

MAXIMISING THE α -PRODUCTION IN BRAIN TUMOURS UNDER DIFFERENT EQUIVALENT DOSE CONFIGURATIONS IN BNCT

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ABSTRACT

The ^{10}B concentration, the relative biological effectiveness factors for ^{10}B as well as fast neutrons, together with the equivalent dose limit set for healthy tissue, affect the optimal BNCT source neutron energy for treating brain tumours. Having source neutrons of a few keV together with neutrons of a few eV, ensure that, under all imaginable circumstances, a maximum of α -particles can be delivered in the tumour.

1. Introduction

On investigating the optimal source neutron energy in BNCT for brain tumours in order to improve the design for a new neutron filter in Petten, it soon became apparent that there is no agreement on the values of the factors translating the physical dose into the equivalent (biological) one. These factors enclose the relative biological effectiveness (RBE) factors, the ^{10}B concentration and knowledge on the source gammas. By setting ranges for these factors, determined by currently used values, and calculating for every configuration the optimal source neutron energy, fundamental knowledge can be obtained about which factors are of influence. The optimal source neutron energy is the outcome of an optimization, which allows most of the neutrons to react with ^{10}B present at certain tumour positions under the constraint of not exceeding a pre-set equivalent dose limit in healthy tissue.

2. Set-up

A cubic phantom is irradiated with neutrons from a 60mm radius disc shaped source with 22 discrete neutron energies, logarithmically chosen between 0.1eV and 1MeV. The calculations are carried out with the Monte Carlo code MCNP4c2 [1]. The neutrons are mono-directional and first hit a 5mm layer of skin and after that a 5mm layer of cranium before reaching the brain. All tissue compositions and densities are from the ICRU46 report [2]. Positioned along the beam centre line within the phantom, at every millimeter there is a small MCNP tally (volume 78.5mm^3) to calculate the dose as a function of depth in the phantom. Equation (1) shows how the equivalent dose H in every tally i in the phantom is determined:

$$H_i = (C_{10B} \cdot CBE_{10B} \cdot D_{10B})_i + RBE_{thn} \cdot (D_{thn})_i + (RBE_{fn} \cdot D_{fn})_i + RBE_g \cdot (D_g + \gamma_{sg} \cdot D_{sg})_i \quad (1)$$

The CBE_{10B} in this equation is in fact a compound adjusted RBE and the C_{10B} is the concentration of ^{10}B . The D 's represent the absorbed doses for the thermal neutrons (thn), the fast neutrons (fn) and induced gammas (g). The absorbed dose for the source gammas (sg) is given per source gamma and therefore has to be corrected with the term γ_{sg} . Table 1 shows the ranges of the parameters that are varied in equation (1). The ranges are mainly based on the BSH [3] and BPA [4] treatment protocols used in Petten and on a

boron uptake study [5]. Since these protocols are based on current literature as well, it is of no surprise that these ranges practically include all values used in BNCT literature (see for example [6]). After a MCNP calculation is performed in which all tissues contain 10ppm of ^{10}B , a post-processing program calculates all the different configurations. The total number of configurations is just over 4.5 million.

	$C_{10\text{B}}$ [ppm]	$\text{CBE}_{10\text{B}}$ [-]	RBE_{thn} [-]	RBE_{fn} [-]	RBE_{g} [-]	sg energy [MeV]	γ_{sg} [-]
Skin	0-80 step 10	0-4 step 1	1-5 step 1	1-6 step 1	0.5-1 step 0.5	(sg=source gamma)	0,
Cranium	0-20 step 10	0-2 step 1		1-6 step 1		1,5 and	1/20
Brain	0-30 step 10	0-2 step 1		1-6 step 1		10	and 1/10

Table 1. All varied parameters in this study with their ranges and step sizes .

Of course, the treatment should be halted when a certain pre-set equivalent dose limit is reached somewhere in the healthy tissue. In this study, 2 values for the ratio concerning the equivalent dose limit in skin and the equivalent dose limit in brain, are investigated. The equivalent dose limit in skin and brain are monitored at a point (actually having the size of a tally).

3 Results

The lower graph in Figure 1 presents the percentage of parameter configurations having a certain optimal source neutron energy for treating tumours between 20mm and 80mm from the skin, under the constraint that the allowed equivalent dose in skin is three times lower than in brain. Over 80% of the configurations lie between 1keV and 10keV. The solid lines indicate the regions below 5% configurations: there are for example a few percent configurations having an optimal source neutron energy of 100keV for a tumour at 80mm, in the upper graph of Figure 1. In this upper figure the maximum allowed equivalent dose in skin is three times higher than in brain.

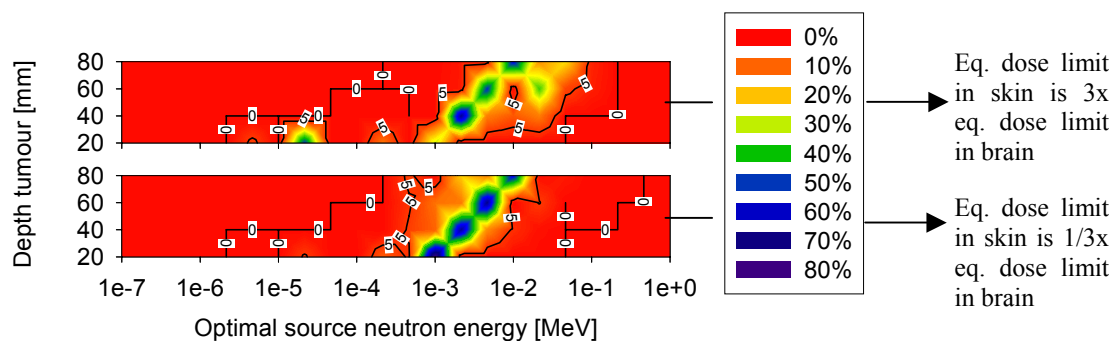


Figure 1. Percentage of parameter configurations having a certain optimal source neutron energy as a function of tumour depth. The two graphs correspond with the setting of the equivalent dose limits.

3.1 Improvements

After this presentation of what source neutron energy ensures the maximum alpha production in the tumour, a logical follow-up question is: is it necessary to provide all these source neutron energies? To investigate this, the number of alphas generated by the optimal neutrons are compared with the number of alphas produced by 10keV source

neutrons. This reference energy of 10keV is chosen since it is a dominant value present in many epithermal based treatment beams. Figure 2 shows, for the same dose limiting cases as in Figure 1, the percentage of maximum improvement in alpha production. For example in the lower graph, for superficially located tumours, there are configurations in which the optimal source neutron energy delivers 600% more alphas (is 7 times better) in the tumour as will be the case with 10keV source neutrons. Notice that, maximum improvements of 100% and higher, are roughly always below 1keV source neutron energy. Further note that for dose limiting ratios, which allow a higher dose in skin (upper graph Figure 2), the improvements are not that spectacular.

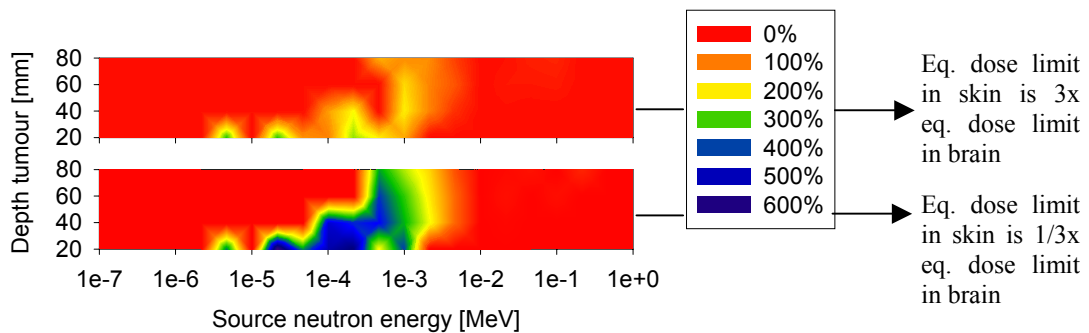


Figure 2. Maximum improvements in produced alpha particles in the tumour using the optimal source neutron energy or 10keV source neutrons. The two graphs correspond with the setting of the equivalent dose limits.

4. Conclusions

This paper is an abstract from an extensive parameter study. There is clarity concerning which parameters are of direct influence on the optimal source neutron energy; i.e. C_{10B} , CBE_{10B} and the RBE_{fn} . The optimal source neutron energy delivers a maximum of alphas in the tumour under certain equivalent dose limiting constraints. It turns out that the definition of the tissue equivalent dose limit is of great influence too. Another important conclusion from the alpha production improvement results (see Figure 2), is that it seems that to use a neutron source of a few keV and a neutron source in the order of eV's would improve the treatment. An optimisation study has to be carried out.

This study strongly points in the direction that having available both source neutrons of a few keV and in the order of eV's, the nuclear physicist in BNCT could deliver, no matter the circumstances, most of the alphas in the tumour.

5. References

1. Briesmeister, J. F. MCNP - A General Monte Carlo N-Particle Transport Code, Version 4C, LA-13709-M, LANL, 2000.
2. Photon, Electron, Proton and Neutron Interaction Data for Body Tissues. ICRU Report 46; 1992
3. Sauerwein, W et al. Postoperative Treatment of glioblastoma with BNCT at the Petten Irradiation Facility. Protocol 11961; 1999
4. Wittig, A et al. Early phase II study on BNCT in metastatic malignant melanoma using the boron carrier BPA. EORTC protocol 11011; 2003
5. Hideghéty K. et al. Tissue uptake of BSH in patients with glioblastoma in the EORTC 11961 phase I BNCT trial. *J Neurooncol.* 2003 Mar-Apr;62(1-2):145-56.
6. Nigg D.W. Some recent trends and progress in the physics and biophysics of neutron capture therapy. *Progr. In Nuclear Energy*, Vol 35, No 1 pp 79-127, 1999