International Academic Institute for Science and Technology

International Academic Journal of Science and Engineering Vol. 1, No. 2, 2014, pp. 17-25.

ISSN 2454-3896

International Academic Journal of Science and Engineering

www.iaiest.com

Determination of proper neutron beam energy spectrum for penetration depth in liver BNCT

Marziyeh Kabirian[a], Dariush Sardari[b], Farshid Babapour[c]

[a]*Master Student, Islamic Azad University, Science and Research Branch, Department of Medical Radiation Engineering, Tehran, Iran.*

[b]*Assistant Professor, Islamic Azad University ,Science and Research Branch, Department of Medical Radiation Engineering, Tehran, Iran.*

[c]*Assistant Professor, Islamic Azad University ,Science and Research Branch, Department of Medical Radiation Engineering, Tehran, Iran.*

Abstract

Cancer treatment with neutron capture in Boron is a recently developed method in treatment of malignant tumor, capable of destroying cancerous cells plus a little side of effect. In BNCT the radiation damage is selectively concentrated according to biodistribution of Boron –carrying molecules. This makes BNCT a viable method in treatment of liver metastatic cancer. In the present study, with the use of ORNL computational phantom and MCNP Monte Carlo Code, an epithermal neutron beam with varying energy between 1eV to 10keV was simulated and the depth-dose curves in healthy tissue for tumors located at 2cm,4cm and 6cm beneath surface were obtained. Two figures of merit was employed to assess the optimum neutron energy: 1- The ratio of tumor absorbed dose to maximum healthy tissue absorbed dose called Therapeutic Gain, 2- The ratio of skin absorbed dose to maximum healthy tissue absorbed dose. This criteria makes possible assessment of epithermal neutron beam quality in liver

Keywords: Neutron capture in boron, Metastatic cancer, Computational phantom, Monte Carlo Code, Therapeutic Gain.

Introduction:

Boron neutron capture therapy is an experimental form of radiation therapy , based on the infusion of a borated compound followed by thermal neutron irradiation. Radiation beam creates a dose in the tumor through boron absorption which is applied in order to destroy cancer cells damaging the adjacent cells. (Barth et al 2005). The base of therapy in Boron neutron capture therapy includes two elements:
1.Boron compound 10 that can fully concentrate in tumor cells 2. Neutron bombardment of the intended area in the appropriate intensity and energy (Vujic and Costes 1997) . Thermal neutrons are captured by nuclei ^{10}B and ^{10}B is transformed to ^{11}B which is in an excited state. The nucleus of the atom stays in the excited state in a very short time. Then ^{11}B is split and resulting in high LET radiation of α-particle and recoil ^{7}Li nucleus. In about 94% of cases, gamma rays are also emitted. These heavy particles locally deposit their energy of 2.34 MeV in a range of 5-9 μm around cancerous cell,which corresponds to the cell diameter .Fundamental reaction of neutron with boron in the vicinity of the nucleus makes it likely to break DNA, resulting in cell death in 95% of cases.(MIT 2008) .

Theoretical basis of research:

The liver is the most common target of metastases from many primary tumors (e.g. colorectal cancer, breast, lung, etc. (Vitale et al., 1986). Primary and metastatic liver cancers are highly fatal especially after resection of multiple individual tumors (Allen et al.,1997). The response rate for nonresectable hepatocellular carcinoma to traditional radiation treatment or chemotherapy is very poor. However, some current results indicate that the thermal neutron irradiation of the whole liver with a ^{10}B compound could be a way to destroy all the liver metastases (Pinelli et al., 2002)..Ideal reatment should kill more cancerous cells plus a little side of effect Since there isn't any successful treatment for many malignant tumors such as liver, so boron neutron capture therapy can be superior to conventional methods of treatment. In addition,the possibility to gain a selective effect based on the boron distribution rather than on the irradiation field, makes BNCT a valid option in the treatment of tumours that invade whole organs, as in the case of metastatic spreads. Also a higher dose will be delivered to tumour cells with the minimum dose reached to normal tissue during neutron irradiation increases the survival fraction and therapeutic gain.

Research Background:

This method was first used by Pinelly et al in 2001 in Pavia, Italy .BNCT was applied to an isolated liver suffering from diffuse metastasis, which was pre-treated.A neutron isotropic field was applied from the experimental reactor at Department Nuclear and Theoretical physics at University of Pavia.

Due to the success of the treatment,another patient with a liver metastasis was treated by using this method by Zonta et al in 2009 . The results obtained in removing liver metastatic motivate other research groups to use organ transplanting method in their studies. For the TRIGA reactor in Pavia, a newconfiguration 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.

Bortolussi et al were done other researches in Pavia by using epithermal neutron beam for lung tumor without removing the organ. A large clinical trials were devoted to treating liver tumors in Argentina and in the reactor RA-3,facilities were established for radiating the removed lung and liver. 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 BNCT reported very promising results for head and neck cancer by Kankaanranta et al in 2007.

In the recent studies,Poras using the isotope S-33 as an alternative for the B-10 in neutron capture therapy which is suitable for superficial tumors such as melanoma of the eye. Other studies by Horiguchi et al indicate the optimal radiation techniques for recurrent breast cancers in BNCT. Considering the existing neutron sources, only beams resulted from research nuclear reactors were applied which were considered as one of the limitations of this method due to the impossibility of their establishment in hospital.

Previous studies dealt with lung metastatic and tumors and the obtained results confirmed the accuracy of using BNCT treatment for lung tumors and metastatic. A recent study was conducted by Krstic et al to evaluate the dose distribution for local hepatic tumors by using MCNP simulation code and phantom ORNL. Tumor location was selected by the $3 \times 3 \times 3\, cm^3$ cube filled with $1 cm^3$ size voxels and the tumor was irradiated in anterior-posterior AP and posterior-anterior PA geometry and the Depth dose distributions in case of thermal neutrons in AP geometry and thermal neutrons in PA geometry were obtained. Finally, according to the figures obtained it has been shown that boron neutron capture therapy is a proper method for the treatment of liver tumors.

In the present study, outlining the dose profile as a function of depth in the liver tissue containing boron and linking the shooting neutron energy and depth of the tumor in the liver are among the applied goals of the investigation and improving the quality of therapy per radiation neutrons is its general. In this study, it is assumed that the source of neutron beams is thermal reactor, tumors are located in 2cm,4cm and 6cm depth in the liver and the energy of the incident neutron beam is determined depending on depth of tumor.

Research methodology:

In order to determinate the proper energy for liver tumors,dose distribution and tumor absorbed dose should calculated.So the Monte Carlo Code and computational model of the male Oak Ridge National Laboratory were used here to simulate tumours in the liver.

Research tools:

The present simulation study was performed by using mathematical phantoms ORNL (2009, Eckerman; 200 7, Krstic) in order to simulate a tumor in the liver and dose distribution calculation. In this study, a single-direction, single-energy and x axis-balanced disc spring was used in order to determine the suitable energy of neutrons for the treatment of a spherical tumor 2 cm in diameter2,4 and 6cm in depth in

the liver in boron neutron capture therapy and the neutron beam with radius 5cm was used (IAEA, 2001). Based on ICRP Publication 89, the reference mass of the liver for adult male is 1800 g and for adult female 1400 g. Thus, liver is rather large organ, and one could expect that by using epithermal neutrons as primary incident radiation instead of thermal ones, the neutron radiation would penetrate much deeper to the cancerous tissue. As the epithermal neutrons scatter and slow down in the tissue to the thermal energy range, they presumably create a much better thermal flux distribution inside the liver that can be achieved by using pure thermal radiation .Also because of the nature of neutron interactions, BNCT analyses rely heavily on the use of Monte Carlo simulations. Calculations are necessary to predict the distribution of the dose released in the liver by a neutron beam of a known energy profile.

Tally segment card FS was used to divide the cylindrical volumes into tally segments along beam axis inside phantom . In this project the tally F4 representing the average flux within a cell was used. The resulted consequences have been multiplied in card FM. These coefficients convert moderate flux over the cell into biological effective dose. For the dose conversion, pointwise KERMA factors and energymass absorption coefficients from ICRU-46 were directly input with DE and DF cards and RBE factors were considered to calculate the equivalent dose coefficients in Table 1.

Table 1: dose components and RBE factors

Dose components	Reaction	RBE or CF
D_B	$^{10}B(n,\alpha)^{7}Li$	Healthy Tissue:1.32 Tumor:3.8
D_N	$^{14}N(n,p)^{14}C$	3.2
D_H	$^{1}H(n,n')^{1}H$	3.2
D_γ	$^{1}H(n,\gamma)^{2}H$	1

Finally equivalent dose was calculated according to below equation.

$$+RB$$

To determine the effects of neutron energy and depth of the tumor in the liver, the total absorbed dose calculations and also calculations for each elements of dose resulted from of the boron, hydrogen, nitrogen capture reaction and proton recoile were performed for various groups of neutron energy and various depths of tumor in the liver and figures of merit were analyzed. The therapeutic ratio was discussed as a function of the neutron energy and in total, 10^7neutron histories were simulated in order to obtain calculation uncertainty smaller than three percent in almost all cases.

The Analysis of Data:

The aim of our study is determine the appropriate energy of neutrons for shallow and deep-seated liver tumors by using MIRD 5 phantom and MCNP simulation code. For this purpose epithermal neutron beams with varying energy between 1eV to 10keV were simulated and Calculations have been

performed by means of the MCNP4C which was used to simulate neutron transport from the source to the target organs.

Research Findings:

Beam obtained from a BSA includes three neutron energy groups. When such a contaminated spectrum is encountered with tissues, 4 parts of the original physical dose should be considered:

1.Boron dose(D_B) 2.Gamma dose(D_γ) 3.Thermal neutron dose( ) 4.Fast neutron dose(D)

The depth-dose curves with for components dose have been obtained as a function of depth in healthy tissue. The following curves represent the dose distribution in healthy tissue in segments along beam axis.

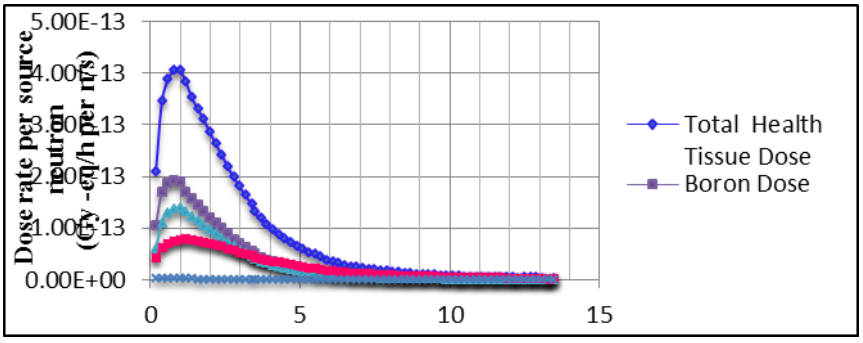


Fig.1.Depth dose distributions in healthy tissue with 1eV neutron energy

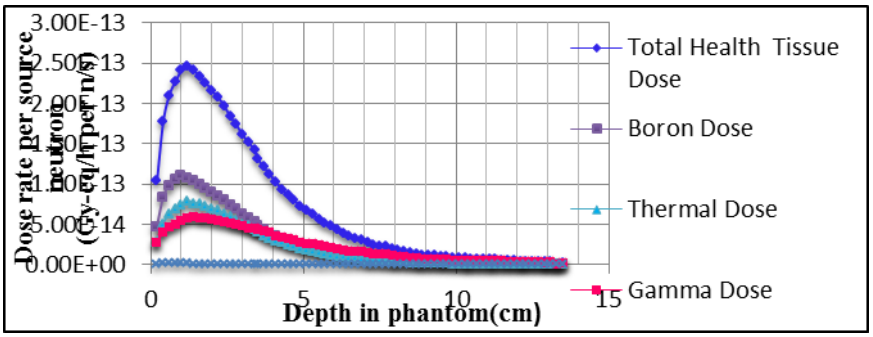


Fig.2.Depth dose distributions in healthy tissue with 10eV neutron energy

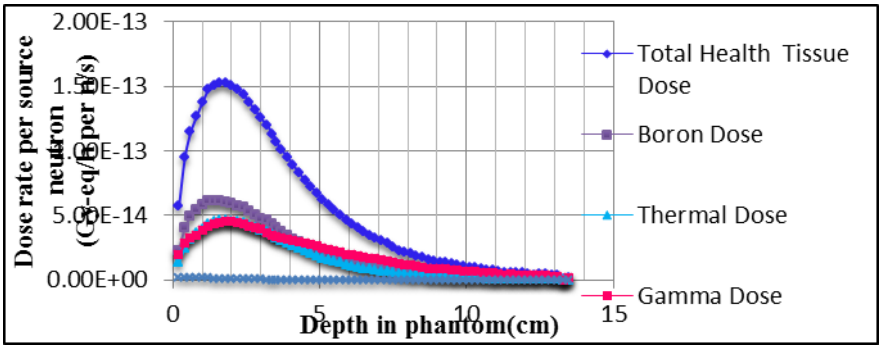


Fig.3.Depth dose distributions in healthy tissue with 100eV neutron energy

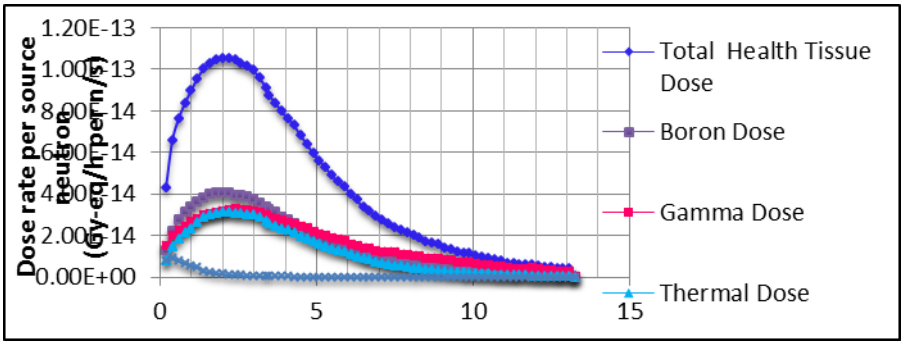


Fig.4.Depth dose distributions in healthy tissue with 1keV neutron energy

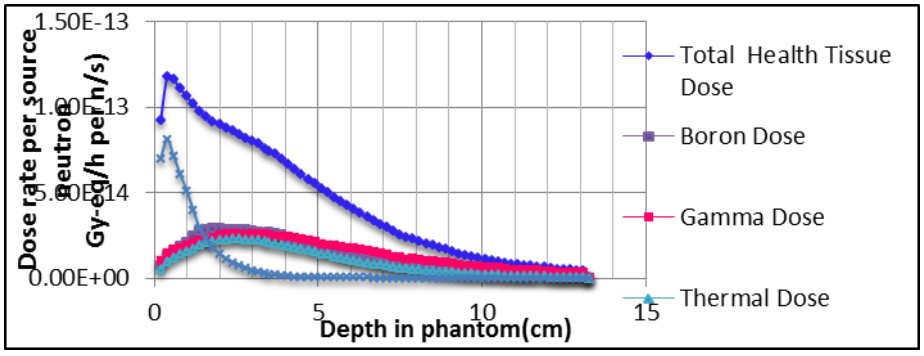


Fig.5.Depth dose distributions in healthy tissue with 10keV neutron energy

In order to find out at which energy the neutrons are the most useful therapeutically for a tumor at a given depth, T wo figures of merit was employed to assess the optimum neutron energy: 1- The ratio of

tumor absorbed dose to maximum healthy tissue absorbed dose called Therapeutic Gain, 2- The ratio of skin absorbed dose to maximum healthy tissue absorbed dose.
Table 2 shows the obtained therapeutic gain in the studied energies of tumor in depths 2,4 and 6cm and ratio of skin dose to the maximum healthy tissue dose.

Table 2.Therapeutic gain at the depths of 2, 4 and 6 cm and absorbed dose to the skin with the mono-directional neutron beam in the liver phantom.

Neutron Beam Energy	Therapeutic gain			Skin to max healthy tissue
	At 2cm	At 4cm	At 6cm	
1eV	5.34	2.36	8.10e-01	5.14e-01
10eV	5.86	3.97	1.79	4.23-01
100eV	5.57	4.78	2.55	3.74e-01
1keV	4.58	4.99	2.68	4.12e-014
10keV	3.30	4.50	2.83	7.83e-01

The optimal neutron beam should minimize the skin dose and maximize the tumor dose. The maximum healthy tissue dose is limited by Brookhaven National Laboratory's(BNL) clinical trial protocol which specifies that the absorbed dose to the healthy tissues must not exceed 12.5 Gy-equivalent anywhere in the soft tissue and we limit the absorbed skin dose to 8 Gy-equivalent.
According to the presented calculations, when the permissible the healthy tissue dose is limited to 12.5 Gy, the favorable therapeutic gain has been obtained for a tumor in depth 2 cm in energies1-100eV and for a tumor in depth 4 cm in energies 1-5 keV and finally for a tumor in depth 6 cm in phantom of the liver, energy range of 5-10 keV is also desirable. It is obvious that treatment by greater therapeutic gain can be done better. However, it is necessary to consider the limitation in absorbed dose by skin. So according to what is mentioned above, one of the other criteria for evaluation of beam energy is ratio of skin absorbed dose to maximum healthy tissue absorbed dose. If the skin absorbed dose and maximum healthy tissue dose are limited to 8 and 12.5Gy, respectively,then the ratio of them should not exceed $8/12.5 = 0.64$. This dose limit im-poses neutron energies in the range 1eV to less than 8keV. So in order to determine optimal energy of neutron beam, the most therapeutic gain should be considered while skin equivalent dose shouldn't exceed the permissible limit. With regarding to the mentioned facts, optimized neutron beam for a tumor in depth 6 cm is limited 5keV to less than 8 keV.

Conclusion:

After many studies and comparisons to similar works(Koivunoro,2004), using anthropomorphic computational phantoms like what was used in this study is preferred for the liver than using simple geometric shapes. Since the excessive dose for the skin can be accompanied by such effects as erythema, waxing and skin necrosis, so in addition to consider the therapeutic values, it is so important to take the ratio of tumor absorbed dose to maximum healthy tissue dose into account. The present simulation study was done in order *to Determination of proper neutron beam energy spectrum for penetration depth in liver BNCT***.** In this study, the basic components of dose were calculated.Therapeutic gain is fundamentally depended on proton dose and nucleus of recoiled carbon during hydrogen and oxygen capture reaction and also on gamma rays. When the neutron flow rate is high, the dose resulted from boron capture takes a large share in the total dose, resulting in its significant role in increasing the amount of therapeutic gain. From the results, it seems that for deep tumors , energy range as 5-8 keV is optimum and maximum energy efficiency of about 8 keV was obtained. For shallow tumors (2 and 4 cm), relatively high therapeutic gain was obtained in more neutron beams having energy less than 5keV.

Practical suggestions:

As a final comment, it is believed that due to the fact that the used MIRD phantom describes human anatomy by using simple mathematical equations in analytic geometry ,then it only gives us an approximation of the dose distribution in the organs. But using the tomography phantom based on three-dimensional imaging techniques such as MRI and CT gives more accurate distribution of the dose, and finally it is recommended that in order to verify the simulation results, results of code will be compared with the actual results in clinicalcal culations and it can be estimated in the results of tumor response to a neutron beam and improvement of patient.

References:

Allen,B.J., Wallace,S.A., and Carolan, M.G. (1997). Can Epithermal Boron Neutron Capture Therapy Treat Primary and Metastatic Liver Cancer? Advances in Neutron Capture Therapy Vol. I. Medicine and Physics (edited by Larsson.B, Crawford.J , Weinreich.R) Elsevier Science p. 118.

Barth, R. F., Coderre, J. A.,Graca,M.,Vicente. H., Blue,s T. E .(2005). Boron neutroncapture therapy of cancer : current status and future prospects. Clin cancer Res . 11(11). p. 3987-4002.

Bortolussi,S.(2011). Simulation of the neutron flux in the irradiation facility at RA-3 reactor. Appl. Radiat. Isot. 69. 1924.

Eckerman. K. F., Cristy. M., Ryman, J. C. (2009). The ORNL Mathematical Phantom Series. Oak Ridge National Laboratory Report.(Oak Ridge.TN. USA. 1996) Updated 08 April .

Horiguchi,.H, Nakamura,T., Kumada,H., Yanagie,H., Suzuki,M. (2011). Sagawa.H.Appl. Radiat. Isot. 69.1882.

IAEA.(2001). Current status of neutron capture therapy. IAEA-TECDOC-1223.

Kankaanranta ,L.(2007). Int. J. Radiation Oncol. Biol.Phys. 69. 475 .

Koivunoro.H., Lou, T. P., Reijonen,J., Leung,K.N. (2004). A D-D/D-T Fusion based neutron generator system for liver BNCT . Proceedings of the Sixth International Topical . Meeting on Nuclear

Applications of Accelerator Technology,AccApp'03, June 1–5. 2003. San D ie go . California.USA.

Krstic,D., Nikezic,D. (2007). Comp. Phys. Commun. 176. 33.

Krstic,D., Jovanovic,Z.,Markovic,V.,Nikezic,D.,Urosevic,V. (2014). MCNP simulation of the dose distribution in liver cancer treatment for BNC therapy. Cent. Eur. J. Phys. 12(10) 714-71.

MIT. (2008). The Basics of Boron Neutron Capture Therapy.online .

Pinelli,T., Altieri,S., Fossati,F., Zonta,A., Ferrari,C., Prati,U., Roveda. L., Ngnitejeu Tata, S., Barni ,S., Ferguson,D. M., in: Hawthorne,M. F., Shelly, K., Wiersema,R. J., (editors). (2001). Frontiers in Neutron Capture Therapy. (NewYork, Kluwer, Plenum) pp. 1427-40.

Pinelli,T., Zonta,A., Altieri,S., Fossati,F., Bruschi,P.,Ferrari,C., Prati,U., Roveda,L., NgnitejeuTata,S., Zonta,C., Barni,S., Chiari, P., Nano,R.(2002).TAORMINA:from the first idea to the application on the humanliver. In: Sauerwein, W., Moss, R., Wittig, A. (Eds.).Proceedings of the 10th International Congress on NeutronCapture Therapy. Essen. Germany. September 8–13 Research and Development in Neutron Capture Therapy.Monduzzi Editore, Bologna. pp. 1065–1072.

Porras.I.(2008). Phys. Med. Biol. 57.L1 .

Vitale,G.C., Heuser, L.S., Polk,Jr.(1986). Malignant tumors of the liver,Surg. Clin. North Am. 66, 723.

Vujic,J., and Costes,S.(1997). An Overview of Boron Neutron Capture Therapy and Desired Characteristics of Neutron Beam. Nuclear Sciences Bulletin.March 97.invited paper .

Zonta,A.(2006) . J. Phys.Conference Series 41. 484.

Zonta,A.,Pinelli,T.,Prati,U., Roveda,L.,Ferrari,C., Clerici,A.M., Zonta,C.,Mazzini.G., Dionigi,P., Altieri,S., Bortolussi,S., Bruschi,P., Fossati,F. (2009).Extra-corporeal liver BNCT for the treatment diffuse metastases:What was learned and what is still to be learned,Applied Rdaiation And Isotopes 67.S67-S75.