A Feasibility Study of the SLOWPOKE-2 Reactor as a Neutron Source for Boron Neutron Cancer Treatment

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Introduction

Over the past decade, there has been a continued interest in the development of Boron Neutron Capture Therapy (BNCT) as a potential treatment for cancerous tumours and especially certain brain tumours. In this method, advantage is taken of the nuclear properties of certain elements such as boron. A special boron carrier drug, designed to be selectively taken up by the cancer cells, is administered to the patient. The cancerous part of the body is then irradiated by thermal or epithermal neutrons. The predominant thermal neutron cross section in the carrier drug yields a ^{10}B(n, ")^{7}Li reaction which results in heavy recoil particles having sufficient energy and range to damage only the cell in which the boron compound was situated. Thus a high boron concentration in the tumor provides preferential cell death in that tissue. Healthy tissue with its lower concentration of boron receives a much smaller dose. The advantage of epithermal neutrons over thermal neutrons is that they can penetrate the skull, moderated, becoming a useable thermal neutron source. Research reactors or accelerators can be used as a source of neutrons. Although work is being done on the development of a suitable accelerator, BNCT becomes clinically attractive only if a sufficiently high epithermal neutron flux can be delivered to the target tissue. To date, only reactor based facilities have been able to meet the required flux levels.(1)

BNCT has been performed in Japan for many years. The early phases of the clinical trials are underway at three research reactor facilities, two of which are in the USA and one in Europe. Several other research reactors are modifying their irradiation facilities to enable BNCT research to be performed. Some entrepreneurial groups, including physicians, are even trying to get purposely built facilities funded. Many research reactors owners/operators are expectantly hoping that this treatment will be successful and that it will enable them to increase the utilization or even to prevent shutdown of their reactors.

Theory

Absorption of a thermal neutrons by boron produces the (n,") reaction, shown in Figure 1. This reaction produces an alpha particle, a lithium ion and a gamma ray. The alpha and lithium nuclei have a range of approximately 4-7 micrometers, sharing between them 2.3-2.8 MeV. The Linear Energy Transfer (LET) of the heavy recoil particles is sufficient enough, such that all of its energy is deposited within a cell The rationale for BNCT is based on the fact that the capture cross section of normal tissue elements for thermal neutrons is two orders of magnitude less than boron-10. . The gamma radiation produced contributes very little to the cancerous cell but must be evaluated at the normal tissue to ensure dose is within acceptable limits. Based on the percentage of the elements in tissue, their capture cross section and the types of radiation emitted in this reaction, only a fraction of these interactions with hydrogen (gammas) and nitrogen (protons) contribute significantly to the dose delivered to normal tissues by capture reactions (^{1}H(n, ()^{2}H) and (^{14}N(n,p)^{14}C). Cancerous cells are also effected by this reaction, but in comparison to the heavy recoil particle damage, it is minimal. Without the heavy recoil LET deposition in the cancerous cells (Li and "), the ratio of the total patient dose to the elimination of cancerous cells would be unacceptable. Gamma radiation emanating from the reactor also has to be considered.

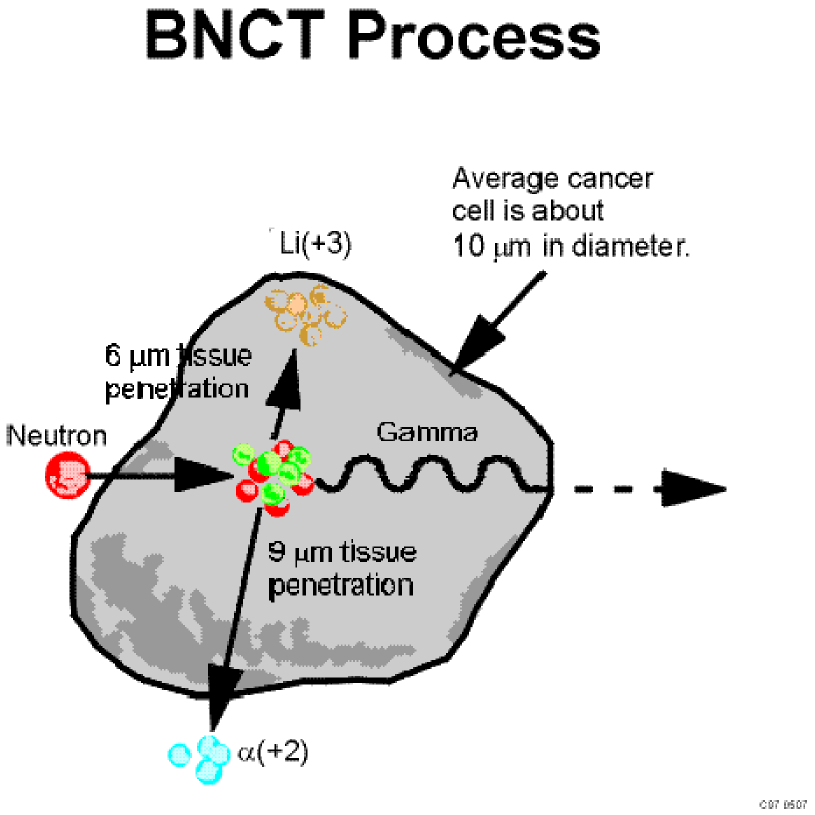

Figure 1: BNCT Process

Alpha particles, unlike some forms of radiation, such as X-rays, do not require oxygen to enhance their biological effectiveness. A rapidly expanding tumour frequently outgrows its blood supply, so that some regions receive less oxygen than normal tissues do. As a result of this oxygen depletion, the tumor can become more resistant to the effects of conventional photon or electron (i.e. low LET) radiation therapy. Tumor sensitivity to alpha particles is retained, however, because the particles, not needing oxygen, can attack all parts of a tumor with equal effectiveness.[2]

Because boron is ideally taken up only in malignant cells, the BNCT process offers the possibility of highly selective destruction of malignant tissue, with cellular-level sparing of neighbouring normal tissue since the neutron sources used for BNCT are, themselves, designed to minimize normal tissue damage to the physical extent possible.

In the past in Japan, the neutrons beams used for BNCT have a characteristic neutron energy that corresponds at incidence to thermal equilibrium with tissue at body temperature (about 0.025 eV).(2) The current trend has been to utilize epithermal-neutron beams (neutrons having energies in the range of 0.4 eV to 10 keV) (1) to produce the required thermal neutron flux at depth (2.5 cm), since these somewhat higher-energy neutrons will penetrate deeper into the irradiation volume before slowing to thermal energy, yet they are still not sufficient energy to inflict unacceptable damage to intervening normal tissue. This procedure allows for thermal neutron energies at the tumor without surgical removal of the skull. The required epithermal neutron flux should be equal or greater than 1×10^9 n/cm^2 s.(1) This flux ensures effective thermal neutron flux at the cellular level for reduced treatment times.

Dose Limits

BNCT, like all other forms of cancer treatment, has the potential to injure the normal tissue. It is not possible to eliminate all of the injurious components. BNCT-related processes that may injure the brain include low and fast energy neutrons interactions, as well as gamma rays as they interact with all elements naturally present in the healthy cells. Achievable tumor-boron concentrations allow tumor destruction while limiting normal brain effects from these reactions. Successful treatments, obviously, require limiting the injurious reactions to healthy cells and maximizing the boron reaction within the tumor.

Dose limits ensure acceptable levels of healthy cell deaths. As per reference (1), the defined dose limits for the gamma and fast neutron dose contribution per epithermal neutron is:

a. less than 1×10^{-10} cGy/cm^2 s for fast neutrons;

b. In the order of 10^{-11} cGy/cm^2 s for gammas; and

c. Thermal neutron dose contribution is minimized as practicable but minimal dose is considered acceptable and unavoidable, as described in the following paragraph.

Although the thermal neutron capture cross-sections for the elements in normal tissue are several orders of magnitude lower than for ^{10}B, two of these, hydrogen and nitrogen, are present in such high concentrations that their neutron capture contributes significantly to the total absorbed dose. In order to reduce this "background" dose it is essential that the tumor attain high ^{10}B concentrations so that neutron fluence (n/cm^2) delivered can be held to a minimum, thereby minimizing the (n,p) reaction with nitrogen (^{14}N(n,p)^{14}C) and the (n,() reaction with hydrogen (^{1}H(n,()^{2}H) and maximizing the ^{10}B(n,") ^{7}Li reaction.

SLOWPOKE-2 Research Reactor

The Royal Military College of Canada (RMC) has fitted a 20 kW SLOWPOKE -2 nuclear reactor (Safe LOW POwer Kritical Experiment) for research, training, radiography. The reactor can provide a stable thermal neutron flux of $1x10^{12}$ n/cm^2 s at the inner irradiation sites. The SLOWPOKE -2 is a pool type reactor, light water moderated and cooled. The core, composed of 198 Low Enriched Uranium (LEU) Dioxide (UO2) fuel rods (approximately 1 kg U-235), is located at the bottom of the reactor container below more than 4 m of water. The water in the container acts as the moderator, the coolant and the shielding. The pool water provides additional shielding. A single central cadmium rod controls the reactor.

The SLOWPOKE -2 has been designed with a large negative temperature reactivity coefficient and a limited excess reactivity (4 mk maximum). The moderator density reduces with increased temperature, rendering the SLOWPOKE -2 in inherently safe. Therefore, it is licensed for automatic unattended operation. There are five inner irradiation sites located in the beryllium annulus (where the flux is the highest), and five outer irradiation sites, located between the annulus and the reactor container (see Figure 2).

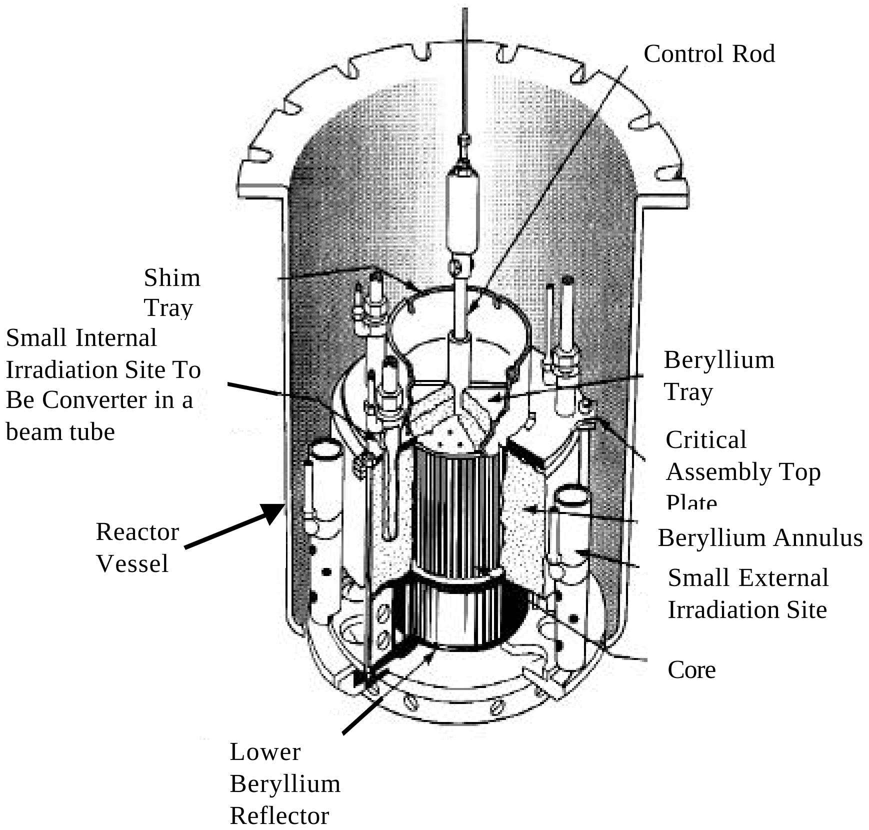

Figure 2: Three Dimension View of the Reactor

The time required for each treatment is linearly dependent on the epithermal flux at the treatment site. The recommended treatment time for an epithermal flux of 1×10^9 n/cm^2 s is 15 minutes.(2) A decrease in this flux requires a longer treatment time. Treatment time must also be limited to an interval during which the patient can be restrained from moving, making a treatment time of less than one hour desirable. This shows that a flux less than optimal can be overcome by increasing treatment time, but it is impractical to use an epithermal flux lower than 1×10^8 n/cm^2 s.(1) The brain tumour treatment drug BSH (boron 10 based) has a tumour residency half life of approximately 4.5 hours. Half of the boron is eliminated from the tumour during this time interval, hence, the boron neutron reaction rate in the tumour is halved, while the rate of injurious reactions to the healthy cells from neutron/cell interactions remains unchanged. Therefore, in a maximum one-hour treatment time, the effect of the boron half-life is negligible. Since small research reactors, shown in table 1, such as the Musashi reactor can be designed to fulfil the role of a neutron source for BNCT, it seemed appropriate to consider the SLOWPOKE Nuclear Reactors for the same role. (1)

Results and Discussion

The reactors detailed in Table 1 were examined and compared in order to assist in the selection process for an optimal beam tube design for the required epithermal flux.

Table #1 - Comparisons of Beam Parameters in Air for Different Reactors

	BMRR	MURR	GTRR	Musashi
Reactor Power (MW)	3	10	5	0.1
Distance (core-FPC) (cm)	90	95	90	100
Distance (FPC-head) (cm)	105	215	170	75
Thermal Flux @ FPC (10^{13} n/cm^2 s)	0.08	0.07	1.7	0.5
^{235}U in FPC (kg)	8.0	4.4	2.4	1.68
Fission Heat (kW)	72	32	600	2.0
Epithermal Flux at Head (10^{10} n/cm^2 s)	1.2	0.25	3.4	0.034
Fast Dose/epi-neutron @head (10^{-11} cGy/cm^2 s)	2.8	1.8	1.0	4.3

NOTE: MURR – Missouri University Research Reactor
GTRR – Georgia Institute of Technology Research Reactor
BMRR – Brookhaven Medical research Reactor
Slab – Generic Slab Core Research Reactor
Musashi – TRIGA-II type Reactor

Options Investigated

This section details the investigation into the ability of the existing, low powered, SLOWPOKE nuclear reactors to produce sufficient flux to be of use as a BNCT research or treatment tool. This project was mainly concerned with determining whether or not an epithermal neutron flux of $1x10^9 \ {}^{n}/_{cm^2 s}$ at the exit of a beam tube could be achieved. Several configurations using the RMC SLOWPOKE 2 nuclear reactor as a reference were investigated as detailed in table 2.

Options	Description	Epithermal Flux @ beam exit ($n/cm^2 \cdot s$)
Tangential Beam Tube	Uses one of the internal radiation sites, see figure 1. **Advantages**: minimal modification required, uses a region of high epithermal flux in the reactor. **Disadvantages**: long beam tube, diameter of beam tube is restricted due to irradiation site size.	$3x10^4$
Radial Beam Tube	Positioned at reactor container, see figure 2. **Advantages**: shorter beam tube, larger diameter. **Disadvantages**: requires significant modifications.	$6.25x10^7$
Radial Beam Tube	Positioned at reactor container, see figure 2 with fission plate. **Advantages**: shorter beam tube, larger diameter and higher flux. **Disadvantages**: requires significant modifications and additional fissile material.	$4.7x10^8$
Radial Beam Tube	Positioned at reactor core, see figure 3. **Advantages**: short beam tube, larger diameter. **Disadvantages**: requires significant modifications including modifications to the reactor container.	$2.8x10^8$
Radial Beam Tube	Positioned at reactor core, see figure 3 including fission plate. **Advantages**: short beam tube, larger diameter and higher flux. **Disadvantages**: requires significant modifications including modifications to the reactor container and additional fissile material.	$2.2x10^9$

Epithermal flux calculations were based on the following general beam tube equation:

$$f_o = \frac{f_i}{16\left({}^{L}/_{D}\right)^2} = \frac{2x10^{10} \ {}^{n_{epi}}/_{cm^2 s}}{16\left({}^{400cm}/_{2cm}\right)^2} = 3x10^4 \ {}^{n_{epi}}/_{cm^2 s} \qquad [1]$$

where f_i is the epithermal neutron flux at the entrance to the beam tube in (n/cm^2·s) which is taken from reference (4). L is the length of the beam tube in cm. D is the diameter of the beam tube in cm. Equation 1 is taken from reference (3).

Fission plates are sub-critical assemblies containing various quantities of fissile material. A fission plate converter (FPC) used between the reactor core and the treatment port results in sub-critical multiplication of the neutron flux, giving a higher epithermal neutron flux (compresses energy spectrum flux levels to epithermal range). Table 1 shows various research reactors and the change in flux levels attainable with the addition of the described fission plate. MCNP calculations, reference (1), indicate that the epithermal neutron flux could be increased by as much as 670%, while actually reducing the fast neutron dose. An in house MCNP calculation using a SLOPOKE-2 type fuel rod weighing 1 kg, yielded an epithermal neutron flux increase of only 34%. Although this is significantly lower than the result previously quoted, it is believed that once the design of the fission plate is optimized, a similar result could be obtained.

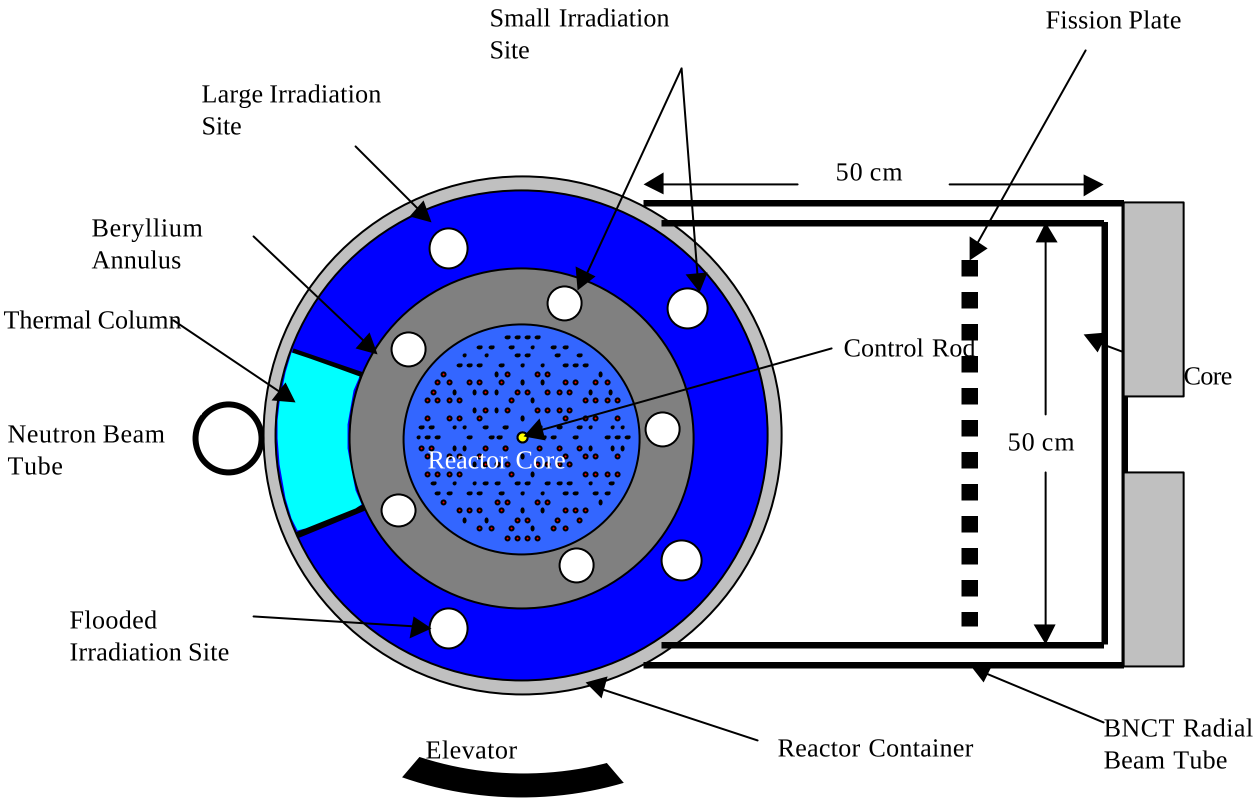

Figure 3: Radial Beam Tube Configuration at Container

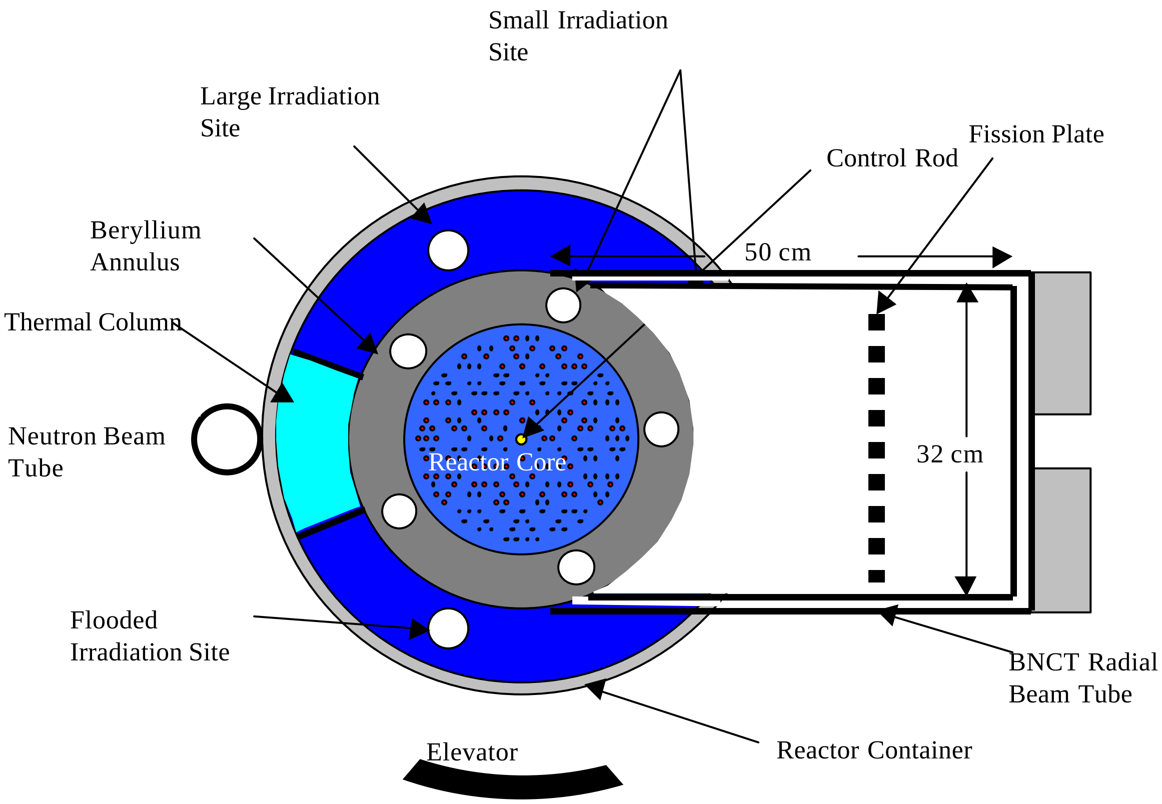

Figure 4: Radial Beam Tube at Beryllium Annulus

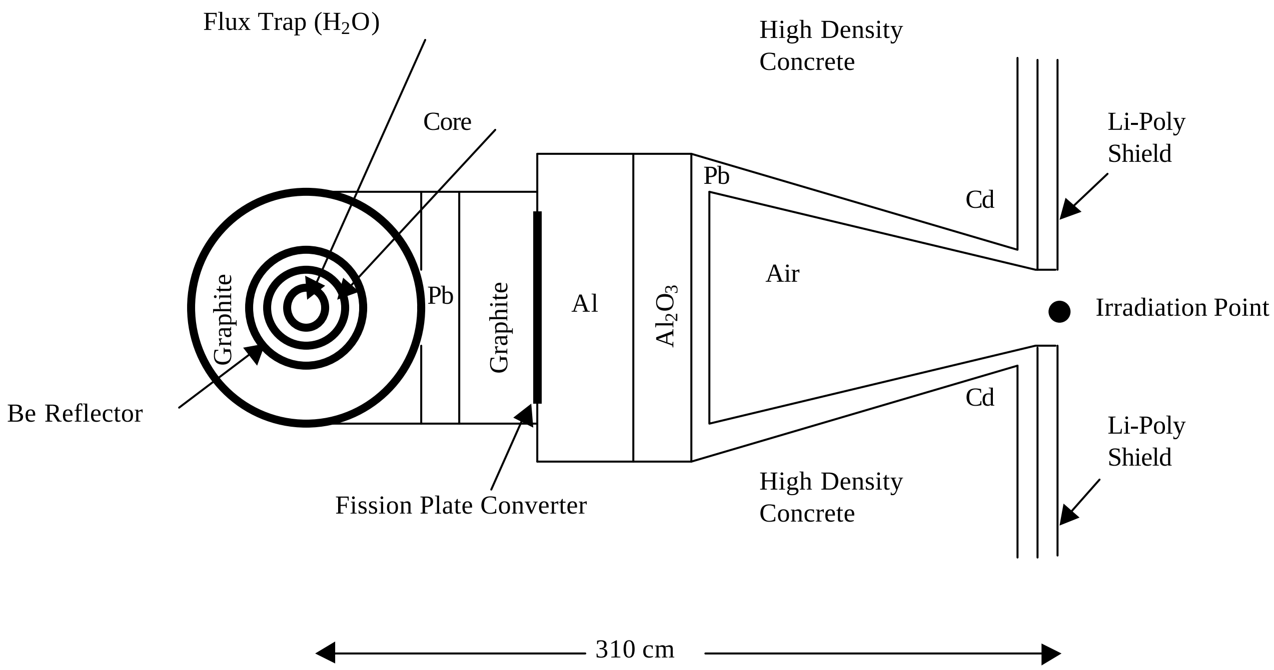

Figure 5: MURR Reactor Layout

This calculation was used to model and evaluate the neutron flux of the MURR using the configuration shown in Figure 5. The thermal neutron flux at the fission plate location (without the plate) was set to 3.5x10^{9} $^{n_{epi}}/_{cm^2 s}$ [2]. The distance from the plate to the exit end of the beam tube was estimated at 200cm based on Figure 5. The diameter of the tube is 1m (1). The epithermal to thermal neutron flux ratio was assumed to be similar to that of the SLOWPOKE-2, so the calculated flux is;

$$f_o = \frac{f_i}{16\left(L/D\right)^2} = \frac{0.018x0.07x10^{13}\ ^{n_{epi}}/_{cm^2 s}}{16\left(200cm/100cm\right)^2} = 2x10^8\ ^{n_{epi}}/_{cm^2 s}$$

. Assuming that the fission plate increases the epithermal neutron flux by 670%, then the epithermal neutron flux becomes 1.54x10^{9} $^{n_{epi}}/_{cm^2 s}$. This simple calculation compares well with the MCNP value of 2.5 x10^{9} $^{n_{epi}}/_{cm^2 s}$, listed in reference (1), which validates our calculations.

Conclusions

Current literature has shown that BNCT is a fairly old technique, although it is just recently becoming more popular as the science becomes better understood. The United States, Japan and Europe are devoting a great amount of money and effort into the development of BNCT treatment sites, including reactor based treatment facilities. The authors were unable to find any Canadian research literature or development within Canada in the field of BNCT. This is an opportunity to be a Canadian innovator in this field.

The results of this project are a simple look at the feasibility of using the SLOWPOKE-2 as a research tool or as a neutron source for BNCT. Initial indications are that a radial beam tube attached to the reactor container wall could be used as a research tool, to help develop beam tube, fission plate, flux simulations, neutron energy spectrums and dose estimations in the field of BNCT.

Based on these initial estimations it seems likely that one could design a practical beam tube for the SLOWPOKE-2, producing more that 1 x10^{8} $^{n_{epi}}/_{cm^2 s}$ epithermal neutron flux with doses less than 1x10^{-10} $^{cGy\ cm^2}/_{n}$ for the fast neutron component and less than10^{-11} $^{cGy\ cm^2}/_{n}$ for the gamma rays components. The SLOWPOKE-2 reactor could be proven acceptable as adequate as a human treatment site for BNCT in the future, but at present it seems more likely that the SLOWPOKE-2 reactor could be used for experimental investigation of the technique.

At this time, Canada has no operating or planned BNCT facility, therefore a proposal for a research reactor to test and validate simulations and calculations could lead to valuable research within this field. As well, there are other SLOWPOKE reactors in Canada that could be utilized for this application if further studies confirm that the SLOWPOKE-2 is suitable for BNCT research.

References

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