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Author for correspondence:
Navid Khaledi, Institute of Modern Physics, Fudan University, Shanghai 200433, China.
Tel: +86-13162274707.
E-mail: khaledi@fudan.educn

Is the proton–boron fusion therapy effective?

Navid Khaledi[1,2], Xufei Wang[1,2], Roghiye B. Hosseinabadi[3] and Farhad Samiei[4]

[1]Institute of Modern Physics, Fudan University, Shanghai 200433, China; [2]Key Laboratory of Nuclear Physics and Ion-Beam Application (MOE), Fudan University, Shanghai 200433, China; [3]Department of Environmental Health, Khoy University of Medical Science, Khoy, Iran and [4]Radiation Oncology Department, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Introduction: In the recent years, some publications (mainly from one group of authors) have dealt with the effectiveness of proton–boron fusion therapy (PBFT). This theory is based on the Q-value of three produced α particles in the reaction of protons with boron (^{11}B). They claim that this reaction significantly increases the absorbed dose in the target volume. However, the current study would re-evaluate their method to show if PBFT is really effective.
Methods and materials: A parallel 80-MeV proton beam was irradiated on a water medium in a cubic boron uptake region (BUR). The two-dimensional dose distribution and percentage depth dose of protons, alphas and all particles were calculated using tally F6 and mesh-tallies by Monte Carlo N Particle Transport code.
Results: The results not only showed that the dose enhancement in BUR is neglectable but also the higher density of BUR in comparison with water led to decrement of dose in this region. Because of low cross section of boron for proton beam (<100 mb), the α particles' dose is 1,000 times lower than the proton dose.
Conclusions: The physical aspects and the simulation results did not show any effectiveness of the PBFT for proton therapy dose enhancement.

Introduction

Different techniques and methods are being used for improving the effectiveness of radiation therapy, to increase the target dose and reduce the delivered dose to surrounding healthy tissues. One of the methods is delivering a radio-sensitisation agent to the target to intensify cumulative dose by physical phenomenon like photoelectric or nuclear fusion. In proton therapy, some studies have been done to evaluate the proton dose enhancement by fusion-released energy. In this theory, when a proton collides with ^{11}B nuclei, the $^{11}B(p,\alpha)2\alpha + \gamma$ (719-keV prompt gamma) reaction occurs. The Q-value of this reaction is 8·6 MeV, which means that one ionising particle (proton) produces three ionising particles (alpha) with higher relative biological effectiveness.

The first study on radio-sensitivity by fusion was introduced in 2014.[1]

Yoon et al.[1] simulated the irradiation of an 80-MeV proton beam on a water phantom by Monte Carlo (MC) N Particle Transport (MCNPX) computer programming, also known as coding (Los Alamos National Laboratory).[2] They inserted a cubic of boron-11 (^{11}B density = 2·08 g/cm^3) in the water phantom at the Bragg peak depth to magnify the peak. A maximum of 79·5% increment in the peak height was reported. So, it was claimed that the proton–boron fusion therapy (PBFT) method can increase the proton therapy dose to the treatment target. Consequently, they proposed further studies on the effectiveness of their concept.

In 2016, Jung et al. published another article about PBFT for 60-, 70-, 80- and 90-MeV proton beams with boron concentrations of 14·4, 16·8, 19·2, 21·6 and 25·0 mg/g^3. Although they used a pure ^{11}B in the boron uptake region (BUR), they assumed that the mentioned concentration is obtained by changing the amount (size) of ^{11}B in the water phantom. Latterly, a 96·62% amplification of proton dose was reported.[3] Therefore, it was concluded that this method decreases the normal tissues dose, and it can be used for an accelerated treatment.

In March 2017, the same researchers presented the results of treatment planning simulation for a simple phantom that had volumes for planning target volume (PTV) and organ at risk (OAR).[4] Again, they used a cubic BUR with pure ^{11}B. They reported the dose increment to PTV and better sparing of the OAR in the cases with BUR placement. As a result of this research, they point to the requirement of additional investigations to benchmark the possible clinical applications.

In February 2017, Jung et al. compared PBFT with boron neutron capture therapy (BNCT) by MC simulation.[5] The energy range was 75–85 MeV with 1-MeV steps. The concentration of the boron was 1·04 mg/g. They used this high-level concentration to observe the amplification of proton peak. The results were similar to their previous works. In addition, they suggest that the produced prompt gamma ray in the PBFT fusion reaction may be used for imaging purposes (which was investigated in their following publication[6]). In addition, they concluded that the PBFT benefits from the advantages of both BNCT and proton therapy.

In all of the above papers that are published by a unique research group, the Bragg peak occurred inside the pure or very high concentration of boron cube. Furthermore, the results are based on MCNPX simulations.

In January 2018, a paper published by Cirrone et al. concentrated on the first experimental proof of PBFT.[7] Their in vitro study reported a significant cell lethality and chromosome aberration in a PBFT case. However, their findings were questioned by Mazzone et al., some months later.[8] Mazzone et al. performed some MC calculations by GEANT4[9] and, consequently, indicated that the results cannot demonstrate the dose enhancement for the in vitro setup because the yield of alpha particles is too low to affect the proton therapy dose. In addition, any boron carrier agents such as boronophenylalanine have a small uptake in the tumour. The mentioned in vitro investigation[7] will not be prepared in the current study, because it was prepared by the above-mentioned study,[8] and it has a different structure than our work. However, the first group's results[1,3–5] will only be dealt on to see whether the used ^{11}B concentration is realistic? And also how much is the proton dose enhancement by the produced alpha particles? In fact, the current study contests the results of specific literatures[1,3–5] in terms of physical scientific basis and validity of the MCNPX simulation. Therefore, the cross section of the $^{11}B(p,\alpha)2\alpha$ reaction, as well as simulation of interaction between proton beam and a BUR inside a water phantom, was investigated.

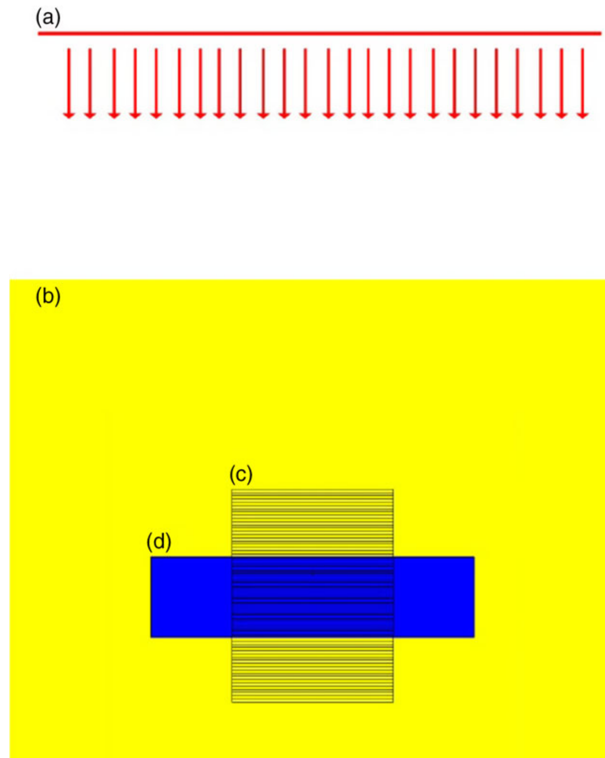

Figure 1. The circular proton source (a), the water phantom (b), the dose scoring cells (c) and the BUR (d).

Materials and Methods

For unifying the conditions between this and the mentioned studies,[1,3–5] it was tried to apply same situations, methods and tools as much as possible. Accordingly, the MCNPX code version 2.6[10] was also used in this study. The calculation MODE was set to electron, proton and alpha (e, h and a) particles. In MCNP, the MODE is used to define the type of source particles to be tracked. The particles' importance (IMP) was set as unit. The IMP keyword tells MCNP what weight to assign to particles inside a cell (inside BUR, water phantom, air, etc.). Furthermore, to include the alpha and proton capture, the energy cut-off (CUT) was set to zero. If the energy of a particle becomes lower than CUT value, its tracking is stopped. MCNP has some calculation functions named Tally that are used for scoring different radiation parameters such as flux, current, kerma, dose and energy deposition. For calculating the absorbed dose and the energy deposition, F6 tally and mesh-tally types 1 and 3 were employed. The F6 tally without the plus character (+F6) only calculates the indicated specific particle's dose. However, the +F6 tally scores the energy deposition from all particles. The mesh-tally type 1 with the predefined *PEDEP* keyword acts like the F6 tally. Consequently, the mesh-tally type 3 is an equivalent to +F6 tally. However, the mesh-tallies score the energy deposition per unit of volume, not unit of mass. Therefore, the mesh-tallies are not suitable for a heterogeneous medium.

The circular proton surface source diameter was 4 cm and its energy considered as 80 MeV that irradiated on a water phantom with a 2-cm diameter BUR with a thickness of 0·5 cm at the depth of 5·1 cm (Figure 1).

The MCNP uses Data Libraries or Model Physics depending on the energy range, the isotope and the particle type. For proton particles, the data libraries (LA150[11] and ENDF/B-VII[12]) are available only for limited isotopes that do not include the boron. Therefore, the MCNP applies model physics instead.

To obtain the proton and alpha percentage depth doses, the depth of 4·4 to 5·8 cm of the water phantom (including the BUR) was divided into 200-micron-thick cells. These cells score the absorbed dose at every 200-micron-step depths by tally F6. Consequently, a same strategy was employed through the mesh-tally types 1 and 3.

Results

Mesh-tally results (energy deposition)

As described above, the mesh-tallies do not score the dose; they calculate energy deposition per unit of volume. As shown in Figure 2, the total energy deposition for all particles (protons and alphas) shows 92% increment in the peak height with the BUR, in comparison to without the BUR case. By inserting the BUR, the continuous-slowing-down approximation (CSDA) range was decreased from 5·4 to 5·2 cm.

Figure 3 shows the alpha particles' energy deposition per unit of volume. By inserting the BUR, an energy deposition peak is appeared. This peak is the result of three alpha particles' production per each proton–boron interaction. Here, the CSDA ranges with and without the BUR are 5·15 and 5·1 cm, respectively.

The comparison of total particles' and alpha particles' energy deposition in the phantom, with and without the BUR, can be seen in Figure 4. The peak height of the total energy deposition is 500 times of alpha particles with BUR insertion.

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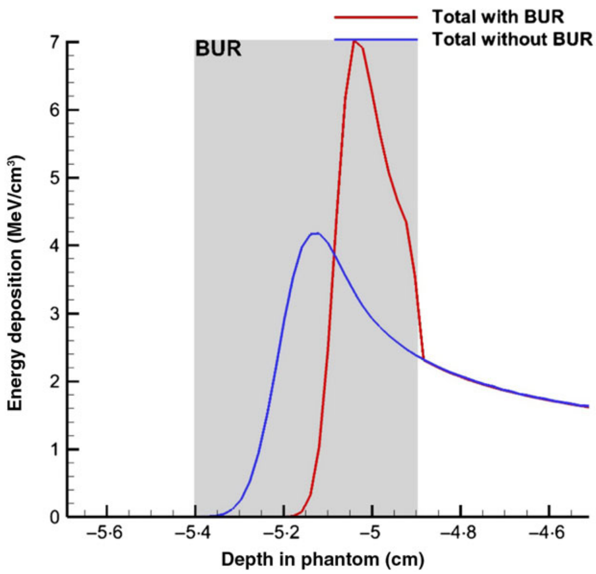

Figure 2. The total energy deposition per unit of volume for all particles in water phantom with and without the BUR.

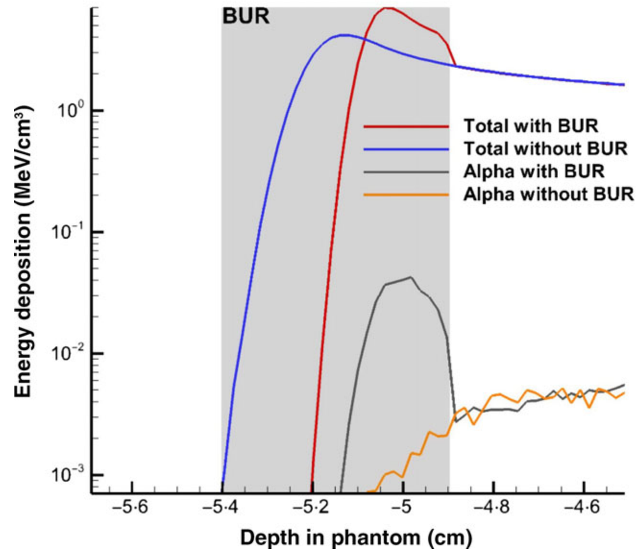

Figure 4. Comparison between total particles' and alpha particles' energy deposition with and without the BUR.

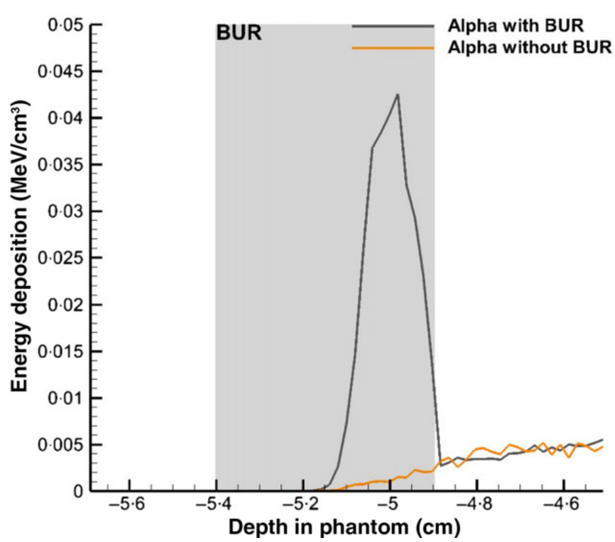

Figure 3. The alpha particles' energy deposition per unit of volume in water phantom with and without the BUR.

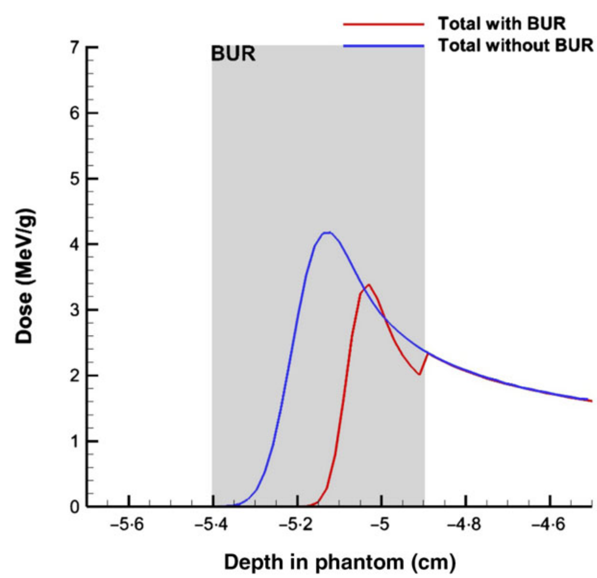

Figure 5. Total dose of all particles with and without the BUR.

F6 and +F6 tallies results (dose)

By considering the density of BUR (2·08 g/cm^3) through +F6 tally, the total dose of all particles is shown in Figure 5. The Bragg peak shows a 20% decrease in the height by taking into account the BUR. Consequently, the alpha particles' dose, calculated by F6 tally, has been shown in Figure 6. The total particles' and alpha particles' Bragg peaks with the BUR show a significant reduction in comparison with their energy deposition curves (Figures 2–4). In addition, the total particles' dose is 500 times of alpha particles (Figure 7).

Discussions

The B11(p,2α)He4 interaction with a Q-value of 8·6 MeV has a maximum cross section of 800-mb (millibarn) peak (Figure 8).[13,14] This cross-section value is quite low for having significant interactions and, correspondingly, desirable alpha particles' dose to boost the primary proton dose. Compared with similar nuclear fusion reactions that are being used in clinic, such as BNCT in which ^{10}B has a cross section of 3,837 b for thermal neutrons, the 800 mb is quite low. In addition, the indicated cross-section peak (800 mb) occurs at the end of protons range, after the Bragg peak,[15,16] where the energy of incident protons falls to below 1 MeV. Therefore, in the Bragg peak region, the cross section is less than 800 mb.

The proton beam energy in our study was 80 MeV that is similar to[1,3–5] the 80-MeV[1]; 60-, 70-, 80-, 90-MeV[3]; 60- to 120-MeV[4]; 75- to 85-MeV[5] protons that were used in the mentioned papers. Furthermore, they used pure ^{11}B cubics[1,3,4] as proton dose booster, which was done in the current work as well. However, no

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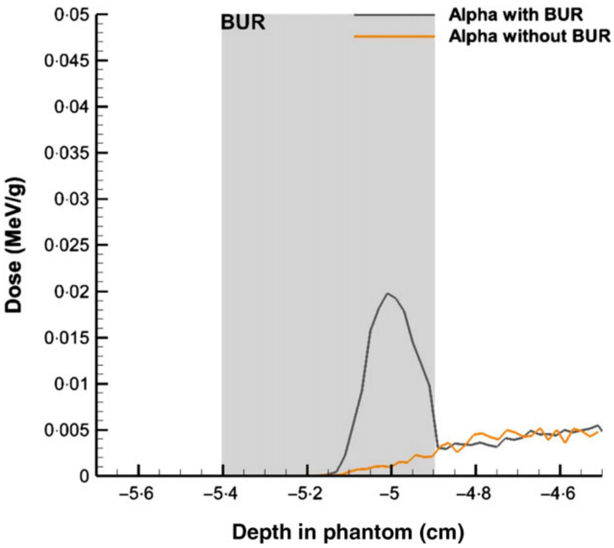

Figure 6. The alpha particles' dose with and without the BUR.

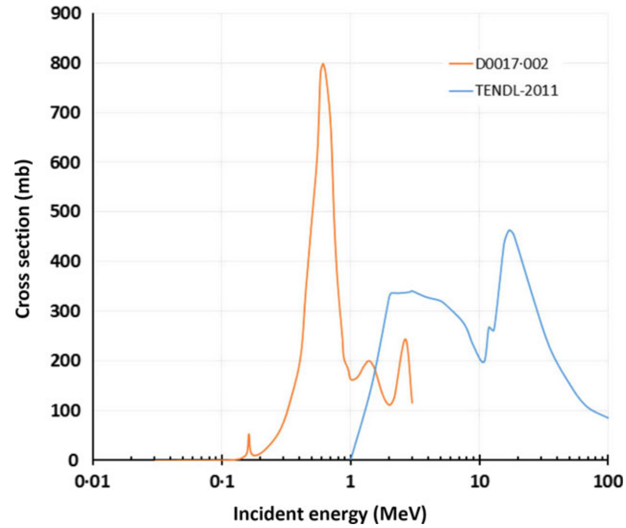

Figure 8. The cross section of B11(p,2α)He4 interaction according to TENDL-2011[14] and JANIS (D0017·002).[13]

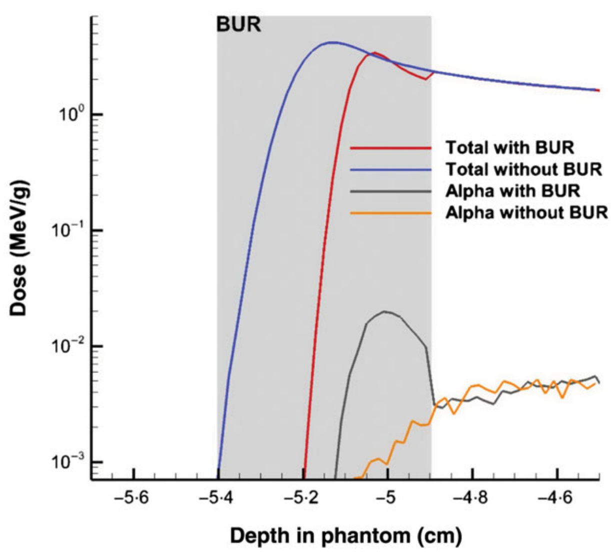

Figure 7. Comparison between total particles' and alpha particles' dose with and without the BUR.

enhancement was seen in the proton 'dose' that has a full agreement with the physical basis of the low cross-section fusion of ^{11}B.

As mentioned above, the MCNPX uses model physics for interaction between protons and boron, so there are no experimental data libraries. The model physics in MCNP applied in a specific range of energy that the code uses in purely theoretical-based calculations (model) for particle transport, instead of experimentally obtained libraries. This range of energy varies for different isotopes and particles. However, the literatures[1,3,5,6] talk about using the 'default library' in their MCNPX calculations, while there is no 'default' library available.

The maximum non-toxic concentration of boron in tumour is under 100 μg/g,[17–19] but the literature concentrations were hundreds of clinical values, varied from 1 g/g (100%)[1,4] to 1·04 mg/g[5] and 25 mg/g.[3]

As shown in Figures 6 and 7, the alpha particles' Bragg peak had a neglectable amplitude in comparison with the protons dose. However, the mentioned studies reported 79·5[1] to 96·62%[3] increase in the Bragg peak intensity. These reported increments are similar to Figure 2 in the current study, which is the energy deposition per unit of volume. In addition, even in terms of energy deposition, the amplification is due to the higher mass density of boron in comparison with the water, not alpha particles' energy deposition.

Despite the analytical and theoretical methods used in this work, it is recommended that an experimental research is done to investigate the real word. Because of the analytical part of the current work and the results of the past works,[1,3–5] the results are based on the MCNPX simulation, which uses model physics, not experimental data. For instance, a similar setup can be established with a dosimetric film sandwiched in solid water and BUR. The film sheet is parallel with the irradiating proton beam. As an alternative, the gel dosimetry can be applied.

Conclusion

The published literature presents the energy deposition enhancement, not the dose. The energy deposition enhancement is due to the higher density of the boron in comparison with water, not the alpha production. In addition, at the presented levels of concentrations in the literature, they are higher than the tolerable level for human body.

Our findings demonstrated that the PBFT is an ineffective and unrealistic method in proton therapy.

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