Monte Carlo Investigation of the Depth-dose Profile of Proton Beams and Carbon Ions in Water, Skeletal Muscle, Adipose Tissue, and Cortical Bone for Hadron Therapy Applications

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Abstract. In this study, the depth-dose profile in water, skeletal muscle, adipose tissue, and cortical bone irradiated using incident beams of protons and carbon ions were simulated at different incident energies using the open source software GEANT4 version 10.3.2 via GATE v.8.0. The depth where the Bragg peaks of protons with incident energies of 75 MeV, 100 MeV, 130 MeV, 150 MeV, and 160 MeV in different materials were determined and the results were compared with the experimental data from the National Institute of Standards and Technology (NIST) database. The corresponding energy for incident carbon ion beam that yields the same Bragg peak position as the incident proton beams were also investigated. The depth-dose profile obtained using carbon ions show better dose conformation, but the presence of dose tail was observed. This suggests that further investigation of the RBE of the secondary fragments is necessary to understand their underlying impact to the carbon ion treatment in general.

1. Introduction

The fundamental goal of radiotherapy is to achieve precise dose localization in the target tumor while minimizing the damage to surrounding normal tissues. Each type of incident beam in radiotherapy shows a distinct depth-dose profile. While the conventional radiotherapy utilizes photon and electron beams in the management of malignant tumors, proton therapy also received a lot of attention. Proton therapy offers an advantage over the conventional radiotherapy modalities due to its depth-dose distribution characterized by a small entrance dose, sharp increase of dose in a well-defined depth and the rapid dose fall-off beyond the maximum dose deposition at the distal edge. The well-defined range and the small lateral beam spread make it possible to deliver the dose with millimeter precision. The point of maximum energy deposition is called Bragg peak and this feature allows high dose deposition...
to a locally restricted volume [1].

Nowadays, the interest in carbon ion radiotherapy is rapidly increasing as well due to the depth-dose profile of carbon ion possessing the same features to that of proton beams but with higher relative biological effectiveness (RBE) [2]. Carbon ion beams also deliver a larger mean energy per unit length (linear energy transfer (LET)) of their trajectory in the body compared with proton or photon incident beams. Carbon ion beams which are high-LET radiation, cause double-strand DNA break, which is essential for cancer cells’ death [3].

This study aims to simulate the depth-dose profile of proton beam in water and other biological materials, determining the position of the Bragg peak (i.e. range) at different incident energies, and determined the energies of incident carbon ions which can produce approximately the same range or position of the Bragg peak as the chosen proton beam energies.

1.1. Theoretical Background
Protons interact with matter and lose energy primarily through electromagnetic interactions with the atomic electrons. In general, the interactions of protons in matter can be classified into three categories according to the proton energy regions: a) interactions with atomic electrons, b) interactions with the atomic nucleus, and c) interactions with the atoms as a whole below 0.01 MeV [4]. The latter occurs only at very low energies and can be ignored in the case of proton dosimetry for radiotherapy. The proton interaction with atomic nucleus includes the inelastic scattering, Rutherford scattering and nuclear reactions.

Protons and carbon ions slow down and deposit energy along their tracks within the material and this mechanism determines the distribution of absorbed dose. In this slowing down process, excitation and ionization of the atoms of the material take place. If sufficient energy is imparted to an atomic electron, this electron can, in turn, cause subsequent ionization. In general, the interaction of protons and carbon ions with matter is described by the Bethe–Bloch formula which describes the rate of energy loss of the incident particle [5]-[6] given by the following equation:

\[
\frac{1}{\rho} \frac{dE}{dx} = K \frac{Z}{A} \beta^2 \left[ 1 - \frac{2m_e c^2 \beta^2 \gamma T_{\text{max}}}{\gamma^2} - \frac{\delta(\beta \gamma)}{2} - \frac{C}{Z} \right]
\]

where \( \rho \) is the density of the traversed material or medium, \( K \) is a constant with numerical value of 0.307 MeV cm\(^2\)/g, \( z \) is the charge of the incident particle, \( m_e \) is the electron mass, \( c \) is the speed of light, and \( Z \) and \( A \) are the atomic number and atomic mass of the material respectively. \( I \) is the mean excitation energy, \( \beta^2 \) is the atomic transitions correction, \( \delta(\beta \gamma) \) is the density effect correction to ionization energy loss, \( C/Z \) is the shell corrections at low energies and \( T_{\text{max}} \) is the maximum transferrable kinetic energy per collision. The density correction (important for high energies) and shell correction (relevant for small energies) can be neglected since these are relevant for large gamma-factor of the incident particle [7]. The shell correction is of paramount importance only at the lower energy. This correction is therefore, not much interest to high-energy physics applications. It treats effects at very low particle momentum when the particle’s velocity is comparable or lower than the orbital velocity of the bound atomic electrons [6], [8].

2. Materials and Methods

2.1. GATE and GEANT4 Simulation Toolkit
The Monte Carlo simulations are conducted using the Geometry and Tracking version 4 (GEANT4) package via GEANT4 Application for Tomography Emission (GATE) [9]-[10] version 8.0. GATE enables the modelling of emission tomography, transmission tomography and radiation therapy. GATE is based on GEANT4 which is an object oriented toolkit for the simulation of particle interactions with matter and provides advanced functionality for all domains typical of detector
simulation: geometry and material modelling, description of particle properties, physics processes, tracking, event and run management, detector response modelling, user interface and visualization [10].

2.2. Simulation setup

The virtual setup is shown in Figure 1. The monoenergetic pencil beam source is placed 11 cm away from the center of the target and is directed towards the +x-axis. The material of the box target or phantom, with dimension of 20 cm × 20 cm × 20 cm, is varied using water (ρ=1.00 g/cm³), skeletal muscle (ρ=1.04 g/cm³), adipose tissue (ρ=0.92 g/cm³), and cortical bone (ρ=1.85 g/cm³). The compositions of the biological materials are adopted from the National Institute of Standards and Technology (NIST) database [11]. The reference coordinate system used for the position and direction of the recorded particles is the same frame of the world.

![Figure 1. The virtual setup of the simulation.](image)

The physics list Quark Gluon String Pre-compound Binary Cascade (QGSP_BIC) is utilized. A proton beam with $1 \times 10^6$ primaries is set with energies of 75 MeV, 100 MeV, 130 MeV, 150 MeV and 160 MeV. After the simulations for these proton beam energies irradiated into the target, the corresponding carbon ion beams with approximately the same proton range, i.e. the same depth of maximum deposition or Bragg peak position is determined via trial and error procedure. The results of the simulations are recorded in ROOT files which contain the amount of dose received by each voxel.

3. Results and Discussion

The depth-dose profiles of carbon ions and proton beams traversing water are shown in Figure 2. The depth-dose profiles exhibit small entrance dose and the sharp increase of dose in a well-defined depth and the rapid dose fall-off beyond the maximum dose deposition i.e., the Bragg peak which is located approximately at the end of the incident beam range. These results are supported by the Bethe-Bloch formula (1) which suggests that the energy loss is inversely proportional to the square of the velocity of the incident particle [5]-[6]. This means that upon entering the target, the incident particles, both protons and carbon ions, have maximum energy and therefore maximum velocity. The faster the incident particle moves, the lesser the time for the particle to undergo Coulomb interaction with the atomic electrons and nucleus of the target material. Since the incident particles penetrate matter at very high speed, they leave a very small portion of their energy at shallower depths. As these particles traverse the material and interact with the atomic electrons, they begin to slow down and eventually lose more energy during interactions. As a result, these particles lose more energy, and consequently deposit more energy as they slow down until they reach their range and deposit the maximum dose at this depth. These characteristics suggest better dose conformation over the conventional photon and electron radiotherapy. The carbon ions have sharper Bragg peak than the proton beam due to their greater mass and even higher charge than protons. This implies that carbon ions have higher LET and consequently, higher relative biological effectiveness (RBE) compared to protons [12]-[13].
The results show that a 75 MeV proton beam can penetrate around 44.30 mm in water, approximately the same depth is achieved with carbon ions of 1660 MeV or 138.33 MeV/u (energy per nucleon) where u is the number of nucleons of the incident particle (12 for carbon ions). It can be observed that higher carbon ion beam energy is required to achieve the same range as a proton beam at lower energy. The reason for this is the higher rate of energy loss or linear energy transfer (LET) of carbon ions compared to protons. A 100 MeV proton beam has almost the same range as 187.50 MeV/u carbon ions, 130 MeV proton beam has almost the same range as the 246.67 MeV/u carbon ions, 150 MeV proton beam had approximately equal range as the 285.42 MeV/u carbon ions, and lastly, 160 MeV proton beam has approximately the same range as the 306.83 MeV/u carbon ions.

Figure 2. Depth-dose profiles of proton and carbon ion beams in water. The doses are normalized with respect to the corresponding maximum values for easy comparison of the locations of the Bragg peak.

Table 1. Comparison of the simulated values of range of the proton beams in water, skeletal muscle, adipose tissue, and cortical bone to the values of range from NIST proton database [11].

| Energy of incident proton beam (MeV) | Range (mm) | Water | % difference | Range (mm) | Skeletal muscle | % difference | Range (mm) | Adipose tissue | % difference | Range (mm) | Cortical bone | % difference |
|-------------------------------------|------------|-------|--------------|------------|----------------|--------------|------------|----------------|--------------|------------|---------------|--------------|
|                                     | CSDA       | Monte Carlo Simulated |          | CSDA       | Monte Carlo Simulated |          | CSDA       | Monte Carlo Simulated |          | CSDA       | Monte Carlo Simulated |          |
| 75                                  | 46.18      | 44.30 | 4.07         | 44.88      | 42.20 | 3.74         | 44.88      | 42.20 | 3.74         | 44.88      | 42.20 | 3.74         | 78.01       | 72.38 | 4.33         |
| 100                                 | 77.18      | 75.25 | 2.50         | 75.02      | 72.21 | 2.41         | 75.02      | 72.21 | 2.41         | 75.02      | 72.21 | 2.41         | 106.22      | 99.22 | 6.75         |
| 130                                 | --         | 120.19 | --          | --         | 116.56 | --          | --         | 116.56 | --          | --         | 116.56 | --          | --         | --    | --          |
| 150                                 | 157.70     | 154.29 | 2.16         | 153.37     | 150.20 | 2.07         | 153.37     | 150.20 | 2.07         | 153.37     | 150.20 | 2.07         | 192.93      | 187.16 | 3.06         |
| 160                                 | --         | 172.20 | --          | --         | 168.27 | --          | --         | 168.27 | --          | --         | 168.27 | --          | --         | --    | --          |

The range of proton beams at different incident energies irradiated in various target materials are tabulated in Table 1. The simulated ranges are compared with the experimental values of range from the NIST proton database [11], [14] particularly the continuous-slowing-down approximation (CSDA) ranges. CSDA range is a very close approximation to the average path length travelled by a charged particle as it slows down to rest. It is obtained by integrating the reciprocal of the total stopping power with respect to energy. The results of the simulations show good agreement with the results from NIST proton database with no more than 4.07 % difference.

Increasing the incident energy of carbon ions yields an increase of the range however, projectiles
with a longer range suffer more straggling and nuclear fragmentation [2], [15]. So despite the determination of the finite range of the carbon ions, small amount of dose is observed behind the Bragg peak which appears like a tail. This dose tail is deposited via ionization processes caused by the fragments, which were created by the collisions of the carbon ions with the atomic nucleus of the material [16]. Shown in Figure 3 is the number of top most abundant secondary fragments plotted against depth. A significant amount of secondary particles such as protons, alpha particles, and fragments of helium, boron, lithium, and beryllium are detected beyond the position of the Bragg peak and hence the most likely contributors of dose deposited in this region. These secondary fragments also cause broadening of the lateral dose deposition and widen the Bragg peaks as confirmed in [15], [17]. In general, these results show that secondary fragments, which are lighter compared to the incident carbon ions, have longer range and hence responsible for the energy deposition beyond the range of the incident primaries.

**Figure 3.** Number of secondary fragments vs depth in water irradiated with primary $^{12}$C ion beam at (a) 138.33 MeV/u, and (b) 306.83 MeV/u. The Bragg peaks located at depths 44.30 mm and 172.20 mm respectively.

4. Conclusion
The range of the simulated proton beams are compared with the experimental values from NIST database and show good agreement with percentage difference no greater than 4.07%. The energies of carbon ions with approximately the same stopping range as the pre-chosen proton beam energies are determined. The depth-dose profile obtained using carbon ions show narrower Bragg peak suggesting better dose conformation, but the presence of dose tail suggests dose deposition due to secondary particles. The results show significant amount of secondary protons, alpha particles, and fragments of helium, boron, lithium, and beryllium. Investigation of the RBE of these secondary fragments is necessary to understand their underlying impact to the treatment. In general, it was found that the range of carbon ions and protons is dependent on the energy of the incident particle and on the target material.

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References

[1] W. Bragg and R. Kleeman, “On the α-particles of radium and their loss of range in passing through various atoms and molecules”, Phil Mag vol. 10, pp. 318-340, 1905.

[2] O. Mohamad, H. Makishima and T. Kamada, “Evolution of Carbon Ion Radiotherapy at the National Institute of Radiological Sciences in Japan”, Cancers, Vol. 10, pp. 66-88, 2018.

[3] H. Tsuji, T. Kamada, M. Baba, et al., “Clinical Advantages of Carbon Ion Radiotherapy”, New J Physics, vol. 10, 2008.

[4] L. Verhey, H. Blattman, P. Deluca, et al., “ICRU Report 59: Clinical proton dosimetry. Part 1: Beam production, beam delivery and measurement of the absorbed dose”, J ICRU, vol. 30, no.2, 1998.

[5] C. Juan, M. Crispin-Ortuzar and M. Aslaninejad, “Depth-dose distribution of proton beams using inelastic collision cross sections of liquid water,” Nucl Instr Meth Phys Res B, vol. 269, pp. 1861-1882, 2011.

[6] W. R. Leo, Techniques for Nuclear and Particle Physics Experiments: A How-to Approach, New York: Springer-Verlag Berlin Heidelberg, 1994, ch. 2 pp. 17-30.

[7] L. Bianchini, Selected Exercises in Particle and Nuclear Physics, Springer International Publishing AG, ch. 2, pp. 107-111, 2018.

[8] D. Groom, “Energy loss in matter by heavy particles,” Particle Data Group Notes PDG-93-06, 1993.

[9] S. Agostinelli, J. Allison, K. Amako, J. Apostolakis, H. Araujo, P. Arce, et al., “GEANT4 - a simulation toolkit”, Nuclear Instruments and Methods in Physics Research, vol. 506, pp. 250-303, 2013.

[10] S. Agostinelli, J. Allison, K. Amako, J. Apostolakis, H. Araujo, P. Arce, et al., “GEANT4 - a simulation toolkit”, Nuclear Instruments and Methods in Physics Research, vol. 506, pp. 250-303, 2013.

[11] M. Berger, J. Coursey, M. Zucker, J. Chang, (2015). Stopping-Power and Range Tables for Electrons, Protons and Helium Ions. Available: http://www.nist.gov/pml/data/star.

[12] T. Takatsuji, I. Yoshikawa and M. Sasaki, “Generalized Concept of the LET-RBE Relationship of Radiation-induced Chromosome Aberration and Cell Death,” Journal of Radiation Research, vol. 40, no. 1, pp. 59-69, 1999.

[13] H. Paganetti, “Relative biological effectiveness (RBE) values for proton beam radiotherapy, variations and a function of biological endpoint, dose, and linear energy transfer,” Phys. Med. Biol., vol. 59, pp. R419-R472, 2014.

[14] M. Berger, J. Coursey, M. Zucker, J. Chang, (2015). Stopping-Power and Range Tables for Electrons, Protons and Helium Ions. Available: http://www.nist.gov/pml/data/star.

[15] I. Mishustin, I. Pshenichnov and W. Grener, “Modeling heavy-ion energy deposition in extended media”, Eur. Phys. J. D. vol. 60, pp. 109-114, 2010.

[16] T. Kubiak, “Carbon Ion Radiotherapy-Advantage, Technical Aspects and Perspectives,” Joint Institute for Nuclear Research, pp. 44-45, 2013.

[17] C. Terracciano, “Analysis and Interpretation of Carbon Ion Fragmentation in the Bragg Peak Energy Range”, Scuola Dottorale in Scienze Matematiche e Fisiche, 2014.