

A Treatment Planning Comparison of BPA- or BSH-based BNCT of Malignant Gliomas

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Introduction

Accurate delivery of the prescribed dose during clinical BNCT requires knowledge (or reasonably valid assumptions) about the boron concentrations in tumor and normal tissues. For conversion of physical dose (Gy) into photon-equivalent dose (Gy-Eq), relative biological effectiveness (RBE) and/or compound-adjusted biological effectiveness (CBE) factors are required for each tissue. The BNCT treatment planning software requires input of the following values: the boron concentration in blood and tumor, RBEs in brain, tumor and skin for the high-LET beam components, the CBE factors for brain, tumor, and skin, and the RBE for the gamma component.

In addition to the ongoing clinical BNCT program in Japan using BSH and the planned trial in Europe with BSH, there is interest among several BNCT groups in the USA in BSH-based BNCT. There is some uncertainty in the BNCT community and literature about the parameters to be considered for BSH regarding tumor/blood ¹⁰B concentration ratio (range: 0.5:1 to 2.2:1) [1,2], CBE factor in brain (range: 0.37 to 0.5)[3,4], and CBE factor in tumor (range: 1.2 to 2.3)[5,6]. In the present work, we applied different combinations of these parameters and used BNCT treatment planning software with actual patient geometry for a direct comparison of a BPA-based plan to the plan that would be obtained for patient treatment with BMRR epithermal neutron beam using BSH.

Materials and Methods

Treatment plans for BSH using different combinations of the input parameters (Table 1) were prepared and compared to the BPA plan used for a representative glioblastoma patient treated at Brookhaven National Laboratory. Treatment planning procedures and parameters used for estimation of radiation doses delivered during BPA-based BNCT are described in this volume by Capala et al. [7]. All treatment plans used a single-field exposure and were run with a prescribed limit of 12.6 Gy-Eq as the maximum dose to a 1 cm³ volume of normal brain outside of the tumor volume (contrast enhanced volume on MRI scan) delivered in a single fraction.

Results and Discussion

Results of these simulations are listed in Table 1. Average doses to the whole brain volume were approximately 4 Gy-Eq and were similar with BPA and BSH. The BPA-based treatment delivered a minimum of 38.1 Gy-Eq to the deepest portion of the tumor. The doses to the tumor volume were considerably lower with BSH in all cases except those involving the most favorable

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set of assumptions. Typical dose volume histogram obtained from BPA-based treatment plan was shown in Figure 1 along with examples of dose-volume histograms that resulted from different sets of assumptions regarding ^{10}B concentration in the blood and ^{10}B tumor-to-blood ratio for BSH-based treatment plans (Figure 1). Only the most optimistic BSH-based treatment plan, which assumed CBE values of 0.37 and 2.3 for the brain and the tumor, respectively, ^{10}B concentration in the blood of 30 ppm and ^{10}B tumor-to-blood ratio of 2:1, produced dose-volume histograms comparable to those obtained using BPA as a boron delivery agent.

In this work we have, for BSH, used CBE factors and ^{10}B concentrations that, to the best of our knowledge, span the range of published values from both animal experiments and clinical studies. Published reports of BSH biodistribution in animal tumor models have generally shown that the boron concentration in the tumor is only about 50% of that in the blood, i.e. a tumor-to-blood ratio of 0.5:1. A recent report from Japan [1] described BSH biodistribution data from 39 patients. The ^{10}B concentrations reported for tumor and blood were 26.5 ± 3.4 and 12.7 ± 0.8 $\mu\text{g } ^{10}\text{B/g}$, respectively, for a tumor-to-blood ratio of 2.1:1. The tumor-to-blood concentration ratios used for the simulations in this report were varied from 1:1 to 2:1. Treatment plans 1 - 9 (Table 1), represent various combinations of the input parameters for BSH. Plan 1 uses the values reported by Hatanaka [1]. Plans 2-9 use tumor-to-blood ratios of 1:1 (Plans 2 -5) and 2:1 (plans 6-9) at two different blood boron concentrations, 20 and 30 ppm, respectively. In addition, at each blood boron concentration, two sets of CBE factors were used as a way of exploring the effect of uncertainty in these parameters. The plans using 0.5 as the CBE factor for brain and 1.2 as the CBE factor for tumor are considered a "worst case", whereas the combination 0.37 as the CBE factor for brain and 2.3 as the CBE factor for tumor is considered a "best case" scenario for BSH-based BNCT. Our results showed that if BSH were used in the current BNL protocol (BMRR epithermal neutron beam, single fraction), only very optimistic assumptions regarding CBE factors, and ^{10}B distribution would produce the radiation doses comparable to those obtained using BPA. However, computer simulations are only as good as their input assumptions. It is possible that new approaches to BSH-mediated boron delivery, as reported by Barth et al. [6] or Haselberger et al. [7] in this volume may improve the ^{10}B distribution. It is also possible that a favorable micro-distribution of BSH-delivered ^{10}B in human tumor cells, as reported by Otersen et al. [8], may increase the effectiveness of the treatment. The influence of fractionation and neutron beam characteristics (other than at BMRR) on the doses delivered to tumor and normal tissues during BSH-based BNCT remains to be explored.

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Figure Legend

Figure 1. Examples of dose volume histograms for normal brain and tumor obtained for BPA (A - plan #10) or BSH using a range of possible blood/tumor ^{10}B concentrations and CBE values (B- plan #1, C - plan #8, D- plan #9, E - plan #6, F - plan #7).

Table 1. Summary of results obtained from treatment plans using BPA or BSH.

Compound	BSH									BPA
	20			30		40		60		
¹⁰ B in the blood (ppm)	12.7	20		30		20		30		12.7
¹⁰ B in the tumor (ppm)	26.5	20		30		40		60		44.
CBE in the brain	0.5	0.5	0.37	0.5	0.37	0.5	0.37	0.5	0.37	1.3
CBE in the tumor	2.3	1.2	2.3	1.2	2.3	1.2	2.3	1.2	2.3	3.8
γ RBE	1	1	1	1	1	1	1	1	1	1
Beam high-LET RBE	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2
Time or irradiation at 3 MW reactor power (min)	51	45	49	39	44	45	49	39	44	38
Peak brain dose	12.6	12.6	12.6	12.6	12.6	12.6	12.6	12.6	12.6	12.6
Average brain dose of which:	4.2	4.1	4.2	4.0	4.1	4.1	4.2	4.0	4.1	4.0
boron	0.7	1.0	0.8	1.3	1.1	1.0	0.8	1.3	1.1	1.3
gamma	2.2	2.0	2.1	1.7	1.9	2.0	2.1	1.7	1.9	1.7
N-14	0.6	0.5	0.6	0.5	0.5	0.5	0.6	0.5	0.5	0.4
fast n	0.7	0.7	0.7	0.6	0.6	0.7	0.7	0.6	0.6	0.6
Peak tumor dose	35.8	17.9	28.5	19.5	27.1	47.5	31.4	29.3	59.3	60.1
Average tumor dose of which:	32.6	16.4	26.0	17.8	31.4	24.6	43.0	28.5	53.4	54.6
boron	23.3	8.2	17.0	10.7	22.7	16.4	34.0	21.3	45.5	47.7
gamma	5.0	4.4	4.7	3.8	4.2	4.4	4.7	3.8	4.2	4.9
N-14	2.0	1.8	2.0	1.6	1.8	1.8	2.0	1.5	1.8	1.5
fast n	2.3	2.0	2.2	1.8	2.0	2.0	2.2	1.8	2.0	1.7
Minimum tumor dose	23.8	12.5	17.8	13.3	22.3	18.1	30.9	20.6	37.9	38.1
Treatment plan #	1	2	3	4	5	6	7	8	9	10











