INEL/CON-97-00694
CONF-971125--

Reactor beam calculations to determine optimum delivery of epithermal neutrons for treatment of brain tumors

F.J. Wheeler, D.W. Nigg, Idaho National Engineering & Environmental Laboratory, Idaho Falls, ID, USA
J. Capala, Brookhaven National Laboratory, Upton NY, USA
P. Watkins, C. Vroegindeweij, Joint Research Centre, Petten, The Netherlands
I. Auterinen, T. Seppälä, Technical Research Centre of Finland, Helsinki Finland

RECEIVED
NOV 21 1997
OSTI

INTRODUCTION

Studies were performed to assess theoretical tumor control probability (TCP) for brain-tumor treatment with boron neutron capture therapy (BNCT) using epithermal neutron sources from reactors. The existing epithermal-neutron beams at the Brookhaven Medical Research Reactor Facility (BMRR), the Petten High Flux Reactor Facility (HFR) and the Finnish Research Reactor 1 (FIR1) have been analyzed and characterized using common analytical and measurement methods allowing for this inter-comparison.

Each of these three facilities is unique and each offers an advantage in some aspect of BNCT, but none of these existing facilities excel in all neutron-beam attributes as related to BNCT. A comparison is therefore also shown for a near-optimum reactor beam which does not currently exist but which would be feasible with existing technology. This hypothetical beam is designated BNCT_1 and has a spectrum similar to the FIR-1, the mono-directionality of the HFR and the intensity of the BMRR. A beam very similar to the BNCT_1 could perhaps be achieved with modification of the BMRR, HFR, or FIR, and could certainly be realized in a new facility with today's technology.

DESCRIPTION of MODEL and METHODS

The BMRR and FIR1 reactors and beam structures were modeled using the DORT[1] discrete-ordinates code and the HFR was modeled using the MCNP[2] Monte Carlo code. MRI images of a male volunteer were used to construct a B-spline head model using the BNCT_Rtpe[3] treatment planning software. The rtt_MC Monte Carlo module of the BNCT_Rtpe system was used for dose distributions within the head where a simulated treatment volume was constructed. For calculation of TCP, the Porter[4] model was employed using empirical data from Laramore[5]. This theoretical model is not intended to represent any individual patient, or brain-tumor patients in general. It simply is a method of comparing various beam/drug combinations in a manner that provides meaningful relative results. The TCP was calculated as an integral over the treatment volume of the Porter function:

$$TCP = e^{-N_0 * FS}$$

MASTER

DISTRIBUTION OF THIS DOCUMENT IS UNLIMITED

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible electronic image products. Images are produced from the best available original document.

where FS = fractional survival of clonogens
N_o = number of clonogens prior to irradiation

and

$$FS = e^{-D/D_0}$$

where: D = absorbed biological-weighted dose to the tumor cells
D_0= inverse radiosensitivity of the tumor system

Laramore's TCP relationship is quite well matched for a "typical" brain tumor with selection of the model parameters D_0 and $N_0 = 3.2 \times 10^5$ cm^{-3}.

The drugs compared were boronated phenyalaline-fructose (BPA-F) and a hypothetical drug with assumed characteristics offering advantage compared to BPA-F.

The biological dose is defined as the weighted sum of the four principal components of the total dose. The gamma dose weighting is unity, the proton-dose (both from ^{14}N capture events and from hydrogen recoil) is multiplied by a relative biological effectiveness (RBE) of 3.2 except for the HFR where a value of 3.9 is used. The ^{10}B component is weighted by a drug-and-tissue-specific compound factor (CF). The CF used for BPA-F was 1.3 and 3.8 for healthy brain and tumor respectively. The correspondence CF for the hypothetical drug were 0.33 and 3.0. For BPA-F, the ^{10}B concentration was 14.9 parts per million (ppm) in blood and 50 ppm in tumor. For the hypothetical drug, ^{10}B concentration was assumed to be 15 ppm in blood and 67 ppm in tumor. The biological half life of ^{10}B in tumor was set at 6 hours for BPA-F. The 10B concentration was assumed constant for the fictitious drug.

SELECTED RESULTS

The BMRR facility has the greater source intensity which is an advantage in that the effect of biological decay of ^{10}B in tumor tissue is less. The HFR epithermal-neutron beam is remarkable in that the neutron current-to-flux ratio is near unity; a very forward-directed beam. This mono-directionality is a favorable attribute of the neutron beam because it results in better penetration and is quite efficient for generation of thermal-neutron flux at depth. The FIR1 beam has an advantage because the contaminating gamma and fast-neutron dose components are very low and this allows for more thermal fluence to tumor cells before healthy-tissue tolerance is reached. The hypothetical beam was assumed to have the favorable spectrum of the FIR1 beam, the mono-directionality of the HFR beam and an intensity at least as great as the BMRR beam.

There were two tumor models. A shallow tumor was simulated by constructing a treatment volume with maximum depth from skin of 6 cm. A second, deeper tumor was simulated assuming an 8-cm depth. Results for TCP can only be interpreted in a relative sense since, in practice, it is not possible to obtain the data required for a calculation of TCP for an individual patient. Figures 1a and 1b show a comparison of model results for TCP for the three reactor beams and for the hypothetical reactor beam with BPA-F for the two tumor models. These results are for single-field irradiations to show the comparison between beams. In practice, for deeper tumors, two

fields are applied for better target coverage. The comparison using the hypothetical improved drug is shown in Figure 1c. In Figure 1c, the calculated results are shown for the BMRR and BNCT_1 both for BPA-F and for the hypothetical drug.

The comparison shows that as expected, theoretical tumor response is quite sensitive to beam attribute, and, even though better neutron sources are coming on line, a large gain is yet to be realized by further improvements in beam quality. There is a significant effort to develop new drugs with better distribution and concentration characteristics and that will also result in large gains, but it is very important to realize that any improvement in drug is significantly enhanced when the highest possible quality neutron beam is also utilized.

REFERENCES

1. Rhoades, R. Childs, "Updated Version of the DOT4 One and Two Dimensional Neutron/Photon Transport Code. Oak Ridge National Lab., ORNL-5851 (1982).

2. Briesmeister, ed. "MCNP-A General Monte Carlo Code for Neutron and Photon Transport", Los Alamos National Lab. LA-7396-M, Rev 2 (1986)

3. Wheeler, D.E. Wessol, R. Babcock, D.W. Nigg, C.A. Atkinson, and J. Evans, "Improvements in Patient Treatment Planning Systems", Cancer Neutron Capture Therapy, edited by Mishima; Plenum Press, New York, 1996

4. Porter, "The Statistics of Dose/Cure Relationships for Irradiated Tumors", Brit. Jour. Radiology, 53, 210-227, 1980

5. Laramore, F.J. Wheeler, D.E. Wessol, K.J. Stelzer and T.W. Griffin, "A BNCT Tumor Control Curve for Malignant Glioma from Fast Neutron Radiotherapy data: Implications for Beam Delivery and Compound Selection." Seventh International Symposium on Neutron Capture for Cancer, held in Zurich Switzerland, Sept. 1996, in publication.

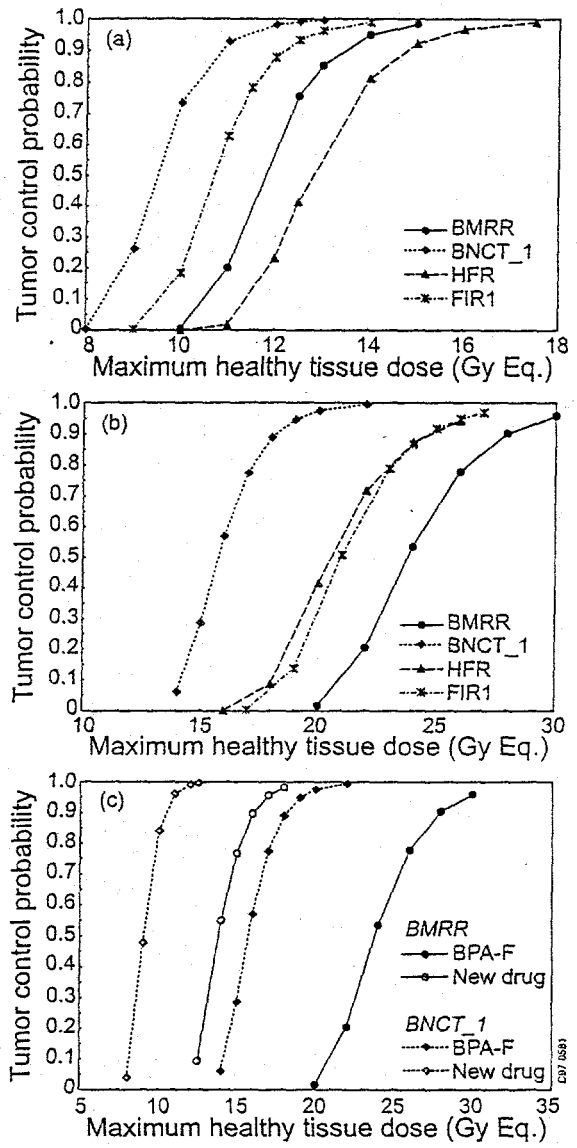

Figure 1. Calculated theoretical TCP using the Porter model with Laramore parameters: (a) values for three existing facilities and the hypothetical BNCT_1 facility for 6-cm tumor depth; (b) values for three existing facilities and for BNCT_1 for 8-cm tumor depth; (c) values for BMRR and BNCT_1 for a drug now in use (BPA-F) and for a hypothetical new drug for 8-cm-deep tumor.