Characteristics of the new THOR epithermal neutron beam for BNCT

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Abstract

A characterization of the new Tsing Hua open-pool reactor (THOR) epithermal neutron beam designed for boron neutron capture therapy (BNCT) has been performed. The facility is currently under construction and expected in completion in March 2004. The designed epithermal neutron flux for 1 MW power is $1.7 \times 10^{9}$ n cm$^{-2}$ s$^{-1}$ in air at the beam exit, accompanied by photon and fast neutron absorbed dose rates of 0.21 and 0.47 mGy s$^{-1}$, respectively. With $^{10}$B concentrations in normal tissue and tumor of 11.4 and 40 ppm, the calculated advantage depth dose rate to the modified Snyder head phantom is 0.53 RBE-Gy min$^{-1}$ at the advantage depth of 85 mm, giving an advantage ratio of 4.8. The dose patterns determined by the NCTPlan treatment planning system using the new THOR beam for a patient treated in the Harvard–MIT clinical trial were compared with results of the MITR-II M67 beam. The present study confirms the suitability of the new THOR beam for possible BNCT clinical trials.

Keywords: Tsing Hua open-pool reactor; THOR; Boron neutron capture therapy; BNCT

1. Introduction

A new beam of epithermal neutrons is being constructed in the removable portion of the thermal column of the Tsing Hua open-pool reactor (THOR), a 2 MW research reactor at the National Tsing Hua University in Taiwan. This beam is a modification of the former test beam (Liu et al., 2001) used in the feasibility study for boron neutron capture therapy (BNCT) (Hsu et al., 2003). The new beam will be established for a full spectrum study in BNCT, leading to possible clinical trials and subsequent therapy applications.

This paper reports the characteristics of the new THOR beam and its BNCT performance evaluated using Monte Carlo calculations and treatment planning system (TPS). Depth dose distributions for the separate radiation components in a modified Snyder head phantom (Goorley et al., 2002) were calculated using the MCNP 4C code (Briesmeister, 2000). The advantage depth, advantage depth dose rate and advantage ratio were determined for clinical $^{10}$B concentrations. Dose patterns determined by the NCTPlan TPS (Palmer et al., 2002; González et al., 2002) using the new THOR beam for a patient treated in the Harvard–MIT (Massachussets Institute of Technology) clinical trial for glioblastoma multiforme (GBM) were compared with results of the MITR-II M67 beam. Isodose contours and dose-volume histograms for normal tissue and tumor were investigated. The present work confirms the suitability of the new THOR beam for possible BNCT clinical trials.

2. Materials and methods

THOR is a 2 MW light water-cooled nuclear reactor of the TRIGA type. Its thermal column was modified in
1998 to enable the installation of a test epithermal neutron beam. After feasibility studies for the BNCT in physical and biological experiments, the test beam was dismantled in 2003. Subsequently, a new beam of epithermal neutrons was constructed in order to conduct extensive feasibility studies of the BNCT. The new beam was designed using TORT (Rhoades and Simpson, 1997) and MCNP 4C codes. A surface source, containing photons and neutrons, was calculated at the beam exit. Free beam parameters were also calculated for thermal and epithermal neutron fluxes as well as fast neutron and photon absorbed dose rates. The absorbed dose rates were obtained in-air by convolving surface fluxes with appropriate photon and neutron kerma coefficients.

The surface source was in turn transported into a modified Snyder head phantom for which calculations using the MCNP 4C were again performed. This phantom represents an analytic, multi-shell and ellipsoidal model with heterogeneous compositions. The phantom consists of two ellipsoids that separate the head into regions of cranium, brain and skin. Tissue compositions of the three regions may be taken from the International Commission on Radiation Units and Measurements Report No. 46 (ICRU, 1992). Calculated fluxes and dose rates were tallied in cylindrical cells of 12.7 mm in diameter and 5 mm in height along the central axis of the phantom. All calculations were normalized to a THOR power of 1 MW.

The TPS, NCTPlan, was developed and implemented at MIT and Harvard Medical School and applied in the present work. This TPS has been upgraded and improved several times since its first conception. Its current version is PC-based, running under Windows 95/98/NT and 2000 and written in Microsoft Visual Basic 6.0. The NCTPlan is operated in two distinct parts. In Part 1, tumor margins are identified, entrance and exit points of the beam central axis are defined, and a material mixture of air, bone and tissue is assigned to each voxel of the mathematical model for the patient head created from computed tomography (CT) images. This material assignment is then used for the generation of an MCNP input file. Part 2 of NCTPlan provides the graphical environment for deriving the dose patterns from the results of Monte Carlo radiation transport calculations. These calculations, using MCNP 4B, are performed between Parts 1 and 2. In the present work, NCTPlan was applied using the new THOR beam to a patient treated in the Harvard–MIT phase I clinical trial.

3. Results and discussion

The new beam, with a circular aperture of 140 mm diameter, was designed using TORT and MCNP 4C codes. The calculated in-air thermal (<0.5 eV) and epithermal (0.5–10 keV) neutron fluxes as well as fast neutron (>10 keV) and photon absorbed dose rates at the beam exit are given in Table 1. These beam characteristics meet most of the criteria set by the International Atomic Energy Agency (IAEA, 2001) for desired neutron beam parameters for BNCT. Although the dose rate from the fast neutron component is off the target number, it falls in the range (2.5–13 × 10^{-12} Gy cm^{-2}) towards the lower end of values in existing facilities. The somewhat higher thermal neutron flux is due to the temporary designing of a natural lithium filter at the beam mouth. This filter will be replaced by a ⁶Li filter (depending on its availability) to reduce the thermal neutron flux. The vertical cross-plane profile of the in-air epithermal neutron flux is symmetric about the central axis of the new beam. The beam intensity falls sharply at a few centimeters outside the boundary of the aperture.

The calculated depth profiles for the individual dose components in the modified Snyder head phantom are shown in Fig. 1 for the new beam with THOR power of 1 MW. The ¹⁰B concentrations for BPA (boronated phenylalanine) in tumor and normal tissue were assumed as 40 and 11.4 μg g^{-1}, respectively (Palmer et al., 2002). Here the dose profiles are weighted with

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Quality</th>
<th>$\phi_{\text{epi}}$ (cm^{-2} s^{-1})</th>
<th>$D_{\text{th}}/\phi_{\text{epi}}$ (Gy cm^2)</th>
<th>$D_{r}/\phi_{\text{epi}}$ (Gy cm^2)</th>
<th>$\phi_{\text{th}}/\phi_{\text{epi}}$</th>
<th>$(J_{+}/\phi_{\text{epi}})^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAEA^b</td>
<td>&gt; 109</td>
<td>&lt; 2 × 10^{-13}</td>
<td>&lt; 2 × 10^{-13}</td>
<td>&lt; 0.05</td>
<td>&gt; 0.7</td>
<td></td>
</tr>
<tr>
<td>THOR^c</td>
<td>1.7 × 109</td>
<td>2.8 × 10^{-13}</td>
<td>1.3 × 10^{-13}</td>
<td>0.12</td>
<td>0.81</td>
<td></td>
</tr>
</tbody>
</table>

^a The fraction of epithermal neutrons that are moving in the forward beam direction, i.e. the ratio between the neutron current $J_+$ and the neutron flux $\phi$ for epithermal neutrons.

^b The IAEA recommended target beam parameters desired for BNCT.

^c Free beam data at the beam port for 1 MW THOR power.
appropriate DRF (dose reduction factor) of 0.5 for photons, RBE (relative biological effectiveness) of 3.2 for neutrons, and compound biological effectiveness (CBE) of 1.35 and 3.8 for boron in brain and tumor (Zamenhof et al., 1996; Coderre and Morris, 1999). These profiles have been used to determine the figures of merit, or the so-called advantage parameters. The advantage depth (AD), a measure of the maximum depth at which therapeutic benefit is obtained, is the depth where the total tumor weighted dose is reduced to the maximum total tissue weighted dose. Here AD is 85 mm, greater than the average distance of 80 mm to the midline of an average adult head to ensure a therapeutic ratio above unity for even the deepest seated brain tumors. An advantage ratio (AR) of 4.8 is obtained from the quotient of the total tumor dose and the total tissue dose, both summed from the surface to the AD. Further, the AD dose rate (ADDR), i.e. the therapeutic dose rate at the AD that gives the total dose rate achievable to treat tumor at the maximum useful depth of the beam, of 0.53 RBE-Gy min$^{-1}$ is obtained.

Using designed data of the new THOR beam, the NCTPlan TPS was applied to a patient (ID 98-5) treated in the Harvard–MIT clinical trial for GBM (Palmer et al., 2002). The same irradiation condition and prescription dose as those adopted in the Harvard–MIT clinical trial, i.e. three fields with a total of 12.9 RBE-Gy maximum biologically weighted normal tissue dose, were applied. The treatment plan consisted of two fields (right posterior oblique and vertex) delivered on 1 day and one field (left posterior oblique) on the other day. Since the dose scaling factors of the THOR beam were not available, a unity was assigned to such factors for all types of radiation. Fig. 2 shows isodose contours (left: normal tissue; right: tumor) overlaid on a CT axial plane intersecting the maximum dose point. All doses are labeled in percentage of the prescription dose, which is 12.9 RBE-Gy maximum biologically weighted normal tissue dose. Isodose contours are represented over the whole brain.

Fig. 1. The calculated depth dose profiles for the individual radiation components in the modified Synder head phantom for the new THOR epithermal neutron beam. Here 40 ppm of $^{10}$B in tumor and 3.5:1 tumor-normal ratio are assumed.

Fig. 2. Isodose contours (left: normal tissue; right: tumor) overlaid on a CT axial plane intersecting the maximum dose point. Here doses are labeled in percentage of the prescription dose, which is 12.9 RBE-Gy maximum biologically weighted normal tissue dose. Isodose contours are represented over the whole brain.

Fig. 3. The composite cumulative dose-volume histograms for biologically weighted tumor and normal tissue doses. Here three fields with a total of 12.9 RBE-Gy maximum biologically weighted normal tissue dose, adopted in the Harvard-MIT clinical trial, are applied to the NCTPlan using the new THOR beam.
fields for the THOR beam is 36.7 min. Based on these
comparisons, it is concluded that the THOR beam may be
suitable for BNCT clinical trials even its performance may
not be as perfect as the near optimal performance expected
for the MIT fission converter based (FCB) epithermal
neutron beam.

4. Conclusions

A new beam of epithermal neutrons is constructed at
the National Tsing Hua University in Taiwan. The new
beam is expected in completion in March 2004 and will
be used for a full spectrum study in BNCT leading to
possible clinical trials. Characteristics of this beam and
its BNCT performance were evaluated using the MCNP
4C Monte Carlo code and the NCTPlan TPS.

Free beam parameters including thermal and epither-
mal neutron fluxes as well as fast neutron and photon
absorbed dose rates were calculated and compared to
the IAEA recommended desirable neutron beam values
for BNCT. The THOR beam parameters either meet the
IAEA target values or fall in the range of values in
existing facilities. Calculated phantom depth dose
profiles for the individual radiation components were
used to determine the figures of merit in BNCT, i.e. the
AD, AR and ADDR. Using a 3.5:1 ratio of BPA boron
concentrations in tumor and normal tissue, it was found
that AD = 85 mm, AR = 4.8 and ADDR = 0.53 RBE-
Gy min⁻¹ for 40 ppm ¹⁰B in tumor. These advantage
parameters showed that the required biologically
weighted dose could be delivered within a reasonable
treatment time. For a patient treated in the Harvard–
MIT clinical trial for GBM, the application of the NCTPlan TPS indicated that the THOR beam provided
a much larger dose to the tumor and somewhat larger
dose to the tissue than the MITR-II M677 beam. The
present study confirms the suitability of the new THOR
epithermal neutron beam for possible BNCT clinical
trials.

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