INTRODUCTION

Boron Neutron Capture Therapy (BNCT) is an effective and promising treatment of tumor types which are resistant to conventional therapies. BNCT is a binary treatment modality, first a $^{10}$B compound is delivered to the patient and differently accumulates in cancer cells versus healthy tissue; then, when a high boron concentration ratio between tumor and healthy tissue is reached, the patient is irradiated with neutrons inducing the $^{10}$B(n,α)$^7$Li reaction. The alpha particle emitted and the $^7$Li nuclei created have high Linear Energy Transfer (LET), and an associated high Relative Biological Effectiveness (RBE). The mean free path is about 7 μm and 4 μm for α particle and for $^7$Li, respectively. Considering that the mean cellular diameter is almost in the same order of magnitude, the BNCT technique may therefore be effective in selective tumor cell destruction (1, 2).

Due to their poor tissue penetration, thermal neutrons are only applicable to the direct treatment of tumors which are located near the tissue surface. Epithermal neutrons with an energy range between 1 eV and 10 keV are more...
penetrating and able to reach deep-seated tumors. A typical example is glioblastoma multiforme, a quite aggressive type of brain cancer, by far the most common and malignant of the glial tumors. The application of the BNCT technique in clinical trials requires a neutron beam having a high enough flux level and, mainly, a proper spectrum shape. In order to reduce the irradiation time, the desirable minimum beam intensity should be $1 \times 10^9$ cm$^{-2}$s$^{-1}$. In order to limit the treatment time to reasonable levels (i.e. 1 hour) the requested epithermal neutron flux level should be at least $10^9$ s$^{-1}$, and also well collimated to avoid excessive dose to adjacent healthy tissues [3-5].

A number of candidate neutron sources for BNCT technique can be considered. Neutrons may be generated by nuclear reactors, accelerator-driven systems or generators based on either spontaneous fission of transuranic heavy materials, or exploiting specific nuclear reactions induced by radioactive sources. Radioisotope sources, such as $^{252}$Cf and $^{241}$Am/Be are commonly used for detector calibrations because of low yield and energy up to 10 MeV. Nuclear reactors provide high-intensity neutron beams but are very expensive and considerably sizeable to be used in hospital settings. Additionally, safety and authorization concerns prevent their installation in urban hospitals. Accelerator-driven systems, based on linacs, cyclotrons, or tandem van de Graaff may instead be properly used to yield and tailor an epithermal neutron beam for this purpose. Their cost is generally lower compared to even small research reactors, although they need a series of ancillary systems which may occupy large space [6-8].

DT neutron generators, based on the fusion reaction $^3$H(d,n)$^4$He, may be an attractive choice as they warrant high safety, smaller size and high social acceptability. Furthermore, these neutron sources require low energy deuteron beam (100–400 keV) which is available with smaller, simpler, electrostatic-type accelerators. Last but not least they offer an on/off switching of the emitted neutrons and are less costly. A number of studies on the use of DT neutron generators for BNCT were recently published [4,5,9-12]. The main goal of this study was to optimize a BNCT facility based on a DT neutron generator - which yields $10^{14}$ n s$^{-1}$- in terms of beam shaping assembly (BSA) design ( moderator, gamma ray, fast and thermal neutron filters) and calculate the dose in a simulated head phantom. The facility was designed using the Monte Carlo MCNP version 4B, transport code which is suitable for gamma and neutron calculations [13].

**MATERIALS AND METHODS**

**Neutron source**

DT tubes are based upon deuteron beams bombarding a tritiated target with the resultant yield of fusion neutrons. The neutron spectrum from the DT neutron generator, which was derived by Fantidis et al. [10], has been used for the purposes of this paper. In order to minimize the treatment time in BNCT the epithermal neutron flux has to be sufficiently high ($\approx 10^9$ n cm$^{-2}$ s$^{-1}$). According to Rasouli et al. [11] a fission-converter-based sphere made by natural uranium surrounding the DT source target could be used as neutron multiplier and energy degrader device in order to increase the number of neutrons via fission reaction. Based on results from the MCNP4B calculations, the ratio of neutrons yielded (mainly by fission reactions) per source neutron (N/NO), available over the surface of such a sphere, is peaked for 14 cm radius (figure 1). These results are similar to the previous studies by Martin and Abrahantes[12] and Rasouli et al. [11].

**The MCNP facility modeling**

Different beam-shaping assembly (BSA) configurations were considered, in order to fulfill the parameters required (table 1) [15]. Based on the literature, lead (Pb) was selected as reflector material (8,9). Because of the high (14.1 MeV) mean energy neutrons yielded by DT reactions, a spectrum shifter system is needed in order to slow neutrons down to the required epithermal energy range (1 eV to 10 keV). In order to achieve such a goal, the "ideal" spectrum shifter should provide the following

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nuclear properties: a low down scattering cross section at the epithermal energy range, high removal cross section at higher energies and limited radiative (n, γ) captures. In addition, it should not produce large quantities of gamma-rays by inelastic scattering. In order to produce an epithermal beam, the most suitable materials to moderate neutrons with different combinations and thickness were therefore investigated by Monte Carlo simulations. Fourteen different materials namely, Teflon (CF₂), heavy water (D₂O), Fluental, PbF₄, PbF₂, BiF₃, BiF₅, MgF₂, Al₂O₃, AlF₃, TiF₃, BeD₂, CaF₂ and ⁷LiF were considered.

Neutrons, once being moderated pass through filters, in order to improve the quality of neutron beam. An ideal neutron filter must absorb only the unwanted fast and thermal neutrons without producing gamma rays. Unfortunately such nuclear properties are not fulfilled by existing materials, either in elemental or compound forms. A balanced compromise has therefore to be taken. For such a reason, the selection has been limited to four different materials able to improve the spectrum shape of the neutron beam: Titanium (Ti), Nickel-60 (⁶⁰Ni), Iron (Fe) and titanium alloy (Ti₆Al₁₄V). They have proven to be effective as neutron filtering materials aiming to improve the

![Figure 1. Number of neutrons per neutron source for different thicknesses of natural uranium as a neutron multiplier.](image)

<table>
<thead>
<tr>
<th>BNCT beam port parameters</th>
<th>Recommended value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Φₑpithermal (n cm⁻² s⁻¹)</td>
<td>~10⁹</td>
</tr>
<tr>
<td>Φₑpithermal/Φfast</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Φₑpithermal/Φthermal</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Dₑfast/Φₑpithermal (Gy cm²)</td>
<td>&lt;2 x 10⁻¹³</td>
</tr>
<tr>
<td>Dₑ/Φₑpithermal (Gy cm²)</td>
<td>&lt;2 x 10⁻¹³</td>
</tr>
<tr>
<td>Fast energy group (Φₑfast)</td>
<td>E&gt;10 keV</td>
</tr>
<tr>
<td>Epithermal energy group (Φₑpithermal)</td>
<td>1 eV ≤ E ≤ 10 keV</td>
</tr>
<tr>
<td>Thermal energy group (Φₑthermal)</td>
<td>E&lt;1 eV</td>
</tr>
</tbody>
</table>
epithermal to fast neutron ratio in the BNCT neutron beam. High Z materials, such as lead (Pb) and Bismuth (Bi) are instead suitable in order to remove the gamma component. Moreover, in order to increase the epithermal to thermal ratio materials having a high absorption cross section in thermal range are needed. An absorber material, lithiumed polyethylene (poly-Li), is at last included as delimited to get a collimated neutron beam. The final part of the BSA design includes a delimit with the intention to minimize the dose rate outside of the tumor cells. It should be noted that the unit is designed in the form of coaxial cylinders and the neutron distribution is symmetrical due to the symmetrical geometry considered.

RESULTS

A wide set of computational studies was carried out using the MCNP4B Monte Carlo code. The neutron flux and the dose rate were calculated at the exit of the facility across the 12 cm diameter window using the F2, Fm2 tallies and the DE, DF cards. An accuracy of less than 1% was achieved in all cases. Fourteen different spectrum shifter materials to slow neutrons down to epithermal energy ranges, having different thickness, were therefore investigated. Figure 2 shows the $\Phi_{\text{epithermal}}$ for the studied materials as a function of the moderators’ thickness. In figure 3 the $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ ratio of spectrum shifter candidate materials versus their thickness, is plotted. According to the results the BeD$_2$ and the D$_2$O give the higher $\Phi_{\text{epithermal}}$ Short moderators length, although the flux level quickly drops off with increasing thickness. Taking into account plots in figures 2 and 3, it may be concluded that 19 cm thickness of $^7$LiF provides the optimal balance between $\Phi_{\text{epithermal}}$ and $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ ratio correspondingly.

With the aim to find out the best solution a huge number of configurations have been considered and the simulations show that 19 cm of $^7$LiF housing at the beam axis an additional, truncated cone volume filled with D$_2$O is the optimum choice. The truncated cone moderator has a length of 6 cm and radii 6 and 1 cm with the larger radius close to the source. The conic part increases the $\Phi_{\text{epithermal}}$ and the $\Phi_{\text{thermal}}$ and reduces the $\Phi_{\text{fast}}$. Particularly the introduction of the D$_2$O increases the $\Phi_{\text{epithermal}}$ more than 7% ($3.04 \times 10^{10}$ n cm$^{-2}$ s$^{-1}$ vs. $2.84 \times 10^{10}$ n cm$^{-2}$ s$^{-1}$) and improves the $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ and the $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ by 9.89% and 0.87% respectively. However, both the $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ and the $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ ratios have values (2.89 and 10.49...

![Figure 2. $\Phi_{\text{epithermal}}$ for different thicknesses of moderators.](image)
correspondingly) below from the recommended limits. For these reasons a second moderator should be used.

Figures 4, 5 and 6 show the $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ and the $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ ratios for a number of materials which have been selected as second spectrum shifter versus their thicknesses, whilst 19 cm $^7\text{LiF}$ incorporating a $\text{D}_2\text{O}$ conic part has previously been selected as the first part of the moderator. Even though Fluental is able to provide a larger $\Phi_{\text{epithermal}}$, the $\text{TiF}_3$ seem to be however a better choice because of superior values for $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ and the $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ BSA modeling parameters. Indeed if $\text{TiF}_3$ is selected as spectrum shifter instead of Fluental the BSA shows to have comparable values for the $\Phi_{\text{epithermal}}$, a better performance for the $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ ratio and by far higher values for the $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ ratio. Therefore results revealed that the optimum thickness for the $\text{TiF}_3$ spectrum shifter is 19 cm.

Figure 3. The $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ ratio for different thicknesses of moderators.

Figure 4. $\Phi_{\text{epithermal}}$ for different thicknesses of the second moderator where 19 cm $^7\text{LiF}$ which incorporates a cone made of $\text{D}_2\text{O}$ are selected as the first part of the moderator.
The BSA configuration thus selected allows for improving the quality of the in-air FOM beam parameters, but the $D_{fast}/\Phi_{epithermal}$ (4.57 x 10^{-13} Gy cm^2) and the $D_{th}/\Phi_{epithermal}$ (4.01 x 10^{-12} Gy cm^2) ratios turn out to be above the fixed levels. The value of the $D_{fast}/\Phi_{epithermal}$ shows that the proper selections for a fast neutron filter is required in order to optimize the BSA design. Therefore 4 different materials (Fe, Ti, Al, V, Ti, 60Ni) were examined as fast neutron filters. In figure 7 plots of the calculated $D_{fast}/\Phi_{epithermal}$ ratio for different thickness of the investigated filters, shows that 60Ni is a better choice. However the beam spectra owing to the fast neutron filters show (figure 8) that the presence of the Ti ensures higher $\Phi_{epithermal}$ with slightly lower values for the $D_{fast}/\Phi_{epithermal}$ ratio. Motivated by these results all the BNCT in-air FOM parameters have been calculated and the results are summarized in table 2. From such results it may...
be noted that the Ti filter compared with the $^{60}$Ni provides higher $\Phi_{\text{thermal}}$ and has slightly higher value for the $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ ratio. However the final choice for the fast neutron filter is $^{60}$Ni (with thickness 5 cm) because not only presents comparable values for the $\Phi_{\text{epithermal}}$, $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$, $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ and $\Phi_{\text{fast}}/\Phi_{\text{thermal}}$ but also shows a basically lower level for the $\Phi_{\gamma}/\Phi_{\text{epithermal}}$ ratio. This fact is very important because require a less thick gamma filter with an improvement on the $\Phi_{\text{epithermal}}$ level as well, compared with Ti or $^{60}$Ni.

### Table 2. The relevant with BNCT parameters for 5cm thickness of the investigated fast neutrons filters.

<table>
<thead>
<tr>
<th>Filter</th>
<th>$\Phi_{\text{epithermal}}$ ($\times 10^9$ n cm$^{-2}$s$^{-1}$)</th>
<th>$\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$</th>
<th>$\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$</th>
<th>$\Phi_{\text{fast}}/\Phi_{\text{epithermal}}$ ($\times 10^{-13}$ Gy cm$^2$)</th>
<th>$\Phi_{\gamma}/\Phi_{\text{epithermal}}$ ($\times 10^{-13}$ Gy cm$^2$)</th>
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</thead>
<tbody>
<tr>
<td>Fe</td>
<td>4.31</td>
<td>33.07</td>
<td>96.30</td>
<td>2.60</td>
<td>2.11</td>
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<tr>
<td>$\text{Ti}_2\text{Al}_3\text{V}$</td>
<td>5.55</td>
<td>46.02</td>
<td>23.11</td>
<td>2.85</td>
<td>2.27</td>
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<tr>
<td>Ti</td>
<td>7.52</td>
<td>72.61</td>
<td>34.54</td>
<td>2.14</td>
<td>2.88</td>
</tr>
<tr>
<td>$^{60}$Ni</td>
<td>6.71</td>
<td>78.94</td>
<td>31.94</td>
<td>1.96</td>
<td>1.06</td>
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<td>IAEA criteria</td>
<td>&gt;1</td>
<td>&gt;20</td>
<td>&gt;100</td>
<td>&lt;2</td>
<td>&lt;2</td>
</tr>
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</table>

Figure 7. The $\Phi_{\text{fast}}/\Phi_{\text{epithermal}}$ ratio for different thicknesses of fast neutrons filters.

Figure 8. The neutron spectra for 5cm thickness of the investigated fast neutrons filters.
The $\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$ ratio can be further raised up above the recommended level by using a thin layer of thermal neutron absorber. Just 0.15 cm of Cadmium (Cd) is indeed enough to absorb a large fraction of thermal neutrons with a negligible part of epithermal ones. On the contrary Cadmium has the drawback of high energy gamma rays yield upon neutron capture but this problem may be overcome if the Cd thermal neutron filter placed before of a gamma shield (10). Gamma rays can be attenuated by using appropriate high-Z materials such as the Bi or Pb. Bi is commonly used, since it provides photon attenuation comparable to that from Pb, while limiting the absorption for the neutron beam. Results of comparative calculations are summarized in table 3. Therefore 5.5 cm thickness Bi gamma shielding, completed by 2 cm thickness delimiter made of poly-Li is the last part of the BSA study which is shown in figure 9. Neutron spectra of the proposed facility, calculated in three configurations, without filters, with 5 cm $^{60}$Ni fast neutron filter and for the final BSA configuration are shown in figure 10. The profile of the $\Phi_{\text{epithermal}}$ in front of the BSA is shown in figure 11.

In this study the Snyder’s head phantom, which was derived by the MCNP sample files, is simulated using MCNP4B code. This phantom consists of three ellipsoids for scalp, skull bone and brain. The dimensions and the chemical composition for an adult proceed from ICRU46.

![Table 3. The BNCT parameters for different gamma ray filters.](Image)

![Figure 9. Geometric configuration of the BNCT system -not in scale.](Image)
The spatial distribution of the $\Phi_{\text{thermal}}$, $\Phi_{\text{epithermal}}$, and $\Phi_{\text{fast}}$ in the head phantom along the beam axis for $Z$ direction are illustrated in figure 12. According to the results the $\Phi_{\text{epithermal}}$ and $\Phi_{\text{fast}}$ have the maximum values at the scalp and the flux level drops off with increasing thickness. The maximum $\Phi_{\text{thermal}}$ occurs at a depth of 1.5 - 2.6 cm.

The total absorbed tissue doses ($D_T$) are obtained by combining the four individual dose components, namely gamma ray dose ($D_{\gamma}$), fast neutron dose ($D_{\text{fast}}$), nitrogen dose ($D_N$), boron dose ($D_B$), weighted by their RBE (relative biological effectiveness) factors, using the equation:

$$D_T = w_{\gamma} \times D_{\gamma} + w_{\text{fast}} \times D_{\text{fast}} + w_{N} \times D_N + D_B \times w_B$$

where $w_{\gamma}$ is 1, $w_N$ and $w_{\text{fast}}$ are taken as 3.2 while $w_B$ is 1.3 for boron in tissue and 3.8 for boron in the tumor. In the tumor, a $^{10}$B concentration of 40 ppm was assumed and a 4:1 ratio of $^{10}$B in tumor to healthy brain was also assumed. Figure 13 shows the calculated dose rates in the tumor and healthy tissues at different depth in the head phantom.

**DISCUSSION**

In order to evaluate the proposed facility the results are compared with other published studies which are based on DT or DD neutron generator (table 4). These results (unacceptable values are in italic letters) indicate that only 2
facilities satisfy all the recommended by IAEA criteria; the excellent extensive research from Rasouli et al. (11) and the study are presented which optimizes the previous BSA configurations. As shown in table 4 the proposed facility compared with the study from Rasouli et al. improves the $\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$ ratio by a factor of $\sim 2.2$. At the same time reduces the $D_{\text{fast}}/\Phi_{\text{epithermal}}$ and the $D_{\gamma}/\Phi_{\text{epithermal}}$ by 3.7 and 1.6 times respectively while decreasing the

<table>
<thead>
<tr>
<th>Facility</th>
<th>Neutron yield ($\times 10^{14}$ n s$^{-1}$)</th>
<th>$\Phi_{\text{epithermal}}$ ($\times 10^{9}$ n cm$^{-2}$ s$^{-1}$)</th>
<th>$\Phi_{\text{epithermal}}/\Phi_{\text{fast}}$</th>
<th>$\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}$</th>
<th>$D_{\text{fast}}/\Phi_{\text{epithermal}}$ ($\times 10^{-13}$ Gy cm$^2$)</th>
<th>$D_{\gamma}/\Phi_{\text{epithermal}}$ ($\times 10^{-13}$ Gy cm$^2$)</th>
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<td>&gt;10$^9$</td>
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<td>&gt;100</td>
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<td></td>
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<tr>
<td>Proposed facility</td>
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<td>52.29</td>
<td>107.95</td>
<td>0.179</td>
<td>1.27</td>
</tr>
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<td>1.04</td>
<td>20.21</td>
<td>-</td>
<td>0.67</td>
<td>5.79</td>
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<td>4.43</td>
<td>23.75</td>
<td>121.2</td>
<td>0.59</td>
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<td>2.51</td>
<td>14.4</td>
<td>114.5</td>
<td>3.45</td>
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<td>133</td>
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<td>0.187</td>
<td>0.29</td>
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<td>16.6</td>
<td>6.3</td>
<td>7.3</td>
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<tr>
<td>Fantidis et al. (2013) (18)</td>
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<td>0.00117</td>
<td>20.81</td>
<td>128.81</td>
<td>0.00011</td>
<td>0.00023</td>
</tr>
</tbody>
</table>

Figure 12. Distribution of $\Phi_{\text{thermal}}$, $\Phi_{\text{epithermal}}$ and $\Phi_{\text{fast}}$ in the human head phantom.

Figure 13. Comparison of depth dose profile between tumor and normal tissue.
\(\Phi_{\text{epithermal}}/\Phi_{\text{thermal}}\) ratio by only \(\sim 10.9\%\). The comparison between the proposed facility with a similar facility which proposed by Fantidis et al. \(^{(18)}\) and based on DD neutron generator indicates that the use of DT neutron generator is by far the best solution owing to the fact that DT neutron source provides significant higher \(\Phi_{\text{epithermal}}\) values. Considering that DT neutron generators having \(10^{14} \text{n s}^{-1}\) neutron output may be feasible the proposed facility might be taken into account as an alternative for clinics which cannot afford to build and maintain a small nuclear reactor.

The therapeutic efficacy of neutron beam for the proposed BNCT facility were calculated through its FOM, i.e. Dose Rate (ADDR), Treatment Time (TT), Advantage Depth (AD), Advantage Ratio (AR) and Therapeutic Depth (TD). ADDR is defined as the maximum delivered dose rate to healthy tissue. Bearing in mind that the maximum allowable dose to the healthy tissue is 12.5 Gy \(^{(19)}\), the TT can be estimated. AD indicates the depth in tissue at which the dose to the tumor equals the maximum dose to the healthy tissue. AR is the integral dose that would be delivered to tumor tissue, uniformly distributed within the brain, divided by the integral dose delivered to normal tissue, while TD defines the depth at which the tumor dose falls below twice the maximum dose to healthy brain \(^{(11,20-22)}\).

The in-phantom parameters of the proposed facility and from some previous published studies are listed in table 5 and show a neutron beam which can reach relevant deeply into the brain (AD has value about 6 cm). The TT parameter which indicates the treatment time has a very attractive value (less than 20 min indicating a reasonable treatment time) as a result of the relatively high \(\Phi_{\text{epithermal}}\) Value.

**CONCLUSION**

BNCT is a potentially very useful cancer treatment modality; however only a few facilities are available for clinical trials, since all these facilities are currently based on a nuclear reactor source. In order to find an alternative source for BNCT applications a DT neutron generator has been considered, using the MCNP4B Monte Carlo code. The proposed facility is optimized in terms of the moderator and beam filtering. \(^7\)LiF incorporating a truncated-cone-shaped made of D\(_2\)O and TiF\(_3\) were chosen as the moderator materials. The use of \(^{60}\)Ni as fast neutron filter, Cd as thermal neutron filter and Bi as gamma filter has led to improving the quality of the beam for BNCT. The resulting dose of the radiation emitted from the facility is evaluated defining the FOM in phantom. According to the results obtained, the proposed facility meets all the recommended by IAEA parameters and constitutes an attractive alternative to the nuclear reactors.

**Conflict of interest:** Declared none

<table>
<thead>
<tr>
<th>Facility</th>
<th>ADDR (cGy/min)</th>
<th>TT (min)</th>
<th>AD (cm)</th>
<th>TD (cm)</th>
<th>AR</th>
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<td>R2-O (^{(25)})</td>
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<td>8</td>
<td>5.89</td>
<td>4.26</td>
</tr>
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</table>

Table 5. In-phantom parameters evaluated for the proposed designed BSA and some other facilities.
REFERENCES


17. ICRU46 (1992), International Commission on Radiation Units and Measurements.


