FINAL TECHNICAL REPORT
MICRODOSIMETRY FOR BORON NEUTRON CAPTURE THERAPY
DE - FG02 - 96ER62217

The specific aims of the research proposal were as follows:

- (1) To design and construct small volume tissue equivalent proportional counters for the dosimetry and microdosimetry of high intensity thermal and epithermal neutron beams used in BNCT, and of modified fast neutron beams designed for boron neutron capture enhanced fast neutron therapy (BNCEFNT).
- (2) To develop analytical methods for estimating the biological effectiveness of the absorbed dose in BNCT and BNCEFNT based on the measured microdosimetric spectra.
- (3) To develop an analytical framework for comparing the biological effectiveness of different epithermal neutron beams used in BNCT and BNCEFNT, based on correlated sets of measured microdosimetric spectra and radiobiological data.

Specific aims (1) and (2) were achieved in their entirety and are comprehensively documented in Jay Burmeister's Ph.D. dissertation entitled "Specification of physical and biologically effective absorbed dose in radiation therapies utilizing the boron neutron capture reaction" (Wayne State University, 1999). A copy of this thesis has been filed with the DOE form F241.1 accompanying this report.

Specific aim (3) proved difficult to accomplish because of a lack of sufficient radiobiological data.

Techniques for constructing miniature small volume tissue equivalent proportional counters (TEPCs) were developed. A particularly difficult operation in the construction of these chambers is the positioning of a 10 micrometers diameter central electrode wire through the center of the outer cylindrical electrode with the appropriate field tubes. This was achieved using a micromanipulator while performing the operation under a low power microscope. A total of seven miniature proportional counters were constructed, all were of a cylindrical design and included:

- 1) A 2.5mm diameter x 2.5mm long prototype counter constructed from A150 tissue equivalent plastic (TEP)
- 2) A 2.5mm diameter x 2.5mm long counter constructed from A150 TEP
- 3) A 2.5mm diameter x 2.5mm long counter constructed from A150 TEP loaded with 200 ppm of ^{10}B .
- 4) A 1.5mm diameter x 1.5mm long counter constructed from A150 TEP
- 5) A 1.5mm diameter x 1.5mm long counter constructed from A150 TEP loaded with 200ppm of ^{10}B .
- 6) A 2.5mm diameter x 2.5mm long counter constructed from A181 brain equivalent plastic (BEP).

DOE Patent Clearance Granted

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Date

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- 7) A 2.5mm diameter x 2.5mm long counter constructed from A150 TEP loaded with 640ppm of ^{157}Gd .

All counters were thoroughly characterized with respect to their performance characteristics. Full details of the design, construction calibration and characterization of the proportional counters can be found in chapters 2 through 5 of Burmeister's Ph.D. thesis.

Counters (2) and (3) were used in dosimetric studies of the Brookhaven Laboratory Medical Research Reactor's (BMRR) clinical BNCT beam and the Massachusetts Institute of Technology's Reactor (MITR-II) produced clinical BNCT beam. Using paired A150 and A150 - ^{10}B proportional counters it is possible to determine, the fast neutron absorbed dose, the gamma ray absorbed dose and the boron neutron capture absorbed dose components in the BNCT beams. Measurements were made as a function of depth in a standardized "head" phantom, which was used at each facility. These microdosimetry measurements were also used as a predictor of the neutron RBE as a function of position in the phantom for the BMRR and the MITR-II BNCT beams. No statistically significant differences are observed in the neutron RBE between the BMRR and MITR-II beams.

At Brookhaven National Laboratory (BNL) the BNC dosimetry results from the TEPCs showed poor agreement with both the Monte Carlo treatment planning system (MCTPS) and the foil activation results used by the BNL staff to determine BNC dose. The discrepancy is most pronounced near the surface of the phantom, where the TEPC results are roughly 30% lower than the MCTPS results. At a depth of 10 cm the results differ by less than 8%, which is within the stated uncertainties. The same trend is observed in the off axis results. The thermal neutron fluence in the epithermal beam is significantly higher than that in the ^{252}Cf field used for calibration. However, if there were a dose rate effect on the BNC dose, one would expect to see the same effect on the photon dose measured by the boron-loaded TEPC as well as on the BNC dose. Photon doses extracted from the boron loaded TEPC agree very well with those from the normal (unloaded) TEPC.

Similarly, at Massachusetts Institute of Technology (MIT) the BNC absorbed doses measured with the miniature TEPCs are roughly 20% lower than results from foil activation analysis made by the MIT staff. This discrepancy is in the same direction and almost the same magnitude as the discrepancy seen in the BNL measurements, indicating a systematic error in one or both measurement techniques. Again, the photon absorbed doses measured with the boron-loaded TEPC showed good agreement with those from the normal (unloaded) TEPC and the ionization chamber measurements. This would appear to rule out a BNC dose rate effect or any anomalous effect on the counter performance in general in the epithermal beam.

The dual counter TEPC method used in the work presented here offers the advantage of directly measuring the BNC dose by providing a single event spectrum of the secondary charged particles resulting from boron neutron capture reactions in a simulated microscopic volume. The pulse height spectrum of energy depositions due to individual charged particles traversing the collecting volume of the proportional counter is calibrated based on the physical features of the spectrum and a knowledge of charged particle energy loss in the

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detector volume. Therefore, the secondary charged particle energy distribution from the BNC reaction in tissue equivalent plastic may be measured, in contrast to the alternative technique of measuring the thermal neutron flux by foil activation and inferring the corresponding BNC dose. Dual proportional counter microdosimetry offers significantly more information than a thermal flux measurement or an absorbed dose measurement using an ionization chamber, which is based on integrated charge. The discrepancies between the foil activation measurements and the TEPC measurements raise interesting possibilities for future studies. In principle the direct measurement nature of the dual TEPC method should make it a more reliable BNC dosimetry technique than foil activation.

Measurements were also made in the BMRR and the MITR-II beams using the brain equivalent plastic proportional counter and compared with measurements made with a tissue equivalent plastic counter of identical construction. Although there are relatively small differences in the nitrogen content of muscle tissue and brain tissue in humans, differences in dosimetry in thermal neutron beams can be considerable due to thermal neutron capture by ^{14}N which yields a 580 keV proton. These differences have been observed in microdosimetric measurements made in the BMRR beam. This is an example of a dosimetry problem that cannot be adequately addressed using conventional dosimetry techniques.

The microdosimetric measurements made at the BMRR and MITR-II have shown that microdosimetry using miniature TEPCs is an excellent tool for BNCT dosimetry. Its advantages over conventional dosimetry methods are well demonstrated in this work. This single dosimetry method allows the examination of the entire single-event charged particle spectrum with a relatively simple analysis allowing separation of the different radiation dose components. In addition to accurate evaluation of absorbed dose components, paired TEPC (A150 and A150- ^{10}B counters) microdosimetry furnishes a wealth of information about radiation quality. This information is useful in assessing the relative characteristics of epithermal beams as well as in estimating the biological effectiveness of absorbed dose in BNCT. Justification for TEPC dosimetry in the high intensity beams used for patient treatment as well as the benefits of conducting dosimetry with brain tissue-equivalent plastic have been established. These techniques may be subsequently applied to other operational BNCT facilities as well as to new facilities proposed for BNCT. In this manner, a standard set of data would be available for comparison of the characteristics of different BNCT beams. Radiobiological data collected in the same experimental conditions would allow this data set to be used to develop radiobiological models permitting the prediction of cell survival based on the attributes of the microdosimetric spectra.

Full details of the measurements made at the BMRR and the MITR-II facilities may be found in Chapter 6 of Burmeister's Ph.D. thesis.

During the course of this project a pair of geometrically identical magnesium and magnesium- ^{10}B foil lined ionization chambers was designed and constructed. A series of measurements made with these two chambers plus a similar A150 TEP ionization chamber allows the neutron absorbed dose, gamma ray absorbed dose and boron neutron capture absorbed dose components to be determined. The use of these chambers was demonstrated in the BNCEFNT beam (a modified fast neutron beam) produced by the 48.5 MeV

superconducting cyclotron at Harper Hospital. A full description of this work is contained in Chapter 8 of Burmeister's Ph.D. thesis. These chambers are more convenient to use than proportional counters. Relatively large amounts of data can be collected in a relatively short time by making lateral and depth-dose beam scans in a water phantom. These chambers are presently on loan to the MITR-II BNCT group and they are using them to make a dosimetric study of their new fission convertor beam, which is being developed for BNCT.

In the original grant proposal proportional counter dosimetry studies were proposed at other BNCT and BNCEFNT sites, namely the University of Washington in Seattle, the University of Birmingham BNCT facility in England and the Petten BNCT facility in the Netherlands. However, travel funding was cut from the grant budget on the assumption that the Radiation Oncology Department at Wayne State University (WSU) would be able to cover these expenses. While WSU was able to cover travel expenses for the BNL and MIT visits, fiscal constraints in the School of Medicine at WSU in the later stages of the project did not allow for funding of these other field trips. Towards the end of the project (September 1999) it was proposed that remaining funds be redirected for this purpose, but loss of project personnel (Jay Burmeister completed his Ph.D. in July 1999 and Dr. Chandra Kota was reassigned to clinical duties at the end of January 2000) lead to effective termination of this project January 31, 2000, which prevented these field trips from being completed. Dr Maughan left Wayne State University on July 9, 2000 to take up a new position as Professor, Vice Chairman and Director of Medical Physics in the Radiation Oncology Department at the University of Pennsylvania.

Published Papers and Abstracts Relevant to this Grant

Published Papers

Kota, C. and Maughan, R.L. Microdosimetric analysis of the absorbed dose in boron neutron capture therapy. Radiation Protection Dosim., 70: 555-558; 1997.

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Burmeister, J.B., Kota, C., Yudelev, M. and Maughan, R.L. Paired Mg and Mg(B) ionization chambers for the measurement of boron neutron capture dose in neutron beams. Medical Physics, 26; 2482-2487, 1999.

Kota, C., Maughan, R.L., Burmeister, J. and Forman J.D. A modified fast neutron beam for boron neutron capture enhanced fast neutron therapy. In Advances in Neutron Capture Therapy Volume I, Medicine and Physics, Proceedings of the Seventh International Symposium on Neutron Capture Therapy for Cancer, Zurich, Switzerland, September 4 - 7. Eds. B. Larsson, J. Crawford and R. Weinreich (Elsevier, Amsterdam, 1997) pp. 496-500.

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Burmeister, J., Kota, C. and Maughan, R.L. Microdosimetric studies at several BNCT facilities using miniature tissue equivalent proportional counters. Submitted to "Frontiers in Neutron Capture Therapy" the proceedings of the Eighth International Symposium on Neutron Capture Therapy for Cancer, Eds. Hawthorne, M.F. and Wiersema, R.J. (Plenum Publishing, New York). In press.

Maughan, R.L., Kota, C., Burmeister, J., Levin, K.J., Chuba, P.J., Gaspar, L.E. and Forman, J.D. Progress towards boron neutron capture enhancement of fast neutron therapy at the Harper Hospital neutron therapy facility. Submitted to "Frontiers in Neutron Capture Therapy" the proceedings of the Eighth International Symposium on Neutron Capture Therapy for Cancer, Eds. Hawthorne, M.F. and Wiersema, R.J. (Plenum Publishing, New York). In press.

Burmeister, J., Kota, C., Maughan, R.L. and Yudelev, M. Characterization of modified fast neutron beam for boron neutron capture enhancement of fast neutron therapy. Submitted to "Frontiers in Neutron Capture Therapy" the proceedings of the Eighth International Symposium on Neutron Capture Therapy for Cancer, Eds. Hawthorne, M.F. and Wiersema, R.J. (Plenum Publishing, New York). In press.

Papers in Preparation

Burmeister, J., Kota, C. and Maughan R.L. Miniature tissue equivalent proportional counters for BNCT and BNCEFNT dosimetry. In preparation for submission to Medical Physics

Burmeister, J., Kota, C. and Maughan R.L. Gas gain and site size characterization of miniature cylindrical TEPCs. In preparation for submission to Medical Physics

Burmeister, J., Kota, C. and Maughan R.L. Characterization of Cf-252 radiation spectrum and possibility of BNC enhancement. In preparation for submission to Medical Physics

Burmeister, J., Kota, C. and Maughan R.L. Intercomparison of MITR-II and BMRR BNCT beams. In preparation for submission to Medical Physics

Burmeister, J., Kota, C. and Maughan R.L. Possibilities for BNCEFNT in moderated fast neutron beam. In preparation for submission to Medical Physics

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Burmeister, J., Maughan, R.L. and Kota, C. Miniature low pressure tissue equivalent proportional counters for microdosimetry studies in high flux BNCT and BNCEFNT beams. Medical Physics 24: 1363: 1997.

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