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# Improvement of depth dose distribution using multiple-field irradiation in boron neutron capture therapy

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## HIGHLIGHTS

- We evaluated the dose distribution obtained using multiple-field irradiation in simulation.
- The tumor dose distribution was found to be improved under multiple-field irradiation.
- The normal tissue dose was increased under two- and three-field irradiation, because of the increased irradiation area. However, in this case, the parotid dose was less than the tolerance dose.
- The total irradiation times of the two- and three-field irradiation processes were longer than that of the one-field irradiation. However, if the available neutron intensity is increased and it becomes possible for the patient position to be smoothly set between irradiation stages, two- and three-field irradiation can be applied in one intravenous infusion of boron drugs.

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## ABSTRACT

It is important that improvements are made to depth dose distribution in boron neutron capture therapy, because the neutrons do not reach the innermost regions of the human body. Here, we evaluated the dose distribution obtained using multiple-field irradiation in simulation. From a dose volume histogram analysis, it was found that the mean and minimum tumor doses were increased using two-field irradiation, because of improved dose distribution for deeper-sited tumors.



## 1. Introduction

As of February 2014, over 510 clinical studies have been performed on boron neutron capture therapy (BNCT) at the Kyoto University Research Reactor Institute (KURRI). In recent years, the number of clinical studies performed on the Kyoto University Research Reactor (KUR) (Sakurai and Kobayashi, 2000) have been divided into three categories: Category 1 cases involve brain tumors (Miyatake et al., 2009); Category 2 cases feature head and neck tumors (Kato et al., 2009); and Category 3 cases involve truncal-sited tumors, such as liver and lung cancers (Suzuki et al., 2014, 2007). In BNCT dose evaluation, the appropriate irradiation time is determined by the dose limits of normal tissue such as the mucosa and normal brain tissue. The biological effectiveness of the boron compound of p-boronophenylalanine (BPA), which is used for clinical studies on BNCT, differs for each normal tissue type. In particular, the compound biological effectiveness (CBE) of BPA for mucosa (4.9) is larger than that for normal brain tissue (1.35). In the case of head and neck tumor irradiation treatment, the mucosa dose limit is set as the normal tissue dose limit. Thus, it is difficult to provide a sufficient irradiation dose to deep-sited tumors under these conditions, and it is therefore important to improve the depth dose distribution for head and neck tumors. Two methods of improving the depth dose distribution exist. Firstly, the treatment beam characteristics can be improved using an optimized beam shaping assembly for not only accelerator-based but reactor-based neutron source (Tanaka et al., 2009; Savolainen et al., 2013; Tung et al., 2004). It has been shown that neutron energy of approximately 10 keV is the most effective for BNCT (Yanch et al., 1991). Fig. 1 shows the tumor dose distribution in water phantom using the irradiation of ideal mono-energy neutron. The dose limit is the

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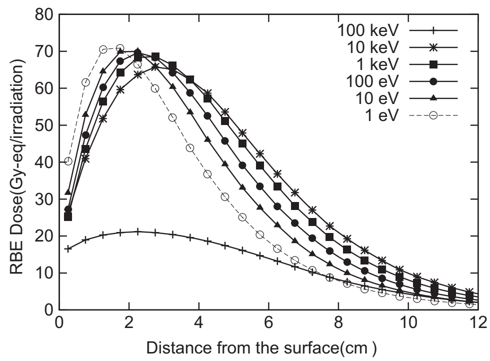


**Fig. 1.** Tumor dose distribution in water phantom for each mono-energy neutron irradiation.

brain dose of 12.5 Gy-eq. The RBE of neutron is 3. CBEs for brain and tumor are 1.35 and 3.8, respectively. Boron concentration and the tumor to blood ratio is assumed to 13 and 3.5, respectively. Tumor dose at the depth deeper than 4 cm irradiated by mono-energy neutron of 10 keV is most large. However, actual moderator is not able to produce the mono-energy neutron. It is difficult to improve the dose distribution using mixed energy neutron beam. The other approach to obtaining improved depth dose distribution is to use the higher tumor to normal tissue boron concentration ratio (Tanaka et al., 2009). Furthermore, the other approach to obtaining improved depth dose distribution is the multiple-field irradiation method. Multiple-field neutron fields have been commonly used in BNCT treatments in western world (Busse et al., 2003; Kankaanranta et al., 2012; Capala et al.,2003). At, KURRI if there is a clear benefit, multi-field irradiation method is applied to clinical study. In this paper, we have evaluated the improvement in dose distribution obtained using two-field irradiation, which was actually performed at KURRI, as compared to one- and three- field irradiation in simulation.

## 2. Materials and methods

We evaluated the dose distribution of two-field irradiation in simulation for two typical patients based on the calculation factors applied in KUR clinical studies, i.e., the boron concentration and the tumor(T)-to-blood(B) boron concentration ratio (T/B). The simulations were performed using the Simulation Environment for Radiotherapy Applications (SERA) software (Wessol et al., 2002), and the simulated two- and three-field irradiation results were compared to those of the one-field irradiation. A quantitative comparison of the depth dose distribution was made through analysis of the dose volume histogram (DVH) for the tumor.

### *2.1. Head and neck tumor case 1*

In this case, the measured boron concentration and the T/B ratio were 25 ppm and 2.7, respectively. Fig. 1 contains a surface remodeling image and an image showing the positions of the tumor and of the normal tissue such as the mucosa, brain, and parotid. One of the two-field irradiation beams was directed towards the front (labeled 'F') and the other was aimed towards the left (labeled 'L'); there was a 90° angle between F and L. We also evaluated the one-field irradiation in the interests of comparison. The one-field irradiation angle was 45° (labeled 'FL'). Finally, we examined the effects of three-field irradiation, using the "F", "L", and "FL" beam directions. In each case, the irradiation time was determined by the mucosa dose limit of 12 Gy-eq.

### *2.2. Head and neck tumor case 2*

In this case, the measured boron concentration and the T/B ratio were 25 ppm and 3.7, respectively. Fig. 2 gives a surface remodeling image along with an image showing the positions of the tumor and of the normal tissue, such as the mucosa, brain, and parotid. One of the two-field irradiation beams was directed towards the right (labeled 'R') and the other was towards the left (labeled 'L'); there was a 180° angle between R and L. We also evaluated the one-field irradiation for comparison, which was directed towards the front (labeled 'F'). Finally, we evaluated three-field irradiation with beam directions of "R", "L", and "F". In each case, the irradiation time was determined by the mucosa dose limit of 10 Gy-eq.

## 3. Results

### *3.1. Head and neck tumor case 1*

Table 1 shows the maximum, minimum, and mean dose values for the tumor, mucosa, and parotid with varying irradiation beam time weightings. In this table, the numeral following the letter symbol indicates the irradiation time weighting. For example, "F1: L2" means that the irradiation time of the left beam is two times greater than that of the front beam. In this study, we selected the irradiation weighting with the largest mean dose as the optimized irradiation parameters.

The irradiation time of the one-field irradiation procedure was

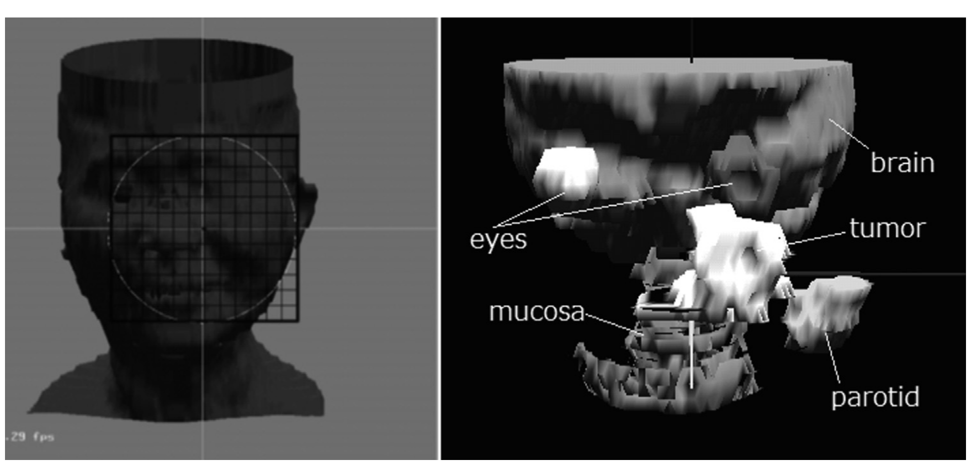


**Fig. 2.** Tumor, mucosa, brain, and parotid position (case 1).