Quantitative analysis of proton boron fusion therapy (PBFT) in various conditions

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1. Introduction

Proton boron fusion reaction was discovered in 1960. In this reaction, an energetic proton reacts with boron (^{11}B), resulting in the generation of excited carbon (^{12}C) [1]. Then, the carbon divides into a 3.74 MeV alpha particle and beryllium (^{8}Be) [3]. In turn, beryllium divides into two alpha particles, each having the energy of 2.74 MeV. Several features make proton boron fusion reaction attractive for radiotherapy applications. First, the pattern of proton dose delivery has Bragg-peak curve characteristics. Damage to normal tissue can be reduced by delivering a critical dose to the tumor cells. Second, although alpha particles are highly energetic, owing to a very short deposition range (< 9 μm), the alpha particles generated by the proton boron fusion reaction are more adequate for tumor-cell destruction than the proton therapy products. For these reasons, we proposed a novel proton boron fusion therapy (PBFT) in our previous research.

From the theoretical point of view, the PBFT has some strong advantages over currently existing radiotherapy methods. First, boron-based tumor targeting is required prior to performing the treatments such as boron-neutron capture therapy (BNCT) [4]. Tumor targeting should be performed before the BNCT by injecting the boronate compound.8 If boron is not taken up by the normal tissue, the normal tissue can be spared the irradiation by alpha particles. When boron uptake occurs in the target region, selective therapy is possible by neutron capture reaction of labeled boron particles in the target region. Likewise, when boron is distributed in the tumor region for the PBFT, the proposed method can represent a more critical discriminative therapy than either the BNCT or conventional particle therapy.

In the conventional proton therapy, in order to deliver a dose to a tumor, the proton beam energy has to be adjusted along the tumor region (e.g., shape and depth). The proton therapy aims at delivering the maximal dose to the tumor by using protons only. In the PBFT, however, the alpha particles that are the products of the proton boron reaction are utilized for treating the tumors. Alpha particle has a greater impact than protons on the tumor therapy. This suggests that protons are not a direct therapeutic factor, but rather a treatment mediator. During the PBFT, we can also make use of the protons Bragg-peak characteristic. The pattern of proton dose delivery follows the Bragg-peak curve, with a low dose being delivered up to a specific range, and a high dose being dramatically delivered to the specific point by the protons. This characteristic is a strong advantage of proton therapy. This advantage can also be used in the PBFT.

The proton in the PBFT is one of the catalysts for inducing of alpha particle generation. When the catalyst passes through a normal tissue, the damage to the normal tissue is reduced owing to the proton's physical characteristics. In addition, many factors can affect the PBFT effectiveness, including the proton flux and the boronate compound dose. Higher boronate compound dose implies high total boron content in the tumor region. The probability of proton boron fusion reaction is increased according to the usage of boronate compound. In order to acquire the probability of proton boron fusion reaction, the clinical maximal allowance of usage of boronate compound was used. Because the dose delivery is dramatically higher in the PBFT, the proton flux can be reduced comparing with the flux used in the conventional proton therapy. By reducing the flux during the PBFT, the damage to the normal tissue can be reduced while retaining the same therapeutic effect on the tumor cells, compared with the conventional proton therapy.

The PBFT research was issued from previous research. Because the main content of previous study was focused on the introduction regarding application possibility of the proton boron fusion reaction to the radiation therapy, it did not contain the quantitative results in several conditions. When the application possibility is raised by the previous, the succeeding research should be progressed to verify the possibility. Thus, the aim of this study was to analyze for proton's maximal dose from the various physical conditions containing proton energies. Monte Carlo simulations were performed in this study to provide theoretical support to the PBFT. All results were interpreted only based on the simulation data. In the PBFT simulations, the most significant factor of the PBFT was amplification of maximal proton dose by boron. The maximal proton dose is reported as the percentage depth dose (PDD) of the protons beam. The maximal proton dose amplification in the PDD occurred because the simulation accounted for the alpha particle protons.

2. Methods and Results

All simulations reported in this article were performed by using the Monte Carlo n-particle extended (MCNPX, Ver. 2.6.0, LANL, NM, USA) simulation toolkit. Basically, the simulated geometry was comprised of a phantom only. There was a point source

of energetic protons near the phantom. These two simulation conditions were fixed to allow for the comparison between different scenarios. The simulated phantom was filled with water, and the phantom's volume was $6 \times 6 \times 10$ cm^3. The boron uptake region (BUR) was inserted into the water-filled phantom. The physical characteristics of the BUR were varied depending on the simulation scenario. The distance between the proton point source and the water phantom surface was 10 cm. The proton source was pointed at the water phantom. The water phantom was partitioned into 100 slabs with 0.1 cm thickness for measuring the proton dose (slab dimensions were $6 \times 6 \times 0.1$ cm^3) [5]. In order to compare the effectiveness of the PBFT using high energy (> 100 MeV), the dose database for dosimetric effect regarding low proton energy with dramatic condition such as maximal allowance usage of the boronate compound was required. The simulation condition of low proton energy was considered preferentially. The PDD values were obtained by using F6 tally (absorbed dose tally, units: MeV/g) in the MCNPX function. To verify the PBFT effectiveness, four simulation scenarios were considered in which different physical variables were varied. The physical variables included the range of proton degradation and the maximal proton dose.

In this scenario, the simulations were performed to confirm that the proton dose changes when the BUR size changes. In general, although the maximal proton dose is amplified following the proton boron reaction, the minimal BUR size allowing such amplification should be determined. The basic simulation conditions were the same for all simulations described here. Four proton beam energy values (60, 70, 80, and 90 MeV) were used to simulate the reaction [6]. For each proton beam energy, the BUR area was 1×1 cm^2 and different BUR thicknesses were considered (0.9, 0.7, 0.5, 0.3, and 0.1 cm), Although the BUR size was changed, in order to maintain the boron concentration, the density of boron region was adjusted. The boron concentration of 25 mg/g was used to simulate. This value was a little bit higher than usage which can be used to clinical application. The BUR center location was adjusted along with the incident proton beam energy. The BUR center locations (regular center) were 3.3 cm (60 MeV), 4.3 cm (70 MeV), 5.5 cm (80 MeV), and 6.8 cm (90 MeV) from the water surface. For each simulation, after the maximal proton dose amplification was calculated, we determined the minimal thickness necessary for effective induction of the proton boron reaction.

In this scenario, the simulations were conducted to verify the variation of the proton PDD with the BUR location. For fixed proton beam energy, varying the BUR location changes the maximal proton dose. With this data, the proton range degradation depending on the target movement can be established and used in the PBFT treatment planning. In this simulation, proton beam energies were the same ones that were used in the first scenario. The BUR area and the boron concentration were the same as well. However, the BUR thickness was set to 0.9 cm. The BUR center location was varied in steps of 0.1 cm, starting from the location 0.6 cm backward of the regular center to the location 0.6 cm forward of the regular center. Maximal proton dose amplification values were obtained for each simulation condition. The variable amplification became especially noticeable when the BUR water boundary was superposed with the point at which the proton dose was maximal.

The third simulation scenario involved varying the proton PDD along with the boron concentration. For boron particles that are distributed in the tumor region by the boronate compound injection, the distribution of boron particles is more concentrated in the middle of the tumor compared with the tumor's fringes. This phenomenon induces inhomogeneity of boron concentration in the tumor region. Although identical conditions are applied in the therapy, such concentration inhomogeneity can yield location-specific therapeutic effectiveness. In this simulation, the variation of proton dose with boron concentration was evaluated. The boron concentration variation was defined as the BUR density variation. The boron concentration values considered in this scenario for different proton beam energies were 14.4, 16.8, 19.2, 21.6, and 25.0 mg/g. The concentration reduction was performed as approximately 15% to observe the evident difference.

The proton beam energy values used in this scenario were the same as those that were used in previously described scenarios. For each simulation, the maximal proton dose amplification was calculated by employing the maximal proton dose in the water without BUR.

The last simulation scenario was constructed that how the amplification of maximal proton dose depends on the proton beam energy when the location of the BUR was fixed in the water. Two simulations were performed. First, the amplification of maximal proton dose with varying the proton beam energy was calculated when the BUR center location was adjusted to be in the point of maximal proton dose. The proton beam energy was varied from 55 MeV to 95 MeV in 1 MeV steps. The BUR size was not changed in order to maintain the same reaction conditions. The BUR center location was adjusted by 0.1 cm or 0.2 cm for each 1 MeV step of energy change. Second, when the BUR location was fixed, the amplification of maximal proton dose was calculated for different proton beam energies. Because the BUR location was fixed, the impact of the energy range modulation on the target region could be evaluated. Four BUR locations (3.3, 4.3, 5.5, and 6.8 cm) were used as benchmarks in these simulations. These benchmark locations were deduced from the PDDs of four proton beam energies (60, 70, 80, and 90 MeV) obtained from the water phantom without BUR. All other simulation conditions were the same ones as in previously described simulation scenarios.

To determine the maximal proton dose, preliminary simulations were performed before obtaining the main

simulation results. Figure 1 shows both the proton PDDs obtained under normal conditions and the amplified proton PDDs obtained following the proton boron reaction. The proton PDDs obtained under normal conditions were set as 100%. When the points of maximal proton dose were located within the BUR, maximal proton dose was amplified in all four cases (proton energies: 60, 70, 80, and 90 MeV). Points of maximal proton dose (60, 70, 80, and 90 MeV) were located at the depth of 3.3, 4.3, 5.5, and 6.8 cm, respectively. In all cases, the amplification exceeded 50%.

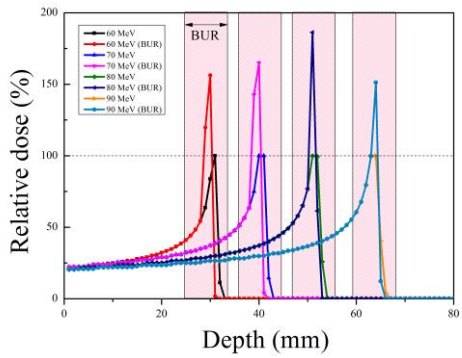

Figure 1. Relative proton dose for different proton beam energies. Four proton beam energies of 60, 70, 80, and 90 MeV were used and the points of maximal proton dose were 3.3 cm, 4.3 cm, 5.5 cm, and 6.8 cm, respectively.

From these preliminary simulations, we determined the points of maximal proton dose depending on the representative four proton beam energies for the benchmark setting. Results of this simulation are quantified in Figure 2. The BUR size variation was defined as the BUR thickness variation. The fiducial level was adjusted to 100% (relative dose level); this fiducial level was calibrated by the maximal dose at the proton beam PDD. For proton beam energies of 60 MeV and 70 MeV, dose amplification was obtained for the BUR thicknesses above 0.3 cm. In the case of 80 MeV and 90 MeV beams, amplification was obtained for the BUR thicknesses above 0.5 cm and 0.7 cm, respectively.

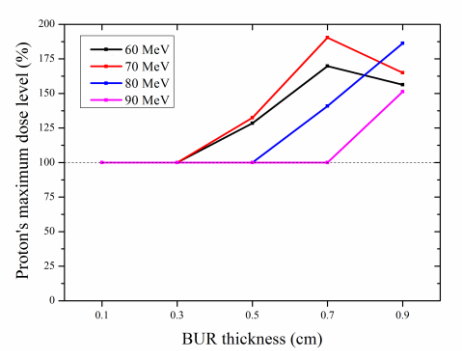

Figure 2. Amplification of proton dose vs. the boron uptake region (BUR) thickness. Four proton beam energies (60, 70, 80, and 90 MeV) were used in this simulation.

Figure 3 demonstrates the dependence of amplification on the BUR movement. Definitely, the BUR movement changes the BUR location. The main result is the change in amplification at the water-BUR surface boundary. In Figure 3, the x axis is the 'Distance difference'. It reports the distance between the boundary and the point at which the proton dose is maximal. Negative distance corresponds to the case in which the point of maximal proton dose is located within the BUR. Although the point of maximal proton dose was not included because of some distance difference, amplification of maximal proton dose was observed in all cases. On average, maximal proton dose amplification occurred at a distance of 0.2 cm ahead of the BUR.

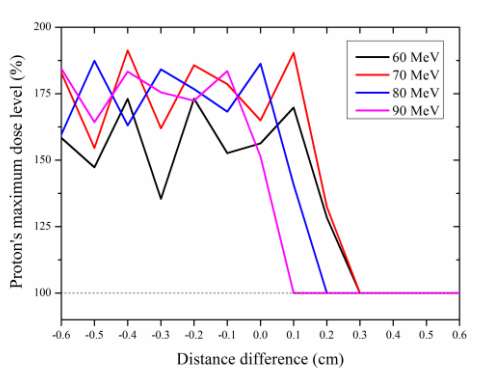

Figure 3. Amplification of proton dose vs. the location of boron uptake region (BUR). The proton beam conditions were characterized by the four proton beam energies as in previously described simulations. The x axis shows the distance from the BUR surface to the point at which the proton dose was maximal.

In the original research, it was shown that the amplification by proton boron fusion reaction depends on the concentration of boron particles in the target region. In the third simulation, we calculated the dependence of maximal proton dose amplification on the boron concentration. The boron concentration was changed by varying the density while keeping the BUR size constant. Some results pertaining to the maximal proton dose in Figure 4 fell short of those obtained under normal conditions (100%). Commonly, for all four proton beam energies, the maximal proton dose tended to increase with increasing boron concentration.

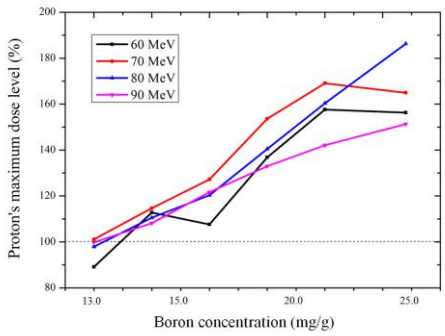

Figure 4. Amplification of proton dose vs. the boron concentration. The proton beam conditions were characterized by the four proton beam energies as in previously described simulations.

The maximal dose difference between the PDD obtained in normal conditions and the PDD obtained by proton boron reaction-related amplification was calculated by using the results of the PDD simulations. In all simulations, the proton beam energy was varied from 60 MeV to 90 MeV in 1 MeV steps. The maximal amplification was 96.62% (obtained at 89 MeV), and the minimal amplification was 53.36% (obtained at 80 MeV). The average amplification was 63.12%.

Proton dose amplification vs. the proton beam energy is shown in Figure 5 for different BUR locations. Because the BUR center locations were based on the locations of maximal proton dose points for different proton energies, the maximal dose is worth noticing. In general, larger proton beam energy yielded stronger amplification. Above a certain proton beam energy value, the dose exhibited dramatic amplification, and for even higher energies, the average amplification was maintained at 50%.

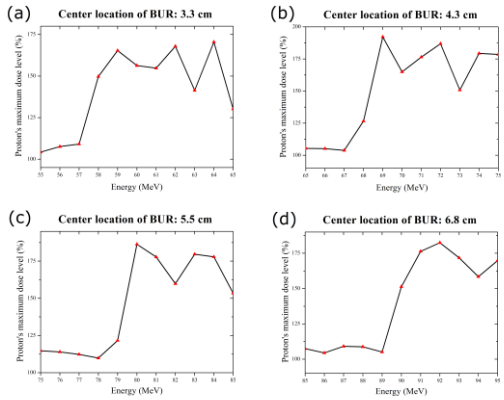

Figure 5. Dependence of dose amplification on the proton beam energy for different boron uptake region (BUR) locations. The BUR center locations were adjusted for the maximal proton dose for four representative energy values. The energies 60, 70, 80, and 90 MeV corresponded, respectively, to the following locations: (a) 3.3 cm, (b) 4.3 cm, (c) 5.5 cm, and (d) 6.8 cm.

3. Conclusions

In this study, the effectiveness of the PBFT with respect to several physical parameters was evaluated quantitatively by using Monte Carlo simulations. We confirmed that the PBFT can be used to perform critical discriminative therapy. Also, the results of our studies can be used for constructing the PFBT dose database that can be utilized in treatment planning systems (TPSs). In the future studies, the PBFT effectiveness will be validated experimentally.

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