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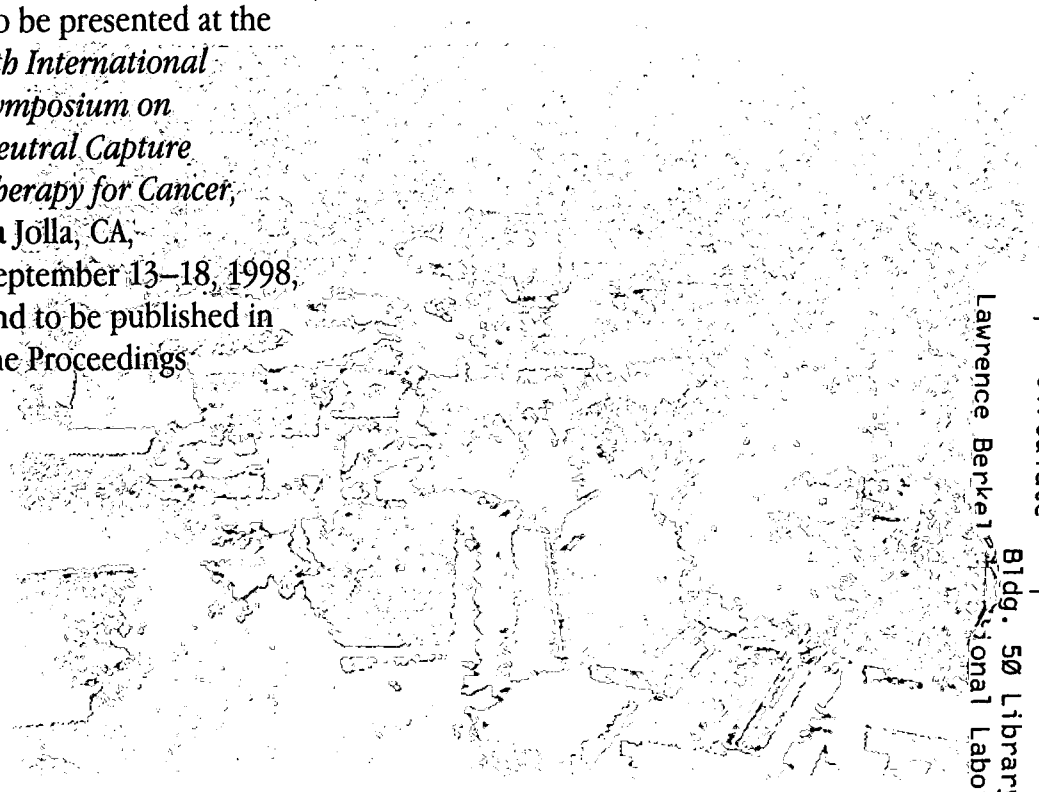

DISCLAIMER

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Development of a Neutron Energy-Biased In-Air Figure-of-Merit for Predicting In-Phantom BNCT Neutron Beam Characteristics.*

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1 INTRODUCTION

Maximizing the efficacy of a Boron Neutron Capture Therapy (BNCT) modality requires improvements in two areas: development of better boron-delivering drugs and better tailoring of the epithermal neutron beam. Previous attempts at the latter have not always been successful in predicting optimal in-phantom results, often assuming that all neutrons within a certain "useful" energy range are equally valuable for BNCT purposes. Some studies have recognized that higher energy epithermal neutrons (~10 keV) and more forward-directed neutrons provide more penetrating beams. This results in higher tumor doses at centerline phantom depths. The exact effect of neutron beam energy spectrum shaping for BNCT has

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Figure-of-Merit		BMRR	LBNL
In-Air	D_f/Φ_{epi} [Gy/(n/cm^2)]	4.8×10^{-13}	8.9×10^{-13}
	D_γ/Φ_{epi} [Gy/(n/cm^2)]	2.0×10^{-13}	3.2×10^{-13}
In-Phantom	RBE Equiv. tumor dose (8cm) (Gy-Eq.)	14.5	23.4
	Advantage depth (cm)	8.4	9.9
	RBE Equiv. D_f at $D_{tis.}$(Max.) (Gy-Eq.)	2.05	0.632

Table 1: Figures-of-merit for two neutron beams. The LBNL beam has a higher fast dose in-air than the BMRR beam, but a lower in-phantom fast dose contribution to $D_{tis.}$(Max.), as well as superior in-phantom qualities. Equivalent doses are calculated assuming a maximum normal tissue tolerence of 12.5 Gy-eq. and using BMRR-defined clinical RBEs and compound factors.

phantom analysis, which is often not used since it is computationally time consuming and the results of different studies may not be comparable unless each use exactly the same phantom geometry and boron-delivering drug parameters.

Table 1 shows how D_f/Φ_{epi} and D_γ/Φ_{epi} can be misleading predictors of in-phantom behavior. Two neutron sources are evaluated: the beam currently used in clinical trials at the Brookhaven Medical Research Reactor (BMRR),[2] and an accelerator-based source designed at LBNL. The LBNL design is an improvement on previous[3] designs, with modifications including a lead reflector, and a cylindrical moderator consisting of 28 cm of Fluental (69% AlF_3, 30% Al, 1% LiF) followed by 6 cm of Teflon. The neutron source for this design is the ^{7}Li(p,n) reaction, utilizing 2.4 MeV protons. The in-phantom figures-of-merit demonstrate the superiority of the more penetrating LBNL beam, but the in-air figures-of-merit predict the opposite. Examination of the depth-dose response in Figure 1 shows why this is true. While the LBNL beam has a significantly higher in-air fast dose than the BMRR beam, the neutrons that contribute to this dose have much lower energies than the neutrons in the BMRR beam. Thus, these neutrons are absorbed more quickly and actually contribute a lower dose component to the treatment-limiting maximum tissue dose than in the BMRR beam. Also, the more penetrating LBNL beam provides a deeper point of maximum tissue dose, where the fast component is a smaller fraction of the total dose. Therefore, these in-air figures-of-merit are of limited use in determining the quality of a particular neutron beam.

Pursuit of a more useful in-air figure-of-merit remains an elusive, yet highly desirable goal.

weighted tumor dose at the brain midpoint to the maximum RBE-weighted tissue dose:

$$TG_{bm} = \frac{D_{tumor}(Midpoint)}{D_{tis.}(Max.)} \tag{1}$$

$$D_{tumor/tis.} = CF_{tumor/tis.} \cdot D_B + RBE_N \cdot D_N + RBE_H \cdot D_H + RBE_\gamma \cdot D_\gamma \tag{2}$$

where D_B, D_N, D_H, and D_γ refer respectively to the physical doses due to the $^{10}B(n,\alpha)$ boron, $^{14}N(n,p)$ nitrogen, $^{1}H(n,n')$ proton-recoil, and the γ dose via the $^{1}H(n,\gamma)$ capture reaction. The physical doses were multiplied by a corresponding compound factor (CF) or relative biological effectiveness (RBE). Boron concentrations and compound factors were used as established[4] for the boron compound *p*-boronphenylalanine (BPA) along with RBEs as established in the dose calculation protocol for clinical trials at the BMRR: normal tissue ^{10}B concentration: 13 ppm; normal tissue compound factor: 1.3; tumor ^{10}B concentration: 45.5 ppm; tumor compound factor: 3.8; RBE_N: 3.2; RBE_H: 3.2; and RBE_γ: 1.0. Because TG_{bm} is a ratio, it is independent of an actual defined limit on $D_{tis.}(Max.)$.

With TG_{bm} established as an appropriate in-phantom figure-of-merit for gauging beam quality, an in-air parameter can be sought to predict this quantity as a function of the neutron spectrum.

3 NEUTRON ENERGY DOSE RESPONSE

3.1 Modeling

The first step in predicting the dose response of any neutron energy spectrum was modeling a large number (~100) of nearly monoenergetic neutron energy distributions through a head phantom using the MCNP[5] Monte Carlo code. Each simulation consisted of a monodirectional neutron beam with a narrow, uniform energy distribution, incident onto the full surface of a head phantom. A modified *Snyder*[6] head phantom was used, consisting of skin, bone, and brain in the geometry with surfaces described by the following equations:

$$(\frac{X}{6.5})^2 + (\frac{Y}{6})^2 + (\frac{Z}{9})^2 = 1 \tag{3}$$

3.2 Moderator Optimization

This new method of evaluating an in-air neutron beam spectrum was initially tested by comparing the TG_{bm} prediction against that calculated with the INEEL Monte Carlo treatment planning code, BNCT_RTPE.[9] There are many differences in these two models, including elemental composition, phantom geometry, beam size, and angular distribution. Therefore, the values of TG_{bm} calculated with each method were expected to be quite different. However, each method should produce the same results in judging different neutron spectra against each other. Figure 2 shows that for two different moderators (Al/AlF_3 and D_2O), the same thickness of moderator is predicted as optimal, independent of the model chosen. It should be noted that because the database includes data only from monodirectional neutrons, which are inherently more penetrating, it cannot be used to produce accurate absolute doses and can only be used to gauge different neutron spectra of similar J/Φ against each other. In particular, if there are additional constraints on treatment other than a maximum tissue dose (eg: surface dose or treatment time), great care must be taken to not misinterpret the results given by the database. For instance, previous LBNL optimization constraints have placed a limit of 10.0 Gy-eq on the surface dose, in addition to a maximum tissue dose constraint of 12.5 Gy-eq. In beams where BNCT_RTPE calculates a surface dose of 10.0 Gy-eq, the database response is only 8.5 Gy-eq. This seems to be a consistent underrepresentation for beams with a typical J/Φ of $\sim$0.8. This should be considered when a skin dose constraint is applied. To be fully useful in predicting dose responses, however, the database should be expanded to allow for angular dependence.

3.3 The Ideal Neutron Spectrum

Using a Monte Carlo code such as BNCT_RTPE or MCNP can take many hours or days of computer time, whereas evaluating an in-air neutron spectrum with the predetermined energy-dependant dose response database is instantaneous. Because the database allows instantaneous evaluation of a neutron energy spectrum, it becomes a powerful tool in determining the effect of changing existing neutron beams, or in quickly evaluating hypothetical neutron spectra.

This ability to instantly evaluate any input spectrum allows investigation into determining an "ideal" neutron spectrum for BNCT, which would produce the maximum value of

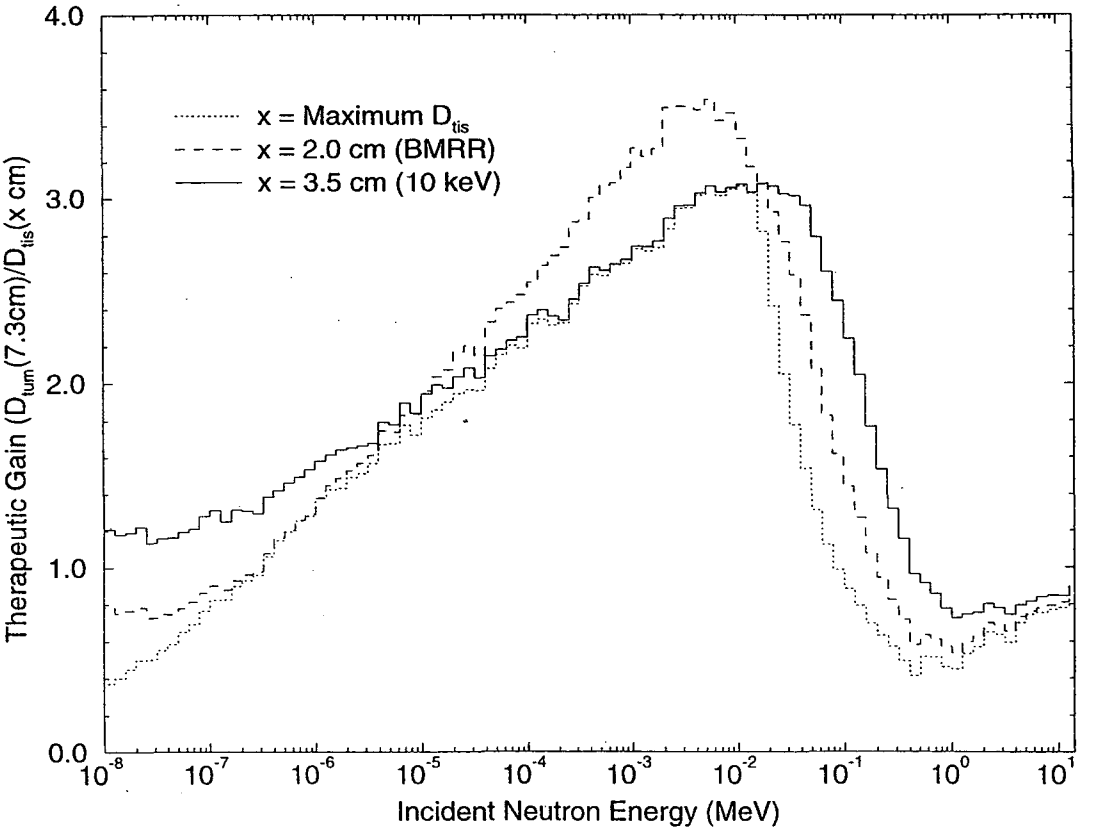

Figure 3: Therapeutic Gain at the brain midpoint as a function of neutron energy, representative of dose responses with peaks at 2.0 cm, 3.5 cm, or where produced by the nearly monoenergetic beam.

a real beam, which may be at up to 3.5 cm depth, will be vastly different. This becomes problematic in that neutrons of a particular energy will be of different worth to different beams. For instance, 40 keV neutrons might lower the TG_{bm} of a beam with a tissue dose maximum at 2.0 cm, but the same energy neutrons may raise TG_{bm} in a beam with a dose maximum at 3.5 MeV.

Therefore, TG_{bm}(2.0cm) and TG_{bm}(3.5cm) have also been plotted in Figure 3. These values are defined as in Equation 1, with the exception that D_{tis}(Max.) is assumed to be at 2.0 cm and 3.5 cm, respectively. These values were chosen as they represent two extremes in maximum dose position. The BMRR tissue dose peaks at 2.0 cm, while the maximum depth at which monodirectional beams peak are at 3.5 cm. If the LBNL spectrum were monodirectional, it would peak close to 3.5 cm. It's actual peak is at 2.9 cm, the TG_{bm} curve for which looks similar to that of a 3.5 cm peak. By plotting TG_{bm} this way, the dose

maximum in the 3.5 cm line. Because these energies individually have TG_{bm} maxima at 3.5 cm, their contribution to the dose at 2.0 cm is lower. It is nearly impossible, however, to conceive of a neutron spectrum which is composed primarily of neutrons at this energy, yet which has a maximum at 2.0 cm and this artifact cannot be exploited to produce a higher TG_{bm} than 3.

The ideal neutron spectrum for BNCT is therefore shown, as in Figure 4, to be a spread of energies between ~4 keV and ~40 keV, so long as the number of neutrons above ~20 keV is kept low enough to not adversely affect the position of D_{tis}(Max.). Also shown are the BMRR beam and the LBNL accelerator-produced Fluental/Teflon-moderated beam. The LBNL beam is quite close to the ideal spectrum, demonstrating that there are few advantages to be gained by further alteration of the energy spectrum. The dose response database predicts that the BMRR, LBNL, and ideal spectra yield, respectively, a TG_{bm} of 2.0, 2.9 and 3.0. Again, these values assume that each spectrum is made purely monodirectional and only reflect the relative differences in energy spectrum.

4 CONCLUSIONS

This study has demonstrated the strong importance of the shape of the neutron energy spectrum for usage in BNCT, which we have taken advantage of in shaping a nearly ideal spectrum. Our accelerator-based spectrum produces a monodirectional TG_{bm} that is within 5% of the maximum that can be realized, leading us to conclude that future beam shaping should focus on improving directionality and beam intensity. The dose response database has proven a valuable tool in instantaneous evaluation of an in-air spectrum to predict in-phantom parameters. However, to be fully applicable, it must be expanded to account for the angular distribution of a neutron beam. It would also benefit from expansion to allow for variable beam sizes and phantom geometries, after which it can be distributed for public use in optimizing neutron beam designs.

[9] Nigg, D. W., Wheeler, F. J., Wessol, D. E., Capala, J., Chada, M., "Computational Dosimetry adn Treatment Planning for Boron Neutron Capture Therapy," *J. Neuro-Oncol.*, **33**, 93-104 (1997).

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