

# A Small-Animal Irradiation Facility for Neutron Capture Therapy Research at the RA-3 Research Reactor

## 2007 ANS/ENS International Meeting

Emiliano Pozzi  
David W. Nigg  
Marcelo Miller  
Silvia I. Thorp  
Amanda E. Schwint  
Elisa M. Heber  
Veronica A. Trivillin  
Leandro Zarza  
Guillermo Estryk

November 2007

This is a preprint of a paper intended for publication in a journal or proceedings. Since changes may be made before publication, this preprint should not be cited or reproduced without permission of the author. This document was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, or any of their employees, makes any warranty, expressed or implied, or assumes any legal liability or responsibility for any third party's use, or the results of such use, of any information, apparatus, product or process disclosed in this report, or represents that its use by such third party would not infringe privately owned rights. The views expressed in this paper are not necessarily those of the United States Government or the sponsoring agency.

The INL is a  
U.S. Department of Energy  
National Laboratory  
operated by  
Battelle Energy Alliance



# A Small-Animal Irradiation Facility for Neutron Capture Therapy Research at the RA-3 Research Reactor

Emiliano Pozzi<sup>1</sup>, David W. Nigg<sup>2</sup>, Marcelo Miller<sup>1</sup>, Silvia I. Thorp<sup>1</sup>, Amanda E. Schwint<sup>1</sup>, Elisa M. Heber<sup>1</sup>,  
Veronica A. Trivillin<sup>1</sup>, Leandro Zarza<sup>1</sup>, Guillermo Estryk<sup>1</sup>

1. *Comisión Nacional de Energía Atómica, Buenos Aires, Argentina*
2. *Idaho National Laboratory, P.O. Box 1625, Idaho Falls ID 83415 USA.*

## INTRODUCTION

The National Atomic Energy Commission of Argentina (CNEA) has constructed a thermal neutron source for use in Boron Neutron Capture Therapy (BNCT) applications at the RA-3 research reactor facility located in Buenos Aires. The Idaho National Laboratory (INL) and CNEA have jointly conducted some initial neutronic characterization measurements for this source.

The RA-3 reactor (Figure 1) is of the open pool type, with 20% enriched uranium plate fuel and light water coolant. A graphite thermal column is situated on one side of the reactor as shown. A tunnel penetrating the graphite structure enables the insertion of samples while the reactor is in normal operation. Samples up to 14 cm height and 15 cm width are accommodated.

## METHODS AND MATERIALS

RA-3 is being considered for small-animal radiobiological studies, at first using an animal model based on induced tumors of the oral mucosa in the hamster cheek pouch [1, 2]. Shielding of the body of the animal from the thermal neutron flux while exposing the everted cheek pouch is accomplished using an enclosure fabricated from plates composed of a 6 mm layer of lithium carbonate enriched to 95% in lithium-6 sealed between thin sheets of Lucite™ (Figure 2). A Lucite phantom of the shape and size of a typical Syrian hamster is shown in position in the shield enclosure. With an actual animal, the cheek pouch is everted onto the protruding shelf on one end of the shield, which is placed in the irradiation cavity with the pouch shelf on the upstream side.

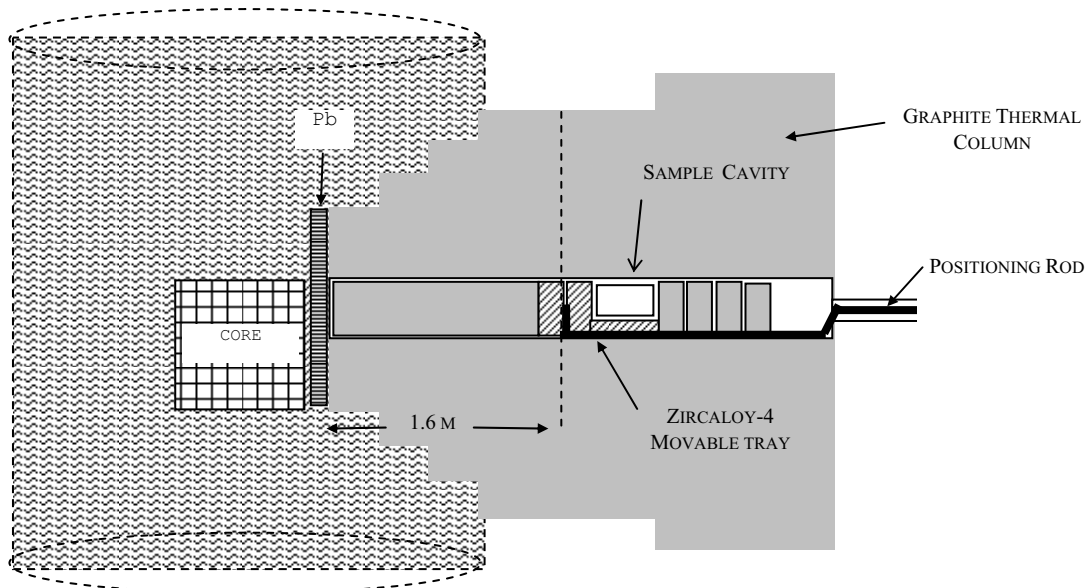


Figure 1. RA-3 reactor and thermal column.



Figure 2. Thermal neutron shielding enclosure with hamster phantom.

Measurements of the neutron flux at the irradiation location were performed using simplified extensions of neutron activation techniques [3] that have been adapted for BNCT applications by the INL. All irradiations were conducted at a reactor power of 8 MW.

The free-field neutron flux spectrum at the irradiation location, without the shield enclosure, was characterized using foils composed of: 1) bare gold, 2) gold, indium, tungsten, manganese and copper enclosed in cadmium and, 3) indium enclosed in boron-10. This provided 7 linearly-independent spectral response functions covering the energy range from thermal to about 1 MeV.

Measurements to determine the spatial distribution of the thermal and above-thermal neutron flux at 12 locations on the surface of, and within, the hamster phantom and at three locations on the pouch shelf were based on activation of copper-gold flux wires approximately 7 mm in length and 1 mm in diameter. Each wire had a mass of approximately 70 mg and was composed of copper alloyed with 1.55 percent gold by weight. This provided two linearly-independent activation responses (neutron capture in Cu-63 and Au-197).

## RESULTS

The measured activities were used to unfold 2-group neutron spectra using an overdetermined least-square fitting method [3] with effective cross sections for the foils and wires computed using the MCNP [4]

code with a graphite moderated fission source spectrum. With the foils this procedure yielded a free-field thermal flux of  $7.1 \times 10^9$  n/cm<sup>2</sup>-s and a fast flux of  $2.5 \times 10^6$  n/cm<sup>2</sup>-s, with estimated uncertainties of approximately 6% ( $1\sigma$ ). The cadmium ratio for the gold foils was approximately 4100, indicating a very well-thermalized neutron field, with negligible radiation dose component from hydrogen recoil in tissue.

In the case of the phantom, the thermal neutron flux at the outermost position on the pouch shelf was  $5.4 \times 10^9$  n/cm<sup>2</sup>-s, with an uncertainty of approximately 8%. This is about 25% lower than is the case for the free-field flux at this location, and is largely due to local flux depression by the shield enclosure. The wire measurements also show that the thermal neutron flux at all locations within the shield container is at least a factor of 20 lower than the flux on the shelf. This implies that the boron dose to the whole body will be correspondingly smaller relative to the dose in the target tissue, conservatively assuming the same boron concentration in all tissues.

## DISCUSSION

RA-3 should be a useful irradiation facility for BNCT-related small-animal studies. The fast-neutron dose will be insignificant compared to the thermal-neutron induced boron neutron capture dose in the presence of clinically-relevant (~30 ppm) quantities of <sup>10</sup>B. The absolute thermal flux magnitude is sufficient to conduct irradiations achieving clinically useful BNCT target tissue dose levels in times of 30 minutes or less. The lithium shielding should reduce whole-body boron and nitrogen capture doses to acceptable levels.

Efforts are ongoing to characterize the incident gamma field within the enclosure and to develop appropriate procedures for management of tritium produced in the shield enclosure. This will be followed by normal-tissue radiation tolerance measurements and, ultimately, various small-animal BNCT radiobiological research studies.

## ACKNOWLEDGEMENTS

INL participation in this work was sponsored by the United States Department of Energy, National Nuclear Security Administration Sister Laboratory Program via DOE Idaho Operations Office Contract DE-AC07-05ID14517.

## REFERENCES

1. E.L. KREIMANN, M.E. ITOIZ, A. DAGROSA, R. GARAVAGLIA, S. FARIAS, D. BATISTONI, A. SCHWINT, The Hamster Cheek Pouch as a Model of Oral Cancer for Boron Neutron Capture Therapy Studies: Selective Delivery of Boron by boronophenylalanine, *Cancer Research* **61**: 8775-8781 (2001).
2. V.A. TRIVILLIN, E.M. HEBER, D.W. NIGG, M.E. ITOIZ, O. CALZETTA, H. BLAUMANN, J. LONGHINO, A. SCHWINT, Therapeutic success of Boron Neutron Capture Therapy (BNCT) mediated by a chemically non-selective boron agent in an experimental model of oral cancer: A new paradigm in BNCT radiobiology, *Radiation Research* **166**: 387-396 (2006).
3. D.W. NIGG, C.A. WEMPLE, R. RISLER, J.K. HARTWELL, Y.D. HARKER, G.E. LARAMORE, Modification of the University of Washington Neutron Radiotherapy Facility for Optimization of Neutron Capture Enhanced Fast-Neutron Therapy, *Med. Phys.* **27**:359-367, 2000.
4. J.F. BREISMEISTER, "MCNP – A General Monte Carlo N-Particle Transport Code", Version 4C, LA-13709-M, Los Alamos National Laboratory, USA (2000).