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TECHNICAL ASPECTS OF BORON NEUTRON CAPTURE THERAPY AT THE BNL MEDICAL RESEARCH REACTOR*

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Reactor Description

The Brookhaven Medical Research Reactor, BMRR, is a three megawatt, (3 MW) heterogeneous, tank-type, light water cooled and moderated, graphite reflected reactor, which was designed for biomedical studies. It became operational in 1959. It provides thermal and epithermal neutron beams suitable for research studies such as radiation therapy of various types of tumors. The BMRR is housed in an 18.3 meter diameter cylindrical gas-tight steel building, connected to the Brookhaven Medical Research Center by a system of air locks. The core was originally loaded with 2.24 kg of ^{235}U in 17 fuel elements having standard curved plate, MTR, design. Most of the core components, including the reactor vessel and cooling water system, are made of aluminum. Spaces not occupied by fuel elements, control rods, or instrumentation within the cylindrical vessel are filled with graphite, which is air cooled.

BMRR has thermal and epithermal experimental treatment rooms on the west and east sides of the reactor. Three thimbles, cast in a concrete shield without shutters, are located on the north side. One of these is a radial beam thimble and is used to irradiate biological samples for evaluating their ^{10}B content by determining the prompt gamma-rays produced in neutron capture. This facility has a PC-based control system to sequentially irradiate and measure up to a hundred samples/day. Samples can be changed manually or automatically. One tangential thimble was used for experiments in neutron moderation but is currently blocked. The third thimble, having a pneumatic system (P_n tube) to convey samples to the edge of the graphite reflector zone, is used for radio-nuclide production and neutron activation analysis. In addition, there is a broad beam facility located at the end of the thermal column on the south side of the BMRR. It is five feet by five feet by three and one half feet deep and has been used for irradiation of large samples and large animals.

Reactor Improvements

Early BNL work in Boron Neutron Capture Therapy (BNCT) used a beam of thermal neutrons for experimental treatment of brain tumors. Research elsewhere and at BNL indicated that higher energy neutrons would be required to treat deep seated brain tumors. Epithermal neutrons would be thermalized as they penetrated the brain and peak thermal neutron flux densities would occur at the depth of brain tumors. One of the two BMRR thermal port shutters was modified in 1988 to include plates of aluminum and aluminum oxide to provide an epithermal port. Lithium carbonate in polyethylene was added in 1991 around the bismuth port to reduce the neutron flux density coming from outside the port. To enhance the epithermal neutron flux density, the two vertical thimbles A-3 (core edge) and E-3 (in core) were replaced with fuel elements. There are now four fuel elements of 190 grams each and twenty-eight fuel elements of 140 grams each for a total of 4.68 kg of ^{235}U in the core.

We have proposed to replace the epithermal shutter with a fission converter plate shutter. It is estimated

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that the new shutter would increase the epithermal neutron flux density by a factor of seven and the epithermal/fast neutron ratio by a factor of two, compared to treatment room (table 1). The new shutter would contain a uranium fission converter with uranium plates enriched in ^{235}U to slightly less than 20%. The fission converter will consist of four fission converter elements located in a narrow tank bolted to the back of the lower section of the shutter. Fission spectrum neutrons will be produced in the fission converter from thermal neutrons leaking from the graphite reflector region surrounding the BMRR core. Aluminum and aluminum oxide installed in the shutter window assembly will moderate the fission neutrons to the desired optimum epithermal energy at the treatment port. With the shutter in the raised position and the window assembly opposite the core, an epithermal beam will be produced. With the shutter in the lowered position and window assembly not exposed to the core, no epithermal beam is produced.

Forced water flowing upward past the elements in the tank would remove the fission heat. Heated water would flow from the tank into a cooling system consisting of a heat exchanger, pump, piping and instrumentation, which would enable monitoring of the cooling system performance and provide signals for trip functions.

Plant modifications, such as the aluminum plates described above, have led to increased epithermal neutron flux densities and larger ratios of epithermal neutron flux to thermal neutron, fast neutron and gamma ray dose rate as shown in table 1.

Table 1

BMRR Experimental Facilities Flux in n/cm^2/sec. at 3 MW

Facility	Thermal Flux	Fast Flux	Gamma Dose	Sample Size
P_n Tube	$1. \times 10^{13}$	$3. \times 10^{11}$		1 1/8" x 4"
Radial Hole	$3. \times 10^{12}$	$1. \times 10^{10}$		1" dia. x 4"
Broad Beam	1.28×10^{10}		1000 r/min(1)	5’ wide x 5’ high x 3’ deep.
Treat.Room 1	$6. \times 10^{10}$ (thermal)			10" x 10"
Treat.Room 2	2.7×10^{9} (epi-thermal)		10" x 10"	

Notes:
(1) With cadmium screen down

BNCT Program

In 1936, Locher[1] proposed that medical research could be advanced by destroying cancerous cells using neutrons. 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.

BNCT involves the minor stable nuclide of boron (^{10}B), which has an isotopic abundance of 19.8% and a cross section of 3838×10^{-24} cm^2 (barns) for absorbing a thermal neutron and emitting an alpha particle. ^{4}He with an energy of 1.47 MeV has a range of 10.1 μm (in water) and an average linear energy transfer, LET, of 150 keV/μm. The residual nucleus, ^{7}Li, with an energy of 0.85 MeV has 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 nearby healthy cells would be relatively unaffected.

In clinical trials of BNCT in the 1950s and early 1960s, no technique was available that allowed prompt estimates of the patient’s blood and/or tissue ^{10}B concentration to help plan the duration of the irradiation and total BNCT dose. Radiation damage to scalp became an early complication. Considerable variation existed from patient to patient in the ^{10}B concentration in their blood. The unavailability of boron containing compounds preferentially concentrating in tumors was an additional problem. No epithermal ports were available to provide adequate flux of thermal neutrons at depth. To minimize the absorption of thermal neutrons in tissues overlying the tumor, scalp and and skull had to be temporarily reflected to directly expose the tumor to thermal neutrons. The modifications made to the BMRR in the past few years permit BNCT for brain tumors without the need to reflect scalp and bone flaps.

Radiation workers are monitored via a TLD badge (read once a month) and a self-reading dosimeter during each experiment. An early concern was raised about whether workers would be subject to a significant dose rate from working with patients who have been irradiated. The gamma ray doses for the representative key personnel involved in the care of the first 12 patients receiving BNCT are listed in table 2. These workers did not receive unusually high exposures.

Table 2

Gamma Doses in Millirem to Personnel during BNCT Irradiations

Staff Member	Patient #												Patient	Total	Avg.
	1	2	3	4	5	6	7	8	9	10	11	12	Treated	Dose	Dose
Responsible Physician	1	1	2	1	4	1	4	3	4	3	6	2	12	32	2.7
Radiation Oncologist	0	2	0	2	5	4	2	7	1	2	-	-	10	25	2.5
Nurse	2	3	0	-	0	1	5	3	6	5	5	5	11	35	3.2
Medical Physicist	1	2	0	1	2	1	-	1	6	2	7	2	11	25	2.3
Health Physicist	1	-	2	-	1	-	3	-	0	-	2	1	7	10	1.4

Clinical BNCT dose-escalation research protocols were initiated in September 1994. A total of 30 patients with glioblastoma multiforme have received BNCT to date. The first 10 patients receiving BNCT have had long enough post-BNCT follow-up to lead us to conclude that at the radiation doses delivered in the first ten patients: a) There was no clinical or radiological evidence of damage to the normal brain; b) The side-effects of the treatment were minimal and, c) The median duration of palliation following one session of BNCT was comparable to the median duration achieved following 30 sessions of conventional radiation therapy with or without chemotherapy.

Preclinical studies were performed to study the effect of BNCT on ocular melanoma.

Research continues using the P_n tube for irradiations such as radio-nuclide production and neutron activation analysis at various thermal neutron flux density levels up to 10^{13} neutrons/sec/cm^2.

Summary

Modifications have been made to the BMRR to significantly increase the available epithermal neutron flux density to a patient. The above data indicates that even with the increasing flux values, dose to the attending personnel has remained minimal.

References

1. G.L.Locher, Amer. J. Roentgen. Radium Therapy 36 1 (July 1936).

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