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Title

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DESIGNING AN EPITHERMAL NEUTRON BEAM FOR BORON NEUTRON CAPTURE THERAPY FOR THE FUSION REACTIONS ${}^2\text{H}(d, n){}^3\text{He}$ AND ${}^3\text{H}(d, n){}^4\text{He}$ ¹.

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Abstract

A beam shaping assembly has been designed to moderate high energy neutrons from the fusion reactions ${}^2\text{H}(d, n){}^3\text{He}$ and ${}^3\text{H}(d, n){}^4\text{He}$ for use in boron neutron capture therapy. The low neutron yield of the ${}^2\text{H}(d, n){}^3\text{He}$ reaction led to unacceptably long treatment times. However, a 160 mA deuteron beam of energy 400 keV led to a treatment time of 120 minutes with the reaction ${}^3\text{H}(d, n){}^4\text{He}$. Equivalent doses of 9.6 Gy-Eq and 21.9 Gy-Eq to the skin and to a 8 cm deep tumor respectively have been computed.

I INTRODUCTION

The main goal of this study is to identify some alternative accelerator-based reactions that could result in an accelerator and target system simpler and less expensive than current ones, while satisfying all of the requirements for boron neutron capture therapy (BNCT). The need for epithermal neutrons with energy distribution peaking around 10 keV [1] has led different groups to focus their research on the two candidate reactions ${}^7\text{Li}(p, n)$ and ${}^9\text{Be}(p, n)$ that generate neutrons in the energy range of hundreds of keV. To the best of authors knowledge, the feasibility of generating neutrons for BNCT with the fusion reactions ${}^2\text{H}(d, n){}^3\text{He}$ (DD) and ${}^3\text{H}(d, n){}^4\text{He}$ (DT) has not been investigated in detail so far, due to the difficulty of moderating high energy neutrons of 2.43 and 14.1 MeV respectively. The advantage of these neutron sources is the low energy required for the deuteron beam. While the protons for the ${}^7\text{Li}(p, n)$ or ${}^9\text{Be}(p, n)$ reactions need to be accelerated between 2.5 and 4.0 MeV, the deuteron beam en-

ergy required for DD and DT lies between 100 keV and 400 keV. Due to this lower energy, smaller accelerators with higher currents can be utilized. In this paper we present a preliminary study to determine which moderators, if any, are the most suitable to decrease the initial neutron energies to therapeutically useful regions, without large losses in neutron beam intensity. The Monte-Carlo codes MCNP [2] and BNCT_RTPE [3] are used for the neutron transport calculation through the moderators and for the treatment planning, respectively.

II BACKGROUND

Boron Neutron Capture Therapy (BNCT) is a binary cancer therapy modality which is very appealing due to its potential for selective cell killing [4]. This therapy is being investigated for several types of cancers including Glioblastoma Multiforme, a highly malignant and therapeutically persistent brain tumor, for which conventional therapies like chemotherapy, surgery, and radiotherapy are not successful.

BNCT brings together two components which assume selectivity in cell killing. The first component is the delivery of ${}^{10}\text{B}$ — a stable isotope of boron with a large cross-section for thermal neutron absorption — preferentially to the tumor cells with help of tumor-seeking compounds. The second component is a beam of low energy neutrons reaching the tumor cells. When a thermal neutron is captured by ${}^{10}\text{B}$, the reaction ${}^{10}\text{B}(n, \alpha){}^7\text{Li}$ occurs, releasing two high-energy ions. Due to the high LET and RBE of these ions, only tumor cells in close proximity to the fission reaction are damaged, leaving adjacent healthy cells unaffected.

Glioblastoma Multiforme is characterized by a tumor mass often located near the center of the brain with accompanying microscopic fingerlets spreading

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throughout the surrounding healthy tissues. The ideal neutron beam to use for irradiation would have to deliver thermal neutrons to the deep-seated tumor mass.

An accepted figure-of-merit to measure the neutron beam quality is based on biological criteria and has been defined in Brookhaven National Laboratory's (BNL) clinical trial protocol [5] as the equivalent dose to the tumor at the centerline of the brain (which corresponds to a depth of 8 cm). This dose is limited by the same protocol which specifies that the equivalent dose to the healthy tissues must not exceed 12.5 Gy-Eq anywhere in the brain. Even though no dose limit has been set by BNL's protocol on the skin, radiation effects in the skin are non-stochastic and a mild skin reddening, which is not permanent, is observed at doses of approximately 8 Gy [6]. Thus the dose to the skin should be minimized to limit potential carcinogenic effects.

One constraint on this radiation therapy is the treatment time. The boron bearing tumor-seeking compound bound to the tumor cells diffuses away after a few hours and the treatment becomes then less efficient. On the other side, for the comfort of the patient, a five hour treatment is undesirable. A fractionated radiation scheme can be adopted, but this option still limits the total treatment time to a few hours or tens of hours. The neutron flux thus has to be high enough.

III DOSIMETRIC PROPERTIES OF MONO-ENERGETIC NEUTRON BEAMS

The center of the brain is the most difficult part to reach due to neutron absorption by healthy tissues. In order to deliver thermal neutrons to tumors 8 cm deep, previous studies [1] showed that we ideally need to supply epithermal neutrons with an energy distribution peaking around 10 keV. The high hydrogen content of the brain slows down the entering epithermal neutrons in such a way that they reach the desired depth thermalized. Neutrons with lower energy contribute less significantly to the dose at the center of the brain because they do not penetrate to this depth. However, they contribute to the dose at shallower depths. Neutrons with energies higher than 40 keV increase the dose to the healthy tissues at the surface of the brain by recoiling proton reactions and are thus therapeutically not as useful.

In order to investigate the dosimetric properties of high-energy neutrons up to 14 MeV (the previous study [1] did not go above 800 keV), we carried out an MCNP [2] simulation study for monoenergetic and

monodirectional beams irradiating the ellipsoidal head of the MIRD5 anthropomorphic phantom [7]. Although this study is not directly applicable to the realistic neutron beams, it provided us with insight and guidance in the design of beam shaping assemblies (BSA).

The neutron beam used for this simulation study was 12 cm in diameter, has an angle of 37.35 degrees with the axis of the MIRD 5 phantom backbone in the sagittal plane and is normal to the upper forehead of the phantom. The monodirectionality of the beam simulates the most penetrating beam achievable. The relative biological effectivenesses (RBE) and boron concentrations used for the dose computation were taken from values used in BNL's protocol [5].

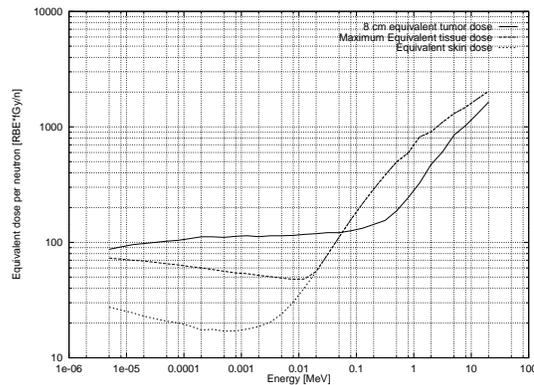


Figure 1: Equivalent doses versus neutron energy.

Figure 1 shows the equivalent tumor dose (D_{tu}) at 8 cm, the maximum equivalent tissue dose (MD_{ti}), and the equivalent skin dose (D_{sk}) per neutron, as a function of neutron energy for monoenergetic and monodirectional beams. The ratio D_{tu}/MD_{ti} has a maximum between 8 and 12 keV equal to 2.4. It decreases slowly for energies below 8 keV, rapidly for energies above 12 keV, and becomes less than unity above 57 keV. Neutrons with energies above 57 keV contribute more to the healthy tissue dose than to the tumor dose at 8 cm. In addition, MD_{ti} increases rapidly for energies above 20 keV. For instance, one 14 MeV neutron contributes as much to MD_{ti} as forty 10 keV neutrons. For these reasons, the neutron energy range above ~ 40 keV is therapeutically undesirable. Since MD_{ti} can not exceed 12.5 Gy-Eq, the theoretical maximum D_{tu} is 30 Gy-Eq with a 8 to 12 keV neutron beam. The number of neutrons required to reach 30 Gy-Eq is 2.6×10^{14} . If we limit D_{sk} to 8 Gy-Eq [6], the ratio D_{sk}/MD_{ti} should not exceed $8/12.5 = 0.64$, which suggests the neutron energy around 8 keV. A more detailed study of a neutron energy-based methodology for predicting in-phantom neutron beam characteristics will be published in [8].

IV METHODOLOGY FOR THE OPTIMIZATION OF THE BEAM-SHAPING ASSEMBLY (BSA)

Neutrons from both fusion reactions have to be moderated down to the desired epithermal energy range. The remainder of this study focuses on determining different combinations of materials to shape the most suitable neutron beam.

Although the study of the dosimetric properties of the monoenergetic neutron beams presented in Sec. III gave us guidance in searching for an optimal beam, the work by Bleuel et al. [9] was extremely helpful in providing an in-depth analysis of the epithermal beam shapes that can produce superior depth-dose distributions.

The neutron source is characterized as follows. Neutrons are emitted isotropically in 2π and monoenergetically across a 5 cm radius flat circular surface. The source is distributed uniformly over the surface of the disk. The assumption of isotropy has to be discussed in detail. Concerning DT, the high Q value for the reaction makes the neutron energy relatively insensitive to the angle of emission for the region of low deuteron energy (~ 100 keV) [10]. The neutrons are emitted practically isotropically in the center-of-mass system below this energy. Thus, angular isotropy in the lab system is an adequate approximation for deuteron beams with energies up to 400 keV [10]. For DD, the angular distribution in the center-of-mass system is anisotropic. A better modeling of the source accounting for the angular distribution would be required but this is beyond the scope of these preliminary calculations.

Source neutrons enter a 25 cm in diameter cylindrical BSA [9] with the monoenergetic neutron distribution corresponding to DD or DT. They travel through the BSA composed of several layers of different materials until they reach the other side where the patient is located. The axial length of the BSA depends on the desired moderation. The BSA is surrounded by a thin (0.5 mm) layer of ${}^6\text{LiF}$ and a 30 cm thick Al_2O_3 reflector. The materials considered for moderation in this study were found in the BNCT literature and are Pb , Fe , Bi , D_2O , LiF with different ${}^6\text{Li}$ enrichments, a mixture 40% Al and 60% AlF_3 , and MgF_2 . The Monte-Carlo code MCNP [2] is used to simulate the neutron transport through the BSA.

The materials have first been analyzed separately to determine their effect on the neutron spectrum. Neutron spectra are measured at the exit of the BSA across a 20 cm diameter circular window. Different combinations of materials have then been considered, the goal

being to produce an intense, broad energy epithermal beam peaking around 8 keV with the fast and thermal neutron components reduced to a minimum level. Finally, the diameter of the beam shaping assembly and the reflector material have been changed to see the impact of these parameters on the neutron flux and energy distribution.

For the dose computations with BNCT_RTPE [3], the boron concentrations and RBE values are taken from BNL's protocol [5]. The energy and angular dependent neutron and photon distributions are determined by MCNP [2] across the 20 cm BSA exit window aforementioned, and are used for the radiation transport through the phantom head and the 13.4 cm thick lithiated polyethylene delimiter separating the BSA from the phantom head [9]. The neutron beam is 12 cm in diameter after the delimiter.

V SELECTION OF FILTERS

It is worth briefly examining the neutron cross sections of the different materials considered; the data are taken from the MCNP [2] cross section library. As shown in

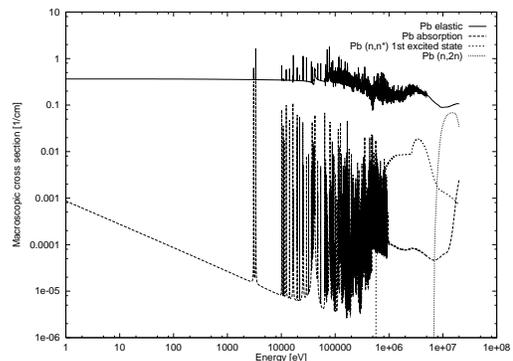


Figure 2: *Pb* macroscopic cross sections.

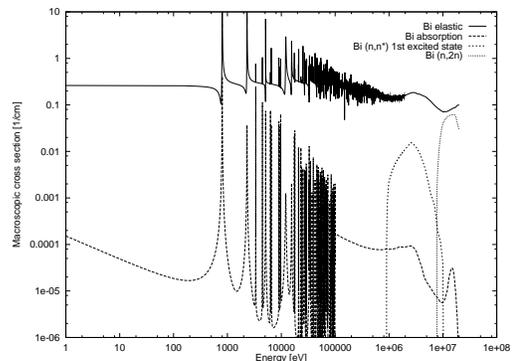


Figure 3: *Bi* macroscopic cross sections.

Fig. 2 and 3, lead and bismuth have high cross-section

for the $(n, 2n)$ reactions at energies above 10 MeV. Lead and bismuth can be used on the incoming 14.1 MeV neutrons from the DT reaction. For every high energy neutron absorbed, two lower energy neutrons are generated. On the other side, lead is also a good photon absorber. Thin layers of lead will be used at the end of the moderation to decrease the undesired photon dose.

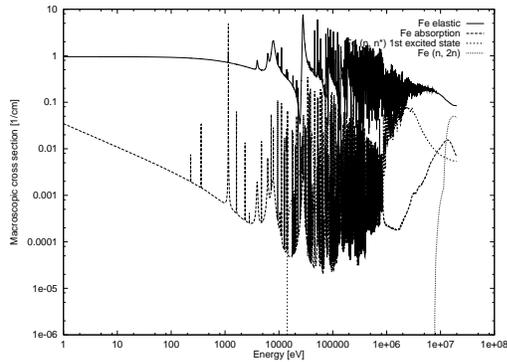


Figure 4: Fe macroscopic cross sections.

Iron has a less pronounced $(n, 2n)$ reaction and a higher absorption cross section than lead. However, iron is a good moderator at high energies due to its high inelastic scattering cross-section above 860 keV. Moreover, it has a window at 20 keV with low cross-sections, just around the desired neutron energy. Thus, iron is used to moderate neutrons from both reactions.

Though widely utilized as a neutron moderator, heavy water is of no interest in our case. Because of the light element 2H , D_2O thermalizes neutrons very quickly and shifts the neutron spectrum down to below epithermal energies.

The next moderator analyzed was 7LiF [11], the heavier element 7Li does not shift the neutron spec-

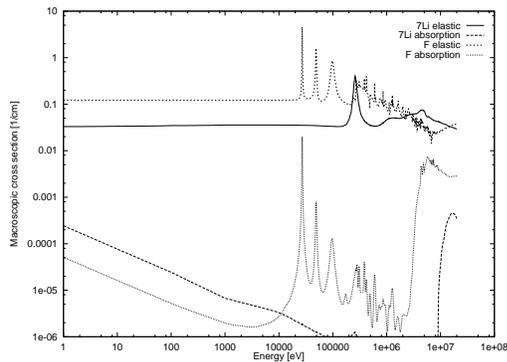


Figure 5: 7LiF macroscopic cross sections.

trum down as fast as 2H but is still very effective in slowing down neutrons in a short distance. Figure 5 shows the cross section of 7LiF . The elastic scatter-

ing resonance structure of F extending down to 27 keV can be used beneficially to downscatter neutrons above this energy. The absorption and elastic cross sections of 6LiF are shown in Fig. 6. The increasing absorp-

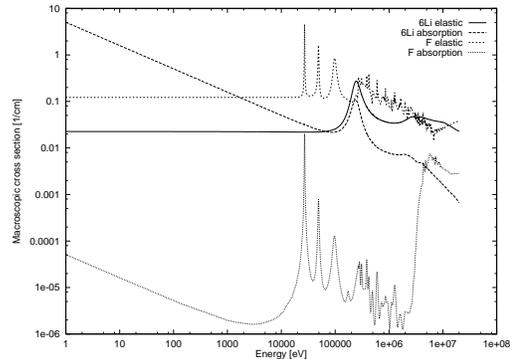


Figure 6: 6LiF macroscopic cross sections.

tion cross section of 6Li for decreasing neutron energies makes this compound an excellent thermal neutron filter. In summary, lithium fluoride has the interesting properties of decreasing the neutron energy in a somewhat more controllable way than D_2O , of restricting the number of neutrons above 27 keV, and of being a good thermal neutron filter if 6Li is present. It will be used in that perspective later when combinations of materials will be considered.

As we can observe in Fig. 7, the mixture 40% Al /60% AlF_3 [12] is interesting in the sense that the

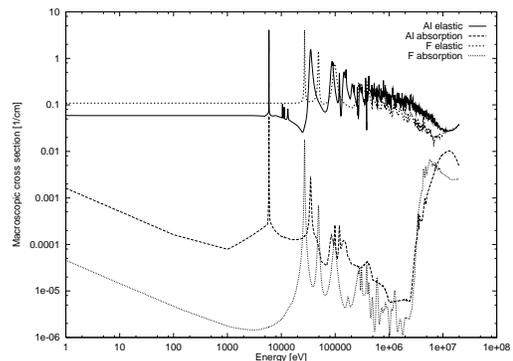


Figure 7: 40% Al /60% AlF_3 macroscopic cross sections.

elastic scattering resonances of Al supplement exactly the ones of F from 27 keV up to the high energy tail, except for a narrow energy range around 70 keV. This resonance structure at high energies will preferentially reduce the number of neutrons above 27 keV.

MgF_2 has properties similar to the mixture 40% Al / 60% AlF_3 but appeared to be worse because more narrow energy ranges are not covered by resonances above 27 keV. It has thus been abandoned.

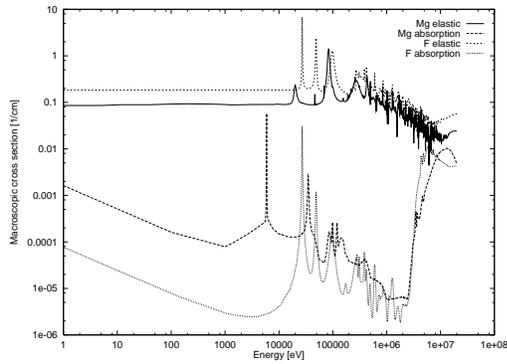


Figure 8: MgF_2 macroscopic cross sections.

VI MODERATION FOR DD.

In a first stage, the moderators 7LiF and 40%Al/60%AlF₃ have been simulated separately. Starting with 2.43 MeV neutrons, the neutron energy distributions as a function of the BSA thickness are shown in Fig.

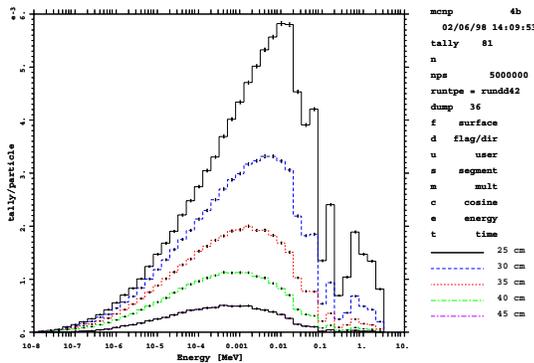


Figure 9: Neutron energy distribution as a function 7LiF moderator thickness.

9. 7LiF shifts the spectrum toward lower energies and the flux of neutrons with energies above 100 keV is reduced to very low levels. The dips at 100 and 250 keV in the spectra correspond to the elastic resonances of F and 7Li respectively (see Fig. 5). On the downside of this moderator, the peak is shifted to lower than 8 keV as the moderation proceeds. The mixture 40%Al/60%AlF₃ exhibits a well-defined peak at 15 keV, which is close to our target energy. However, the high energy tail of the spectra and particularly the narrow range around 70 keV — corresponding to energies not covered by elastic resonances in Fig. 7 — persist. In summary, 7LiF and 40%Al/60%AlF₃ could be used beneficially in combination with other moderators to achieve the desired epithermal energy distribution.

Several combinations of materials have been tested. The optimal combination of materials that we came up with was 30 cm of 7LiF and 18 cm of

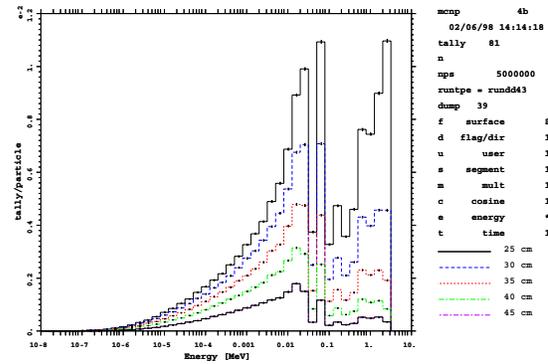


Figure 10: Neutron energy distribution as a function of 40%Al/60%AlF₃ moderator thickness.

40%Al/60%AlF₃. The neutron spectrum after moderation, the total equivalent doses to the tumor and healthy tissues (with its components) are shown in Fig.

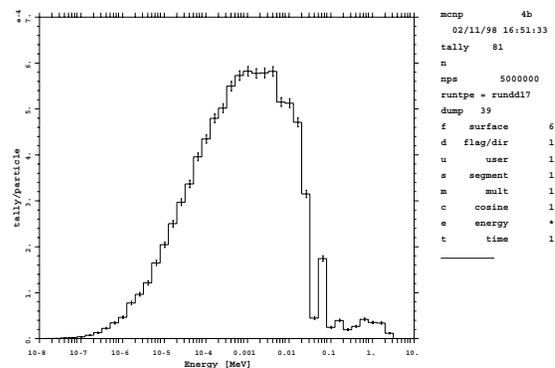


Figure 11: Neutron energy distribution after moderation corresponding to DD.

11 and 12. The equivalent tumor dose to the desired depth of 8 cm with this moderation is 18 Gy-Eq. The equivalent skin dose is 8.9 Gy-Eq. Accounting for the neutron yield of DD — which is $8.5 \times 10^9 n/sec/mA$ for a 400 keV beam [13] — this moderation would lead to a treatment time of 840 hours for a 5 mA deuteron beam. Another combination of materials — namely 5 cm of Fe to downscatter inelastically the fast neutrons, 25 cm of 7LiF , 24 cm of 40%Al/60%AlF₃ and 1 mm of Pb to reduce the photon dose — resulted in a 18.2 Gy-Eq equivalent tumor dose to the center of the brain and a 8.2 Gy-Eq skin dose but led to a 1540 hours treatment time. This unacceptably large treatment time could probably be reduced by using several beams, by increasing the beam intensity, or by improving the beam shaping assembly.

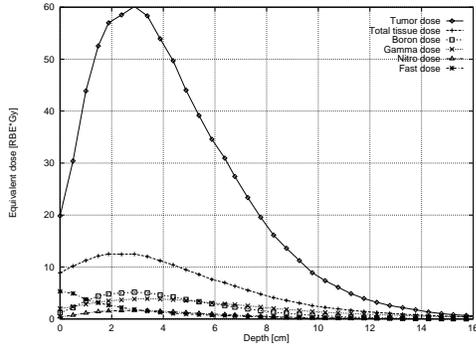


Figure 12: Total equivalent doses to the tumor and healthy tissues (with its components) corresponding to DD.

VII MODERATION FOR DT.

DT has been considered next for the neutron yield is more than one order of magnitude higher than DD. Figures 13 and 14 show the neutron energy distributions

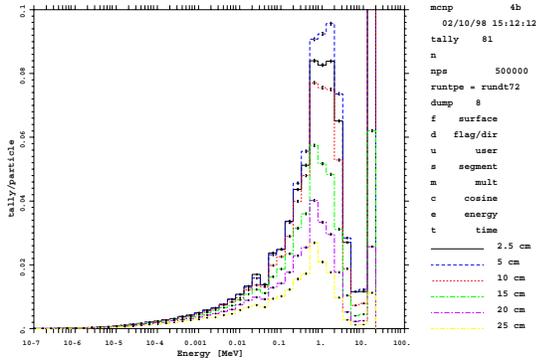


Figure 13: Neutron energy distribution as a function of Pb moderator thickness.

for different thicknesses of lead and bismuth for 14.1 MeV entering neutrons. Due to the $(n, 2n)$ reactions, the neutron flux increases in the first 5 cm. This neutron multiplication is slightly more pronounced for lead. Figure 15 shows the same graph for iron. The shapes of the spectra for lead and bismuth exhibit clear peaks at around 1 MeV, with less-sharply defined peaks around 25 and 250 keV for iron. Neutrons passing through iron are moderated to slightly lower energies than in the cases of lead or bismuth, and the 14.1 MeV ones are better suppressed. In order to take advantage of the properties shown in Figs. 13, 14 and 15, a 5 cm layer of lead or bismuth followed by a thicker layer of iron are used at the beginning of the moderation.

The emphasis in the design of a BSA was on decreasing the high energy neutron flux to a level as low as possible. The best moderator design we came up with

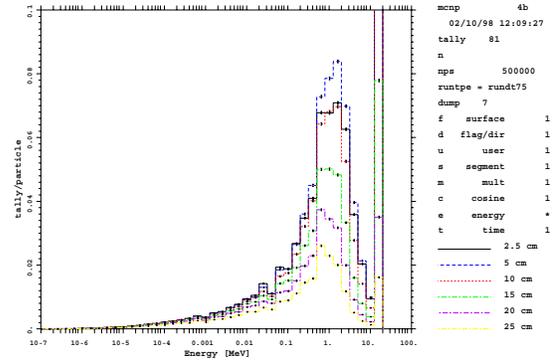


Figure 14: Neutron energy distribution as a function of Bi moderator thickness.

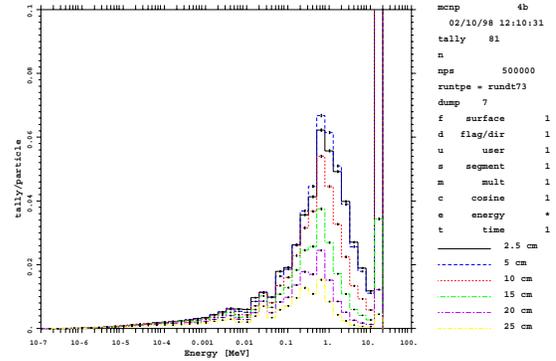


Figure 15: Neutron energy distribution as a function of Fe moderator thickness.

was 5 cm of Bi , 50 cm of Fe , 24 cm of 40% Al /60% AlF_3 , 1 mm of 6LiF and 1 mm of Pb . Bismuth was used to generate more neutrons with the $(n, 2n)$ reactions, iron to decrease the fast neutron flux in the range of 1 to 14 MeV, the mixture 40% Al /60% AlF_3 to decrease the fast neutron flux in the range of 90 keV and higher, and eventually the thin layers of 6LiF and Pb to decrease the thermal neutron and photon fluxes respectively. With this BSA, the equivalent tumor dose at 8 cm is 18.2 Gy-Eq and the equivalent skin dose is 11.35 Gy-Eq. Simulations with a 5 cm slab of lead instead of bismuth at the entrance of the moderator gave slightly worse results, especially concerning the fast neutron flux. The neutron spectrum after moderation is shown in Fig. 16. We observe that the number of neutrons with energies greater than 3 MeV has been reduced to about a hundredth of the number of neutrons at 15 keV.

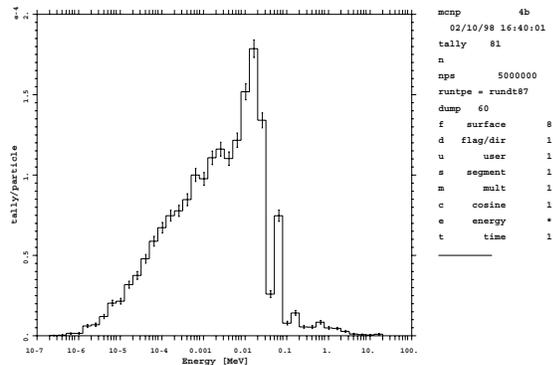


Figure 16: Neutron energy distribution after moderation corresponding to DT with a 25 cm diameter BSA.

VIII EFFECT OF THE BSA DIAMETER ON THE BEAM CHARACTERISTICS

The optimal combination of materials being determined, the next step consisted in modifying the diameter of the cylindrical beam shaping assembly, which has been kept at 25 cm so far. A few simulations with greater diameters revealed the interesting behavior shown in Fig. 17. The treatment time decreases, the

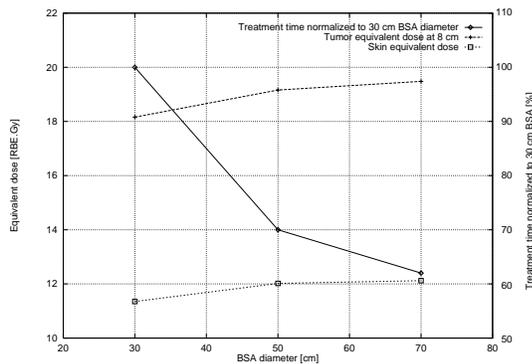


Figure 17: Treatment time normalized to 30 cm BSA diameter treatment time, tumor equivalent dose at 8 cm and equivalent dose to the skin as a function of the BSA diameter.

tumor equivalent dose at 8 cm increases as well as the equivalent dose to the skin. The neutron spectrum after moderation corresponding to the 70 cm diameter BSA is shown in Fig. 18. As we can observe, the fast neutron flux is lower, the epithermal neutron flux is higher and the neutron energy distribution exhibits a sharper peak

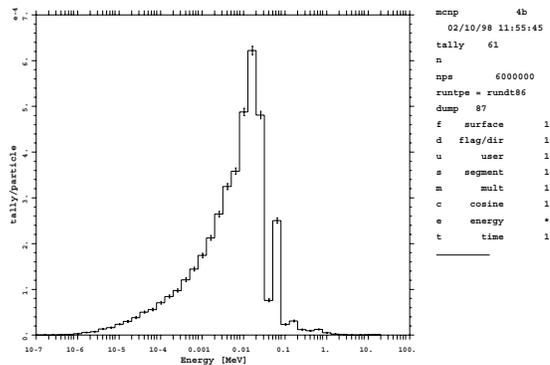


Figure 18: Neutron energy distribution after moderation corresponding to DT with a 70 cm diameter BSA.

at 15 keV, which is a slightly too high energy for the skin. The equivalent tumor dose at 8 cm depth is 19.5 Gy-Eq and the equivalent skin dose is 12.1 Gy-Eq. In the last part of this study, the BSA is further optimized to minimize the dose to the skin.

IX OPTIMAL BSA FOR DT

Source neutrons are now emitted isotropically in 4π across a 5 cm diameter flat circular surface. A brief study for the moderators led to the conclusions that a) the thickness of the Al_2O_3 reflector could be decreased to 17.5 cm without affecting the neutron fluxes and thus without increasing the treatment time significantly, b) lead exhibited better characteristics than Al_2O_3 or graphite as a reflector material. The best BSA we came up with is composed of layers of Bi , Fe , 40% Al /60% AlF_3 , 6LiF and Pb . The thin layer of 6LiF surrounding the BSA has been removed as it did not decrease the thermal neutron flux component of the beam significantly.

The neutron spectrum and dose distribution corresponding to this BSA are shown in Fig. 19 and 20.

The equivalent tumor and skin doses are 21.9 Gy-Eq and 9.6 Gy-Eq, respectively.

The neutron yield for DT is considerably higher than for DD. With 400 keV and 22 mA for the deuteron beam, a neutron yield up to $6 \cdot 10^{12} n/sec$ has been obtained by R. Booth et al. [14] in 1977. For our BSA design, a 160 mA beam intensity would then lead to treatment times of 120 minutes using a single beam. Taking advantage of the small sizes of the ion sources, accelerators and moderators, two beams could easily be used in parallel. By increasing the beam intensity and the number of beams, treatment times could be reduced to less than an hour.

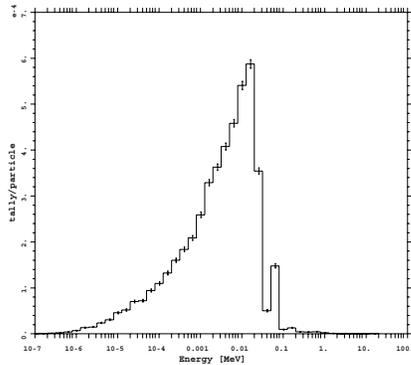


Figure 19: Neutron energy distribution after moderation corresponding to the optimal BSA for DT.

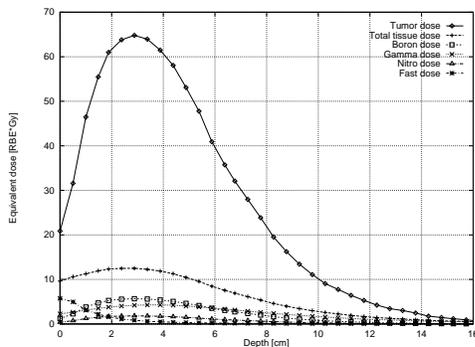


Figure 20: Total equivalent doses to the tumor and healthy tissues (with its components) corresponding to the optimal BSA for DT.

X CONCLUSION

Two fusion reactions have been studied to determine whether they could be used as neutron sources in the context of BNCT. Our analysis shows that the low neutron yield of DD seems to be an obstacle for its use in this therapy. On the other hand, we have shown that the high-energy neutrons from DT could be moderated to around 8 to 10 keV without reducing the neutron flux to a negligible level. With our current beam-shaping assembly design, the equivalent tumor dose at the center of the brain is 21.9 Gy-Eq and the equivalent skin dose is 9.6 Gy-Eq. With this reaction, treatment times of 120 minutes could be computed using a single deuteron beam of 400 keV and 160 mA. A multiple beam configuration could increase the tumor dose at the center of the brain and reduce the treatment time to less than one hour. However, the high deuteron beam intensity might cause problems with the tritiated target, which have not been considered so far.

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