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An Intermediate Energy Neutron Beam for NCT at MURR*

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ABSTRACT

The University of Missouri Research Reactor (MURR) is one of the high flux reactors in the USA and it can be used to produce an intense beam of intermediate energy neutrons for neutron capture therapy. Two methods are being evaluated at MURR to produce such a beam. The first uses a moderator of Al_2O_3 replacing part of the graphite and water on one side of the core of the reactor to produce a source of predominantly intermediate energy neutrons. The second method is a filter of ^{238}U between the core and the patient position to pass only intermediate energy neutrons. The results of these evaluations are presented in this paper along with an outline of the other resources at the University of Missouri-Columbia that are available to support an NCT program.

I. INTRODUCTION

In neutron capture therapy (NCT)[1], boron that has been selectively implanted in a tumor is fissioned by thermal neutrons. The high LET fission products deliver a large dose to the tumor while the triggering particles, the neutrons, deliver a lower dose to the healthy tissue. Past research has used beams of thermal neutrons, but recent trends are toward development of an intermediate energy beam that will allow the neutrons to penetrate several centimeters into a patient before these neutrons are moderated to thermal energy at the location of the tumor.

At MURR two methods of producing an intermediate energy beam are being studied. The first method is a moderator of Al_2O_3 placed near the core to give a source flux of intermediate energy neutrons. The second method is a filter of ^{238}U placed between the source and the patient. This filter passes only intermediate energy neutrons. The results to date of the studies of these two methods are presented in this paper.

II. Al_2O_3 MODERATED BEAM

A. Calculations The diffussion code DISNEL has been used to calculate the neutron flux in the core, moderator and out to a patient position in the MURR. First, DISNEL calculations were made of the MURR as it is usually

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configured to confirm that DISNEL and the parameters being used give the correct fluxes. Comparisons with the original design calculations and with flux measurements that have been made over the 20 years of operation of MURR indicate that DISNEL is working satisfactorily.

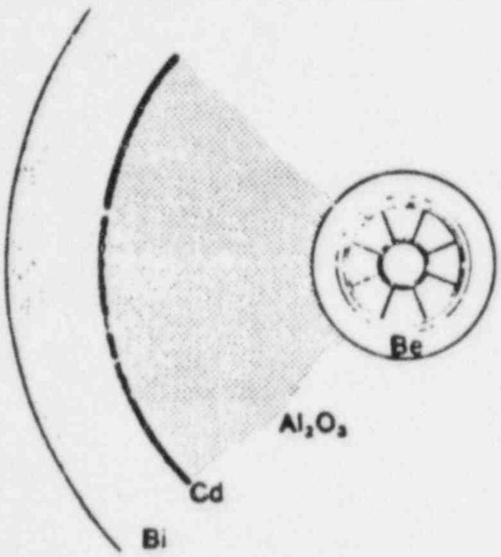

Fig. 1

Figure 1 shows the cylindrical geometry that was used to approximate the MURR for the moderator calculations. The Be reflector was not replaced with Al_2O_3 because replacing the Be in the reactor would be difficult and would reduce the reactivity a little. Leaving the Be reflector does reduce the intermediate flux some as compared to replacing this zone with Al_2O_3. For the calculations, the graphite and water reflector out to an 80 cm radius have been replaced with Al_2O_3. Outside the Al_2O_3 moderator is a 35 cm shield of Bi. Following the Al_2O_3 and before the Bi is 0.25 cm of Cd to reduce the thermal neutron flux. The patient position is at 2 m from the core centerline.

Since the diffusion code DISNEL does not simulate boundaries well, the fluxes have been calculated for Bi out to 2 m. Then the flux at 115 cm has been reduced by a factor of 2 for flux suppression by a beam. A source size of 40 cm x 40 cm has been selected and the flux at the patient has been calculated by the beam equation

$$\Phi = \Phi_s \frac{A_1 A_2}{4 \pi d^2}$$

where Φ_s is the source flux, A_1 is the source area, A_2 is 1 cm^2 and d is the distance from the source to the patient.

Figure 2 shows the intermediate flux (0.15 eV to 9.1 keV), the thermal (< 0.15 eV) flux and the fast flux (9.1 keV to 10 MeV) calculated for the above geometry. The 9.1 keV transition was selected as the division between intermediate and fast fluxes because this was the division between two groups in the DISNEL code and thus was convenient. The Be is around the core and the Al_2O_3 moderator extends out to 80 cm. A 0.25 cm layer of Cd is bewtween the Al_2O_3 and the Bi, and the Bi is 35 cm thick. There is 0.2% of Li metal added to the Bi. In Figure 2, as the radius increases, the fast flux is suppressed much faster than the intermediate flux decreases. At the outer edge of the Bi the fluxes drop because of flux suppression, and at the patient position, 2 m from the

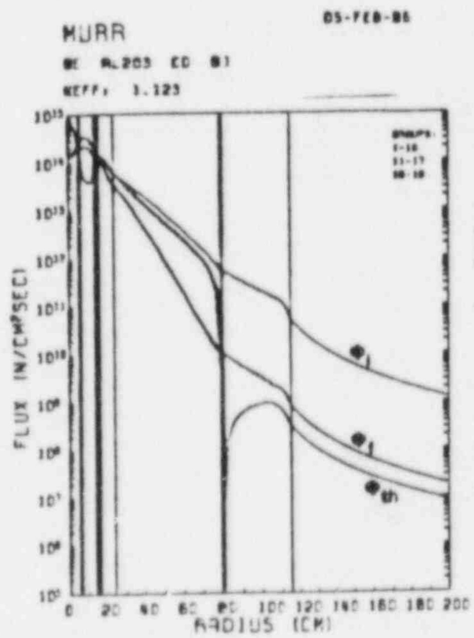

Fig. 2

center of the core, the intermediate current is 1.3 X 10^9 n/cm^{2}sec, while the fast current is smaller by about two orders of magnitude. Figure 3 shows the neutron flux spectrum at the patient position. The flux is truly peaked in the intermediate range and most of the dose to the patient will come from the intermediate energy neutrons. Table 1 summarizes the neutron currents and Kerma.

Most of the dose to the patient by gamma rays comes from thermal neutron capture in the Cd and in the Al of Al_2O_3. As a first approximation of the gamma dose, the MURR core and the Al_2O_3, Cd, and Bi moderator sections were treated as infinite slab volumetric photon sources 1 to 10 MeV in increments of 1 MeV. To establish the spectrum and the magnitude of the gammas coming from the core, the ^{235}U prompt photon spectra[2] and the known MURR gamma-heating were used as benchmarks. The core volumetric source strength spectra was estimated and treated as constant over the diameter of the core. In the moderator sections it was found that the major contribution to the photon dose was from thermal neutron (n,γ) reactions with Al and Cd. The volumetric photon source strength in these regions varied with the thermal neutron flux.

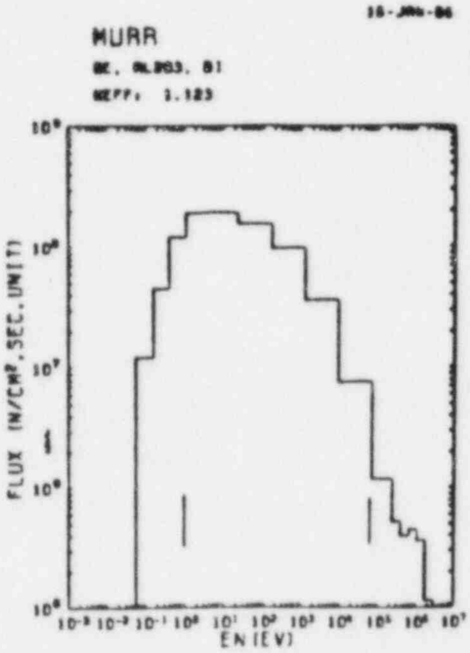

Fig. 3

Table 1. Fluxes and Doses at Patient Position with Al_2O_3 Moderator	
Intermediate flux	1.3 x 10^9 n/cm^{2}sec
Kerma from intermediate flux with boron (50 μgm/gm)	21 Gy/hr
Kerma from intermediate flux without boron	0.3 Gy/hr
Thermal Flux (thermal Maxwellian)	9.3 x 10^6 n/cm^{2}sec
Kerma from thermal flux with boron (50 μgm/gm)	0.14 Gy/hr
Kerma from thermal flux without boron	0.005 Gy/hr
Fast flux	2 x 10^7 n/cm^{2}sec
Kerma from fast flux	0.3 Gy/hr
Kerma from gamma rays	0.8 Gy/hr
Kerma from $^{10}B(n,\delta)^7Li$ gamma ray	0.9 Gy/hr

The calculations of the dose for uncollided and in-scattered photons were performed using ray analysis technique and the Burger build-up formula.[3] The results of this first approximation are that 35 cm of Bi keeps the photon dose rate to the patient to 0.8 Gy/hr. The fractional contributions of this dose rate from (n,γ) reactions in Al, Cd, and Bi are about 23%, 73%, and 4% respectively. Most of that portion from the Bi originates near the outer edge of the shield. Bismuth with a small amount of Li^6 would further reduce the thermal neutron dose to the patient. If small amounts of Li^6 were also in the Al_2O_3, the number of $Al(n,\gamma)$ reactions would be reduced, thus reducing the gamma dose and/or the thickness of the Bi shield required, and the need for Cd.

Alumina should be a good moderator in a reactor. It is a common substance and may be easily obtained with a high purity. Silica (SiO_2) is the main impurity found in Al_2O_3 and this poses no problem in neutron moderation or radioisotope production. Alumina is a hard white ceramic that is commercially available at a cost of about $6000 per cu yd, with densities ranging from 3.4 to 3.95 gm/cm^3, and it can be purchased in preformed shapes. The highest density Al_2O_3 is preferred for neutron moderation and photon shielding, thus a density of 3.95 gm/cm^3 was used in all calculations. Alumina has a melting point of 2323°C with a suggested maximum use-temperature of 1540°C. Alumina is an insulator with a thermal conductivity of 25 W/mK at 130°C, and a low thermal expansion of 3.4×10^{-6}/°C in the range of 25-700°C, thus low heat conducting may pose a problem with gamma-heating, and ways to cool the moderator blocks are being investigated. Alumina is relatively inert, insoluble in water and would only be affected superficially in the bond phase if hydrofluoric acid or strong caustics were present. Alumina is relatively inert to radiation damage and should hold up well close to the core.

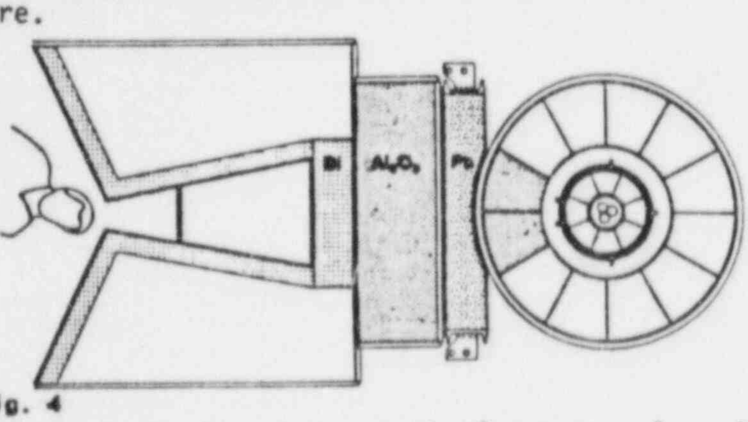

Fig. 4

B. MURR Geometry The actual MURR is not quite as simple as is represented in Figure 1. Figure 4 shows a section at the mid plane. The graphite wedges on the west side of the core can be replaced with wedges of Al_2O_3. The 6 inches of lead that shield the thermal column will be difficult to move, but leaving it in is not too much of a compromise since Pb reduces the neutron fluxes very slowly as the radius increases. Next comes the pool liner, which is about 3/4 inch of Al, and this is not much of a compromise. Next Al_2O_3 would be stacked in the thermal column followed by Bi.

A tank that can be filled and drained quickly would fill the space between the Bi and the patient, and a high density liquid filling the tank would act as a radiation shutter. An alternate design for a shutter is sliding doors following the Bi. The fluxes and doses with the actual geometry should be similar to the fluxes and doses calculated for the simpler geometry.

III. ^{238}U FILTERS

A. Measurements Several years ago measurements were made at MURR of the spectra of neutrons passing through several different thicknessess of natural U metal.[4] A Bonner sphere detector was used as the energy spectrometer and the code BONAB was used to process the data. Figure 5 shows these data, which indicate that a thick ^{238}U filter does pass only intermediate energy neutrons. At the time these spectra were measured, a spectrum with zero thickness of U was not measured so that it is difficult to convert these data to transmissions or put the spectra on an absolute scale.

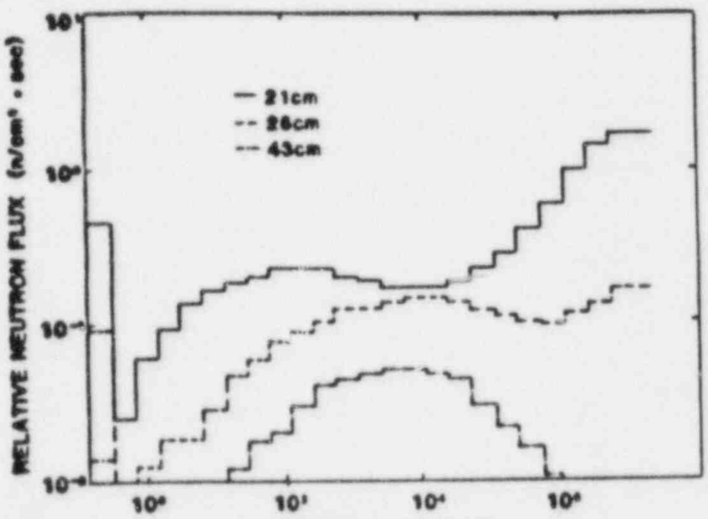

Fig. 5

B. Calculations The transmission of thick filters of ^{238}U have been calculated using the total cross sections of ^{238}U as given by ENDF/B-V. Neutrons interact with matter by the neutron-nuclei reaction and the probability that neutrons of a specific energy react with nuclei is expressed as a cross section $\sigma(E)$. The attenuation of a beam of neutrons through a filter can be described by the formula $I(E) = I_0(E)e^{-nx\sigma}$, where the number of neutrons $I(E)$ that pass thru a filter of length x and atom density n is equal to the product of the original number of neutrons from some source, $I_0(E)$, times the exponential of the product of the cross section, length, and atom density.

In order to calculate the spectrum of neutrons that would be passed by a thick ^{238}U filter, the initial source flux of MURR was considered. F.Y. Tsang has shown that a flux profile of the outer edge of the Be reflector for MURR can be calculated from the following equations:

1) For the thermal region (0.0001eV-0.64eV) the equation is
   $\phi(E) = 1.35 \times 10^{14} \times e^{-E/0.028} \times E/(0.028)^2 \times 10^6$ in units of n/cm^2-sec-MeV
2) For the resonance region (0.64eV-0.8MeV), the equation is
   $\phi(E) = 5.698 \times 10^{12} \times 1/E$ n/cm^2-sec-MeV
3) For the fast spectrum (0.8MeV->10.0MeV) the equation is
   $\phi(E) = 4.794 \times 10^{13}e^{-E}\sinh(2E)^{1/2}$ n/cm^2-sec-MeV

These three primary energy regions were applied to the 25 energy group structure used in previous filter measurements at MURR. Equation 1 applies to BONABS groups 1 and 2 (thermal to 6.826×10^{-7} MeV); equation 2 applies to BONABS groups 3 thru 21 (6.826×10^{-7} MeV to -9.072×10^{-1} MeV); and equation 3 applies to BONABS groups 22 thru 25 (9.072×10^{-1} to 2.5×10^{1} MeV). One further group was added to the calculations to include energies over the BONABS limits but suggested by the ENDF/B data.

The data used to calculate the intensity, I(E), or the flux, $\phi(E)$, was derived from ENDF/B data supplied as a series of (E,σ) pairs. These data pairs represent a series of ascending but unequally spaced points describing a function f(x). To integrate this function and thus derive I(E), the rectangular method of integration was modified where $\Delta E = (E_{i+1} - E_{i-1})/2$. The equation describing the total flux for an energy group becomes $\Sigma I(E) = \Sigma(I_o(E)e^{-\sigma nx}\Delta E)$, where $\Sigma I(E)$ has limits equal to the specific limits for the BONABS group being calculated.

The attenuation relationship, or the transmission factor, is the ratio of the number of neutrons passed through the filter to the number of neutrons incident to the filter, and is defined by the equation $T = \Sigma I(E)/\Sigma I_o(E)$. This transmission factor was also calculated for each BONABS group.

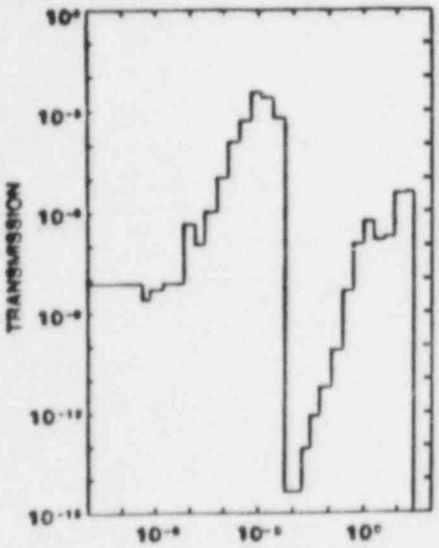

Fig. 6 NEUTRON ENERGY (MeV)

Figure 6 shows the transmission that was calculated for a filter of ^{238}U that is 43 cm long. One notes that the transmission is small in the thermal region and increases as the neutron energy approaches the keV region, but drops suddenly near 4keV. This drop corresponds to the energy at which ENDF/B stops treating individual nuclear resonances and shifts to a smoothed average value. Thus, above 4 keV the transmission calculations for thick filters probably exclude transmission through some windows and underestimate the transmission. This transmission curve indicates that the number of intermediate energy neutrons through a thick ^{238}U filter may be 50-100 times more than the number of neutrons transmitted at the single window at 186 keV. The peak of the band passed by this filter is centered at 1 keV.

Possibilities of gamma ray contributions to patient dose exist with any filter. Other U filters have a reported gamma contribution of < 1 mR/hr at neutron fluxes of $\sim 10^5$ n/cm^2-sec. Very low gamma flux is to be expected of a metal with a density greater than lead and a large mass energy attenuation coefficient. With a 43 cm long filter there is 850 gm/cm^2 of material in the beam.

Possible problems that need to be assessed include the probability of thermal flux activation of the 0.2% ^{235}U found in depleted ^{238}U and the subsequent production of fission neutrons and gamma rays at the less self-attenuated patient exposed end of the filter. Also, physical properties of ^{238}U as a metal need to be investigated, including malleability, any pyrophoric attributes, melting point, and thermal conductance.

Depleted ^{238}U is a readily available metal/radionuclide that has a commercially reported cost of $15.00/kg in bulk form. Shipping regulations are delineated by NRC Regulation 75.31. MURR has three sections of ^{238}U currently on hand to use as a filter, enabling the expected implementation of further Bonner sphere tests.[4]

The above indicates that ^{238}U possesses the qualities of a good filter, adequate neutron flux over a desired energy range with minimal gamma ray contribution to dose, and a reasonable cost factor. Rough calculation starting with a source flux of the MURR, a 100 cm x 100 cm source area, a source to patient distance of 2 m and the transmissions of figure 6 show that an intermediate flux of near 10^9 n/cm^{2}sec could be obtained at the patient position.

IV. OTHER RESOURCES IN COLUMBIA

Besides the research reactor as a source of neutrons, there are other resources at the reactor facility, at the University of Missouri-Columbia, and in the city of Columbia that can add to the effectiveness of an NCT program.

A. At MURR There is room on the reactor floor and a shielded room can be added at the irradiation position; Figure 7 shows a sketch of such a room. The door, which will have several windows for viewing the patient, will roll back and forth on the tracks that are already in place. A shutter will need to be added in the irradiator, and one possible shutter, as shown in Figure 4, is a tank that can be rapidly drained and filled with a high density liquid.

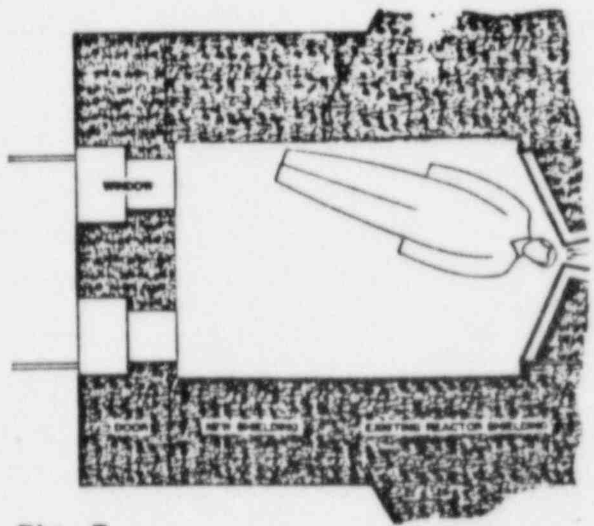

Fig. 7

The NCT irradiation facility at MURR would be accessible to patients by the path through the front door of the reactor building, through the air lock, down the elevator, and across the beam port floor to the irradiation room. Five hospitals are within one to five miles of the front door, and patients would be shuttled by car or ambulance.

The reactor now operates at 10 MW more than 150 hours a week--more than 91% of the time. The reactor is shut down for 4 to 16 hours on Thursdays for maintenance. Neutrons will be available most of the time. The cost of operating the reactor is shared by a number of users, so the cost of operating an NCT program would be relatively modest. At MURR, a program is underway to increase the power of the reactor to 30 MW, which will increase the flux by a factor of three.

B. At the University The University of Missouri at Columbia has a medical school on campus about one mile from the MURR. This school has a radiology department including diagnostics and therapy. The medical school has a professional staff of 300 faculty and a hospital of 495 beds. The School of Veterinary Medicine is also at the Columbia campus with an excellent staff and animal care facilities.

C. In Columbia Besides the University's medical center, there are five other hospitals and/or cancer research facilities in Columbia. These are Boone Hospital Center, a 334 bed hospital with radiation treatment facilities; Columbia Regional Hospital, a 301 bed hospital with radiation treatment facilities; Ellis Fischel State Cancer Center, a state supported cancer treatment center with 64 beds and radiation treatment facilities; and the Cancer Research Center, a private cancer research institution. These are all within five miles of the MURR. In addition to these facilities, there is, across the street from the University Medical Center, the Harry S. Truman Veterans Administration Hospital, with a nuclear medicine department.

V. OTHER RADIOTHERAPY AND DIAGNOSTICS

The MURR has participated for many years in the development of radioisotopes for diagnostics and therapy. For many years the MURR supplied the most widely used diagnostic radioisotope precursor, Mo-99, and in fifteen years delivered over a million Curies. Recently the MURR has been actively developing and supplying new radioisotope generator designs. The new gel generator designs for the Mo-99/Tc-99m and Sn-113/In-113m systems developed at MURR are uniquely suitable for efficient, inexpensive production of medical generators and for their widespread distribution in large, developing countries such as China. We have recently heard from our Chinese contact and both of these generators are now in use in China. In addition, MURR produces isotopes for the quantitation of osteoporosis (calcium loss in bone) and for basic studies of the cause and treatment of hypertension and cystic fibrosis. Researchers at MURR have also participated in the development of a new ^{99m}Tc diagnostic nuclear medicine agent for measuring blood flow in the brain that is now being marketed by Amersham.

For a number of years MURR has provided iridium seeds for the radiotherapeutic treatment of cancer, and has also supplied isotopes such as Re-186 for research into radiotherapy using tumor-specific bone and antibody agents. The Re-186 phosphonate bone agent, for example, will help to relieve the often intractable pain associated with bone metastases from breast, lung and prostate cancer, and may serve to reduce the size of such bone tumors. This and similar agents may also effectively eliminate micrometastases to bone in cancer patients before they become detectable by other means, thus serving as a prophylactic treatment.

Currently at least seven different reactor produced isotopes are under investigation at MURR for such varied uses as the treatment of metastatic liver cancer using Y-90 glass microspheres, therapy to palliate the pain of bone cancer, radiotherapy of tumors using labeled antibodies, and radiation treatment of rheumatoid arthritis. Two of these radiotherapeutic drugs have been submitted to the FDA for Investigational New Drug exemptions to permit human trials, and a third is nearing that stage, with the rest at earlier stages of active development. The use of reactor-produced beta-emitters for radiotherapy is on the verge of a great expansion in which MURR will play an important role. The MURR has a proven track record of development of methods for cancer diagnosis and therapy.

VI. CONCLUSIONS

The effectiveness of an Al_2O_3 moderator and a ^{238}U filter have been evaluated to see whether either could produce a beam of intermediate energy neutrons starting with the flux of the MURR. The Al_2O_3 moderator looks very promising yielding a current of $> 10^9$ intermediate energy neutrons at the patient position but very few fast neutrons or gamma rays. The ^{238}U filter is also promising, with fluxes of intermediate energy neutrons near 10^9. Either or both such beams could be implemented at MURR once MURR is given the go ahead.

ACKNOWLEDGMENTS

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REFERENCES

1. Proceedings of the Second International Symposium on Neutron Capture Therapy, Teikyo University, Tokyo, October 18-21, 1985, ed. H. Hatanaka, Nishimura-Elsevier, Japan-Holland (in press).

2. S. Glasstone and A. Sesonke, Nuclear Reactor Engineering, page 112, Van Nostrand Reinhold Co., New York, NY (1967).

3. A.B. Chilton, J.K. Shultis, and R.E. Faw, Principles of Radiation Shielding, chapters 5, 6, 7, Prentice-Hall, Englewood Cliffs, NJ (1984).

4. W.H. Miller and R.M. Brugger, Additional Experimental Tests of the Bonner Sphere Neutron Spectrometer, Nucl. Instrum. and Meth., A236(1985)333.