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Range versus density dependence of proton-therapy beams in human tissues

Márius Pavlovič[a,*], Milan Pavúk[a], Andreas Hammerle[b], Vladimír Nečas[a]

[a] Faculty of Electrical Engineering and Information Technology, Slovak University of Technology in Bratislava, Ilkovičova 3, 81219 Bratislava, Slovak Republic
[b] University of Applied Sciences in Wiener Neustadt, Johannes-Gutenberg-Strasse 3, A-2700 Wiener Neustadt, Austria

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ABSTRACT

Range versus density dependence of proton-therapy beams in human tissues is discussed in the paper. The main attention is paid to energy-scaling of simple fitting functions that fit the range-to-density dependence for single proton-beam energies. These functions have been found by fitting ranges obtained with the aid of the Monte Carlo module of SRIM2013. The simulations have been run for 28 human tissues at 8 energies from 60 MeV to 220 MeV. It has been shown that a fitting function that depends solely on the target density can be found at each proton-beam energy. After the energy-scaling, the fitted ranges have been compared with the Monte Carlo ranges. We conclude that the final energy-scaled fitting function provides ranges within 0.4% of the Monte Carlo range (on average), which is less than 30% of the natural range-straggling (1.4% of the Monte Carlo range on average). The worst data-point has an off-set from the fitting function less than 1.7% of the Monte Carlo range.

1. Introduction

Ion therapy is a promising and modern cancer-treatment modality that profits from favourable interaction mechanism of ions with matter (Bragg peak, inverse dose profile) [1]. This interaction (including biological effects) is an intensively studied field of material science and radiation biology, and many in-depth theoretical works are available [e.g. [2–7]]. Ion ranges are usually calculated with the aid of simulation computers codes that are validated by dedicated experiments [8]. In many cases, these codes use Monte Carlo technique to simulate the stochastic sequence of collisions of the ions with target atoms, which is a time-consuming approach. Another option – using tabulated data – is suffering from the fact that the tables are inherently discrete and can never contain values for any possible combinations of particle species, energies, and target materials. Parametrization models are therefore necessary to fill the gaps in the discrete tables and data-sets. That is why several authors have proposed analytical models for quick assessment of ion ranges in matter. For example in Ref. [3], Ulmer refers to the so-called Bragg-Kleeman rule in the form:

$$R_{CSDA} = AE^p \tag{1}$$

where R_{CSDA} is the range in a medium by continuous slowing-down approximation, E is the particle kinetic energy, and A and p are parameters that must be determined either by fits to experimental (or simulated) data [9] or by calculations based on integration of the Bethe-Bloch equation. The R_{CSDA} represents the total path-length needed to travel until the particle loses all its kinetic energy. This model predicts ion ranges as a function of ion energy for the same ion species in the same target material. Ulmer derived a generalized formula for different target materials [3]:

$$R_{CSDA} = \frac{1}{\rho}\frac{A_T}{Z_T}\sum_{n=1}^{N}\alpha_n E_I^{p_n} E^n \tag{2}$$

where ρ is the target density, A_T is the nuclear mass number of the target atoms, Z_T is the proton number of the target atoms, α_n are coefficients determined by the integration of the Bethe-Bloch equation [3,4,10,11], E is the projectile kinetic energy and E_I is the atomic ionization energy weighted over all possible transition probabilities of atomic/molecular shells. For special case of therapeutic protons ($E < 300$ MeV) in water ($\rho = 1$ g/cm^3, $E_I = 75.1$ eV, $A_T = 18$, and $Z_T = 10$), Eq. (2) can be simplified to the polynomic function:

$$R_{CSDA} = \sum_{n=1}^{N} a_n E^n \tag{3}$$

The parameters of formulas (2) and (3) are tabulated in Ref. [3] up to $N = 4$, which is claimed to be satisfactory. However, determination of A_T and Z_T – the target characteristics needed for evaluation of Eq. (2) – may be problematic in multi-element tissues with heterogeneities. In *in-vivo* systems, the tissue chemical composition cannot be measured and may also vary in time. Accurate determination of the atomic ionization energy, E_I, is even more difficult. These values are hardly

* Corresponding Author.
E-mail address: marius.pavlovic@stuba.sk (M. Pavlovič).

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known for water, in particular for excitation transitions, let alone for tissue material. For liquid water, 14 different values are listed in Ref. [7], ranging from 67.2 eV to 81.8 eV (covering data obtained by different experiments and measurement methods in 1952–2009). It appears that at present, the most precise measurements of the mean ionization energy of water are the range measurements made in Gesellschaft für Schwerionenforschung Darmstadt by D. Schardt (see Ref. [7] and the references therein). This is in fact partly a motivation of our work to avoid difficulties with the E_I – values and to find a simplified model that does not suffer from scarcity of the entry-data.

Kempe and Brahme [4] proposed a similar model based on the range-to-energy proportionality:

$$R \propto \frac{M_p}{Z_p^2}\frac{M_T}{\rho Z_T}\left(\frac{E}{M_p}\right)^k \tag{4}$$

where R is the so-called practical range (for definition see Ref. [4]), E is the kinetic energy of the projectile, Z_p and M_p is the projectile proton and mass number, respectively, and Z_T and M_T is the proton and mass number of the target, respectively. E/M_p is the kinetic energy per nucleon, which is related to the projectile velocity. Eq. (4) reflects the well-known fact that the range of different particle species at the same kinetic energy per nucleon (*i.e.* at the same velocity) in the same medium is proportional to the particle mass number divided by the square of the particle proton number. Eq. (4) makes it possible to calculate the range of an ion in some target material by scaling the known range of other ion in other target material (provided that the energy exponent k is independent from the stopping power). Assuming the same particle species at the same energy but in different absorbing materials, the range should be proportional to $M_T/(\rho Z_T)$ of the target, which again requires known target chemical composition.

In order to avoid difficulties with chemical composition and target ionization energy, we looked at the dependence of proton ranges on target density. We have found a simple analytical formula for proton range as a function of target density only. This was done for the target materials belonging to the same "family" – to human tissues. The same "family" means that the materials have similar chemical composition and rather restricted span of densities. The human tissues have been our favorite group of materials selected for this study mainly due to the following reasons: (1) the SRIM (Stopping and Ranges of Ions in Matter) compound dictionary contains a large set of materials in this particular category [12]; (2) these materials have rather similar chemical composition and reasonably narrow density-span; (3) the problem is relevant from practical point of view in situations, when exact chemical composition of the target material is difficult to get or when fast but reasonably accurate assessment of proton range is needed.

It should be pointed out that our primary motivation was to explore a possibility of proton-beam range-parametrization using a single target characteristic – the target density. Such a model has not been introduced yet in the literature, hence it is an innovative step with respect to the state-of-the-art. Apart from the density, the existing models rely on known target chemical composition and atomic ionization energy. In many cases, these values are not reliably known. It has been primarily a matter of interest to look for a model that avoids those problematic entry quantities. On the other hand, our model is less general, as it is valid merely for the family of similar materials within a restricted span of target densities and proton-beam energies. Its practical applicability shall be seen in situations, when more sophisticated, complex and general models fail due to the lack of necessary input data. It can also be used as a tool for extremely fast range assessment in the phase of the experiment design and preparation before running time consuming Monte Carlo simulations based for example on FLUKA, GEANT or MCNP-X computer codes. These codes allow also simulating experiments with complex target geometry, but it is always a great advantage to run these simulations with an experiment set-up that is already reasonably close to the final version. Running FLUKA, GEANT, MCNP-X or similar tools just to get particle ranges and stopping powers would not be efficient in simple cases, since these codes are capable of simulating complex problems as far as the target geometry and composition, input beam characteristics, as well as the required output quantities are concerned. On the other hand, SRIM is a well-balanced compromise between the code complexity, accuracy and computation time. It is also user-friendly and easy to operate. That is why it is often used to get ranges and stopping powers both in forms of tables as well as via Monte Carlo simulations. It also provides a so-called "Compound dictionary" that contains pre-defined parameters of the most common target materials classified into several categories, one of them being the "Biological materials – human" that are going to be used in this paper.

2. Materials and methods

Let us define first the basic concepts and quantities that are going to be used through the paper. A data-point is a result of the SRIM Monte Carlo simulation made with 99,999 protons for a particular combination of the proton-beam energy, E, and the target material that is characterized by its density, ρ. The data-points were generated for 8 energies (60 MeV, 100 MeV, 120 MeV, 140 MeV, 150 MeV, 180 MeV, 200 MeV, and 220 MeV) and 28 human-tissue targets taken from the built-in SRIM compound dictionary (category "Biological materials – human", see Table 1). Apart from the kinetic energy, each data-point is characterized by four quantities. The Monte Carlo range, R_{MC}, is the mean value of the projected range depth-distribution (adopted from SRIM). The projected range is the depth in the target where a particle stops. In principle, the projected range must always be slightly shorter than the CSDA-range mentioned before. However, in the energy interval of interest, numerical difference between the R_{MC} and R_{CSDA} is negligible. The range-straggling, S_{MC}, is the square root of the variance of the projected range depth-distribution (adopted from SRIM). It shall be pointed out that the standard deviation of the Monte Carlo range, σ_R, is related to the range-straggling, S_{MC}, by the known relation $\sigma_R = S_{MC}/n$, where n is the square root of the number of simulated particles (in our case, 99,999 protons). The fitted range, R_{FIT} stands for the range calculated according to a fitting formula. Finally, the deviation, D, characterizes the difference between the Monte Carlo range and the fitted range. It is convenient to express the range-straggling, S_{MC}, and the deviation, D, in relative units with respect to the Monte Carlo range. In this relative representation, the deviation becomes:

$$D = \frac{|R_{MC} - R_{FIT}|}{R_{MC}} 100\% \tag{5}$$

Table 1
Human tissues selected from the SRIM built-in compound dictionary and their densities.

Tissue	Density [g/cm^3]	Tissue	Density [g/cm^3]
Adipose tissue	0.92	Ovary	1.05
Skeleton-yellow marrow	0.98	Skeletal muscle	1.05
Mammary gland, #1	0.99	Trachea	1.06
Water (liquid)	1.00	Mammary gland, #3	1.06
Mammary gland, #2	1.02	Human blood, ICRU	1.06
Urinary bladder-urine	1.02	Human skin	1.09
Urinary bladder, full	1.03	Spleen	1.09
Skeleton-red marrow	1.03	Skeleton-cartilage	1.10
Testis	1.04	Skeleton-spongiosa	1.18
Pancreas	1.04	Perinatal rhesus monk	1.40
Prostate	1.04	Cortical bone, age 2–5	1.80
Urinary bladder, empty	1.04	Cortical bone, age 6–13	1.83
Muscle-skeletal, ICRP	1.04	Bone-cortical, ICRP	1.85
Thyroid	1.05	Cortical bone, adult	1.92