Radiol Oncol 1999; 33(1): 69-75.

# Epithermal neutron beam for BNCT at the JSI TRIGA reactor – modelling and experimental verification

**Marko Maučec, Bogdan Glumac, Jože Rant, Edvard Krištof**

*Jožef Stefan Institute, Reactor Physics Division, Ljubljana, Slovenia*

*It has been reported that satisfactory thermal/epithermal neutron beams for Boron Neutron Capture Therapy (BNCT) could be designed at TRIGA research reactors, which are generally perceived as being safe to install and operate in populated areas. This contribution presents the most recent research activities in this field at the Jožef Stefan Institute TRIGA reactor, where an epithermal neutron beam for BNCT is being developed. Experimental verification of Monte Carlo simulation results proves the quality and wide applicability of the developed 3-D model, particularly of the reactor core and irradiation channels. Due to high attenuation of the epithermal neutron flux ($\Phi_{epi} = 4.1 \times 10^6$ n/cm$^2$s, two orders of magnitude below the therapeutic limit) the irradiation facility in the current stage of development is not appropriate for the clinical BNCT treatments. Furthermore, the contribution of the 2.5 mm air gap surrounding the facility is unacceptably high, thus making the relative gamma dose ($D\gamma/\Phi_{epi}$) almost 60-times higher than therapeutically recommended. Nevertheless, using gamma shielding of Pb or Bi and LiF or $Li_2CO_3$ (thermal neutron cut-off), the quality of the epithermal neutron beam would be significantly upgraded and become appropriate for in vitro studies of boron compound transport in malignant tumour cells or smaller laboratory animals.*

*Key words: boron neutron capture therapy; neoplasms-radiotherapy; nuclear reactors*

## Introduction

Boron Neutron Capture Therapy (BNCT)[1] is a bimodal treatment that offers the potential of a highly selective radiation effect - by α particles - while sparing normal tissues. Brain tumours, particularly glioblastoma multiforme (GBM), were chosen as the initial target for BNCT. GBM is an extremely lethal cancer, with no significant advances in therapy in the last two decades. Almost all patients die within two years, even with the best efforts using surgery, external beam therapy and chemotherapy.[1,2]

The central feature in effective BNCT is the selective delivery, concentration and build-up of the naturally occurring 10B isotope in tumour tissue, using one or more advanced drug delivery systems (DDS) such as monoclonal antibody carriers or liposomal deliveries.[3-5] As the tumour is irradiated with low energy neutrons (epithermal neutrons

Received 5 October 1998
Accepted 10 December 1998

Correspondence to: Marko Maučec, MSc, Jožef Stefan Institute, Reactor Physics Division, Jamova 39, POB 3000, 1001 Ljubljana, Slovenia. E-mail: marko.maucec@ijs.si

with 0.4 eV<E<10 keV become thermalized in the surrounding healthy tissue), there is a higher likelihood of the $^{10}B$ nucleus absorbing them than the nuclei of any other elements normally present in tissues. The boron nucleus become unstable and immediately splits into two recoiling ionizing particles, an particle (i.e., a helium nucleus) and a lithium nucleus:

$$n + {}^{10}B \rightarrow {}^{11}B^* \rightarrow {}^{4}He + {}^{7}Li + \gamma$$

These products of the BNCT reaction - $^{10}B(n,\alpha)^7Li$ - are very damaging to tissue, but of short range (the pathlength of particles is about one cell diameter, which is around 10 μm) and are confined to the immediate vicinity of the boron-containing compound which, hopefully, should be concentrated in the tumour. A major appeal of BNCT is that $^7Li$ and energetic α particles are produced by a fission reaction following neutron capture. These heavy particles carrying 2.79 MeV of energy, have a very high ionization density. Another advantage is that they can affect dividing and nondividing tumour cells alike - tumours are known to have a large number of viable but nonactive cells.

Up to the present NCT research in Slovenia has been carried out in a provisional irradiation system, consisting of a „dry cell" adjacent to the thermalizing column (Figure 1) at Jo_ef Stefan Institute (JSI) 250 kW TRIGA Mark II research reactor. The „dry cell" (originally a pool-type storage facility) is a unique advantage of the JSI TRIGA reactor, with approx. ground plan dimensions of 3x3 $m^2$ and additional neutron protection, currently refurbished for experimental purposes. The radiative field cross-section of the thermalizing column is approx. 60x60 $cm^2$, and is rather homogene due to the substantial distance from the core fuel elements. The irradiation field of the experimental set-up is approx. 10x10 $cm^2$, thus enabling irradiation of 9 foils with specimens at the time. The experimental set-up is mainly used for *in vitro* studies in a mixed neutron/gamma irradiation field, with the aim of determining the radiosensitivity of two cell lines: mouse B16F1 melanoma and human MCF7 breast carcinoma.[6,7]

Unfortunately, the contribution of fast neutrons (18.4%) as well as γ-rays (23%) to the total effective dose in the current experimental system is substantial.[6] Since this has a strong negative influence on the verification of $^{10}B$ or thermal neutron effects, as well as on the mortality of prepared cell cultures, the development of an irradiation facility with optimized beam properties (minimised fast neutron and gamma dose and maximised epithermal neutron flux) is indispensable. Hence Monte Carlo modeling, development as well as experimental verification of the epithermal neutron beam in the radial channel of the JSI TRIGA reactor is presented in this paper.

## Methods

### *Monte Carlo modeling of the BNCT irradiation facility in the radial channel of the TRIGA reactor*

The general purpose MCNP4B Monte Carlo code was used for modeling of the TRIGA reactor, together with the ENDF/B-V and ENDF/B-VI continuous cross-section libraries and S(α,β) scattering data from the ENDF/B-IV file.[8] n/γ transport was performed using geometry splitting, weight window (WWG) and direct statistical approach (DSA) variance reduction techniques.[8,9]

A detailed Monte Carlo model of the TRIGA Mark II research reactor has been developed, where all important details concerning the reactor core, graphite reflector, thermal and thermalizing column, irradiation channels and biological shielding were considered (Figure 1). The original TRIGA core

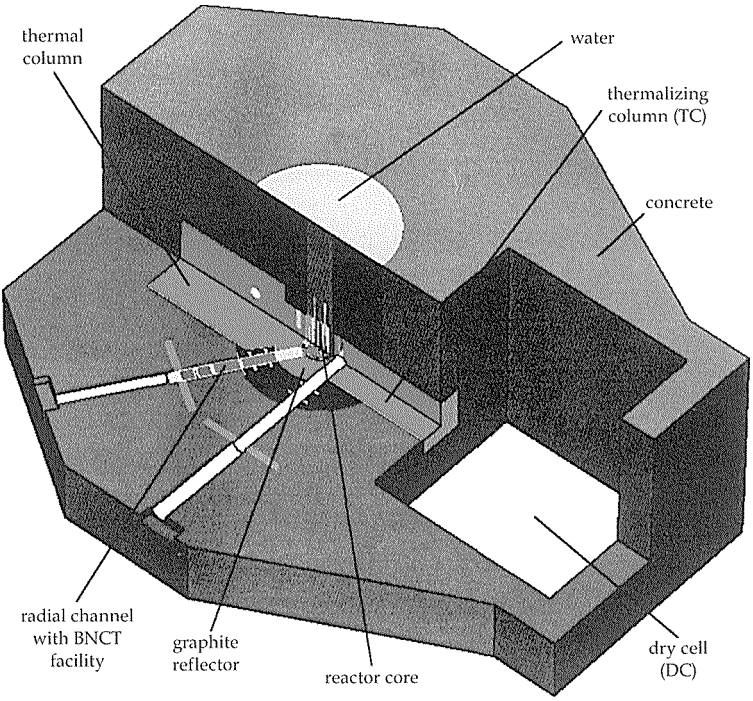


**Figure 1.** 3D Monte Carlo model of the JSI TRIGA Mark II research reactor.

configuration No. 147 was modified in such a manner that three fuel elements were positioned at the inlet of the radial channel. With this set-up (based on an MCNP TRIGA benchmark model[11]), which considered 50 fresh fuel elements with multiplication factor keff being 1.0100 ± 0.0017, the total neutron flux was enhanced by 40%, with a negligible change of neutron spectrum.[10]

On the basis of an extensive Monte Carlo pilot study of epithermal neutron filter and gamma shielding materials, the final configuration of the BNCT irradiation facility was elaborated, consisting of the following elements (Figure 2):[12,13]

- 30 cm Al + 40 cm $Al_2O_3$ (with a density of 2.3 g/cm$^3$, which can be achieved by pressing the $Al_2O_3$ powder (initial density is 1.6 g/cm$^3$) at 400-500 kg/cm$^2$) in a single piece, used as epithermal neutron filter,
- an additional 30 cm $Al_2O_3$ with 0.05 cm of Cd foil, used as a thermal neutron absorber,
- 15 cm Pb, used as a gamma shield and
- 15 cm Pb + 15 cm borated paraffin (90 vol. % $C_{30}H_{62}$ + 10 vol. % boric acid $H_3BO_3$), as additional neutron/gamma shield.

All the elements are cylindrically shaped and equipped with six small stainless steel wheels to enable unrestrained transport through the channel. In addition to numerous benefits offered by this design - easy handling and transportation of filter elements, as well as storage after irradiation - it has one major drawback: an approx. 2.5 mm air gap, leading directly from the reactor core to the irradiation point, thus allowing fast neutrons and gamma rays to stream through the gap and contributing significantly to the total dose. When the calculations were repeated using the MC model without the air gap, the fast neutron and gamma doses were reduced by more than 80%! The results of Monte

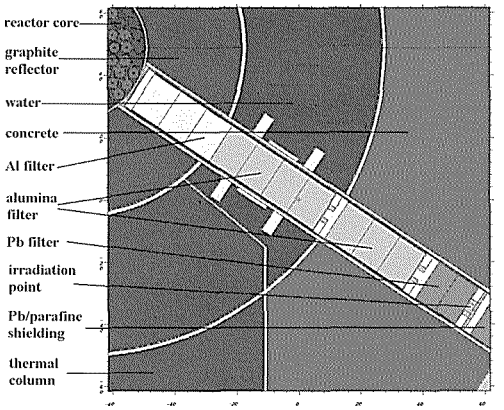


**Figure 2.** MCNP model of the BNCT facility inserted in the radial channel (units in cm).

Carlo calculations at the irradiation point (Figure 2) are presented in Table 1.

*Experimental verification*

Based on the results of MC calculations, the irradiation facility for BNCT treatment was manufactured. The details of elaboration were presented in more detail.[13] The measurements of neutron flux and mixed n/γ field dosimetry were performed with a set[13] of $^{115}$In and $^{197}$Au (n,γ) activation detectors for the thermal and epithermal range. A Cd cover (thickness 0.5 mm) was used in order to determine the cadmium ratio of the field. The integral fluxes in the fast neutron range were measured with the following threshold reactions: $^{115}$In(n,n′)$^{115m}$In, $^{27}$Al(n,p)$^{27}$Mg, $^{56}$Fe(n,p)$^{56}$Mn, $^{64}$Zn(n,p)$^{64}$Cu, $^{24}$Mg(n,p)$^{24}$Na, $^{27}$Al(n,α)$^{24}$Na and $^{19}$F(n,2n)$^{18}$F. Pure metallic foils (In, Al, Fe, Zn and Mg) as well as Teflon™ ($CF_2$) were irradiated with Cd covers. Gamma dose was measured using a set of TLD detectors on the central axis of the channel. In order to absorb the radiation from electrons and soft X-rays from the outside and to affirm the reproducibility of the results, the set was confined in a 1 cm thick holder made of plexiglass. To obtain the neutron spectrum (Figure 3), the detector responses were adjusted with the SAND-II deconvolution code.[14] The systematic error of the experiment was estimated to be less than 3%. The standard deviation over the entire spectrum of detector saturated activities was less than 2%.

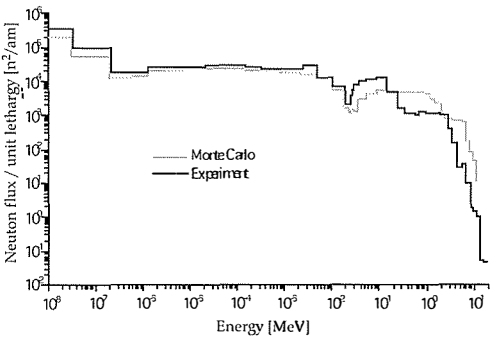


**Figure 3.** Calculated vs. measured neutron flux per unit lethargy.

## Results

Experimental results confirmed 10% higher epithermal neutron flux $\Phi_{epi}$ (0.4 eV < E < 10 keV) at the irradiation point than MC calculated one. This remains two orders of magnitude below the recommended therapeutic limit of $10^9$n/cm$^2$s, thus dictating quite long irradiation times.

Furthermore, the experiment confirmed a surplus of thermal neutrons (E<0.4 eV) ($\Phi_{term}/\Phi_{epi}$ = 1.85 for Monte Carlo calculations results and 1.75 for the experiment). This can be attributed to thermal neutrons that arrive at the irradiation point from surrounding regions, *i.e.* the water and concrete of the reactor biological shield (those emerging from the neutron beam itself were cut-off with the 0.5 mm thick Cd absorber). The measured neutron spectrum (Figure 3) conforms the calculated one; discrepancies emerge only in the fast part of the spectrum (above 10 keV) but still remain within the 10% confidence interval of the Monte Carlo calculated total fast neutron flux.

**Table 1.** Results of MC calculations vs. experiment

| Quantity[c] | Method | | Trerapeutic |
|---|---|---|---|
| | Monte Carlo[a] | Experiment[b] | limit values |
| $\Phi_{nterm}$ (E<0.4 eV) | 6.95e+6 (15) | 7.1e+6 (+10) | / |
| $\Phi_{nepiter}$ (0.4 eV<E<10 keV) | 3.75e+6 (12) | 4.1e+6 (+20) | $>10^9$ |
| $\Phi_{nfast1}$ (10 keV<E<300 keV) | 3.86e+5 (17) | 8.7e+5 (+10)d | / |
| $\Phi_{nfast2}$ (300 keV<E<20 MeV) | 4.83e+5 (15) | / | / |
| $J_{epiter}$ | 2.55e+6 (12) | / | $>5*10^8$ |
| $D_{nfast}$ | 7.04e+6 (13.8) | 7.4e+6 (+15) | / |
| Dγ | 6.07e+7 (11.7) | 8.1e+7 (+45) | / |
| $D_{nfast}/\Phi_{nepiter}$ | 19 | 18 | <5 |
| $D\gamma/\Phi_{nepiter}$ | 162 | 197 | <3 |
| $J_{epi}/\Phi_{epi}$ | 0.68 | / | >0.5 |

[a] -( ) - relative errors in %

[b] - ( ) - discrepancy from Monte Carlo results in %

[c] - units: $\Phi_n$ and - [n/cm$^2$s], $D_{nfast}$ and Dγ - [$10^{-12}$ Gy s$^{-1}$], $D_{nfast}/\Phi_{nepiter}$ and $D\gamma/\Phi n_{epiter}$ - [$10^{-13}$ Gy cm$^2$]

[d] - fast neutron flux, measured in a single energy group (10 keV<E<20 MeV)

To determine the influence of the air gap surrounding the filter configuration on the neutron and gamma dose, the profiles of the neutron and gamma fields were measured using photo-luminescence imaging plates (IP) with a 0.1 mm thick dysprosium screen, frequently used in the direct method of neutron radiography. The imaging plate is exposed with the neutron-activated Dy foil and later scanned with a laser reader. The gamma beam profile at the outlet of the radial channel is presented in Figure 4.

The experimentally measured gamma dose exceeds the calculated one by 33%, thus making the relative gamma dose ($D\gamma/\Phi_{epi}$ in units of $10^{-13}$ Gy cm$^2$) unacceptably high and almost 60-times higher than therapeutically recommended. The contribution of the 2.5 mm air gap is most clearly evident from Figure 5: the gap region is approximately 30-times more irradiated than the filter-covered region in relative PSL (Photo Stimulated Luminescence) units as a function of the spatial co-ordinate.

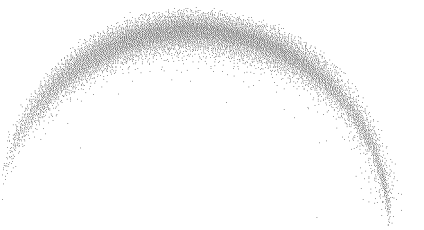

**Figure 4.** The profile of the gamma profile field at the outlet of the channel ($P_{reactor}$ = 2kW, $T_{irrad}$ = 500s).

## Discussion

Experimental verification of the BNCT irradiation facility at the JSI TRIGA reactor proves the quality and wide applicability of the developed 3-D Monte Carlo model, particularly of the reactor core and irradiation channels. The model can easily be extended for the purposes of Prompt Neutron Gamma Activation Analysis (PNGAA), Proton Recoil Spectrometry and

many other activities. It is accurate enough to enable agreement with the experimentally obtained results within the confidence intervals of the Monte Carlo calculations.

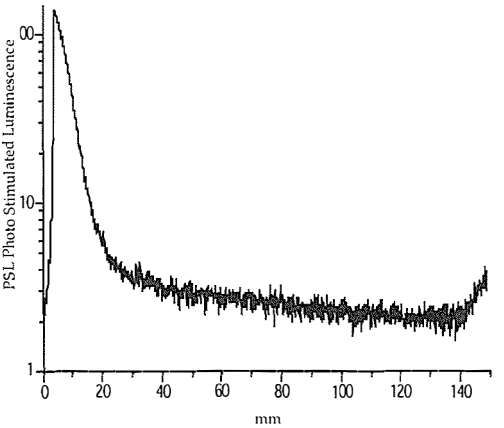


**Figure 5.** Numerical profile of the gamma field in relative PSL units (vertical cross-section of Figure 4).

In the current stage of development, the irradiation facility is not appropriate for clinical BNCT treatments. Due to high attenuation of the epithermal neutron flux, we were obliged to alter the initial design of the facility so as to move the irradiation point from the outlet of the radial channel to the interior immediately behind the lead gamma filter. This makes our radiation facility appropriate for *in vitro* studies of novel techniques of boron entrapment in malignant tumour cells (i.e. by application of electroporation[15,16]) or *in vivo* irradiation of smaller laboratory animals. Using stop (or shelter) made of Pb or Bi (gamma shielding) and LiF or $Li_2CO_3$ (thermal neutron cut-off), the influence of the air-gap on the irradiation point would be significantly reduced, thus increasing the quality of the epithermal neutron beam.

This work represents the first stage of the BNCT research project in Slovenia leading, hopefully, towards further development of a clinical irradiation facility for BNCT treatment of human patients in the thermalizing[17] or thermal column of the Jožef Stefan Institute TRIGA reactor.

## Acknowledgements

The authors would like to express special thanks to dr. Kenneth W. Burn from ENEA, Bologna, Italy for extensive help with the variance reduction method DSA for the Monte Carlo calculations, and to dr. Anthony R. Byrne, Jožef Stefan Institute, Ljubljana, for a thorough review of this paper.

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