A comprehensive study on $^9\text{Be}(d,n)^{10}\text{B}$-based neutron sources for deep tumor treatment.

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# Accelerator-Based BNCT

Nuclear reactions and material properties

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Proton or deut. energy</th>
<th>Neutron Yield [n/mC]</th>
<th>Average neutron energy</th>
<th>Radioactive products</th>
<th>Target Properties: Melting T [Thermal Cond.]</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^7\text{Li}(p,n)^7\text{Be}$</td>
<td>2.5 MeV [Thres: 1.88]</td>
<td>$8.9 \times 10^{11}$</td>
<td>0.33 MeV</td>
<td>Yes *</td>
<td>180ºC [84.7 W/mK]</td>
</tr>
<tr>
<td>$^7\text{Li}(p,n)^7\text{Be}$ “Near Threshold”</td>
<td>1.95 MeV</td>
<td>$2.9 \times 10^{10}$</td>
<td>0.04 MeV</td>
<td>Yes *</td>
<td>180ºC [84.7 W/mK]</td>
</tr>
<tr>
<td>$^9\text{Be}(p,n)^9\text{B}$</td>
<td>4.0 MeV [Thres: 2.06]</td>
<td>$1.0 \times 10^{12}$</td>
<td>1.5 MeV</td>
<td>No**</td>
<td>1287ºC [190 W/mK]</td>
</tr>
<tr>
<td>$^9\text{Be}(d,n)^{10}\text{B}$</td>
<td>1.5 MeV [exoergic]</td>
<td>$1.6 \times 10^{11}$</td>
<td>1.7 MeV</td>
<td>No</td>
<td>1287ºC [190 W/mK]</td>
</tr>
</tbody>
</table>

* 53 day radioactivity from $^7\text{Be}$  
** Very short lived with no gamma emission

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**Advantages of $^9\text{Be}(d,n)^{10}\text{B}$:**

- No residual radioactivity
- Less difficulties related to power dissipation and stability.
- Lower bombarding energy
The $^9$Be(d,n)$^{10}$B reaction
Neutron spectrum & population of $^{10}$B

Exothermic, $Q=4.36$ MeV

Even at low deuteron energies, the residual $^{10}$B may be left in any of the excited states, leading to a neutron spectrum with several “monoenergetic” peaks.

For deuteron energies $< 500$ keV only the ground and first four excited states are accessible.
The $^9$Be(d,n)$^{10}$B reaction

Neutron spectrum & population of $^{10}$B

Population of 6$^{\text{th}}$, 7$^{\text{th}}$ and 8$^{\text{th}}$ excited states (at $\approx 5.1$ MeV) in $^{10}$B:

- These states are preferentially populated as they are accessible (Bonner and Buttler, 1959).
- For these states, the reaction has an effective threshold of $\approx 1$ MeV.
- Mainly decay by alpha emission to $^6$Li (ground state)
The $^9\text{Be}(d,n)^{10}\text{B}$ reaction
Thin vs. Thick targets

**“Thick” target**
A deuteron loses all its energy in the target

Many reactions take place at an energy lower than the 1 MeV threshold, producing high energy neutrons

**“Thin” Target**
A deuteron loses only part of its energy in the target.

All reactions take place at an energy larger than 1 MeV (i.e., in the regime where the 5 MeV states are preferentially populated!)

All deuterons leave the target with $E > 1$ MeV

A “thin” target allows us to eliminate a significant part of the more energetic neutrons
The $^9\text{Be}(d,n)^{10}\text{B}$ reaction

Thin vs. Thick targets

Example:
Deuterons of 1.45 MeV
Thickness of Be: 8 microns

All reactions which would take place at $E< 1$ MeV are eliminated, i.e., many of the more energetic neutrons are not produced.

Capoulat et al., PoS XLASNPA (2014)
Softening the primary spectrum

Why is it important?

Ideal Spectrum

Primary Spectrum

In BNCT neutrons are classified according to the energy as:

<table>
<thead>
<tr>
<th>Type</th>
<th>Energy Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal</td>
<td>&lt;0.5 eV</td>
</tr>
<tr>
<td>Epithermal</td>
<td>0.5 eV-10 keV</td>
</tr>
<tr>
<td>Fast</td>
<td>&gt;10 keV</td>
</tr>
</tbody>
</table>

Highest energy neutrons will not be completely moderated after beam shaping

→ Fast neutrons!
Softening the primary spectrum

Why is it important?

- Fast neutrons will produce high LET protons by the scattering in $^1$H (present in tissues)
- Dose due to these protons is "nonspecific" (i.e., same RBE for normal and tumor tissues)
- Radiotoxicity effects.

$$D = w_B D_B + w_{\text{ther}} D_{\text{ther}} + w_{\text{fast}} D_{\text{fast}} + w_\gamma D_\gamma$$

- $D_B$ → $^{10}$B(n,a)$^7$Li → This is the only "selective" contribution to the total dose
- $D_{\text{fast}}$ → elastic scattering on hydrogen $^1$H(n,n)$^1$H → Non selective
- $D_{\text{ther}}$ → neutron capture on nitrogen $^{14}$N(n,p)$^{14}$C → Non selective
- $D_\gamma$ → Mainly due to radioactive capture on hydrogen $^1$H(n,γ) and a less important contribution due to gamma emissions from the target $^9$Be(d,n)$^{10}$B* and gamma rays produced in the beam shaping process → Non selective

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiobiological weighting factors for each tissue.</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>CBE:</td>
</tr>
<tr>
<td>RBE's:</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
**Beam Shaping Assembly (BSA)**

**Design**

**Objectives:**
- Obtain an epithermal beam.
- Maximize the neutron flux in the patient direction.
- Provide shielding

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**Moderator materials:**
Al, fluorated compounds, Fluental®, PTFE

**Thermal neutron filtering:**
Materials enriched in $^6\text{Li}$ or $^{10}\text{B}$

**Shielding for fast neutrons:**
Hydrogen, polyethylene, Lithiated polyethylene, Borated paraffin.

**Neutron Reflector:**
Lead, Graphite

**Gamma Shielding:**
High Z materials, Lead
**Beam Shaping Assembly (BSA)**

**Optimization**

**Goal:**
- To find the BSA configuration (i.e., length and cross-section) that maximizes the dose to tumor and the treatable range.

**Materials/Methods**
- Simulated depth-dose profiles at the beam centerline in a Snyder’s phantom using the MCNP code.
- Lengths up to 95 cm and CS’ up to 50x50 cm².
Beam Shaping Assembly (BSA)

Optimization results (I): Tumor Dose

- **Beam current:** 30 mA
- **Deuteron energy:** 1.45 MeV
- **Target thickness:** 8 micron

Dose prescription:
- Peak dose to normal brain = 11.0 Gy-Eq

**Peak Dose to Tumor:**
- 1 Fraction (60 min.): 49 Gy-Eq
- 2 Fractions (2x60 min.): 55 Gy-Eq
- “Optimal condition”: 59 Gy-Eq
  in a total irradiation time of ~180 min

**Peak Dose to normal tissues:**
- Peak dose to normal brain is 11.0 Gy-Eq according the adopted prescription.
- Peak dose to skin is about 15 Gy-Eq for all configurations.
**Beam Shaping Assembly (BSA)**

Optimization results (II): Tratable Range

**Beam current:** 30 mA  
**Deuteron energy:** 1.45 MeV  
**Target thickness:** 8 micron

**Dose prescription:**  
Peak dose to normal brain = 11.0 Gy-Eq

**Treatable ranges and depth of maximum dose:**

Treatable range is the region where total tumor doses are higher than 40 Gy-Eq

- 1 Fraction (60 min.): 4.7 cm
- 2 Fractions (2x60 min.): 5.2 cm
- “Optimal condition”: 5.3 cm. in a total irradiation time of 180-200 min

The depth of maximum dose slightly decreases with the treatment time (i.e., with the moderator) due to a higher thermal contribution in the neutron spectrum.
“Best” irradiation conditions:
180-220 min. irradiation time (i.e., moderator lengths from 70 to 74 cm)
Also note that a 2-hour irradiation allows working quite near the “best condition”, in a much more clinically manageable irradiation time.

Fractionated BNCT:
The “best condition” involves too long irradiation times for a single application.
Fractionated schemes come up with a solution.
Fractionated BNCT allows:
- To increase total tumor doses without increasing doses in normal tissues (i.e., best tumor/normal tissue dose ratio)
- To maximize treatable depths.
- To significantly reduce fast dose to normal tissues
- To increase “specific” dose (boron) in tumor (absolute and relative values)
A more realistic case …

Preliminary results

- **NCTPlan** (MCNP-Based Treatment Planning Tool)
- Voxel model of a patient’s head (11025 voxels of 1 cm³)
- Diagnostic: Glioblastoma Multiforme (GBM)
- Size and localization: 4.2 cm³, Occipital Lobe
- Irradiation conditions: Single Field, posterior-anterior direction (not optimized)
- Dose prescription: 11.0 Gy-Eq (Peak dose normal brain)

### Table 1: Adopted Radiobiological Effectivenesses (RBE), Compound Biological Effectiveness (CBE) and $^{10}$B concentration in different tissues (relative to blood)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>RBE Gamma</th>
<th>RBE Thermal/Fast</th>
<th>CBE Boron</th>
<th>$^{10}$B uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>1</td>
<td>3.0</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Brain</td>
<td>1</td>
<td>3.2</td>
<td>1.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Tumor</td>
<td>1</td>
<td>3.2</td>
<td>3.8</td>
<td>3.5</td>
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Boron uptake in blood was taken as 15 ppm.
A more realistic case ...

Preliminary results

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<th>Beam</th>
<th>Time (min.)</th>
<th>Tumor (Gy-Eq)</th>
<th>Normal Brain (Gy-Eq)</th>
<th>Skin (Gy-Eq)</th>
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<td>min.</td>
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<td>min.</td>
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<td>Beryllium</td>
<td>60.4</td>
<td>31.5</td>
<td>42.0</td>
<td>47.2</td>
</tr>
<tr>
<td>Lithium</td>
<td>35.1</td>
<td>37.0</td>
<td>45.0</td>
<td>51.8</td>
</tr>
<tr>
<td>Reference*</td>
<td>45-65</td>
<td>19.8-32.3</td>
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A more realistic case …

Preliminary results

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**Primary neutron spectra**

Total Yield:
- Be: $1.65 \times 10^{11} \text{ mA}^{-1}$
- Li: $5.76 \times 10^{11} \text{ mA}^{-1}$

**Neutron spectra at the beam port**
Final remarks

- A neutron source based on the $^9\text{Be}(d,n)^{10}\text{B}$ reaction was evaluated as an epithermal neutron source for brain tumor treatments through AB-BNCT.

- In particular, the usefulness of a thin target was evaluated.

- Good treatment qualities (comparable to other neutron sources: nuclear reactors, $^7\text{Li}(p,n)$ reaction) are feasible through the following configuration:

  - Beam current: 30 mA
  - Deuteron energy: 1.45 MeV
  - Target thickness: 8 micron

- An additional experiment has been recently carried out (Sept. 2015) which is qualitatively consistent with the data used so far.

  Collaboration CNEA (Argentina) – LPSC Grenoble (France) – LNL (Italy) – University of Seville (Spain).