New Physics: Sae Mulli,
Vol. 69, No. 2, February 2019, pp. 215∼220
http://dx.doi.org/10.3938/NPSM.69.215

Evaluation of Proton-Boron Fusion-Enhanced Proton Therapy (PBFEPT) by Using a Simulation Method

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(Received 11 September 2018 : revised 25 October 2018 : accepted 29 October 2018)

Radiation therapy is a technique for delivering sufficiently high doses to target cells while keeping the dose to neighboring normal tissues as low as possible. As an advanced radiation therapy method, proton therapy has a more ideal dose distribution than either electron or photon therapy due to the Bragg peak. Recently, an enhanced proton therapy based on the proton-boron (^{11}B) fusion reaction was proposed. For this method, alpha emitters from proton-boron fusion reactions are utilized to improve the dose deposition in the target. A few studies have confirmed this method by using the Monte Carlo N-Particle (MCNP) code. In our study, a mathematical method and the GEometry ANd Tracking (GEANT4) toolkit are combined to evaluate and analyze the dose distribution of the proton-boron (^{11}B) fusion-enhanced proton therapy (PBFEPT) method. Calculations of both the emitters of proton-boron (^{11}B) fusion reactions based on related cross-sections and the dose distribution of alpha emitters by using Geant4 toolkit, PBFEPT is found relatively to enhance the dose deposition in the target volume. This results agrees with those of previous studies.

PACS numbers: 42.62.Be, 29.25.-t
Keywords: Proton therapy, Proton-boron (^{11}B) fusion-enhanced proton therapy (PBFEPT), Monte Carlo method

I. BACKGROUND

1. Proton Therapy

As an advanced external radiotherapy method, proton therapy utilizes high energy proton beams rather than photon beams to irradiate the target volume for destroying the target cells. Based on the Bragg peak feature, proton therapy is more professional to conform the shape and depth of a target volume, while reducing the risk to the surrounding normal tissues [1–4].

2. Principles of Proton Boron (^{11}B) Fusion Enhanced Proton Therapy (PBFEPT)

Recently, several non-conventional proton therapy methods are proposed, which are called enhanced proton therapy methods that aim to enhance the dose deposition of the target volume and without the dose increase of normal volumes. One of these methods is proposed based on the Proton Boron (^{11}B) Fusion Reaction (PBFR). In which, when the PBFR takes place, firstly the boron nucleus changes to a carbon (^{12}C) nucleus in an excited state, then the excited carbon nucleus may split into an alpha particle of 3.76 MeV and a beryllium (^{8}Be). Subsequently, the beryllium nucleus decays into two alpha

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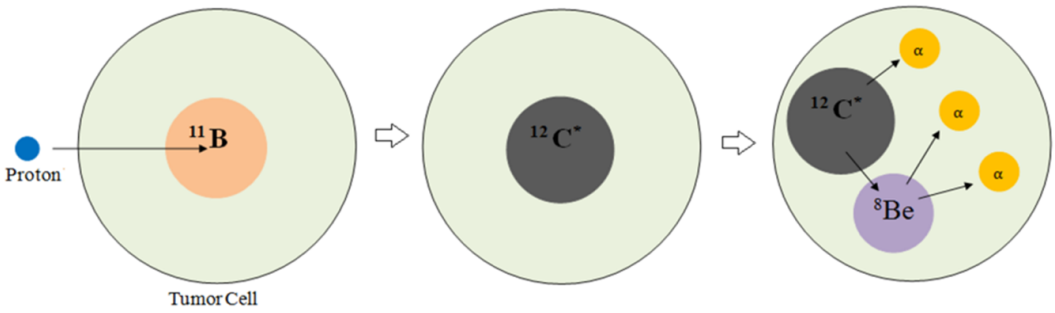

Fig. 1. (Color online) The schematic diagram of PBFR and PBFEPT. In which, the agents contain ^{11}B are injected in advance and can be selected deposited into target cells mostly. With the irradiation of protons, the PBFRs take place, and emit three alpha particles with two kinds of energies. These alpha particles may targeted destroy the local cell due to their short range in cell.

particles with 2.74 MeV. In total, three alpha particles are emitted at the place of PBFR. The processes can be shown in the following equations.

$$\begin{aligned} {}^{11}B + p &\rightarrow {}^{12}C* \\ {}^{12}C* &\rightarrow {}^{8}Be + \alpha \text{ (3.76 MeV)} \\ {}^{8}Be &\rightarrow 2\alpha \text{ (2.74 MeV)} \end{aligned}$$

In summarized:

$$^{11}B + p \rightarrow 3\alpha$$

Therefore, this enhanced proton therapy method can be called Proton Boron (^{11}B) Fusion Enhanced Proton Therapy (PBFEPT). In which, the alpha particles emitted from PBFRs are utilized as the addition targeted radiation to improve the dose deposition in the target cells. The diagram of PBFEPT is shown in Fig. 1.

For this method, a few studies have been carried out confirming this method by the MCNP program [1–3]. In this investigation, the PBFEPT method is studied and evaluated by using combined Mathematical calculation and Geant4 Monte Carlo calculation.

II. METHOD

Because the process of PBFR is not included in Geant4 toolkit, in order to calculate the dose deposition induced by both proton beam and alpha emitters of PBFR, this investigation method consists of two steps. The first step is the calculation of the number of alpha emitters from PBFRs for specified boron concentrations. The second step is calculation of the dose deposition in target volume for various situations. In which, there are no boron in contrast group. Therefore, the dose deposition for contrast group is induced by only proton beam. For other groups that contain different concentration of boron, the dose depositions are induced by both proton beam and alpha emitters from PBFRs.

1. Mathematical Calculation for the Number of Produced Alpha Emitters

For obtaining the number of produced alpha emitter from PBFRs, the number of reactions should be calculated firstly. For PBFRs, the number of reactions can be calculated by using the following equation:

$$R = N^{11}B \times \sigma \times \Phi, \tag{1}$$

where R: number of fusion reactions, $N^{11}B$: atomic number density of ^{11}B, which expresses the concentration of ^{11}B atoms in a volume. Here, the concentration of ^{11}B in natural boron is assigned as 80%. σ: cross section of PBFRs. The cross section for PBFRs has a max peak value of 0.9 barn, when the energy of proton is about 670 keV (The boron is only contained in the target volume, when proton incident into target, collide with boron and induce the PBFRs, the most incident protons is slowing down and their energy is also already reduced to about 670 keV from original higher energy level, such as 100 MeV. Therefore, when the PBFRs take place mostly, the energy of proton is about 670 kev). Here, the max value for cross section of PFFRs (0.9 barn) is used.

Φ: the number of incident protons, here the number is defined as 1.364387×10^9.

Table 1. The number of PBFRs in six groups of sample materials, which have various boron concentrations.

Groups	Mass of Water (g)	Mass of Borax and ^{11}B (g)	Concentration of Borax (weigh %)	Number of PBFRs (R)
A	50.00	0.00, 0.000000	0.00	0
B	49.75	0.25, 0.023094	0.50	304657
C	47.50	2.50, 0.230935	5.00	3046570
D	45.00	5.00, 0.461870	10.00	6083140
E	42.50	7.50, 0. 692805	15.00	9129710
F	40.00	10.00, 0.923740	20.00	12176280

Table 2. The number of alpha emitters with two kinds of energy.

Groups	Number of Alpha Emitters (3.76 MeV)	Number of Alpha Emitters (2.74 MeV)
A	0	0
B	304657	609314
C	3046570	6093140
D	6083140	12166280
E	9129710	18259420
F	12176280	24353560

The Atomic Number Density (N) of ^{11}B can be calculated by using the following equation:

$$N = n/V \tag{2}$$

In which, the V is the volume of ^{11}B that can be calculated, and the Number of Atoms (n) can be obtained by following equation:

$$n = mN_A/M \tag{3}$$

In where: m: the mass of ^{11}B, M: the atomic weight of ^{11}B (is 11.009), N_A: the Avogadro's number (6.022×10^{23} atoms or molecules per gram-mole)

In this investigation, boron delivery material is defined as borax ($Na_2B_4O_7{\cdot}10H_2O$) for comparison with the future experiments results. The six groups of materials including various boron concentrations are assigned as shown in Table 1. Then, the mass of ^{11}B in each groups of materials can be calculated and are shown in Table 1. In which, the material of target volume for Group A is water, and the materials of target volume for Group B to F are various concentration of boron solution. The volume of each group is measured in 20 Celsius degree. Then, by using Eq. (1), (2) and (3), the number of PBFRs for different boron concentration can be calculated and are shown in Table 1.

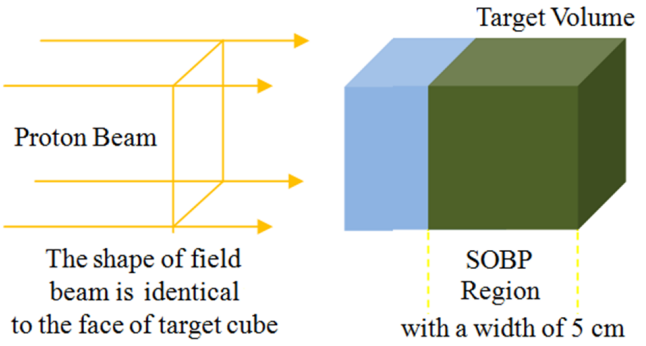

Fig. 2. (Color online) The principle of investigation. The target is defined as a cube with side length of 5 cm, and the thickness of tissues that in front of target is 3 cm. 15 proton beams with assigned energies is used to form a SOBP to cover the volume of target.

Then, the number of two kinds of alpha emitters with different energies can be calculated by using Eq. (4) and (5), and are shown in Table 2.

$$\text{The Alpha Emitters with energy of 3.76 MeV} = R \tag{4}$$

$$\text{The Alpha Emitters with energy of 2.74 MeV} = R \times 2 \tag{5}$$

2. Simulated Calculation

The principle of simulation is shown in Fig. 2. The volume with the name "target volume" is designated as the planning target volume (PTV), which is defined as a cube with a volume of 125 cm^3. The normal tissue in front of the target volume is assigned a thickness as 3 cm, and the material of normal tissue is water.

As for the beam parameters, 15 pristine Bragg peaks are used to create the Spread-out Bragg peak (SOBP) that is used to cover the target volume. In addition,

Table 3. The chemical composition of each group materials for simulation.

Group	Chemical Compositions (Mole Ratio of Each Element)				Density (g/cm^3)
	H	O	Na	B	
A	2	1	0	0	1.9832
B	77.56	38.843	0.018	0.036	0.9875
C	75.68	38.47	0.18	0.36	1.0088
D	73.6	38.06	0.36	0.72	1.0372
E	71.61	37.73	0.55	1.10	1.0654
F	69.56	37.35	0.73	1.46	1.0953

the incident proton beams are assigned as field beams with area of 25 cm^2, which is identical to any face of target volume cube. As a result, the target volume can be completely covered by the SOBP. In simulation, the FTFP_BERT Physics List is applied, which includes all of the interaction processes of alpha particle and proton in matters. For group A, by using specified number of incident protons, the absorbed dose is about 5 cGy for target volume. For groups B to F, the two kinds of alpha emitters with different energy and assigned particle number are uniform distributed in target volume.

For simulation, the chemical compositions of target for each group are defined and summarized in Table 3. Moreover, in order measure the densities, the six groups of materials are prepared, and are measured by using density meter.

III. RESULTS AND ANALYSIS

The results for dose deposition induced by alpha emitters in each group are shown in Table 4. For group A, the dose deposition is null, because no boron is contained in material, accordingly no PBFRs take place. Then, by using the enhanced doses value in Table 4, the total dose deposition induced by both protons and alpha emitters of PBFR for each group can be calculated and shown in Table 5. The calculation results about enhanced dose value induced by alpha emitters for each group are shown in Fig. 3, and the total dose deposition in target volume induced by alpha emitters and proton beam for each group are shown in Fig. 4.

Through analyzing the above calculation results, it can be seen that the absorbed dose of target volume is enhanced due to the alpha emitters from PBFRs when the

Table 4. The dose deposition induced by alpha emitters from PBFRs for each group.

Group	Dose induced by Alpha Emitters of PBFRs (cGy)
A	0.0000
B	0.0793
C	0.4346
D	1.2332
E	1.6890
F	2.5294

Table 5. The total dose deposition in target volume for each group.

Groups	Concentration of Boron (weigh %)	Total Dose Depositions (cGy)	Enhanced Rate %
A	0.00	5.0346	0.0000
B	0.50	5.1039	1.3765
C	5.00	5.4692	8.6323
D	10.00	6.2678	24.5045
E	15.00	6.7236	33.5479
F	20.00	7.5640	50.2403

^{11}B is contained in the target material. Moreover, with the increase of boron concentration, the enhanced rate of dose value is also increased. For Group B and C, the dose enhanced dose rate is lower. Therefore, this means the lower boron concentration may enhance the dose deposition. However, the enhanced value is very ineffective. In contrast to this, it can be seen that for Group D, E and F, the dose is effectively enhanced, especially, the dose enhanced rate achieve to fifty percent in Group F. This suggested us that concentration of boron is a critical important factor to influence the enhanced dose value, and it should be preferentially considered for clinical application.

Based on the theoretical and experimental investigations about PBFR, it can be seen that the highest cross-section of PBFR take place at the proton with energy of 600-700 keV. Also at such energy, the Bragg peaks of proton mostly take place. Therefore, the cross-section of PBFE is lower for higher energy protons in the proximal region of Bragg peak (tumor region), and the most PBFRs take place at the area of Bragg peak [6–11]. In addition, in clinical applications, the boron delivery drugs should be injected to tissue and the concentration

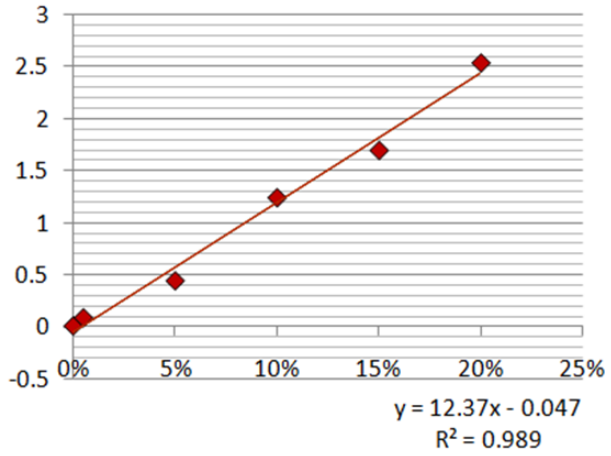

Fig. 3. (Color online) The pure enhanced dose induced by emitters from PBFRs for various borax concentrations. The two fitting lines are obtained according to the 6 groups of calculation results. Here, the linear fit is used and R-squared is a statistical measure of how close the data is to the fitted regression line.

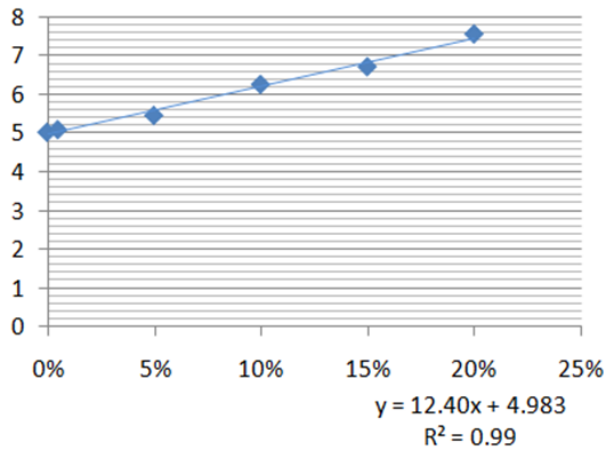

Fig. 4. (Color online) The total dose deposition in target volume for various borax concentrations. The two fitting lines are obtained according to the 6 groups of calculation results. Here, the linear fit is used and R-squared is a statistical measure of how close the data is to the fitted regression line.

of boron in tumor tissues (covered by SOBP) is higher than that in the neighboring normal tissues. Therefore, boron concentration is lower in normal tissues compare to in tumor tissues. This is another reason that makes PBFRs mostly takes place in tumor tissues. As a result, in clinical application of PBFRPT, the PBFRs take place rarely in the upstream area of the tumor tissues (target volume), and the absorbed dose of tumor volume can be enhanced, relatively. Therefore, compared to conventional proton therapy, PBFEPT can enhance the dose ratio of SOBP and proximal region.

Moreover, except the main advantage on distribution of physical dose, other advantages benefit from PBFR can be found, through analyzing the p(^{11}B, 3α) reaction and refering related research. These benefits are summarized as follows.

1. The PBFR has a relative higher cross-section among proton induced fusion reactions [12–14].

2. The alpha emitter has a more ideal oxygen enhancement ratio (OER), linear energy transfer (LET) and relative biological effectiveness (RBE).

3. The PBFR is neutronic (neutron-free), therefore no dose calculation about neutrons is considered [12–17].

4. The alpha emitters with a short path range largely deposit the dose into the local target cells.

5. Correct this phrase can be utilized for a real-time imaging technique [17–19].

As for the boron delivery drugs that used to take the boron into target cells, the sodium borocaptate (BSH) and boronophenylalanine (BPA) which are applied in BNCT (Boron Neutron Capture Therapy) can be considered as the candidate [20,21].

IV. CONCLUSIONS

In this investigation, based on the definition of various boron concentrations, by using mathematical method, the numbers of alpha emitters from PBFR are calculated. Then, through utilizing the Monte Carlo calculation, the interaction of the alpha emitter and materials are simulated, and the dose depositions of alpha emitters are calculated. As a result, the dose depositions in target volume for various boron concentrations are obtained. Through analyzing the results, it can be seen that in PBFEPT the alpha emitters have the potential to enhance the dose deposition for SOBP region compare to the conventional proton therapy. In addition, with the increase of boron concentration in target volume, the enhanced rate is also increased. In conclusion, the PBFEPT can be considered as a candidate of the enhanced proton therapy, which may relatively enhance the dose deposition of target volume, and accordingly enhance the dose ratio of SOBP and proximal region compare to conventional proton therapy.

ACKNOWLEDGEMENTS

This research was supported by grant number 2013M7 A1A1075764.

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