

An epithermal facility for treating brain gliomas at the TAPIRO reactor

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Abstract

An epithermal facility for treating patients with brain gliomas has been designed and is under construction at the fast reactor TAPIRO at ENEA Casaccia (Italy). The calculational design tools employed were the Monte Carlo codes MCNP/MCNPX together with the DSA in-house variance reduction patch. A realistic anthropomorphic phantom (“ADAM”) was included to optimise dose profiles and in-phantom treatment-planning figures-of-merit. The adopted approach was to minimise the treatment time whilst maintaining a reasonable therapeutic ratio. It is shown that TAPIRO, in spite of its low power of 5 kW, is able to provide an epithermal beam that is of good quality and of sufficient intensity to allow a single beam patient irradiation, under conservative assumptions, of 50 min.

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Keywords: Fast reactor; Epithermal column; Monte Carlo; MCNP; Anthropomorphic phantom; Therapeutic figures-of-merit

1. Introduction

TAPIRO at ENEA (Casaccia) is a 5 kW fast reactor with a small, highly enriched, core currently operating an experimental epithermal BNCT facility for phantom irradiations within the biological shield (Agosteo et al., 2003). To treat patients, the neutron beam had to be conducted outside the biological shield, a further 143 cm from the present irradiation position at 119 cm from the core centre, involving a total redesign of the column.

2. Materials and methods

Monte Carlo was used to model the neutron and photon transport in the core, epithermal column and phantom. We employed an in-house variance reduction

optimiser (the “DSA”) (Burn et al., 2000) which is currently patched to MCNP4B (Briesmeister, 1997) and MCNPX2.1.5 (Waters, 1999). Fixed source calculations were executed starting from the fission source spatial distribution in the core (4.23×10^{14} neutrons/s).

The feasibility of treating patients was firstly established by calculating the free beam parameters that provided an immediate comparison with beams of other facilities. Subsequently, a realistic anthropomorphic phantom, “ADAM” (Kramer et al., 1982), was employed to optimise the dose profiles and the following in-phantom treatment-planning figures-of-merit: advantage depth (AD) and therapeutic depth (TD) (depths at which the tumour dose falls below 1 and 2 times the maximum healthy tissue dose respectively), peak therapeutic ratio (PTR), advantage depth dose rate (ADDR) (i.e. the maximum healthy tissue dose), treatment time. We adopted a reasonably wide collimator aperture ($10 \times 14 \text{ cm}^2$ as already employed at Studsvik) and placed ADAM in the most common side-of-cranium irradiation position. The material compositions, ^{10}B

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concentrations and dosimetric conversion factors followed generally accepted standards for BPA and brain gliomas (Zamenhof, 2002). RBE factors of 3.2 and 1.0 were employed for neutrons (at all energies) and γ 's, respectively; a mean high LET energy release of 2.34 MeV per $^{10}\text{B}(n,\alpha)^7\text{Li}$ reaction was assumed; the material compositions in the cranium were defined by ICRU-46 (International Commission on Radiation Units and Measurements, 1992). The ^{10}B concentrations were 15 $\mu\text{g/g}$ for skin, 10 $\mu\text{g/g}$ for tissue under skin and normal brain tissue and 35 $\mu\text{g/g}$ for tumour brain tissue. C/RBE factors were 2.5 for skin and tissue under skin, 1.3 and 3.8 for normal and tumour brain tissue. The ^{10}B concentrations were included in the Monte Carlo transport simulations although such levels of ^{10}B do not perturb the neutron flux. The tumour was not modelled as ^{10}B concentrations of 35 $\mu\text{g/g}$ are still too low to perturb the neutron flux. No ^{10}B was assumed in the skull.

The usual materials employed for epithermal neutron beams were adopted: AlF_3 (1.85 g/cm^3) moderator, nickel reflector, lead collimator, lithiated polyethylene absorber.

3. Results

So as to allow a possible further improvement in the tumour/healthy tissue ^{10}B ratio through optimisation of the time interval between boron introduction and irradiation, we aimed to reduce as much as possible the irradiation time whilst maintaining a reasonable therapeutic ratio. The solution arrived at is shown in Fig. 1. The main characteristics are:

- voiding the window in the outer core reflector so as to increase the fast neutron flux impinging on the AlF_3 epithermal moderator;
- a thickness of 37 cm of moderator;

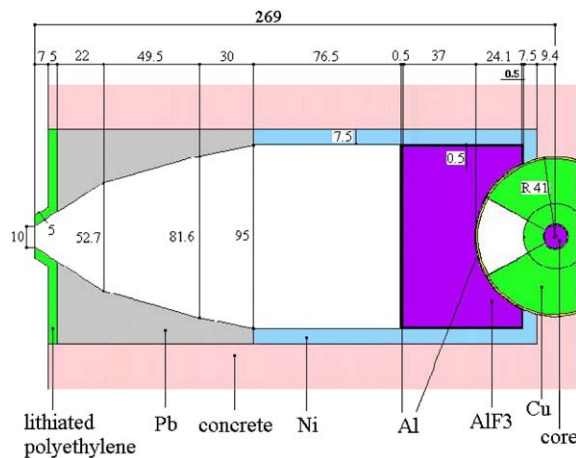


Fig. 1. Section of the epithermal column for patient irradiations (dimensions in cm).

- following the moderator, a cavity of length 76.5 cm surrounded by a relatively thin (7.5 cm) nickel reflector that acts as a discriminating reflecting filter between the fast ($> 10 \text{ keV}$) and epithermal neutron flux (with a higher albedo for the epithermal flux);
- a relatively long (101.5 cm) collimator with a shape that models in a simple fashion a paraboloid followed by a 5 cm thick enriched lithiated polyethylene neutron absorber (as employed, for example, at Espoo);
- a small protruding (7 cm) nozzle to improve the patient's position.

There is no thermal neutron absorber or γ shield within the beam as both contaminations are very low.

The calculated neutron flux spectrum at the collimator aperture is shown in Fig. 2. The calculated standard free beam parameters (averaged over the collimator aperture) are:

Φ_n epith (0.4 eV–10 keV)	$7.99 \times 10^8 \text{ cm}^{-2} \text{ s}^{-1}$
Neutron dose in water $> 10 \text{ keV}/\Phi_n$ epith	$3.38 \times 10^{-13} \text{ Gy cm}^2$
γ whole body dose/ Φ_n epith	$4.12 \times 10^{-13} \text{ Gy cm}^2$
J_n epith/ Φ_n epith	0.73

where the current-to-flux ratio, J_n epith/ Φ_n epith, is a measure of the directionality of the beam (its maximum value is 1 for a mono-directional beam).

Notwithstanding the fact that the fast neutron and γ beam contamination exceed the suggested limits in the literature (IAEA, 2001), the in-phantom results will be seen to be very satisfactory, indicating the importance of the neutron spectrum shape and the limits of such integral quantities.

A section of the ADAM cranium is shown in Fig. 3. The dose was estimated in volume segments of various radial extents around the central axis (the largest radial extent is shown in Fig. 3). The profiles shown in the following figures were obtained by extrapolating to the central axis. In Fig. 4 the single beam dose profiles in healthy tissue (in the whole cranium) and in tumour (only in brain) are shown. Fig. 5 shows the resulting therapeutic ratio (the total tumour dose divided by the maximum healthy tissue dose). Profiles from a bilateral parallel-opposed irradiation are shown in Figs. 6 and 7.

4. Discussion

In Figs. 4 and 6 there are three dose components:

- “neutron” includes both recoil protons and protons from neutron capture in ^{14}N ,

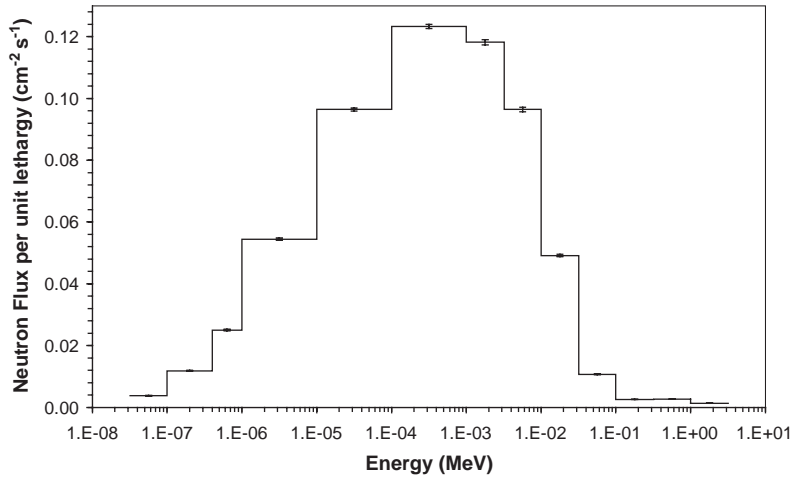


Fig. 2. Neutron flux spectrum calculated at the collimator aperture.

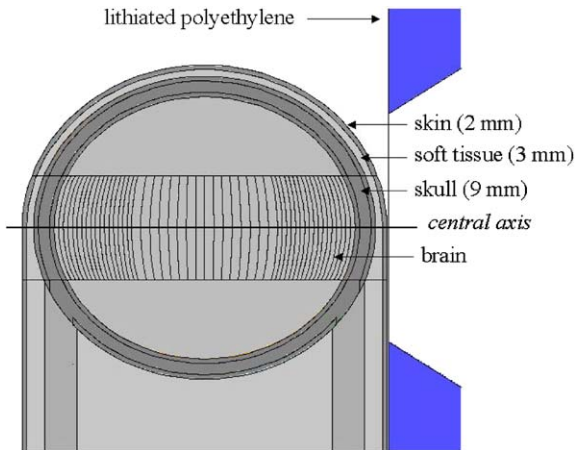


Fig. 3. Section of ADAM cranium with the tally cells. The brain is an ellipsoid with axes 132, 172 and 115mm; it is surrounded by a skull and a scalp consisting of soft tissue and skin.

- “photo-electronic” includes both beam γ 's and γ 's born from neutron capture in the cranium and models the transport of the electrons produced in photon interactions,
- “ ^{10}B ” comprises the high LET products of the $^{10}\text{B}(n,\alpha)^7\text{Li}$ reaction.

For a single beam irradiation, the maximum dose rate to healthy tissue (ADDR) is 0.252 Gy Eq/min situated in the brain near the maximum tumour dose (Fig. 4). Using the constraint of a maximum 12.6 Gy Eq to healthy tissue this implies a treatment time of 50 min. For the two beam irradiation (Fig. 6) the treatment time is 45 min per beam.

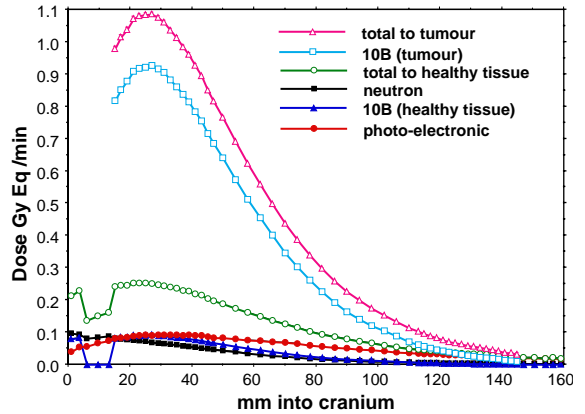


Fig. 4. Dose components to healthy tissue and tumour in ADAM cranium for a single beam.

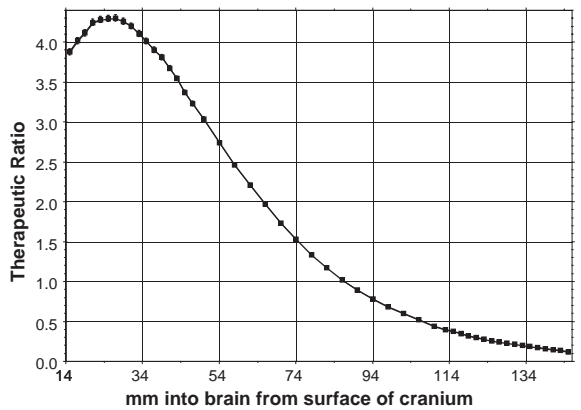


Fig. 5. Therapeutic ratio (tumour dose/maximum healthy tissue dose) in ADAM brain for a single beam.

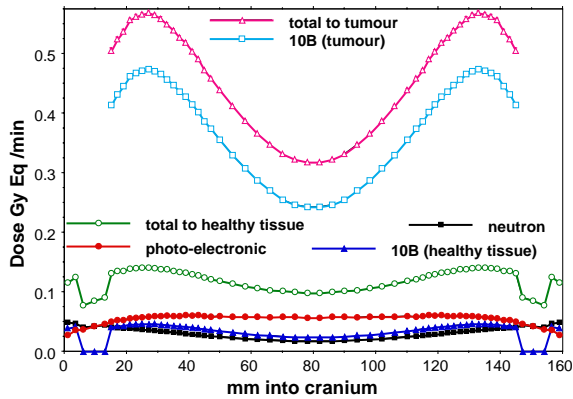


Fig. 6. Dose components to healthy tissue and tumour in ADAM cranium for two parallel-opposed beams.

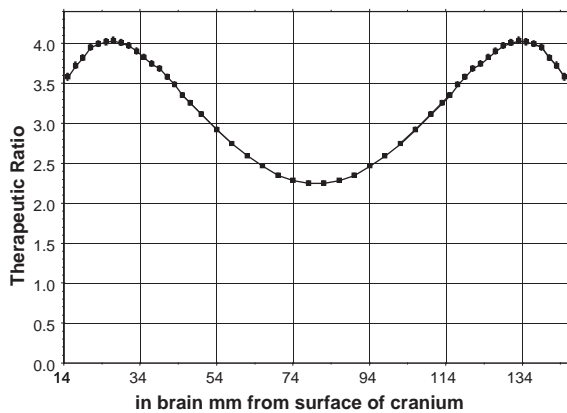


Fig. 7. Therapeutic ratio in ADAM brain for two parallel-opposed beams.

In Figs. 5 and 7 the PTRs are 4.30 and 4.04 for one and two beams, respectively, both at a depth of 13 mm in the brain (27 mm in the cranium). For a single beam the AD and TD are 86 and 66 mm, respectively (measured from the skin surface). In the case of two beams the therapeutic ratio never falls below 2.25. A relative comparison of the various dose contributions together with the position of the maximum dose to healthy tissue indicate that these figures-of-merit are very satisfactory but it must be borne in mind that they are strongly dependent on the hypotheses in the section “Materials and Methods”. For example, the ^{10}B concentration of 10 ppm in healthy brain cells was deliberately chosen to be conservative. More realistic ^{10}B concentrations of 18 ppm in healthy brain cells and 65 ppm in tumour cells (Harling et al., 2002) have also been evaluated. With these ^{10}B concentrations the single beam irradiation results improve as follows: the treatment time reduces from 50 to 39 min, the PTR increases from 4.3 to 5.6, and the AD and TD both increase by 8 mm.

The single beam results are much improved, both in terms of therapeutic ratio and especially of treatment time, compared with those presented previously (see for example (Burn et al., 2002)). This is partly due to improvements in the epithermal column configuration and partly due to the introduction of $S(\alpha,\beta)$ thermal neutron scattering data. However it also results from a simple error in dose normalization, corrected since the previous conference in this series.

At TAPIRO because of the low source strength, filters (e.g. of lithium) may not be employed to harden the spectrum and attempt to increase the penetration depth in the brain as they unacceptably degrade the treatment time. The only handle available to vary the beam is through the thickness of the AlF_3 moderator. Thus a number of aluminium boxes of different depths containing AlF_3 are employed that model a range of moderator thicknesses. Increasing the AlF_3 thickness lowers the dose rate, increases the treatment time but raises slightly the therapeutic ratio and vice versa.

5. Conclusions

TAPIRO can provide a high-quality epithermal beam of sufficient intensity to treat patients with brain gliomas. The epithermal column is currently under construction. All the results presented here are from calculations. Extensive measurements will be required to characterise the facility.

References

- Agosteo, S., Burn, K.W., Casalini, L., Cortesi, M., d’Errico, F., Gambarini, G., Gay, S., Nava, E., Rosi, G., Sarotto, M., 2003. Role of the TAPIRO fast research reactor in neutron capture therapy in Italy. Calculations and measurements. International Conference On Research Reactor, Utilization, Safety, Decommissioning, Fuel and Waste Management, Santiago, Chile.
- Briesmeister, J.F. (Ed.), 1997. MCNP™, A general Monte Carlo N-Particle transport code, version 4B, LA-12625-M.
- Burn, K.W., Gualdrini, G., Nava, E., 2000. Variance reduction with multiple responses. Proceedings of the Conference on Monte Carlo 2000, Lisbon, pp. 687–695.
- Burn, K.W., Casalini, L., Daffara, C., Nava, E., Petrovich, C., Gualdrini, G., Fiorani, O., Perrone, A., Rosi, G., 2002. Design of an epithermal facility for treating patients with brain gliomas at the TAPIRO fast reactor at ENEA Casaccia. Proceedings of the Conference on Research and Development in Neutron Capture Therapy, Essen, pp. 129–134.
- Harling, O.K., Riley, K.J., Newton, T.H., Wilson, B.A., Bernard, J.A., Hu, L.-W., Fonteneau, E.J., Menadier, P.T., Ali, S.J., Sutharshan, B., Kohse, G.E., Ostrovsky, Y., Stahle, P.W., Binns, P.J., Kiger III, W.S., 2002. The Fission Converter-based Epithermal Neutron Irradiation

- Facility at the Massachusetts Institute of Technology Reactor. Nucl. Sci. Eng. 140, 223–240.
- IAEA (International Atomic Energy Agency), 2001. Current Status of Neutron Capture Therapy. IAEA-TECDOC-1223, Vienna.
- International Commission on Radiation Units and Measurements, 1992. Photon, electron, proton and neutron interaction data for body tissue (ICRU Report 46).
- Kramer, R., Zankl, M., Williams, G., Drexler, G. 1982. The calculation of dose from external photon exposures using reference human phantoms and Monte Carlo methods. Part I: the male (ADAM) and female (EVA) adult mathematical phantoms. GSF-Bericht S-885. Gesellschaft für Strahlen und Umweltforschung mbH, Munich, Germany.
- Waters, L.S. (Ed.), 1999. MCNPX™, User's manual, Version 2.1.5. TPO-E83-G-UG-X-00001 Rev. 0 (LANL report).
- Zamenhof, R.G., 2002. Private communication (posted to bncf@listserv.mit.edu, 27/2/2002).