

*Radiation Dosimetry in the BNCT Patient Treatment
Room at the BMRR*

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INTRODUCTION

The Medical Research Reactor at the Brookhaven National Laboratory (BMRR) was a heterogeneous, tank type, light water cooled and moderated, graphite reflected reactor, which was operated on demand at a power level up to 3 mega-watts (MW) for medical and biological research [1]. The reactor first went critical on March 15, 1959, with 17 fresh fuel elements (2.52 kg uranium-235 in a total of 2.7 kg uranium) in the center core. The BMRR had two treatment rooms on opposite sides of the core. It had a predominately thermal neutron beam in the Thermal Neutron Irradiation Facility (TNIF) on the west side of the core. By early 1990, a redesigned beam line had a predominately epithermal neutron beam in the Epithermal Neutron Irradiation Facility (ENIF) on the east side of the core [2].

The ENIF was approximately 11 feet by 21 feet in size with its focal point consisting of a bismuth plate mounted in the wall adjacent to the reactor shield about 36 inches above the floor. The beam originated at a shutter constructed of 0.75 inch steel filled with concrete and weighing ~21 tons. Access to the ENIF was through a pair of hand operated steel shielding doors, each 42 inches wide, 84 inches high and 5 inches thick. The inner door had a 4-inch thick layer of paraffin on the side facing the reactor. The doors 5000 pounds weighed each. Additional shielding material had been added to the entire beam port at reactor wall within the ENIF. The shielding material consisted of 2-inch thick polyethylene sheets, which were impregnated with 95%-enriched ⁶Li in lithium carbonate (Li₂CO₃). The shielding sheets around the port face were designed to allow the insertion of a variety of different beam collimators.

The ENIF served as the Patient Treatment Room, where the epithermal neutron beam was primarily used to perform clinical trials on patients with malignant brain tumors (glioblastoma multiforme). Boron Neutron Capture Therapy (BNCT) was the treatment used in the clinical trials. In 1936, Locher proposed that medical research could be advanced, by destroying cancerous cells using neutrons [3]. He suggested the injection of a soluble, non-toxic compound of boron into superficial cancer, followed by bombardment with slow neutrons, in order to liberate the ionization energy. The minor isotope of boron, ¹⁰B, has an abundance of 19.8%. The ¹⁰B(n, α)⁷Li reaction, as shown in Figure 1, has a thermal neutron cross section of 3.838 x 10⁻²¹ cm². The released ⁴He, which has an energy of 1.47 MeV,

over a range of 10.1 μm (in water) and an average linear energy transfer, LET, of 150 keV/ μm . The residual nucleus, ${}^7\text{Li}$, has an energy of 0.85 MeV with a range of 4.9 μm and an average LET of 170 keV/ μm . Due to the short range of both of these tracks, almost all of the energy is deposited within a cell diameter of where the reaction takes place. If the boron can be selectively targeted in a cancerous cell, only the cancerous cell would be destroyed, while the nearby healthy cells would be relatively unaffected.

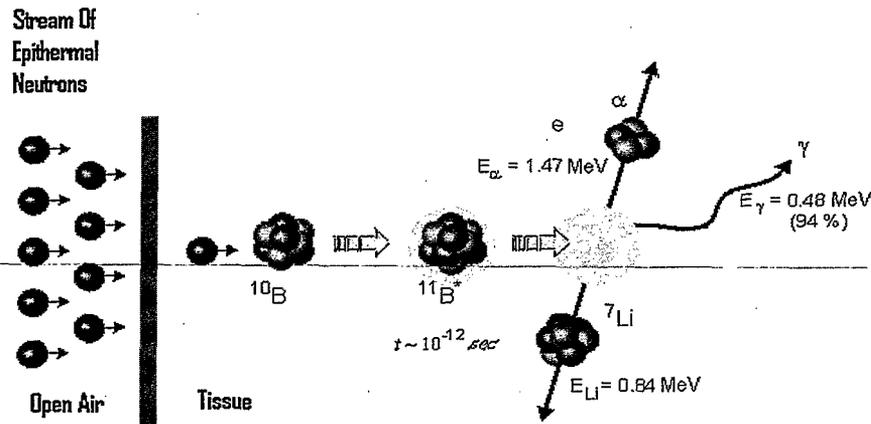


Figure 1. The BNCT mechanism and energy release from reaction of ${}^{10}\text{B}(n,\alpha){}^7\text{Li}$ in tissue.

In BNCT, the patient is initially injected with a boron compound (the last compound of boron that was used was boronophenylalanine-fructose, BPA-F [4]). After the level of the boron in the blood was sampled and determined by prompt photon analysis, the patient was subsequently irradiated with epithermal neutrons. In the earliest measurements performed at the BNL Graphite Research Reactor (BGRR) in the 1950s, thermal neutrons were used. When the initial treatments were performed at the BMRR, thermal neutrons were still being used. The treatments were not successful for a few reasons. The boron compound originally used was not preferentially absorbed in the cancerous cells and the tumors were deep seated (anywhere from 1 inch to 3 inches beneath the scalp surface with an average depth of ~ 2.375 inches) and the thermal neutrons were found to be absorbed in the hydrogenous material of the head, before they could reach these tumor cells.

With the development of the new epithermal neutron beam and a new boron compound, BPA-F, BNCT clinical trials were again begun at the BMRR on September 13, 1994 [5]. From that time, until the trials were suspended after May 20, 1999, a total of fifty-four patients had undergone such clinical BNCT trials at the BMRR. These patients were treated under a series of protocols in which the reactor power was first limited to 2 MW and later raised to 3 MW and the patients were initially irradiated in one session and later they were irradiated in a series of sessions to adjust the irradiation time to the level of boron compound in the blood, (boron was re-measured between sessions). The injected boron compound, BPA-F, was found to be preferentially absorbed in the tumor cells rather than

normal cells with the ratio of up to 4 to 1. To be conservative, this ratio was assumed to be ~3.5 to 1. However, the BMRR had its operations permanently suspended, by the US Department of Energy (USDOE). The final shutdown of the BMRR occurred at 12:19 PM on December 28, 2000. The reactor fuel has since been removed and shipped off-site.

MEASUREMENT PROGRAM

The original critical BMRR core contained 17 fuel elements 93%-enriched in ^{235}U , while the core during the last of the BNCT trials had 32 enriched fuel elements. To control the total amount of neutron and gamma-ray dose that a patient would receive during the clinical trials, a series of measurements were performed both before, during and after the treatment irradiations. Bare gold foils, cadmium covered gold foils and various threshold detector foils were used to determine the neutron flux values. Thermo-luminescent dosimeters (TLD) badges with ^6LiF and ^7LiF chips were used to provide experimental data on the neutron dose rates and gamma-ray dose rates. TLD test badges used $^{6,7}\text{LiF:Mg, Ti}$ as the thermo-luminescent material in the form of solid chips. Three of the chips used were TLD-700 material (chips enriched in ^7Li to 99.93%), while one chip was TLD-600 material (chips enriched in ^6Li to 95.6%). These badges also have filters of plastic, copper and thin aluminized Mylar film of various thicknesses to separate and measure mixed fields of neutrons, electrons and gamma-rays.

THE MONTE CARLO PROGRAM

To calculate the flux of thermal and epithermal neutron beam through simulation of the BMRR core, the shutter assembly and the beam irradiation port, a computational technique and an experimental method to validate these computations were required. We used the Monte Carlo based code, MCNP-4B2 [6], to calculate the neutron and gamma-ray fluxes and absorbed doses, while measurements of the fluxes and doses at the core-shutter interface and at the irradiation port were made using gold foils and TLDs. The MCNP code is a general-purpose Fortran-compiled software package, which can be utilized to model any single particle motion or coupled neutron-photon-electron transport in a three-dimensional geometry consisting of different material regions. We used continuous cross sections for neutron and photon transport and reaction rate calculations and appropriate thermal neutron scattering function, $S_{\alpha\beta}$, to treat neutron interactions with light materials such as H_2O , D_2O , graphite and polyethylene in the MCNP package. To expedite particle tracking, a newer version of the program (MCNP-4C) was used allowing the data processing to be performed on a parallel computing platform. The continuous-run option increased the particle history and reduced the tally's statistical uncertainty.

The measured neutrons varied from thermal neutron energies (0.001 to 0.4 eV) up to fast neutron energies (0.1 to 10.0 MeV). The MCNP program was used to mock up the geometry of the reactor core down to the polyethylene and lithium carbonate collimator on the port face and the patient treatment room, as shown in Figure 2. For efficiency, the heterogeneous reactor core with fuel elements, control rods, water coolant, graphite

moderator, and aluminum fillers was replaced by a homogeneous cylinder with U, H, O, Al, C and B in appropriate nuclide composition. Randomly distributed sources in this region increased particle emission and reaction rate in the entire MCNP geometry thus expediting statistical sampling for tallies. Core peripheral fillers and their surrounding coolant were simulated by an Al-H₂O filled cylindrical shell, which was enclosed within an aluminum pressure vessel wall. To properly simulate the homogenized critical core under different operational conditions, the weight percentage of the nuclides in the model input had to be adjusted according to the recorded fuel inventory and critical rod bank position.

For the shutter-closed case, the BMRR basic design feature of $K_{eff} = 1$ maintained in the graphite reflected critical assembly alone (1.7 m cube) was utilized for the source term check-up. Criticality calculations using the shutter-opened configuration were also performed in order to compare the computed thermal neutron flux with the measured flux at the core-shutter interfacial air gap. In this location, a significant portion of the neutron flux has already been thermalized, so that the downstream neutron beam has a low intensity of epithermal neutrons.

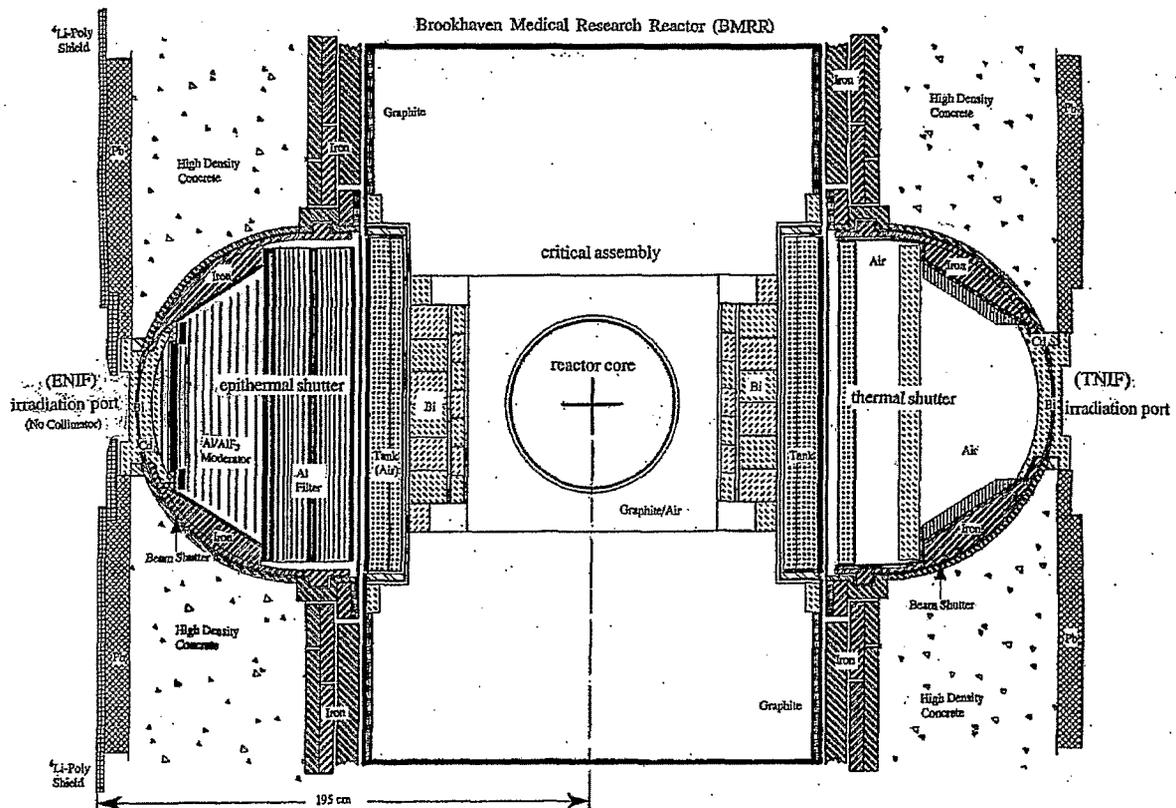


Figure 2. Simulation of ENIF and THIF by the MCNP code shows the symmetry of circular shutter and concrete shield to the critical assembly at reactor center, where homogenized core, moderator, and reflector areas are setup in model.

THE PATIENT TREATMENT ROOM

In the ENIF, the neutron beam was located three feet above the floor in the center of the reactor wall. Radiation shielding in the beam port ended with a bismuth shield. For the BNCT treatment, experimental comparisons were made with the patient in place, with a tissue equivalent head phantom in place to mock up the patient's head position and with the room empty to study the impact of the patient on the background flux and dose rate values. At four inches downstream of the bismuth shutter apex along the beam path, a removable six-inch thick collimator of polyethylene and Li_2CO_3 (95% ^6Li -enriched) is located. The collimator had a concave cavity with an 8-inch diameter on the reactor side tapering to a 4.75-inch diameter on the treatment room side, for optimal beam focusing. When collimator is in place, the axial distribution of the thermal and epithermal neutron fluxes can be shown by the two curves in Figure 3. Note that although the epithermal neutron flux decreases relatively faster than the thermal neutron flux, its absolute value is 27 times larger.

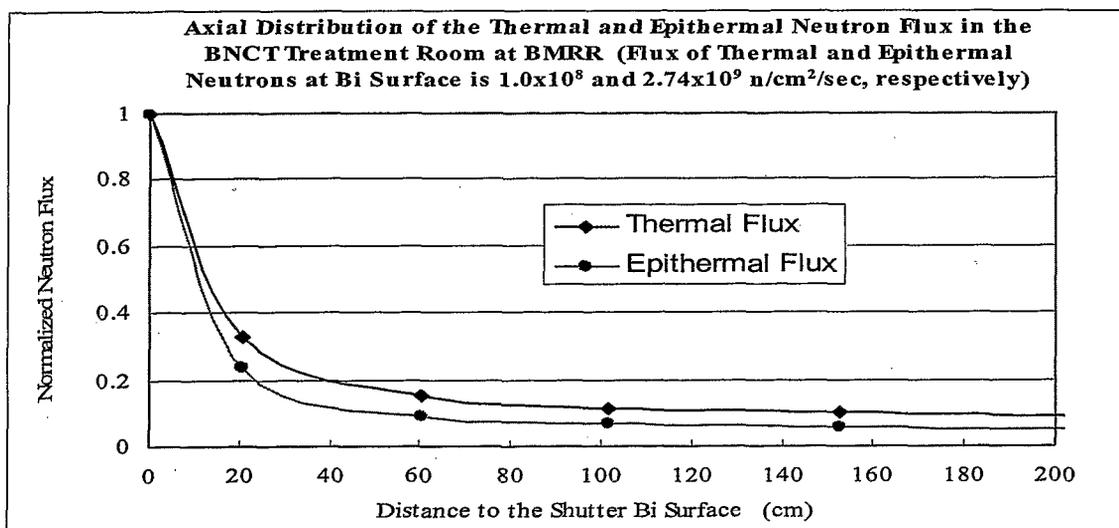


Figure 3. Axial distribution of the thermal and epithermal neutron flux along the beam path starting from the shutter Bi-surface and passing through the Li_2CO_3 -based collimator in the BNCT patient treatment room at ENIF of the BMRR.

NEUTRON AND GAMMA-RAY DOSIMETRY

Before the BNCT clinical trials began in 1994, there was a concern about the response to a patient emergency and the gamma-ray dose rate that would be received by personnel in responding. To obtain an estimate of the gamma-ray dose rate, an ion chamber (Eberline RO2) measured the dose rate at both the port face and at one foot from the port face (the approximate position of a patient). Under the scenario that the reactor went critical and reached a power level of 10 kW, the measured gamma-ray dose rates were 400 $\mu\text{Gy/h}$ (40 milli-Rem/h, mR/h) and 180-200 $\mu\text{Gy/h}$ (18-20 mR/h), respectively. When the reactor power was raised to 3 MW and operated for 20 minutes and the power was dropped to 10

kW, these two dose rates were measured to be 1 mGy/h and 0.4 mGy/h, respectively. After the above operations, and a subsequent 20-minute reactor shutdown, the gamma-ray dose rates remained at the same levels of 1 mGy/h and 0.4 mGy/h.

Another early concern was raised about whether radiation workers would be subject to a significant gamma-ray dose rate from the normal work (non-emergency) with patients who were being irradiated. Gamma-ray dose rates, received by the key staff personnel involved in the care during the treatment, was measured. These workers prepared the room and the patient, operated the shutter, located the patient in the proper position in the room and moved the patient in and out of the room during the treatment. The reactor power level was ~10 kW, whenever these workers were in the treatment room. This included the responsible physician, the radiation oncologist, the nurse, the medical physicist and the health physicist. Results of the measurements, that were taken during the treatment of the first 12 patients undergoing BNCT in the trials, gave average gamma-ray doses received by these staff members that varied from 14 μ Gy or (1.4 mR) to 32 μ Gy (3.2 mR) per individual. The highest gamma-ray dose reading recorded during treatment of any individual patient was 70 μ Gy (7 mR), which was received (for separate patients) by the radiation oncologist and the medical physicist.

The neutron flux was measured and calculated at the 4.75-inch opening of the epithermal beam port collimator. The thermal neutron flux was $\sim 3 \times 10^7$ n/cm²/sec, the epithermal neutron flux was $\sim 6 \times 10^8$ n/cm²/sec and the fast neutron flux was $\sim 2 \times 10^7$ n/cm²/sec. There was reasonable agreement between the MCNP calculations and the various bare gold foil, cadmium covered gold foil and threshold foil measurements used to determine the neutron flux values.

In October 1995, a measurement of the neutron dose rate, at a power level of 3 MW and at a distance of one foot from the collimator, was performed in the ENIF using an Eberline ASP1 "rem-ball" (a neutron sensitive instrument). The resulting dose rate was 1.0 Sv/h (100 R/h). At the same power level, a measurement of the gamma-ray dose rate at one foot from the collimator was 1.0 Gy/h (100 R/h), using an NRC ADM multi-purpose gamma sensitive instrument. In November 1997, neutron and gamma-ray dose rates were measured at the collimator face using monitoring badges with ⁶LiF and ⁷LiF chips. The results were 2.66 Sv/h (266 R/h) and 1.38 Gy/h (138 R/h). Both of these measurements at the collimator face should be larger than those made at 30 cm away due to the geometric factor, which may have a 1/r or 1/r² dependence. This is indeed the case.

A series of experiments [7] on neutron and gamma-ray dose rates were performed in the ENIF between October 1997 and January 1998. The results measured at 3 MW operating power using the TLD personnel monitoring badges with ⁶LiF and ⁷LiF chips are given in Table 1. It can be noted from Table 1 that the neutron and gamma-ray dose rates fall off rapidly as one moves out from the center of the beam. For the empty room, there is a reduction in the neutron dose rate at the reactor face by a factor of 5 to 10 in all directions (3 o'clock, 6 o'clock, 9 o'clock and 12 o'clock) at a distance of two feet from the beam center, compared to the collimator center results. There is a similar reduction of 10 to 30 in

the gamma-ray dose rates. For the area above the collimator, there appears to be much less gamma-ray shielding, resulting in a much larger gamma-ray dose rate under all conditions.

Table 1. Epithermal room neutron and gamma-ray dose rates measured by TLD at 3 MW

Location in Room	Empty Room	Empty Room	Phantom in Place	Phantom in Place	Patient in Place	Patient in Place
	N (Sv/h)	γ (Gy/h)	N (Sv/h)	γ (Gy/h)	N (Sv/h)	γ (Gy/h)
Door	0.21	0.015	0.13	0.008	0.14	0.013
North Window	0.32	0.032	0.19	0.025	0.18	0.037
South Window	0.20	0.017	0.11	0.009	-----	-----
3-ft high (Opp. Wall)	0.45	0.055	0.13	0.032	0.13	0.047
8-ft high (Opp. Wall)	0.41	0.041	0.15	0.032	0.15	0.040
2-ft right (3 O'clock)	0.35	0.048	0.29	0.048	0.52	0.068
2-ft down (6 O'clock)	0.45	0.045	0.28	0.030	0.65	0.085
2-ft left (9 O'clock)	0.32	0.064	0.24	0.051	0.27	0.094
2-ft up (12 O'clock)	0.26	0.150	0.23	0.230	0.30	0.240
4-ft right (3 O'clock)	0.29	0.025	-----	-----	0.14	0.078
Collimator Center	2.66	1.380	-----	-----	-----	-----

----- indicates no measurement was taken at this location

By comparing the data with the patient in place to the data for the empty room, there is obviously neutron scattering back from the patient to the face of the reactor. However, the scattering of the gamma radiation back to the reactor face is larger. Although there is a significant reduction in the neutron dose rate at the 3 foot beam center position on the wall opposite the patient, there appears to be much more absorption of neutrons than gamma radiation by the patient, which is the preferred situation. It might be noted that the head phantom absorbs more gamma radiation than does the patient. More of the average physical dose to the patient's brain (~1.6 times) came from the gamma-ray radiation rather than from the boron-10 neutron capture reaction [8], since much of the neutron radiation was absorbed in penetrating the scalp to reach the tumor.

CONCLUSIONS

The above data indicate a well-characterized neutron beam in the BMRR facilities, where the desired epithermal neutron flux predominates over both fast and thermal neutron fluxes in the ENIF. The residual gamma dose-rate is insignificant at the BNCT treatment room, in which the gamma dose is about one tenth of the neutron dose to the patient at beam port location. Through the use of TLDs, it is also confirmed that gamma dose to the attending personnel is minimal, at a level close to the background radiation. The dose-rate which drops rapidly during post shutdown indicates that emergent access of the facility with no specific body protection would not result in any radiation hazard to response personnel. Good agreement is obtained from various measurement techniques such as TLD and gold-

foil irradiation, and collected data from measurements agree with the theoretical results from MCNP calculations. When a patient is located in front of the beam port during shutter opening, the scattering of gamma rays back to the reactor face has been found to be larger than that of neutrons; however, since the dose decreases with $1/r^2$, the effect from beam scattering is very limited. Based on consistent results from particle transport in the ENIF, it is concluded that during the process of BNCT the dose that deposits at the tumor cell (^{10}B tagged) is much larger than that accumulated from the whole body of the patient, which is, in turn, much larger than that absorbed by the attending personnel to the treatment room.

Clinical BNCT trials of patients with malignant brain tumor were carried out at the BMRR for half a decade (1994-1999), with encouraging results obtained on 54 patients infused with the then recently developed BPA-F compound, followed by irradiation of the high-intensity epithermal neutron beam. The patients selected for these clinical trials had pre-trial survival rates estimated at from 3 to 9 months. The mean post-treatment survival time for all 54 glioblastoma multiforme patients, who were treated under these BNCT protocols, was ~22 months. The survival rate for two of these patients (3.7%) was greater than 5-years. Another patient (1.9%) still survives today (May 2005). The combined 5.6% survival rate of greater than 5-years, and the mean survival time post-BNCT of ~22 months indicates that BNCT, coupled with the use of the BPA-F compound and an epithermal neutron beam, is a promising treatment for the glioblastoma multiforme.

The conclusions from the measurements and the impact on the patient treatment indicated that although the beam at BMRR was well collimated and concentrated for the patient treatment, there was still a need to improve the beam to maximize the epithermal neutron beam compared to the gamma radiation and the fast neutron components of the beam. Work had already begun on the improvement of the epithermal beam with the design of a new beam using a fission converter plate in the shutter [9] at the time that the BMRR was permanently shut down.

The recommendations from the BMRR BNCT clinical trials [8] called for an increase in the boron compound dose and in its time of delivery. These recommendations have since been followed up by the Studsvik's group [10]; a total of 900 mg of BPA-F per kg of body weight compared to a maximum of 330 mg of BPA-F per kg of body weight at BMRR and 6 hours of BPA-F infusion compared to 2 hours of BPA-F infusion at BMRR. Efforts worldwide on finding a successor boron compound to BPA-F, which would have an improved tumor cell to normal cell absorption ratio in the body, is still continuing.

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