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NEUTRONICS ANALYSIS OF THREE BEAM-FILTER ASSEMBLIES FOR AN ACCELERATOR-BASED BNCT FACILITY*

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ABSTRACT

Three moderator materials, AlF\textsubscript{3}/Al, D\textsubscript{2}O and LiF, have been analyzed for clinical usefulness using the reaction $^7\text{Li}(p,n)$ as an accelerator driven neutron source. Proton energies between 2.1 MeV and 2.6 MeV have been investigated. Radiation transport in the reflector/moderator assembly is simulated using the MCNP program. Depth-dose distributions in a head phantom are calculated with the BNCT_RTPE patient treatment planning program from INEEL using the MCNP generated neutron and photon spectra as the subsequent source. Clinical efficacy is compared using the current BMRR protocol for all designs. Depth-dose distributions are compared for a fixed normal tissue tolerance dose of 12.5 Gy-Eq. Radiation analyses also include a complete anthropomorphic phantom. Results of organ and whole body dose components are presented for several designs. Results indicate that high quality accelerator beams may produce clinically favorable treatments to deep-seated tumors when compared to the BMRR beam. Also discussed are problems identified in comparing accelerator and reactor based designs using in-air figures of merit as well as some results of spectrum-averaged RBE’s.

I. INTRODUCTION

\*This work was supported by the Director, Office of Energy Research, Office of Health and Environmental Research of the U. S. Department of Energy under Contract DE-AC03-76SF00098
The design and construction of an accelerator-based BNCT facility for clinical trials is being pursued by a collaboration of LBNL and UCSF researchers. An intense proton beam of about 2.5 MeV impinges on a lithium target generating a high neutron flux. A moderator assembly is required to shape the neutron energy spectrum and produce an epithermal neutron beam optimized for the clinical application. This work presents the results of an optimized design for three different moderator materials.

II. NEUTRON SOURCE MODELING

Double differential neutron yields for the reaction $^7\text{Li}(p,n)^7\text{Be}$ were calculated for varying incident proton energies using Legendre coefficient fits to the cross section provided by Liskien.\(^1\) The reaction $^7\text{Li}(p,n)^7\text{Be}$ displays a large resonance in the forward direction around 2.3 MeV which extends to about 2.5 MeV. Only the reaction $^7\text{Li}(p,n)^7\text{Be}$ is considered. The reaction $^7\text{Li}(p,n)^7\text{Be}^*$ which produces a 0.431 MeV gamma with a threshold of 2.373 MeV in the forward direction and 2.423 MeV in the backward direction, and higher threshold reactions is not included in our treatment. These cross sections are generally only a few percent of the $^7\text{Li}(p,n)^7\text{Be}$ cross section at proton energies less than or equal to 2.5 MeV and therefore not considered important. A detailed description of our source modeling can be found elsewhere.\(^2\)

III. NEUTRON BEAM MODELING

Complete characterization of the neutron beam from its $^7\text{Li}(p,n)$ source, through a filter assembly, and transported through a head phantom, has been carried out in two stages.

The first stage models the neutron beam from the $^7\text{Li}(p,n)$ source through the filter assembly. A three dimensional geometry is specified using the Monte Carlo program MCNP.\(^3\) This geometry includes a 5 cm radius flat circular neutron source, with energy and angular dependence as previously described.\(^2\) The source is distributed uniformly over the surface of this disk. A 1 cm thick aluminum target backing is modeled immediately behind the source, which is then followed by the 12.5 cm radius cylindrical moderator of variable thickness and material. Surrounding the entire moderator and proton beam port is an $\text{Al}_2\text{O}_3$ reflector. Some preliminary studies have shown that other materials may be as suitable for use as a reflector, such as lead or carbon, which exhibit lower gamma production, but as long as the reflector is consistent among simulations, the selection of a particular material was not deemed to have a large effect on the conclusions of this report. Finally, all interface surfaces are lined with 0.05 g/cm\(^2\) of $^6\text{Li}$ (in the form of either $^6\text{LiF}$ or pure $^6\text{Li}$) for filtering of thermal neutrons, with the exception of the front window of the moderator, which is lined with 0.01 g/cm\(^2\) of $^6\text{Li}$.

Three moderator materials were analysed to determine the best beam shaping assembly. The first material, heavy water (D\(_2\)O), was chosen since it has been proposed for several accelerator-based designs\(^4,5,6\) and produces a neutron spectrum similar to those produced by existing reactor-based sources. A second material, aluminum fluoride, is being used in TRIGA reactor-based BNCT research in Finland\(^7\) but has
not previously been applied to an accelerator-based neutron source. Its ability to produce a relatively narrow energy spectrum around 20 keV makes it a promising material choice for BNCT applications. A particular mixture of 60% AlF$_3$ and 40% Al was assumed. The third material, enriched $^7$LiF was chosen for similar reasons and its ability to more adequately filter fast neutrons. These characteristics can be seen from typical neutron spectra in Fig. 1 produced by a given thickness of each material.

The energy and angular dependent neutron and photon spectra are determined by MCNP across a 20 cm surface at the front window of the moderator. This information is then used as the source for a second Monte Carlo model for determination of head phantom depth-dose distributions. This source is characterized by ten equal-intensity angular bins and an energy resolution of five equal-lethargy energy bins per decade. Each moderator typically tends to produce a different characteristic neutron spectra, examples of which are shown in Fig. 1 along with the spectrum produced by the Brookhaven Medical Research Reactor (BMRR) in their current BNCT clinical trials. Each of these spectra have been normalized to the same total fluence, yet it is clear that each spectrum could produce significantly different dose distributions when transported through a human brain. Analyzing the transport of neutrons and photons through a head phantom is therefore necessary to determine the true quality of each beam, which cannot be accurately estimated by using existing in-air parameters such as the useful flux or the ratio of the useful flux to the dose at the exit of the moderator. These beams can be tailored by varying the incident proton energy on the lithium

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Figure 1: Neutron spectra from various moderator materials.
target and by changing the moderator thickness.

The second Monte Carlo model used is the BNCT treatment planning code, BNCT\_RTPE\textsuperscript{10}, developed by INEEL for use in Brookhaven's clinical trials. A lithiated polyethylene beam delimiter identical to the design used in these trials is modeled in BNCT\_RTPE, as well a head phantom based on CT scans. The MCNP binary output file, containing neutron and gamma transport results for the moderator and reflector, is converted to a format that can be read as the input to BNCT\_RTPE for subsequent transport in the head phantom.

The four primary tissue dose components are calculated in the phantom along the centerline of the beam. These are: gamma, neutron-proton recoil, nitrogen neutron capture and boron neutron absorption. Fig. 2 shows the kerma factors in boron-free tissue used to convert fluence to dose. As can be seen, neutron interactions above about 10 keV contribute the majority of their dose via hydrogen elastic scattering or proton recoil, while below 10 keV neutron interactions are dominated by the $^{14}$N(n,p) absorption reaction. Generally in BNCT neutronics these dose components are termed the fast neutron dose component and the nitrogen dose component, respectively. The gamma dose from hydrogen thermal neutron capture and the $^{10}$B(n,\alpha) are tabulated separately. The total dose rates to tissue and tumor were computed:

$$\dot{D}_{total,tis} = \dot{D}_B(z) \cdot CF_{B,tis} + \dot{D}_N(z) \cdot RBE_N$$
$$+ \dot{D}_H(z) \cdot RBE_H + \dot{D}_\gamma$$

(1)
\[
\dot{D}_{total,tum} = \dot{D}_B(z) \cdot CF_{B,tum} + \dot{D}_N(z) \cdot RBE_N + \dot{D}_H(z) \cdot RBE_H + \dot{D}_{\gamma} \tag{2}
\]

where: \( CF_{B,tis} = 1.3, \ CF_{B,tum} = 3.8, \ RBE_N = 3.2, \ RBE_H = 3.2 \). The symbols are defined as follows: \( CF_B \) is the boron dose compound factor, for either tumor or normal tissue, which includes the relative biological effectiveness (RBE), \( RBE_N \) is the RBE for the nitrogen capture dose component, \( RBE_H \) is the RBE for the neutron proton recoil dose component and \( \dot{D} \) is the dose rate for the subscripted component at a given depth, \( z \).

The above values were taken from values used in Brookhaven’s clinical trials.\(^{11} \) Since a patient’s treatment is limited by a certain maximum tissue dose, the treatment time, \( T \), can be calculated:

\[
T = \frac{\dot{D}_{(max-tolerable)}}{\dot{D}_{(max-total,tis)}(z)} \tag{3}
\]

where \( \dot{D}_{(max-total,tis)}(z) \) is the maximum total tissue dose rate in the brain, and \( D_{(max-tolerable)} = 12.5 \text{ Gy-Eq}, \) per Brookhaven protocol.

The total dose delivered over the full treatment time is then the sum of the individual dose rate components over the treatment time.

There is some concern regarding the use of RBE’s measured at BMRR for a fission reactor spectrum and applying these to an accelerator-produced neutron spectrum, particularly for the harder neutron spectrum from the AlF\(_3\)/Al moderator (see Fig. 1). In this work we have used the BMRR fast neutron RBE value of 3.2. As a check we have used the RBE\((E_n)\) values of Blue et. al.\(^{12} \) These authors have developed an expression for the neutron RBE as a function of neutron energy and then normalized the results to the normal tissue tolerance studies performed on the BMRR epithermal neutron beam. When we fold in the normalized RBE\((E_n)\) with the spectra produced by our AlF\(_3\)/Al and D\(_2\)O moderators and the BMRR spectrum (as shown in Fig. 1) we calculate spectrum averaged RBE’s of 3.19, 3.65 and 3.94, respectively. One may infer from this that our use of the BMRR Phase I/II Treatment Protocol fast neutron RBE value of 3.2 is conservative.

IV. FIGURES OF MERIT

It is extremely important in characterizing a neutron beam for BNCT to use accurate and relevant figures of merit. One cannot evaluate the effectiveness of a particular beam based strictly on the flux, or on loosely defined in-air terms, such as “useful flux,” or in-air dose-to-flux ratios, which assume that all neutrons in a certain energy range are all equally ”useful” for BNCT applications and that all neutrons outside that range are not. The relative effect of each neutron energy in treatment varies. Furthermore, the total contribution of a full beam spectrum can provide different dose characteristics that are not calculable by assuming equal importance for each energy, or by attempting to match a particular ”perfect” energy. For these reasons, it is necessary to evaluate the effect of a beam based on analyzing in-phantom depth-dose characteristics.
Evaluating the efficacy of these in-phantom doses can be difficult. When available and applicable, parameters for this study were taken from current BMRR patient treatment protocol. These parameters include RBEs, maximum tissue tolerance dose, and boron loading in tissue and tumor cells.

While clinical data on tissue dose-volume limits was not available, it was felt that allowing too large a portion of the brain to receive a high tissue dose would be undesirable, even if the maximum point tissue tolerance dose criteria and whole brain irradiation limits are met. Therefore, an entrance dose limit of 10.0 Gy-Eq was set. BNCT RTPE calculates entrance dose as the dose to normal brain tissue extrapolated back to zero tissue depth. It was felt that if the entrance dose was limited to the above value, sufficient leeway is allowed to properly optimize other beam characteristics without incurring a high dose (near tolerance) in a large brain tissue volume as well as being a safe limit for the scalp. As will be seen later, one does not gain significant advantages in efficacy by surpassing this limit for the particular designs addressed.

For Boron Neutron Capture Therapy of glioblastoma multiforme, the most penetrating neutron beam possible is desired, keeping within the aforementioned established limits. Other issues, such as total flux intensity (which determines only the treatment time), are largely secondary concerns and should be considered only when they suggest a highly inconvenient scenario, such as abnormally long treatment times.

Several other in-phantom figures of merit were considered to determine the optimal beam for BNCT treatments, including parameters such as advantage depth and advantage ratio. Advantage depth is defined as the depth in the brain at which the tumor dose is equal to the maximum tissue dose in the brain (which has been set at 12.5 Gy-Eq in this analysis). While it is an adequate relative measure of the penetrability of particular neutron beams, it relies heavily on the particular drug boron loading and tissue/tumor boron ratio and does not take the full depth-dose characteristics into account. An equally adequate parameter is the advantage ratio, defined as the ratio of the tumor dose at a particular depth to the maximum tissue dose:

\[ A.R. = \frac{D_z(tumor)}{D_{max}(tissue)} \]

Since the maximum tissue dose has been set at 12.5 Gy-Eq, the tumor dose at a particular depth is an equivalent measure of the beam quality. It was chosen to maximize the total equivalent dose at a depth of 8 cm, roughly the brain midline, as this would be the largest depth one could conceivably treat with a single beam.

V. RESULTS

For each incident proton energy and moderator material, the dose properties of a range of moderator thicknesses were examined. In each case, decreasing the moderator thickness results in an increase in both the 8 cm tumor dose as well as the entrance dose. The moderator thickness is decreased in each simulation until the 10 Gy-Eq entrance dose is reached.

The optimal moderator thickness is the thickness below which the entrance dose would exceed 10 Gy-Eq, within a moderator thickness resolution of 1 cm for practi-
Figure 3: The total and four components of tissue dose components as a function of depth in tissue for the 34 cm AlF₃/Al, 2.4 MeV design, as calculated by BNCT RTPE.

Figure 4: Depth-dose distributions in tumor for BMRR and the three moderator designs. The results for each moderator are chosen based on producing the highest 8 cm tumor dose for a fixed entrance and peak normal tissue dose equivalent.
cality. Exceeding the 10 Gy-Eq entrance dose limit would not lead to significant gains in the 8 cm tumor dose, which makes it an excellent requirement to ensure patient safety while still providing the best possible treatment. Fig. 3 shows the depth-dose components for the 34 cm AlF₃/Al moderator design and an incident proton energy of 2.4 MeV. The total dose curve demonstrates how the 10 Gy-Eq entrance tissue dose and the 12.5 Gy-Eq peak tissue doses are met.

The optimum design for each moderator is specified by the incident proton energy and the moderator thickness and is measured by finding that set of conditions (proton energy, thickness) which produces the highest 8 cm tumor dose equivalent for a fixed entrance and peak normal tissue dose equivalent. As can be seen in Fig. 4 the AlF₃/Al and LiF₃ moderator designs produce tumor doses at 8 cm depth approximately 50% higher than the referenced BMRR design. This is a substantial increase for regions of the brain that are difficult to treat given the fact that typical tumor control curves can rise steeply for relatively small increases in dose. The D₂O results are very similar to the BMRR curve. This 50% increase in modeled depth-dose is the result of a complex tradeoff between many variables resulting in a neutron spectrum outside the moderator which is closer to the ideal spectrum.

VI. PHANTOM DOSIMETRY

Different ¹⁰B delivery agents can result in varying uptakes of boron in many of the body organs. These uptakes will vary with time after drug injection. In this section we calculate major organ doses during a patient irradiation assuming a uniform concentration of 10 ppm ¹⁰B in all organs. Results are tabulated by dose component, including the ¹⁰B dose from the reaction ¹⁰B(n,a). The moderator/reflector assembly together with the anthropromorphic phantom are shown in Fig. 5. Normal ICRU 44 soft tissue elemental composition is used for simplicity with different densities for soft tissue (1 g/cm²), bone (1.48 g/cm²) and the lungs (0.296 g/cm²).

MCNP is used with the MIRD 5 anthropomorphic phantom model.¹³ One can scale these results for actual measured concentrations of ¹⁰B in each organ. Quantifying these doses is important and is the first step in deciding whether or not measures should be taken to reduce these doses. Much of this work has been tabulated elsewhere.¹⁴ The moderator/reflector assembly together with the anthropomorphic phantom are shown in Fig. 5.

Table 1 gives a brief summary of absorbed doses to several organs and to the whole body (W.B.) for the AlF₃/Al moderator design, including the lithiated polyethylene delimiter. Results are tabulated with the MCNP tracklength tally averaged over the entire organ cell. Relative errors are given in parenthesis. Several of the errors are large (>10%) due primarily to the fact that the particular dose component is negligibly small, representing a rare statistical event. Actual calculated values for over 77 cells are available. The absorbed doses are about 2 times higher for the whole body and 30% higher for the brain-average without the delimiter. About 15% of the whole body dose is due to the assumption of uniform 10 ppm concentration of ¹⁰B in the body which may not represent a realistic condition and therefore should be properly adjusted. In addition, one can see that even for high concentrations of ¹⁰B in
Figure 5: Layout of moderator/reflector assembly with delimiter and anthropomorphic phantom used in MCNP calculations. Phantom internal organs not shown.

Table 1: Summary of organ and whole body doses for AlF₃/Al moderator design including the lithiated polyethylene delimiter. Relative errors are given in parenthesis.

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<tr>
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<th>Absorbed Dose (cGy)</th>
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<tbody>
<tr>
<td></td>
<td>Brain</td>
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<tr>
<td>n</td>
<td>29.6</td>
</tr>
<tr>
<td></td>
<td>(0.013)</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>165.6</td>
</tr>
<tr>
<td></td>
<td>(0.02)</td>
</tr>
<tr>
<td>$^{10}$B</td>
<td>85.5</td>
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<tr>
<td></td>
<td>(0.013)</td>
</tr>
<tr>
<td>Total</td>
<td>280.7</td>
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a blood filtering organ like the liver, the boron dose is much smaller than the gamma dose due to thermal neutron capture in hydrogen throughout the body.

VII. SUMMARY

The combination of using MCNP for simulating transport through the moderator and reflector assembly with the use of BNCT RTPE for modeling transport in a head phantom provides an excellent way of analyzing accelerator-produced neutron beams for BNCT. Using an AlF₃/Al moderator produces a neutron spectrum peaked in energy between 10 and 20 keV, close to what may be considered by many to be an ideal beam. The difference between this and highly moderated reactor spectra can lead to significantly improved depth-dose distributions, as much as 50% near the midline of the brain (roughly 8 cm). Using a 20 mA, 2.4 MeV proton accelerator will yield treatment times similar to those at BMRR (less than one hour).

REFERENCES

1. H. Liskien and A. Paulsen, "Neutron Production Cross Sections and Energies for the Reactions ⁷Li(p,n)⁷Be and ⁷Li(p,n)⁷Be*," Atomic Data and Nuclear Data Tables, 15, 57-84 (1975).


