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The role of Monte Carlo simulations in the radiobiological optimization of proton therapy treatment plans

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The number of facilities offering ion radiation therapy to cancer patients has steadily increased over the last decades, being proton therapy the hadron therapy modality more extended as of today [1]. In general, the main advantage of proton beams, as compared with photon conventional radiotherapy, is related to the shape of the depth dose distribution curves they produce, with a sharp maximum dose known as the Bragg peak. Since the depth of the Bragg peak can be regulated according to the beam nominal energy, each radiation field used in a treatment plan can be energetically adjusted so that its maximum dose is placed within the prescribed tumor volume (PTV). Another important advantage of proton therapy, also with respect to light-ion radiation therapy, corresponds to the exit dose, i.e. the dose deposition in tissues and organs downstream the tumor volume, which is negligible with respect to the dose deposited at beam entrance and at the Bragg peak region.

However, the high gradient dose regions produced by proton clinical beams calls for a very accurate modeling of proton propagation through organs and tissues, either as for linear energy transfer (LET) and lateral spread calculations. Especially, it is important to reduce the uncertainties on the value of the mean ionization potential (I-value) in materials relevant for the clinical practice, such as water, to increase the accuracy of LET calculations, and subsequently the beam range calculation in a patient [2]. Furthermore, the radiobiological response of tissues irradiated with protons has been proved to be more complex as compared with photon beam irradiation. Although it is currently established that the relative biological effectiveness (RBE) of protons is 10% larger than mega-voltage photons [3], several models and experimental results have been published recently suggesting a higher RBE value around the Bragg peak region [4].

In this contribution, we show two research activities currently under development by our group within the context described above, in which simulations with the Geant4 Monte Carlo toolkit [5-7] are playing an important role. A first activity aims at providing an accurate I-value for water by means of modeling energy deposition curves measured in water with different light ion beams by Schardt et al. at GSI (Darmstadt, Germany) [8]. Concretely, they obtained the energy deposition as function of the absolute depth in water for protons and ions lighter than ^{16}O , with range values between 5 and 30 cm, approximately; the absolute depth uncertainty reported was 0.2 mm. In our first set of Geant4 simulations, including proton and helium ion beams only, we have obtained a preliminary water I-value of 78.1(5) eV [9], which is compatible with the current I-value recommended by the ICRU, 78(1) eV.

A second Monte Carlo activity is focused on the radiobiological description of proton beams, both macroscopically and microscopically. As for macroscopic description of the radiation quality, we have come up with a more reliable strategy to calculate dose-average LET (LETd) distributions in voxelized geometries, since we showed that the most popular scoring approach is subject to bias [10]. This is of importance as for the use of phenomenological radiobiology models found in the literature [11-13]. As for microscopic approach, we are currently producing a set of distributions of microdosimetric stochastic quantities, such as lineal energy (y) and collisional energy imparted (ϵ_c), to characterize the radiation quality of the proton beam [14]. We also plan to verify the limits of applicability of a relation proposed by Kellerer between the macroscopic LETd and dose-mean lineal energy (yD) [15]. Finally, our ultimate aim is to compare our calculations with experimental measurements, both at Centro Nacional de Aceleradores (CNA, Seville) and proton therapy centers.

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