CONVERTING THE EPITHERMAL COLUMN AT THE TAPIRO FAST REACTOR FROM AN EXPERIMENTAL FACILITY TO ONE FOR TREATING PATIENTS WITH BRAIN GLIOMAS

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ABSTRACT

The TAPIRO fast reactor at ENEA (Casaccia) has a relatively low power (5kW compared with typically 1MW of other research reactors converted to BNCT). Notwithstanding, it is shown that TAPIRO is able to provide a high quality epithermal beam for treating patients with glioblastoma that is of sufficient intensity to allow a single beam irradiation of approximately 50 mins. Monte Carlo has been extensively used in the design stage. The characteristic of a low power source (5kW) suggests that the solutions to the design problems may have implications for other limited neutron source NCT facilities. The new epithermal column is currently under construction.

Introduction

TAPIRO at ENEA (Casaccia) is a 5kW fast reactor with a small, highly enriched, core. In one sector, the concrete biological shield and the outer part of the copper reflector have been removed and replaced by an epithermal column currently used as an experimental facility to irradiate samples within the biological shield /1/ (see Figs. 1 and 2). This irradiation chamber is however totally unsuitable for patients due to its size and difficulty of access. To irradiate patients, the beam had to be conducted to outside the biological shield, a further 143 cm from the present irradiation position at 119 cm from the core centre. Furthermore this had to be done without compromising the standard beam parameters whose calculated values for the experimental column were as follows (compared with IAEA targets in brackets /2/):

$\Phi_{n\ epith\ (0.4\ eV - 10\ keV)}$:	9.8×10^{8} n cm^{-2} s^{-1}	(1.0×10^{9})
Neutron dose in water > 10 keV / $\Phi_{n\ epith}$:	5.3×10^{-13} Gy cm^{2}	(2.0×10^{-13})
γ whole body dose / $\Phi_{n\ epith}$:	3.6×10^{-13} Gy cm^{2}	(2.0×10^{-13})
$J_{n\ epith}$ / $\Phi_{n\ epith}$:	0.79	(> 0.7)

Fig.1. View of the TAPIRO reactor.

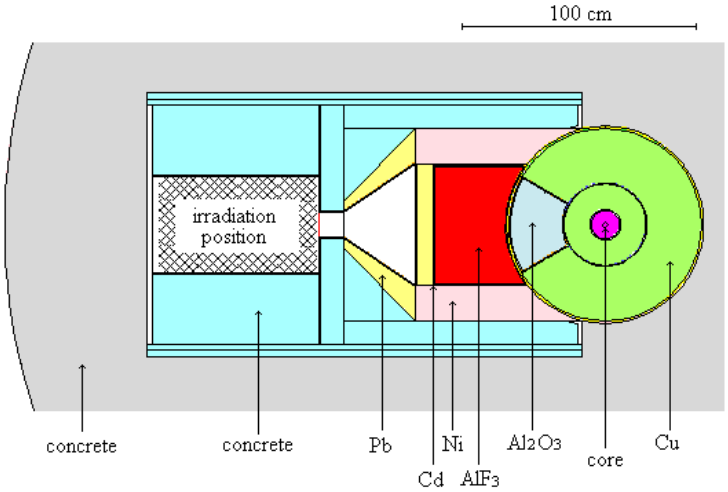

Fig.2. Section of the experimental epithermal column.

Thus clearly the column had to be totally redesigned to maintain the beam parameters to the outside of the shield.

Method

It is well known that designing an epithermal column with Monte Carlo can be extremely time consuming. We employed the in-house Monte Carlo optimizer, the "DSA", that allows the variance reduction parameters to be optimised with respect to several radiation responses simultaneously /3/. The DSA currently uses as vehicles the Monte Carlo codes MCNP4B /4/ or MCNPX2.1.5 /5/. Fixed source calculations were executed starting from the fission source in the core (4.23×10^{14} neutrons/s with a spatial distribution calculated previously in an eigenvalue calculation). To save time, in a first phase the configuration was developed using as criteria the above-mentioned free beam parameters. In a second phase the configuration was fine tuned employing a realistic anthropormorphic phantom ("ADAM" /6/) to calculate dose profiles and the usual in-phantom treatment planning figures-of-merit.

It is worthwhile discussing here the choice of ADAM. Whilst the free beam parameters allow an idea of the feasibility of practicing BNCT and provide an immediate comparison between the beams of different facilities, they do not allow an accurate estimate of the therapeutic figures-of-merit (time, therapeutic ratio, etc.), as they are too integral. However the choice of phantom involves a balance between a more realistic phantom which will give a better idea of the therapeutic figures-of-merit and a simple phantom which may still allow comparisons with other beams. (Furthermore, introduction of a realistic phantom involves choices of material composition, ^{10}B concentrations and C/RBE factors which further mitigate against comparison with other beams.) We erred on the side of a more realistic phantom so as to better predict the single beam therapeutic figures-of-merit. We also chose a reasonably wide collimator aperture: 10×14 cm^2 as employed at Studsvik and placed ADAM in the most common side-of-cranium irradiation position.

The definition of the material composition, ^{10}B concentration and dosimetric conversion factors followed generally accepted standards when using BPA for brain glioma's /7/, that is:

RBE factors of 3.2 and 1.0 were employed for neutrons (at all energies) and for photons respectively; a mean high LET energy release of 2.34 MeV per $^{10}B(n,\alpha)^7Li$ reaction was assumed; the material compositions in the cranium were defined by ICRU-46 (/8/) and the ^{10}B concentrations and C/RBE factors employed were as follows:

Material:	^{10}B (μg/g)	^{10}B C/RBE factors
skin	15	2.5
tissue under skin	10	2.5
skull	0	-
normal brain tissue	10	1.3
tumour brain tissue	35	3.8

The ^{10}B concentrations were included in the materials in the Monte Carlo transport simulations although, as is well known, such levels of ^{10}B do not perturb the neutron flux. The tumour was not modelled as ^{10}B concentrations of 35 μg/g are still too low to perturb the neutron flux.

Results

As will be discussed below, there are a number of therapy parameters and the problem of their joint optimization needs to be defined in some way. The philosophy adopted was to try to reduce as much as possible the treatment time whilst maintaining a reasonable therapeutic ratio. (It will be seen that increasing the dose rate and therefore decreasing the treatment time tends to damage the therapeutic ratio.) The idea here was that as short as possible a treatment time would allow further improvement to be made in the tumour cell/healthy cell ^{10}B ratio, for example by varying the ^{10}B introduction rate and the time interval between end of ^{10}B introduction and irradiation.

The current solution, shown in Fig. 3, exploits the experience of other epithermal BNCT facilities and contains the usual materials known to perform well in this context [aluminium fluoride, nickel, lead, lithiated polyethylene, etc.]. The main characteristics are:

- a thin (5.6 cm) layer of lead in the window in the copper reflector to maintain the criticality level by preferentially reflecting back higher energy neutrons (> 500 keV);
- an AlF_3 moderator (density 1.85 g/cm^3) placed immediately after the window, with a minimum thickness of 31 cm;
- after the moderator, a cavity of length 82.5 cm and of maximum possible radial dimensions, surrounded by a relatively thin (7.5 cm) nickel reflector that acts as a discriminating filter between the fast (> 10 keV) and epithermal neutron flux (with a higher albedo for the epithermal flux);
- a relatively long (101.5 cm) lead 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 at Espoo);
- a small protruding (7 cm) nozzle to improve the patient's position.

Note that there is no thermal neutron absorber (the thermal neutron flux in the column is very low as it is a fast reactor). Also there is no γ shield: there is a background γ flux originating in the column and impinging on the phantom but firstly it is low compared with the γ flux created from neutron captures within the cranium itself and secondly a γ shield lowers the therapeutic neutron flux impinging on the cranium. The standard free beam parameters (calculated averaged over the collimator aperture) are as follows:

$\Phi_{\text{n epith (0.4 eV – 10 keV)}}$:	8.0×10^{8} n cm^{-2} s^{-1}
Neutron dose in water > 10 keV / $\Phi_{\text{n epith}}$:	4.1×10^{-13} Gy cm^2
γ whole body dose / $\Phi_{\text{n epith}}$:	3.5×10^{-13} Gy cm^2
$J_{\text{n epith}}$ / $\Phi_{\text{n epith}}$:	0.73

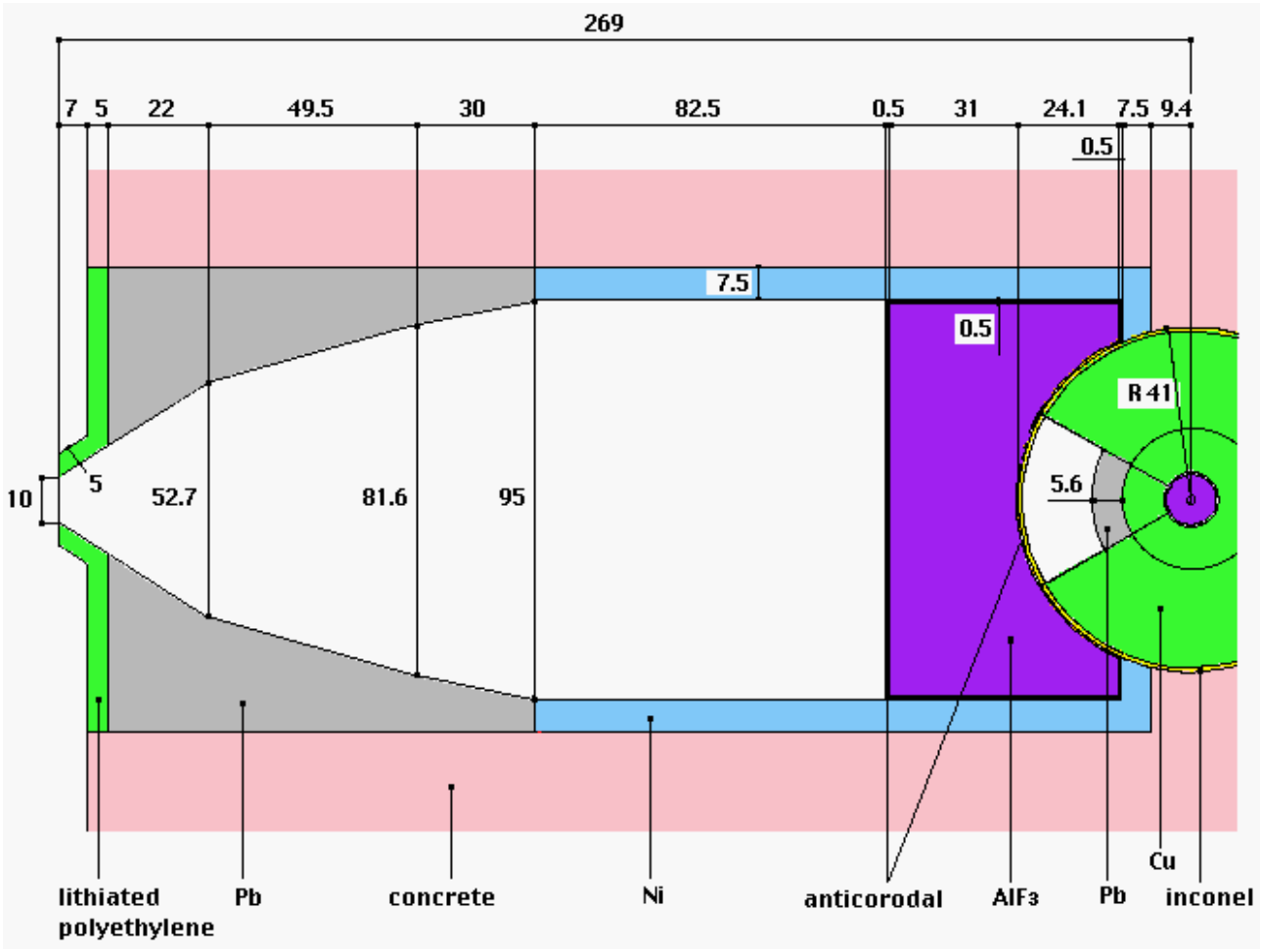

Fig.3. Section of the epithermal column for patient irradiations (dimensions in cm).

The seemingly high neutron and γ background doses in the free beam compared with the IAEA recommendations resulted from the optimization of the dose profiles in the phantom. (It seems that the variation of the neutron energy spectrum within the range: 0.4 eV – 10 keV is critical and is hidden when only the free beam parameters are considered.) Of course the dose profiles are the real result of interest.

Fig. 4 shows a 3-D image of the epithermal column with the ADAM phantom in the side-of-cranium irradiation position. A section of the cranium is in Figs. 5 and 6, the former with the tally cells for the various dose components, the latter showing some radiation simulations. The dose profiles in healthy tissue are shown in Figs. 7a and 7b. Fig. 7c includes the dose to a tumour (which has a meaning only in the brain although values are also shown in the scalp and the skull) and Fig. 7d shows the therapeutic ratio defined by us as the dose to the tumour divided by the maximum dose to healthy tissue. Note that in Fig. 7d the depths are in the brain whilst in the other three figures, the depths are in the cranium.

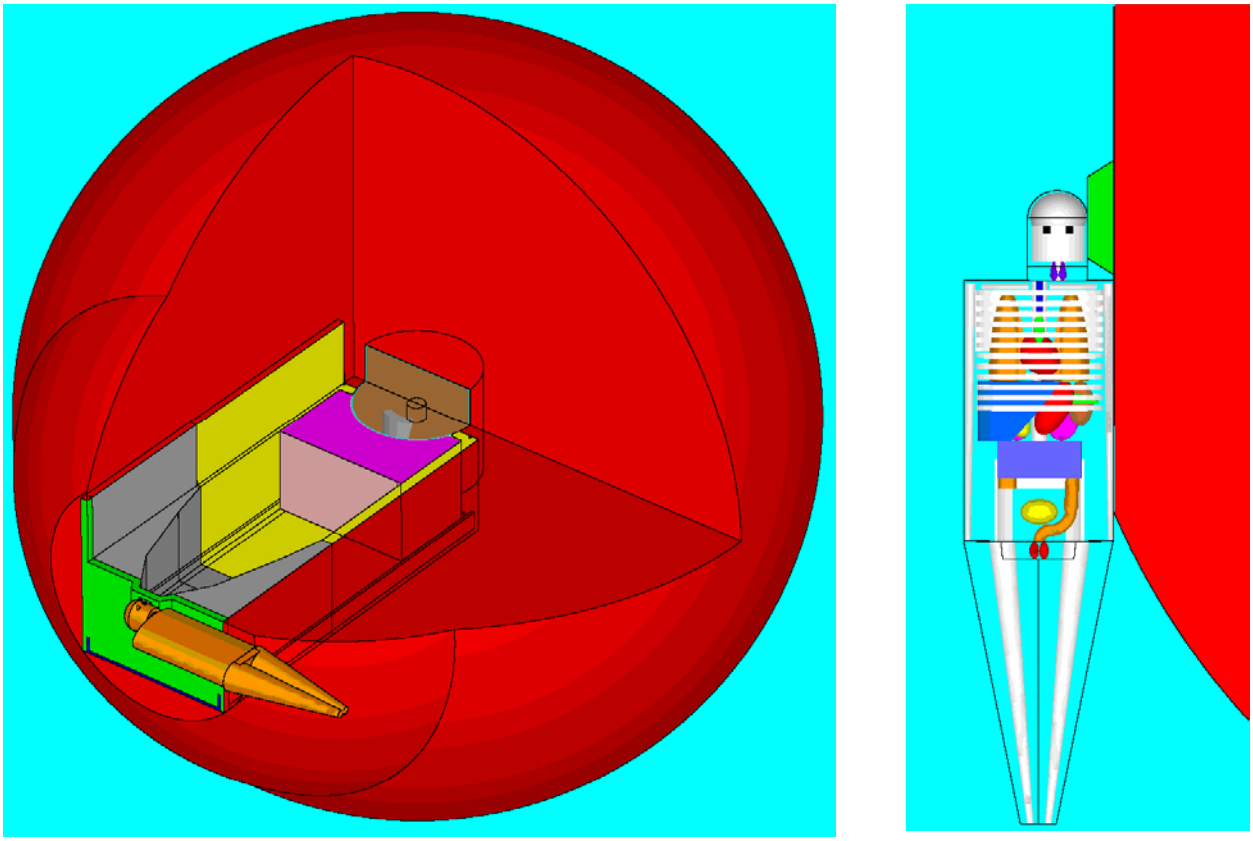

Fig.4. The epithermal column for patient irradiations with the ADAM phantom.

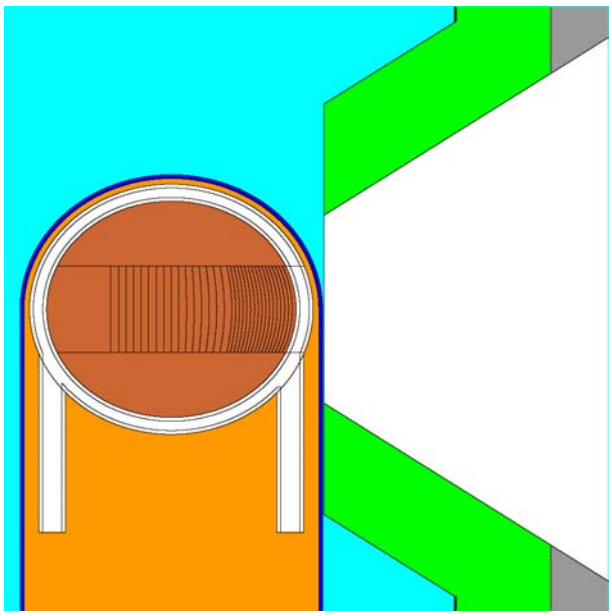

Fig.5. Section of ADAM cranium with the tally cells.

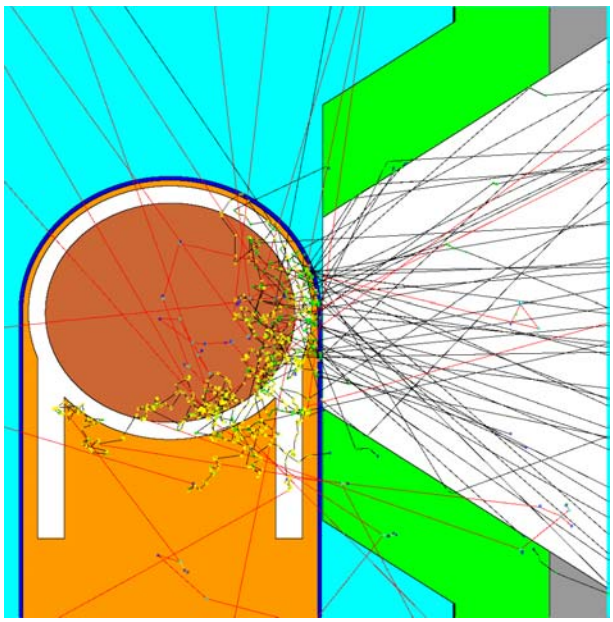

Fig.6. Interaction of the radiation in the cranium.

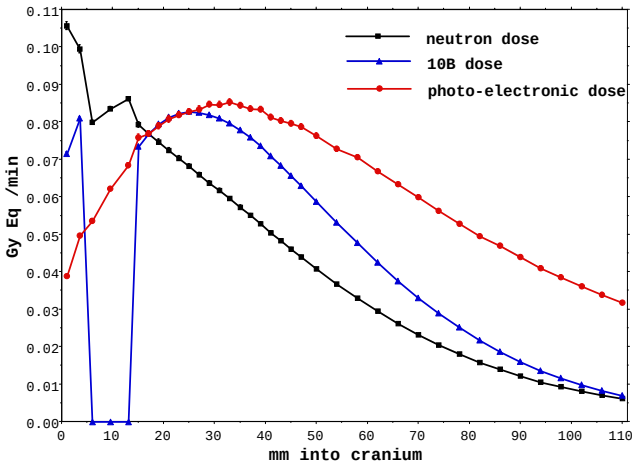

Fig.7a. Dose contributions in healthy tissue in ADAM cranium.

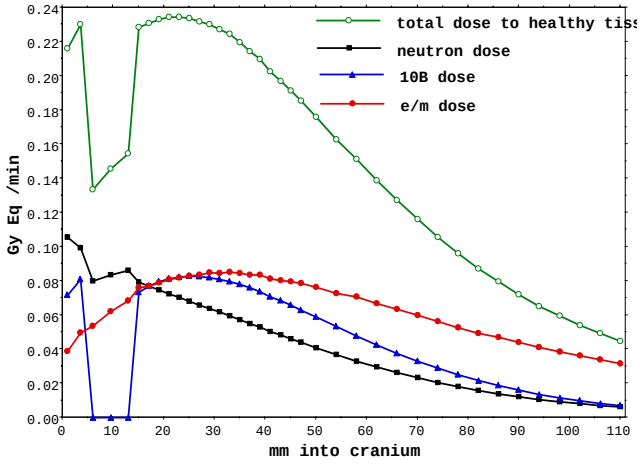

Fig.7b. Total dose in healthy tissue in ADAM cranium.

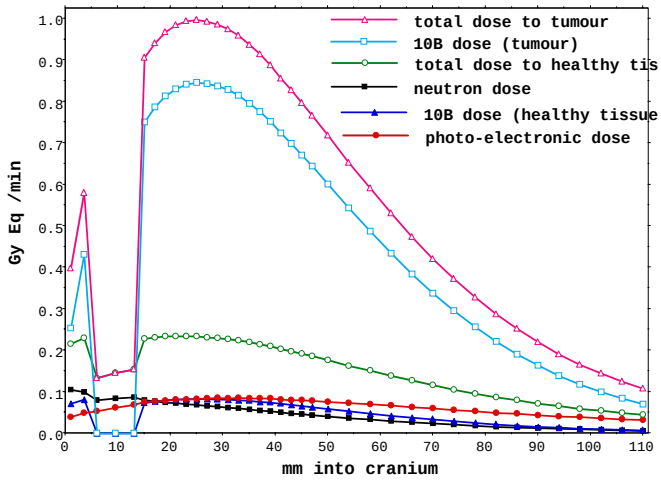

Fig.7c. ^{10}B and total dose in tumour in ADAM cranium.

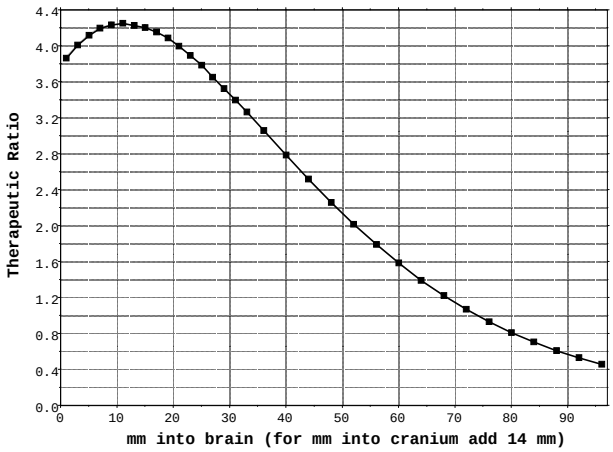

Fig.7d. Therapeutic Ratio in ADAM brain.

Discussion

In Fig. 7a there are three dose components: "neutron" including both recoil protons and protons from neutron capture in ^{14}N, "photo-electronic" including both the beam γ's and γ's born from neutron capture in the cranium and including transport of the electrons produced in the electromagnetic interactions (which lowers the dose up to a depth of 50–60 mm in the cranium and especially in the part near the surface) and "^{10}B" from the high LET products of the ^{10}B(n,α)^{7}Li reaction. In Fig. 7b we see that the maximum dose to healthy tissue is in the brain, which indicates a reasonable beam (if the maximum were in the scalp it would be an indication that there were too high a fast neutron background in the beam). In Fig. 7d the peak therapeutic ratio (PTR) (i.e. maximum dose to tumour) is at a depth of 11 mm in the brain (or 25 mm in the cranium). From Figs. 7b and 7d the standard therapeutic figures-of-merit are as follows (the depths do not include the 14 mm skull and scalp thickness):

Advantage depth (mm):	74
Advantage depth dose rate (Gy Eq / min):	0.2345
Treatment time (max. healthy tissue dose 12.6 Gy Eq.) (min):	54
Therapeutic depth (mm):	52
Peak therapeutic ratio:	4.25

As already discussed, it is difficult to compare these figures-of-merit with those from other beams. A relative comparison of the various dose contributions in Fig. 7a together with the position of the maximum dose to healthy tissue in Fig. 7b seem to indicate that they are good but they are strongly dependent on the hypotheses discussed in the section “Method”.

At other epithermal beams, filters (e.g. of lithium) are employed to harden the spectrum and increase the depth of the point of maximum dose in the brain (thereby increasing also the advantage and therapeutic depths). At TAPIRO because of the low source strength, such filters only degrade the treatment time, without changing much the dose–depth profile. (Eventually administration of heavy water up to for example 20% may be considered as it seems the only means to alter the dose–depth profile.) Thus as for most acceptable configurations the depth–dose profile has the same shape, the PTR and treatment time are the only two parameters that characterize the goodness of a configuration.

This is illustrated in Fig. 8 where for two series of configurations with a slightly different moderator set–up, “A” (with the layer of lead in the window, see Fig. 3) and “B” (with Al_2O_3 in the window), the moderator thickness was varied around its optimum value (“optimum” in a loose sense as used above). The points in Fig. 8 represent different moderator thicknesses. We wish to be as near as possible to the top left part of Fig. 8 (low treatment time, high therapeutic ratio). Instead solutions run along a rough diagonal, bottom left to top right. The current solution (configuration A, 54 min treatment time) is around the beginning of a plateau. As the moderator thickness is further reduced, the PTR begins to badly degrade.

Therefore the only possibility to vary the beam is through the thickness of the AlF_3 moderator. For this reason the moderator is composed of a number of aluminium boxes of different depths containing AlF_3 so as to be able to mock up easily a range of moderator thicknesses; the greater the AlF_3 thickness, the lower the dose rate, the higher the therapeutic ratio and *vice versa*.

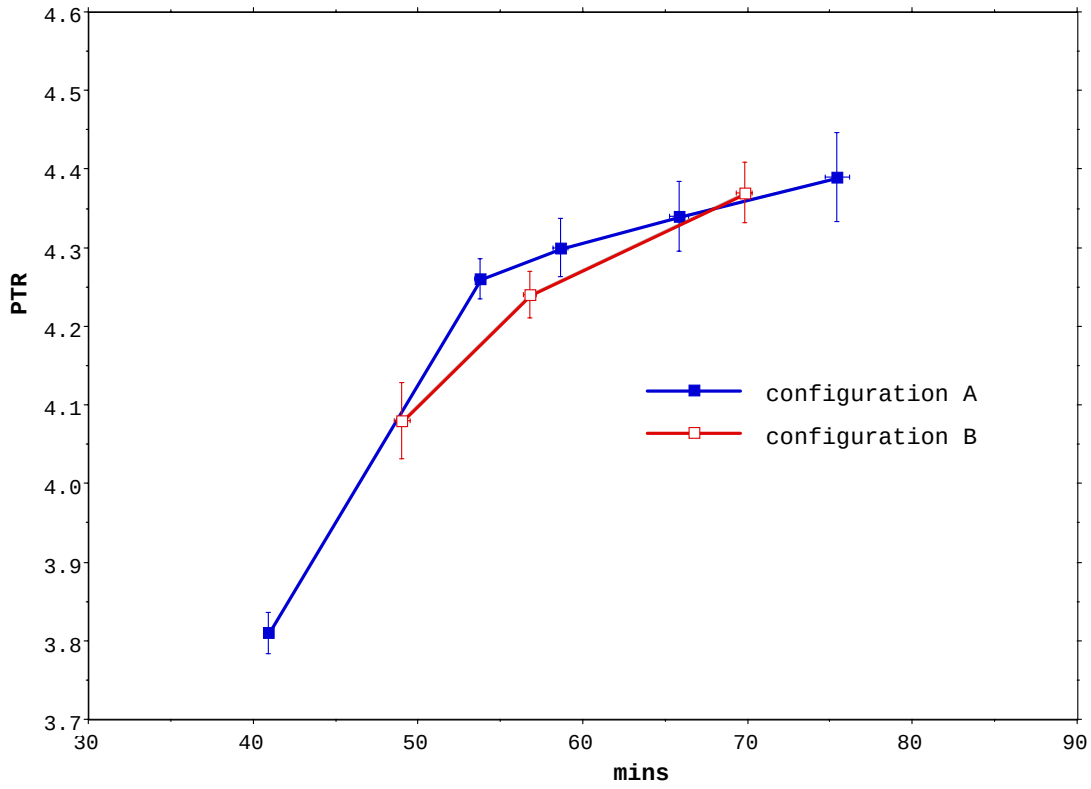

Fig.8. Variation of peak therapeutic ratio and treatment time with different moderator thicknesses.

Concluding Remarks

The column for patient treatment is currently under construction. A number of further modifications have been made to the configuration cited above. The most important ones are the removal of the 5.6 cm layer of lead in the reactor window (as it has been found that criticality can be ensured without it) and the removal of the 7 cm nozzle (a flat surface at the collimator aperture seems to be no worse than a short nozzle – the nozzle should be much longer but this damages the dose rate). These and other small modifications (including reducing the lateral extension of the tally cells – see Fig. 5) should lower somewhat the treatment time whilst maintaining the therapeutic ratio. It is expected that the results for the final configuration will be a little under 50 min treatment time for the single beam. For a typical two beam treatment plan this should result in around 35–40 min per beam.

Finally a word of caution is in order. All the results presented here are from calculations. Extensive investigations will be required for the characterization of the facility. As well as the usual uncertainties associated with the design of a complex epithermal beam, two factors peculiar to TAPIRO might lead to discrepancies between calculation and measurement and performances outside the design parameters:

– the singular reactor design and low power (only one other similar model has been built) imply that care must be taken in evaluating the absolute source strength;

– large amounts of Cu, an unusual element in neutronics, are present and its neutron cross sections are subject to greater uncertainties compared with those of more common elements.

References

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