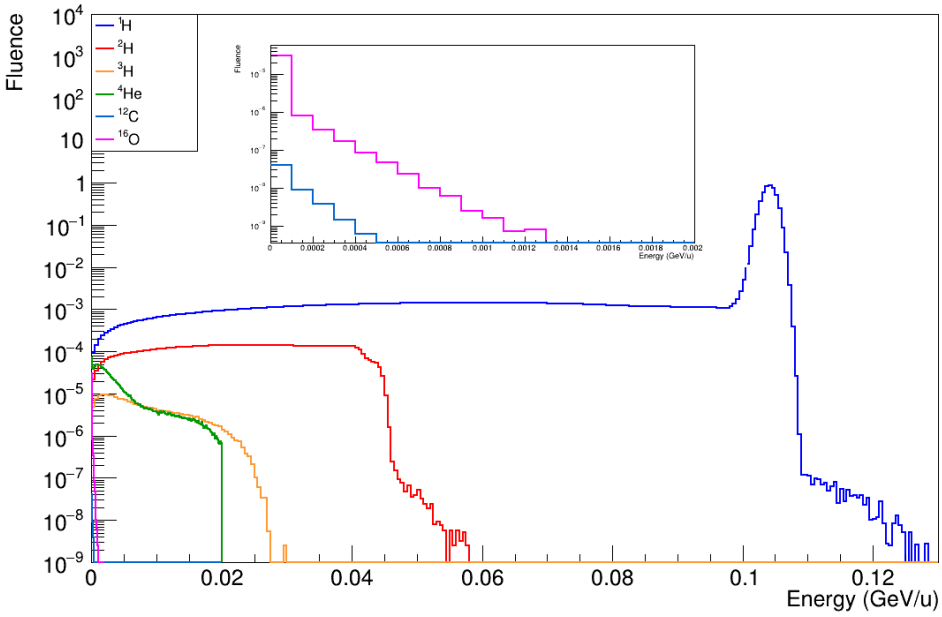


Figure 2: Range distribution of ^{1}H (a), ^{2}H (b), ^{3}H (c), ^{4}He (d), ^{12}C (e) and ^{16}O (f) produced by proton of 160 MeV in water.

Goldhaber formula. The Monte Carlo approach allow a more complete description of the physical processes and the range estimation is therefore more reliable.
The range of heavy fragments is comparable or lower than the radius of the cell nucleus. Therefore there could be a colocalization effect: a spatial overlap between two or more tracks of different fragments in the same area of the cell. Thus the overall biophysical effect estimation of this mixed field, may be complicated by nanoscale effects. This is part of a dedicated forthcoming work. Therefore, it is not a simple issue to determine the contribution of each target fragments to the overall dose.
In conclusion, 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.

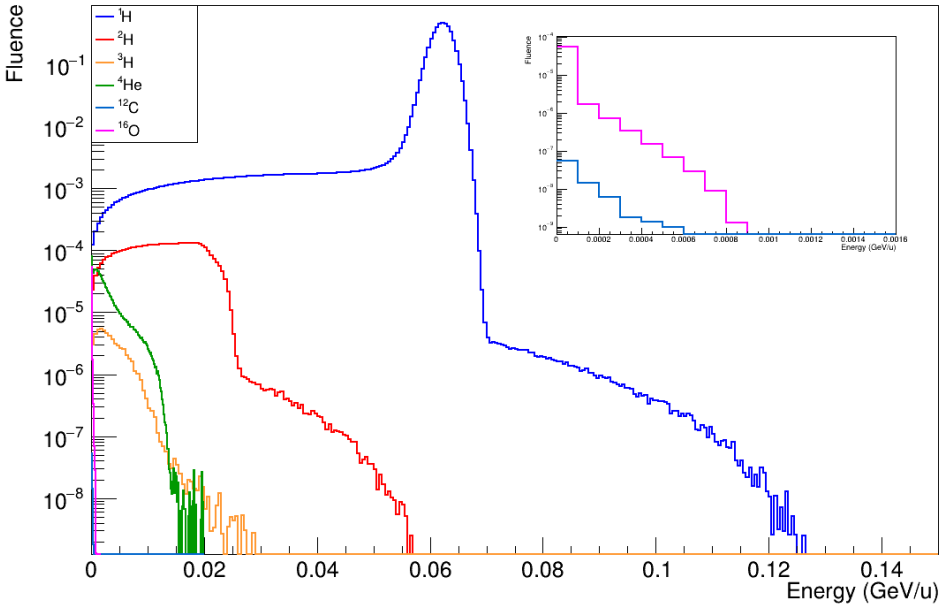


(a)

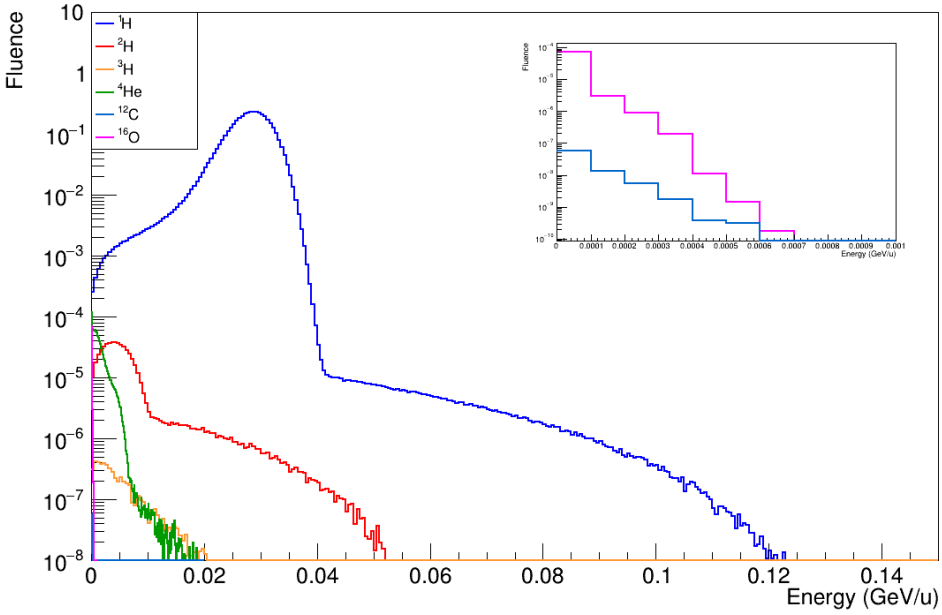


(b)

Figure 3: Fluence of target fragments induced by 150 MeV protons in water at z=2.5 (a) and 7.5 cm (b) (Bragg Peak at 15.8cm).



(a)



(b)

Figure 4: Fluence of target fragments induced by 150 MeV protons in water at 12.5 (a) and 15 cm (b) (Bragg Peak at 15.8cm).

6. Fragments fluence

In order to include the impact of fragmentation and estimate the biological contribution of fragments in TPS, the secondaries production have been evaluated with FLUKA code. In the simulation, the source is a monoenergetic proton beam of 150 MeV. The water phantom is a cylinder of radius 20 cm. The scored quantity is the fluence of each fragments at different depths in a water phantom. FLUKA score the track-length fluence distribution of certain particle with the USRTRACK card combined with an AUXSCORE card. The fluence has been evaluated at different depths in a volume with 1 mm of depth (V=125.6 cm^3): the radius of target was chosen in a way that the full energy of the beam would be deposited inside the volume.
In Figures 3-4, the fluence of fragments produced by proton beam of 150 MeV in water has been reported at different depths. Looking at these results, it emerge that the fluence of proton is characterized by two components: the primary beam (the region with peak) and the secondaries protons. Due to the energy dependence of the nuclear interaction, the energies of fragments are higher in the entrance channel than the Bragg peak region and decrease with increasing depth. Therefore, target fragmentation is more relevant in the entrance region. From the results shown in Fig.3-4, it emerges that the main contributors to the target fragmentation are Hydrogen isotopes, according to [11], but a significant contribution to the dose distribution is given also by Helium fragments [12].

7. Conclusions

The present MC study allows to fully characterize the mixed field generated by proton beams in protontherapy and confirm the expected distribution of high LET and short ranged particles [2].
The mean range of fragments obtained by MC distribution is in the order of 10-100 μm. Thus, these particles deposit all their energy close to their generation point and one or a few cells are directly hit. It is important to note that the range of heavier fragments is less than the radius of the cell nucleus. There could be a colocalization of different particles in a close region of a cell nucleus so the overall biophysical effect is not a simple issue to evaluate.
In order to estimate the effect of target fragmentation on biological dose, the fragments fluence has been evaluated with FLUKA at different depths. From simulation, it emerges that secondary protons are the main contributors to the target fragments but a significant contribution to the dose distribution is given also by Helium fragments. In the framework of MoVe IT project, the creation of a fragments database for the inclusion of target fragmentation in the TPS and is subject of a forthcoming paper.

Acknowledgments

This work was supported by Istituto Nazionale di Fisica Nucleare (project MoVe-IT).

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