Cent. Eur. J. Phys. • 12(10) • 2014 • 714-718
DOI: 10.2478/s11534-014-0507-2

VERSITA

Central European Journal of **Physics**

MCNP simulation of the dose distribution in liver cancer treatment for BNC therapy

Research Article

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Received 18 March 2014; accepted 10 June 2014

Abstract: The **B**oron **N**eutron **C**apture **T**herapy **(BNCT)** is based on selective uptake of boron in tumour tissue compared to the surrounding normal tissue. Infusion of compounds with boron is followed by irradiation with neutrons. Neutron capture on ^{10}B, which gives rise to an alpha particle and recoiled ^{7}Li ion, enables the therapeutic dose to be delivered to tumour tissue while healthy tissue can be spared. Here, therapeutic abilities of BNCT were studied for possible treatment of liver cancer using thermal and epithermal neutron beam. For neutron transport MCNP software was used and doses in organs of interest in ORNL phantom were evaluated. Phantom organs were filled with voxels in order to obtain depth-dose distributions in them. The result suggests that BNCT using an epithermal neutron beam could be applied for liver cancer treatment.

PACS (2008): 87.53.Bn, 24.10.Lx, 87.19.xj

Keywords: Boron Neutron Capture Therapy (BNCT) • Monte Carlo simulation • depth-dose distributions • liver cancer

1. Introduction

Nuclear reaction $^{10}B(n,a)^{7}Li$ is a basic principle of Boron Neutron Capture Therapy (BNCT). High energy alpha particle and recoiled ^{7}Li, created in this reaction produce a large and spatially close ionization in vicinity of the the reaction. The range of reaction products is comparable with the size of cells. Metastatic cells have higher affinity towards boron uptake, so a higher dose will be delivered to tumour cells during neutron irradiation. The normal healthy tissue can be spared from the nuclear reactions if they have not taken up ^{10}B they can be spared from the nuclear reactions. The advantage of this process is even more pronounced when the whole organs such as brain, liver, lung, pancreas and prostate are treated [1–4]. This method was first used in 2001 in Pavia, Italy [5]. BNC Therapy was applied to an isolated liver suffering from diffuse metastasis, which was pre-treated. The blood content was removed through washing and the liver was made hypothermic at temperature of $4^{o}C$. A neutron isotropic field was applied from the experimental reactor at Department Nuclear and Theoretical physics at University of Pavia.

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Liver perfusion with a solution of 10boronophenylalanine (10BPA) ensured that concentration of boron in tumour was about six times greater than that of healthy liver tissue [3]. The therapeutic procedure was successful, and it was applied again in 2003 on different patient. The efficacy of BNCT in destroying the tumour cell populations and the high selectivity of its killing effect was confirmed [3]. No other kind of antineoplastic therapy stands comparison with this one [6]. Liver autotransplant is a hard task both for patient and surgeon. An in situ irradiation of the liver, with the method of hypothermic exsanguineous perfusion, should reduce both the surgical trauma and the time required for the procedure; but in this case a proper shielding of the patient's body and a bed-side source of neutrons would be needed [6]. Results obtained in the elimination of the liver metastases have encouraged other research groups to begin studies and projects for the autotransplant method. For the TRIGA reactor in Pavia, a new configuration of the thermal column was designed by using MCNP calculations that would ensure a better dose uniformity in the explanted organ. Another BNCT research area in Pavia was dedicated to lung tumours, consisting of irradiating the organ with external epithermal neutron beams, without organ explantation. Other clinical trials for liver treatment have been performed in Argentina [7]. A facility for the irradiation of a portion of patients explanted liver and lung was constructed at the RA-3 reactor, Comision Nacional de Energia Atomica, Argentina, [7]. The facility, located in the thermal column, is characterized by the ability to insert and extract samples without the need to shutdown the reactor. The most recent clinical trials with BNC therapy reported very promising results for head and neck cancer [8]. A recent work consists of the study of a different isotope ^{33}S as a alternative to ^{10}B for neutron capture therapy. It could produce an enhancement of the tumour dose near the surface in BNCT treatments or applied to superficial tumours as ocular melanoma [9, 10]. Other studies showed the optimal irradiation technique for BNCT dosimetry of recurrent breast cancers [11]. It was shown that thermal neutron beam was the optimal treatment with shorter irradiation timeas a longer irradiation time was not suitable for actual clinical trials in breast cancer treatments. With respect to the neutron sources, only beams obtained from research fission nuclear reactors have been employed up to now. These are facilities that cannot be built into hospitals and therefore this is a limitation of the technique. However, the new projects of producing the neutron beams from accelerators may lead to a new era in BNCT.

Here authors wanted to investigate BNC therapy efficiency for localised tumors in the liver. In the authors previous paper [12] metastasis and a lung tumor were described. The difference in evaluated dose in tumour and normal lung tissue suggests that this therapy could be applied for treatment of tumours and metastasis in lungs. In this work, the advantages of BNCT therapy for liver tumors are investigated.

2. Material and methods

The computational model of the male Oak Ridge National Laboratory (ORNL) phantom [13, 14] was used here to simulate tumours in the liver. Calculations have been performed by means of the MCNP5/X code [15] which was used to simulate neutron transport from the source to the target organs. The subject liver and surrounding tissue was filled with voxels in order to obtain dose distribution in direction of the beam. Since the tumour is localized inside of liver, a collimated beam was used in order to minimize the dose in healthy tissue. To ensure an isotropic neutron field, the tumour was irradiated in anterior-posterior **AP** and posterior-anterior **PA** geometry. Location of the tumour was chosen as in [16] with the tumour represented by the $3 \times 3 \times 3$ cm^3 cube filed with 1 cm^3 size voxels, as shown on Figure 1.

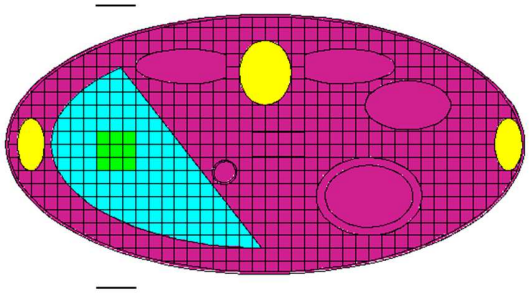

Figure 1. Transversal cross section of ORNL phantom at height z=35 cm

The coordinates of the tumour are x: -13 to -10 cm; y: -2 to 1 cm, and z: 33 to 36 cm. The neutron source position is marked on Figure 1 by the black lines outside of the trunk. The source is the same size as the tumour and collimated with direction towards the tumour. The energy of the neutrons was taken to be 0.025 eV as the representation of thermal neutrons and 1 keV for epithermal neutrons. Two cases were investigated in this study the tumour tissue was injected with both 30 and 45 ppm of boron. For the 30 ppm case, 3 ppm was taken to be absorbed in healthy tissue as in [16]. For the 45 ppm case

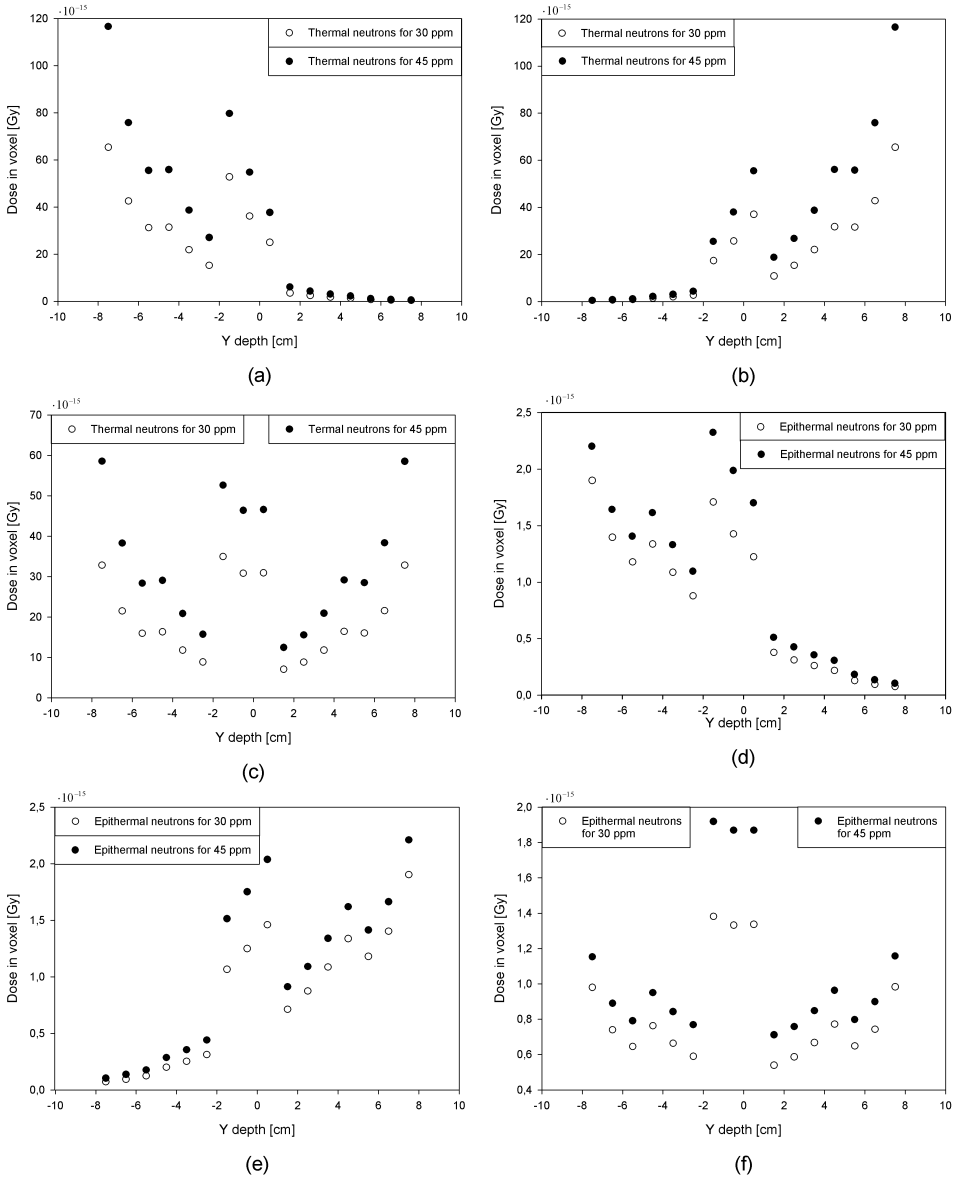

Figure 2. Depth dose distributions in case of: (a) thermal neutrons in AP geometry; (b) thermal neutrons in PA geometry; (c) weighted dose depth distribution for thermal neutrons; (d) epithermal neutrons in AP geometry; (e) epithermal neutrons in PA geometry; (f) weighted dose depth distribution for epithermal neutrons

Table 1. Doses in right kidney and spine [Gy per incident neutron]

	Thermal neutrons		Epithermal neutrons	
Boron concentration	30 ppm	45 ppm	30 ppm	45 ppm
right kidney	$6.71 \cdot 10^{-16}$	$1.17 \cdot 10^{-15}$	$6.66 \cdot 10^{-17}$	$1.13 \cdot 10^{-16}$
spine	$7.11 \cdot 10^{-17}$	$1.08 \cdot 10^{-16}$	$2.25 \cdot 10^{-17}$	$3.43 \cdot 10^{-17}$

8 ppm was taken to be absorbed in healthy tissue [3]. In total, 10^7 neutron histories were simulated in order to obtain calculation uncertainty smaller than two percent in almost all cases. MCNP energy deposition tally-f6 was used for absorbed dose calculation (in Gy per source neutron).

2.1. Results and discussion

The tumour tissue presented in Figure 1 was irradiated with two separate beams in AP and PA geometry with thermal and epithermal neutrons. Y axis dose distribution at the direction that goes through middle of the tumour for AP and PA geometry is presented for thermal neutrons in Figures 2a and 2b, respectively. Doses in these two irradiation cases were weighted with 0.5 and summed to give dose per neutron from both geometries of irradiation in which near uniform field was expected. Summed dose is presented in Figure 2c. For epithermal neutrons dose distributions for AP and PA geometry are presented in Figures 2d and 2e; weighted dose is presented on Figure 2f. Doses on Figure 2 are in Gy per one incident neutron from source. Analyzing graphs for thermal neutrons it can be seen that almost all neutron flux has been absorbed in the side of the trunk from which neutrons are incident. Outside of the tumour, the dose could be practically neglected, when comparing to tumour dose and the dose in opposite side of the trunk. With increasing depth, dose is rapidly decreasing. In the tumour tissue, the dose is higher due to higher concentrations of boron. In order to get a more homogeneous distribution of dose and more effectiveness of irradiation neutron flux was split into two beams from opposite directions. In that way dose to healthy tissue can be reduced to half in one direction. In Figure 2c the weighted dose was shown. It can be seen that dose per neutron is about half the dose in healthy tissues while tumour dose is practically the same when irradiating in both directions. Non uniform depth dose in tumour is consequence of non symmetrical conditions of irradiation. The important thing that should be noticed is the fact that for thermal neutrons and 30 ppm concentration of boron dose in tumour is the same as the dose near the surface of the trunk. For BNCT treatment it is proposed that due to higher concentration of boron in tumour tissue compared with healthy dose in tumour is far greater. For concentration of boron in tumour of 45 ppm, dose in truck is even greater than dose in tumour. Considering epithermal neutron beam situation is more convenient. Figures 2d and 2e show the depth dose distribution for AP and PA geometry where it can be seen that neutrons have enough energy to deliver far greater doses in the tumour tissue compared to the healthy tissue. On Figure 2f it can be seen that the tumour to healthy tissue ratio is greater compared to that of thermal neutrons, which makes them better candidates for BNC therapy. Values of doses are larger in the case of thermal neutrons, up to $60 \cdot 10^{-15}$Gy per neutron, compared with epithermal neutron dose up to $2 \cdot 10^{-15}$Gy per neutron. The tumour to healthy tissue dose ratio is about 4 for epithermal neutrons. In addition doses in nearby organs are calculated also. In this study, the right kidney and the spine are also in the vicinity of the beam. Doses in these two organs are given in Table 1.

2.2. Conclusion

BNC Therapy has been shown as a good approach for selective treatment in some cases of malignant diseases. It has been already shown that this approach has advantages in the treatment of lung metastasis and localized tumours. In the case of the liver BNC Therapy, the method is also shown as a viable method for tumour treatment. Simulations such as this present very helpful pretreatment approach in order to provide insight during treatment planning. Here it was shown that epithermal neutrons are better candidates even though doses from thermal neutrons are larger. Since doses are per source neutrons, a higher exposure with epithermal neutron for same flux as the thermal neutrons can give rise to same dose in tumour tissue, while the dose in healthy tissue will be far lower in case of epithermal neutrons. Surrounding organs in this study receive far lower doses than tissue which is in the way of the beam, due to the collimated beam of neutrons. BNC Therapy has been shown as very powerful method due to selective uptake of boron.

Acknowledgments

This work was supported by Serbian Ministry of Education and Science [Grants No 171021 and 43011].

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