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

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Accelerator-Based BNCT

Nuclear reactions and material properties

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

* 53 day radioactivity from ^{7}Be

** Very short lived with no gamma emission

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

- ✓ No residual radioactivity
- ✓ Less difficulties related to power dissipation and stability.
- ✓ Lower bombarding energy

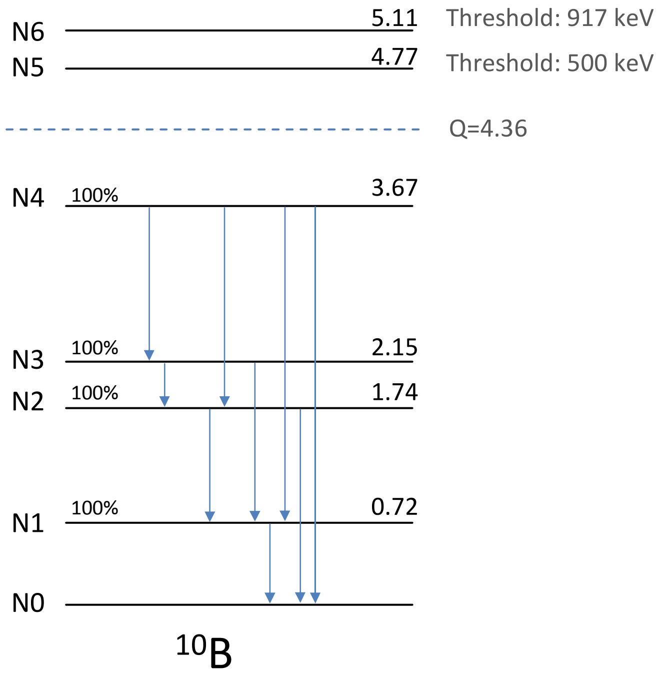
The ^{9}Be(d,n)^{10}B reaction

Neutron spectrum & population of ^{10}B

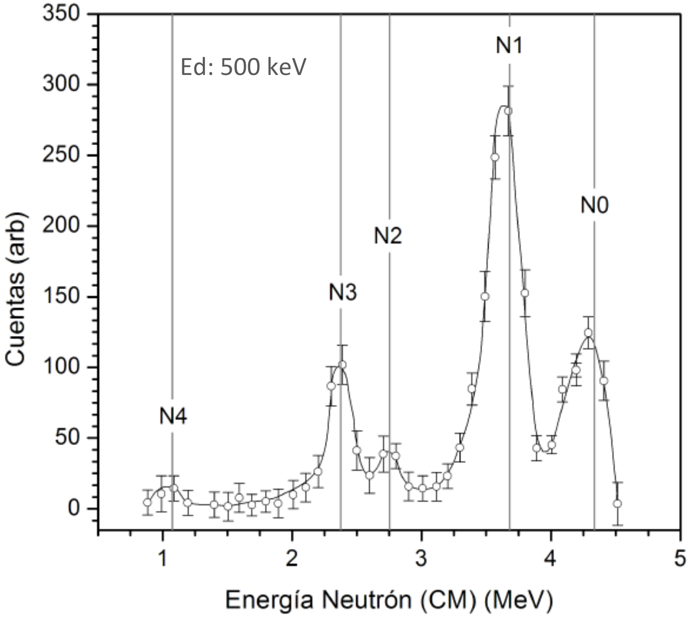
Exothermic, Q=4.36 MeV

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.



Shpetnyi , JETP, 1957

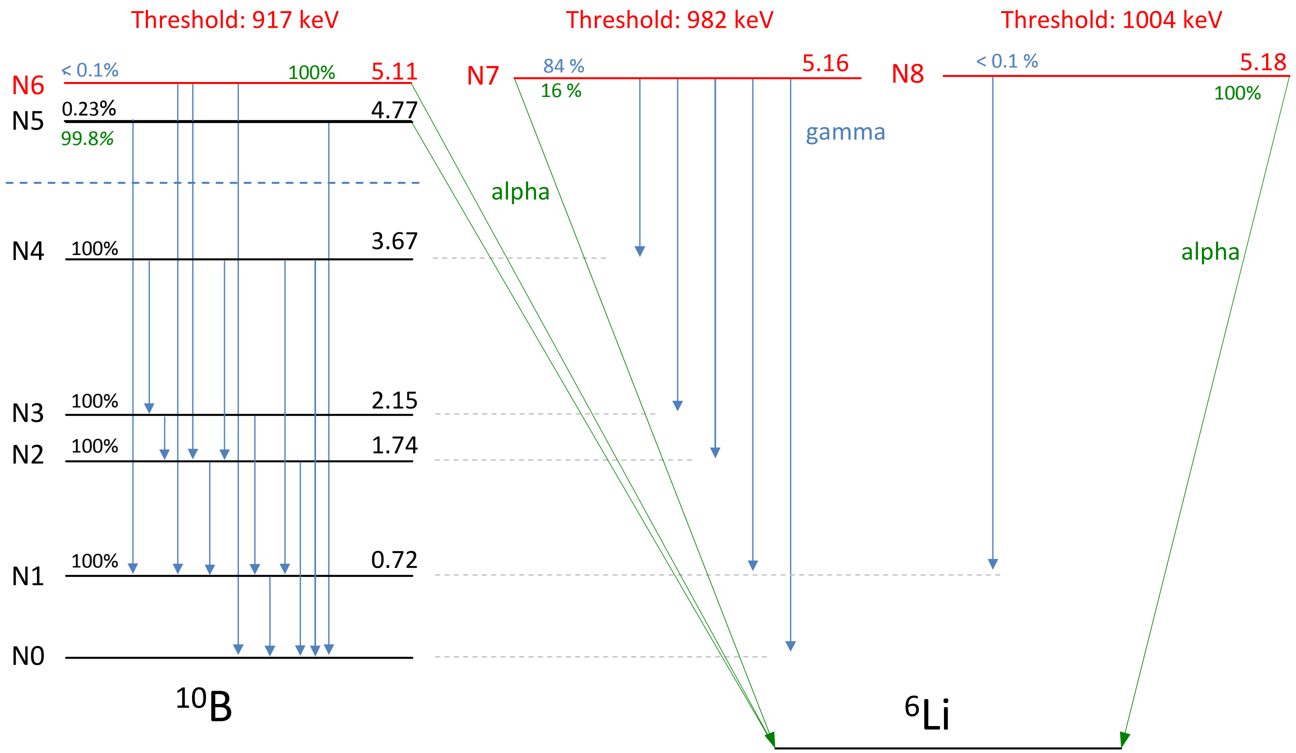


The ^{9}Be(d,n)^{10}B reaction

Neutron spectrum & population of ^{10}B

Population of 6th , 7th and 8th excited states (at ≈ 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 ≈1 MeV.
- Mainly decay by alpha emission to ^{6}Li (ground state)

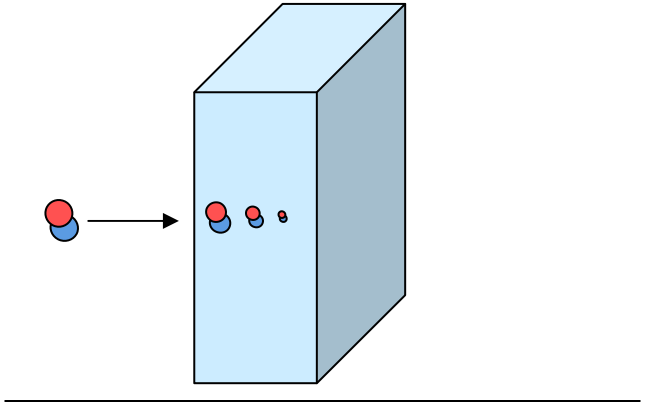


The ^{9}Be(d,n)^{10}B reaction

Thin vs. Thick targets

“Thick” target

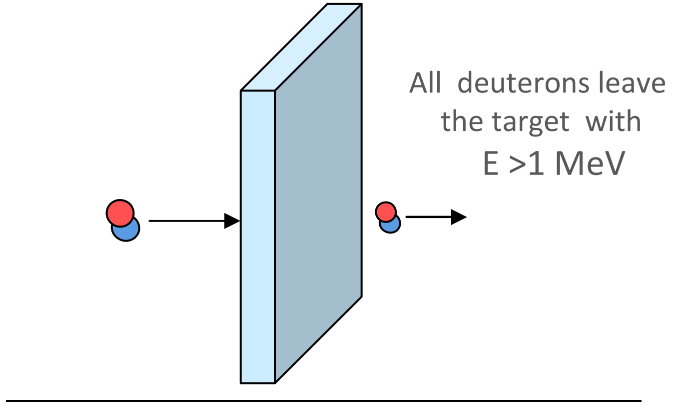
A deuteron looses all its energy in the target



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

“Thin” Target

A deuteron looses only part of its energy in the target.



All deuterons leave the target with E >1 MeV

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

A “thin” target allows us to eliminate a significant part of the more energetic neutrons

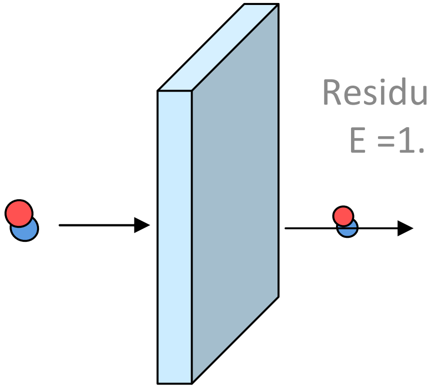
The ^{9}Be(d,n)^{10}B reaction

Thin vs. Thick targets

Example:

Deuterons of 1.45 MeV

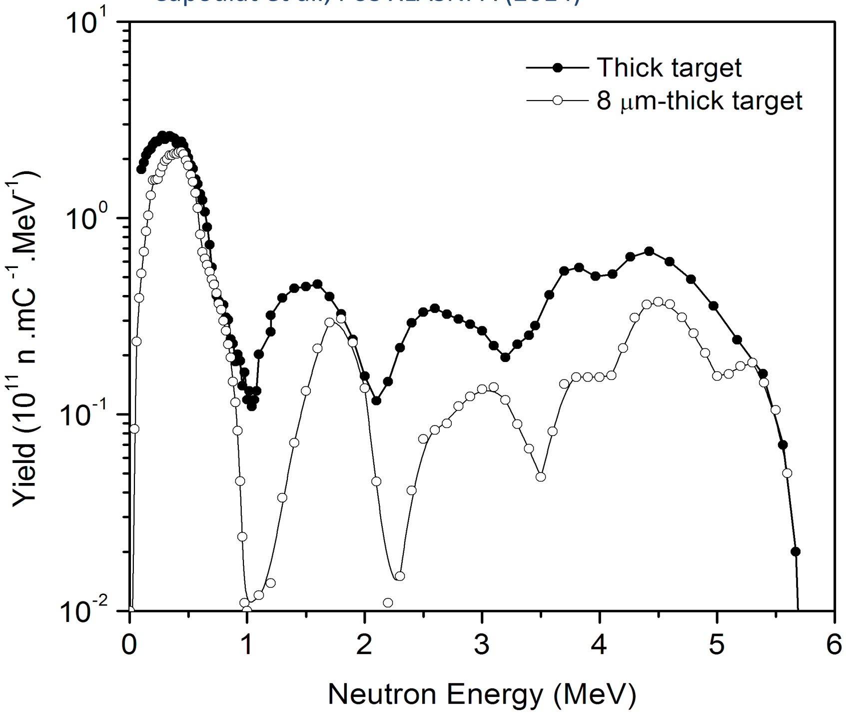
Thickness of Be: 8 microns



Residual Energy

E =1.05 MeV

Capoulat et al., PoS XLASNPA (2014)

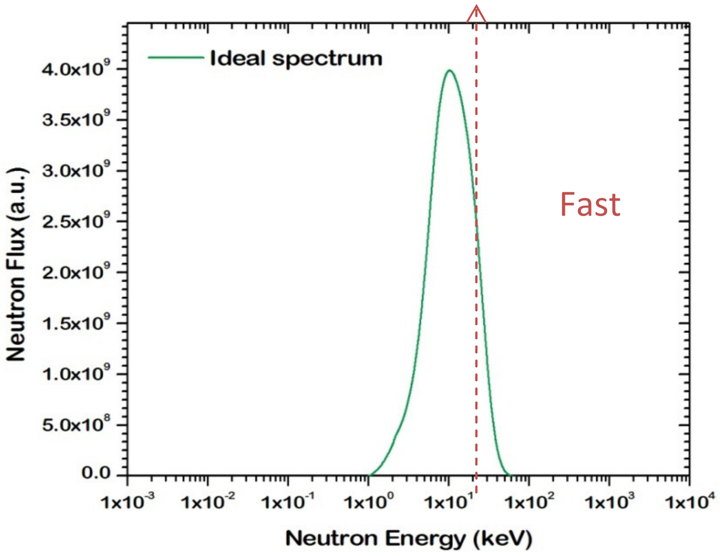


All reactions which would take place at E< 1 MeV are eliminated,
i.e., many of the more energetic neutrons are not produced.

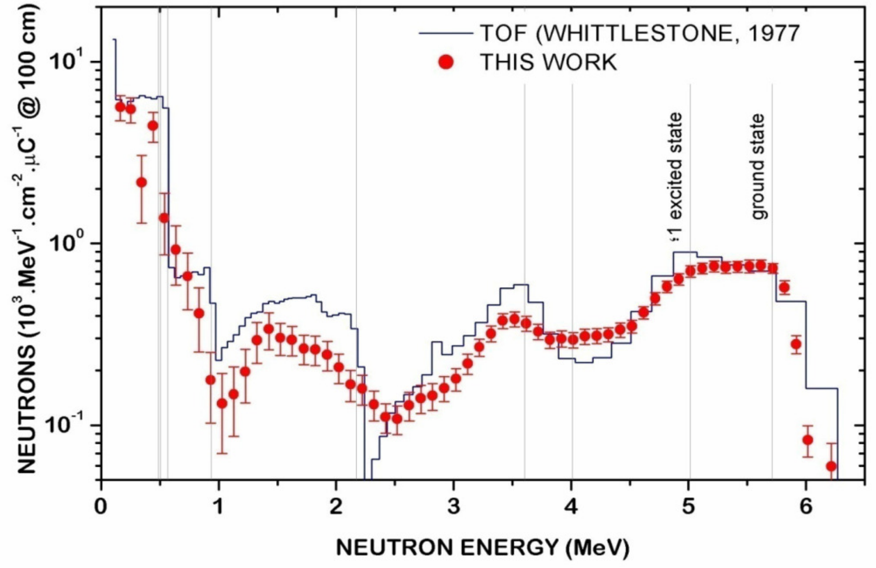
Softening the primary spectrum

Why is it important?

Ideal Spectrum



Primary Spectrum



In BNCT neutrons are classified according to the energy as:

Thermal <0.5 eV
Epithermal 0.5 eV-10 keV
Fast >10 keV

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.

$$D = w_B D_B + w_{Ther} D_{Ther} + w_{Fast} D_{Fast} + w_{\gamma} D_{\gamma}$$

D_B → $^{10}B(n,a)^{7}Li$ → This is the only “selective” contribution to the total dose

D_{Fast} → elastic scattering on hydrogen $^{1}H(n,n)^{1}H$ → Non selective

D_{Ther} → neutron capture on nitrogen $^{14}N(n,p)^{14}C$ → Non selective

$D\gamma$ → Mainly due to radiactive capture on hydrogen $^{1}H(n,\gamma)$ 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

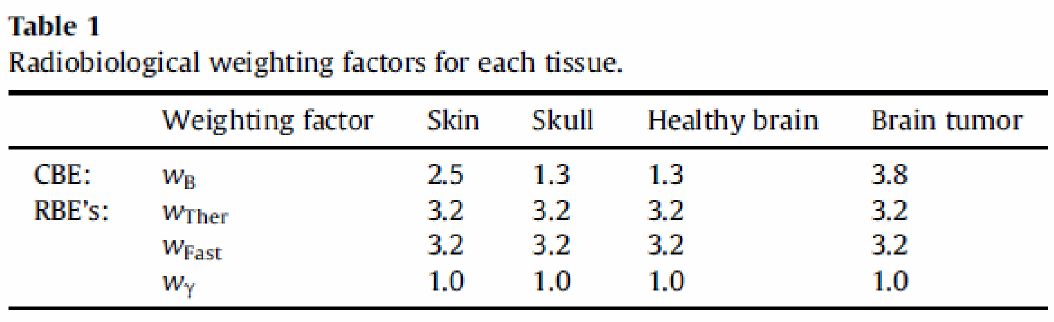


Table 1
Radiobiological weighting factors for each tissue.

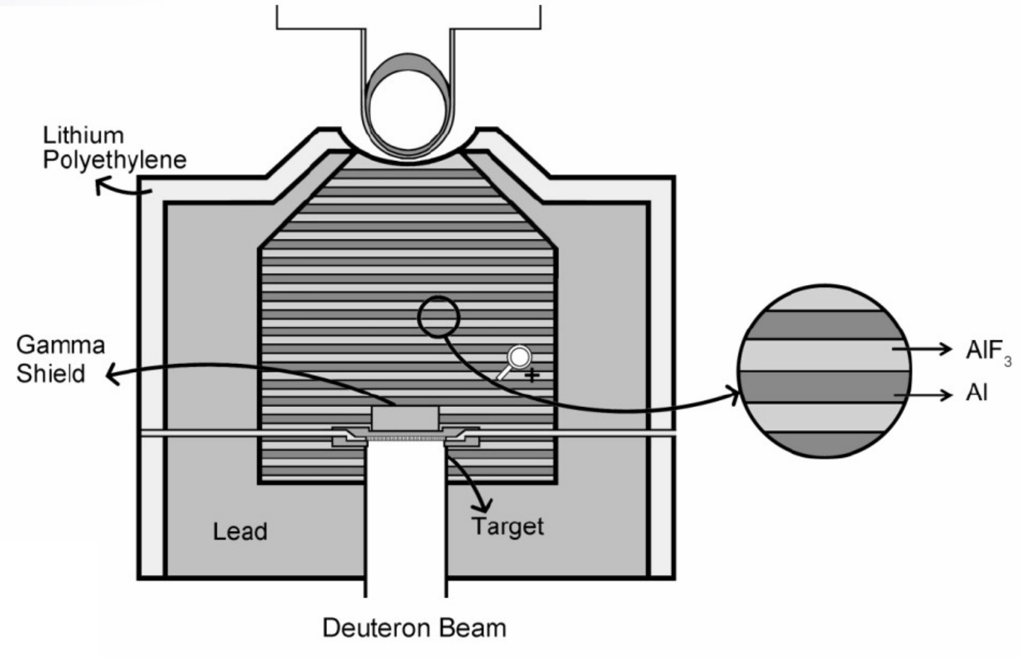
	Weighting factor	Skin	Skull	Healthy brain	Brain tumor
CBE:	w_B	2.5	1.3	1.3	3.8
RBE's:	w_{Ther}	3.2	3.2	3.2	3.2
	w_{Fast}	3.2	3.2	3.2	3.2
	w_{γ}	1.0	1.0	1.0	1.0

Beam Shaping Assembly (BSA)

Design

Objetives:

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



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

Thermal neutron filtering:
Materials enriched in ^{6}Li or ^{10}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)

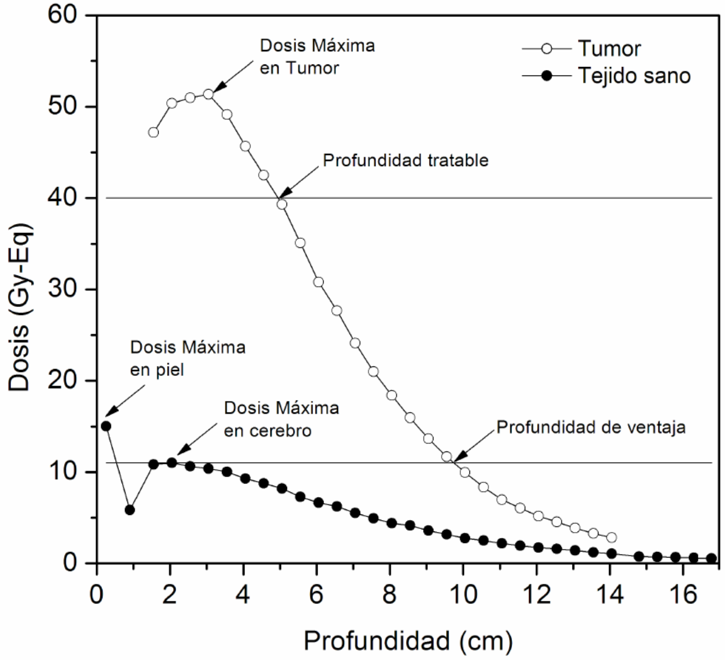
Optimization

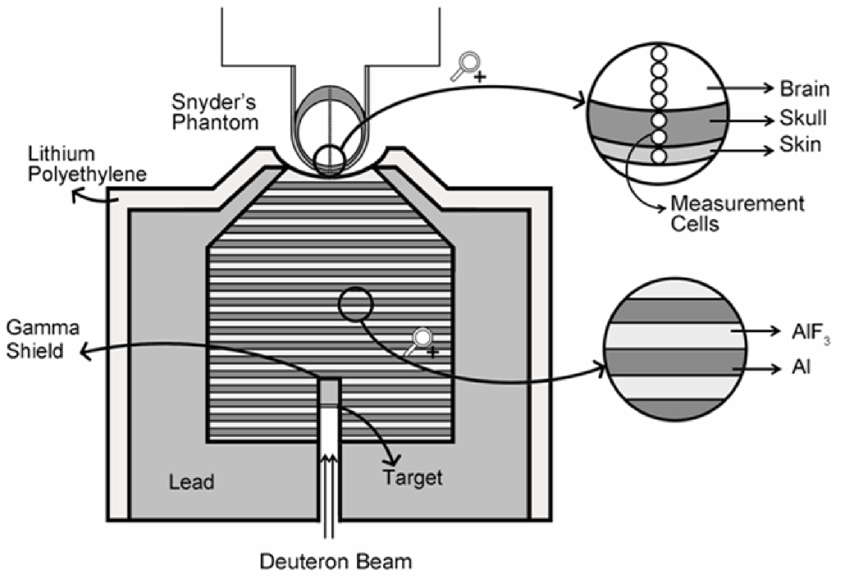
Goal:

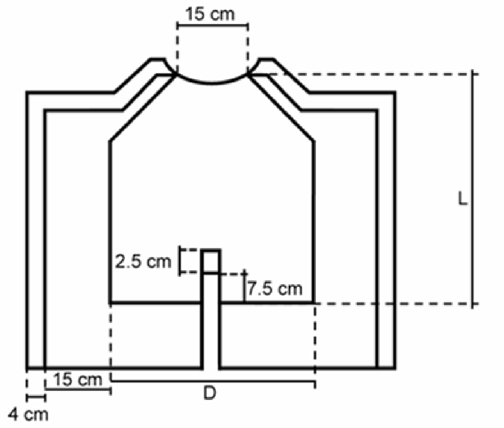
- To find the BSA configuration (i.e., length and cross-section) that maximizes the dose to tumor and the treatable range

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 cm^2







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

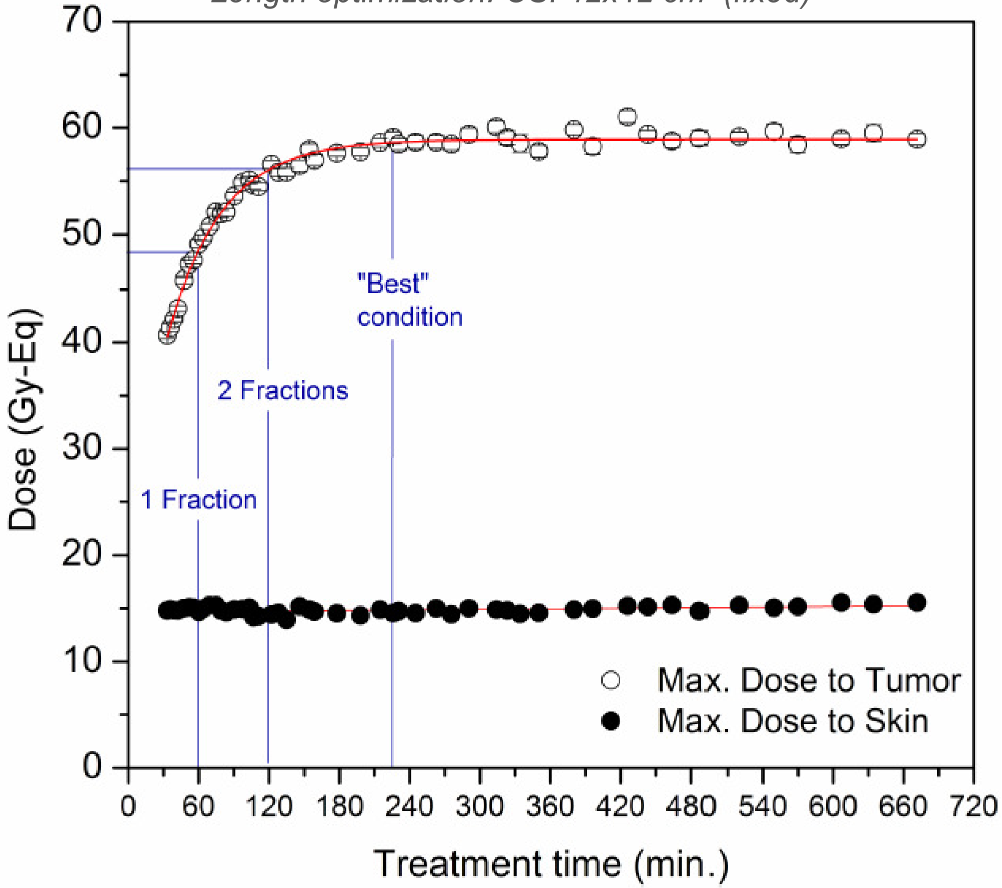
Peak Dose to Tumor:

- 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.

Length optimization. CS: 42x42 cm^2 (fixed)



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

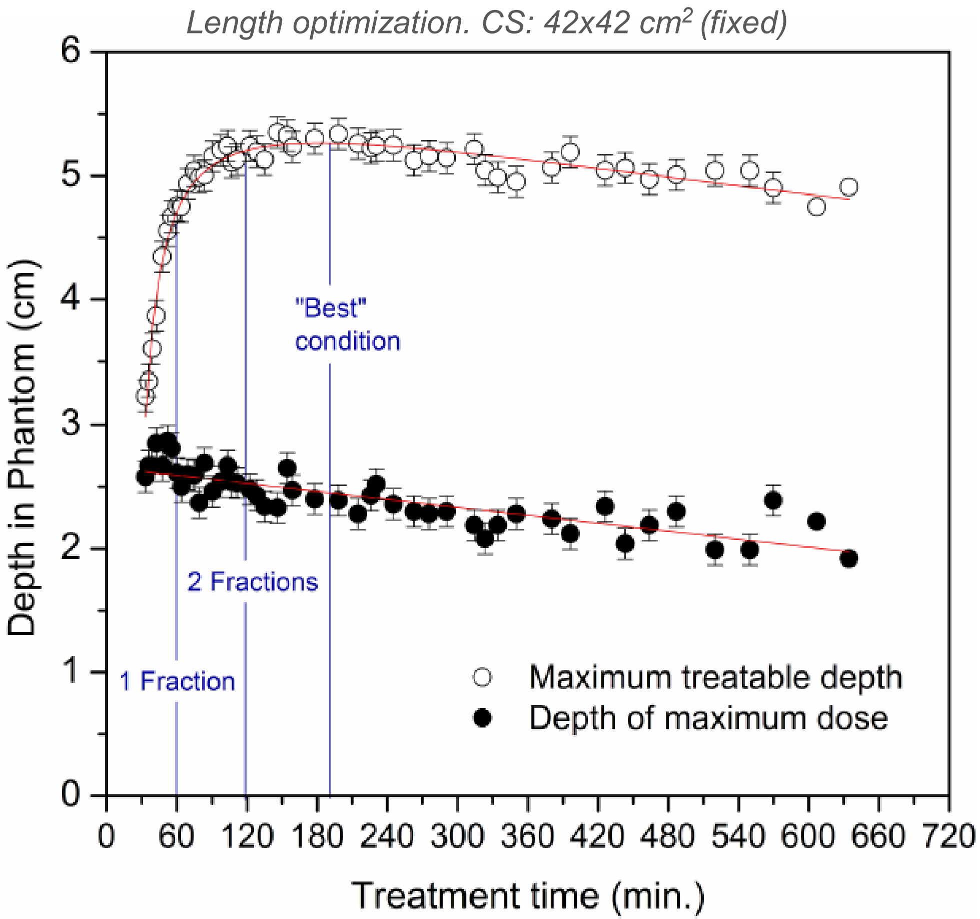
Treatable ranges and depth of maximum dose:

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

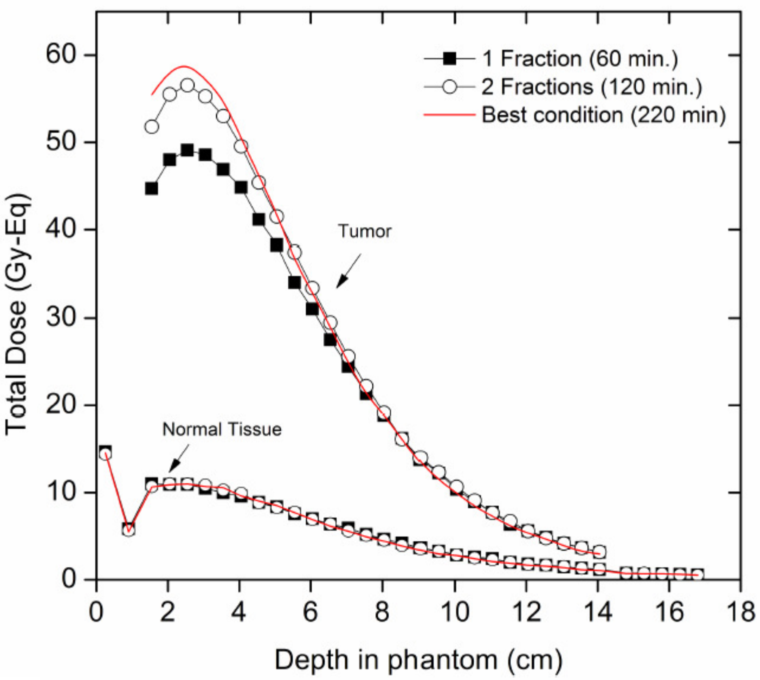
The depth of maximum dose slighltly decreases with the treatment time (i.e., with the moderator) due to a higher thermal contribution in the neutron spectrum.



"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.

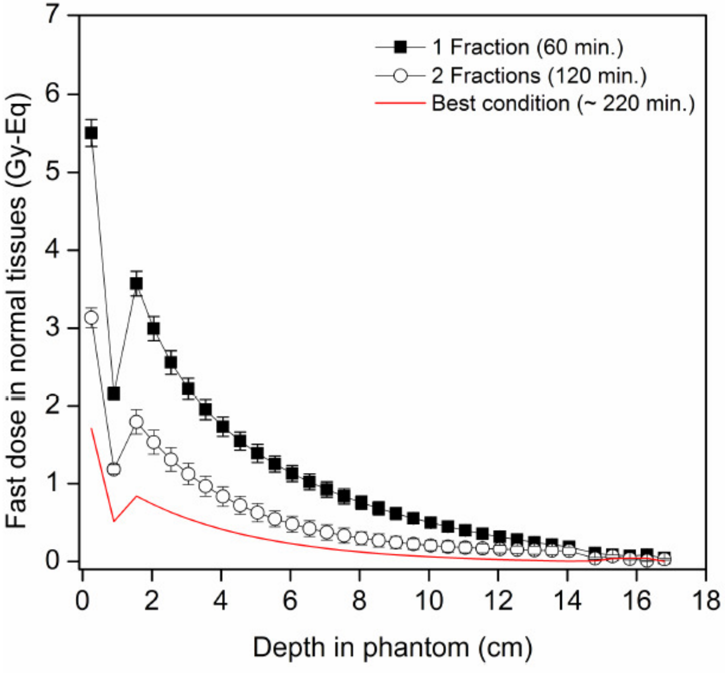


Fractionated BNCT:

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 …

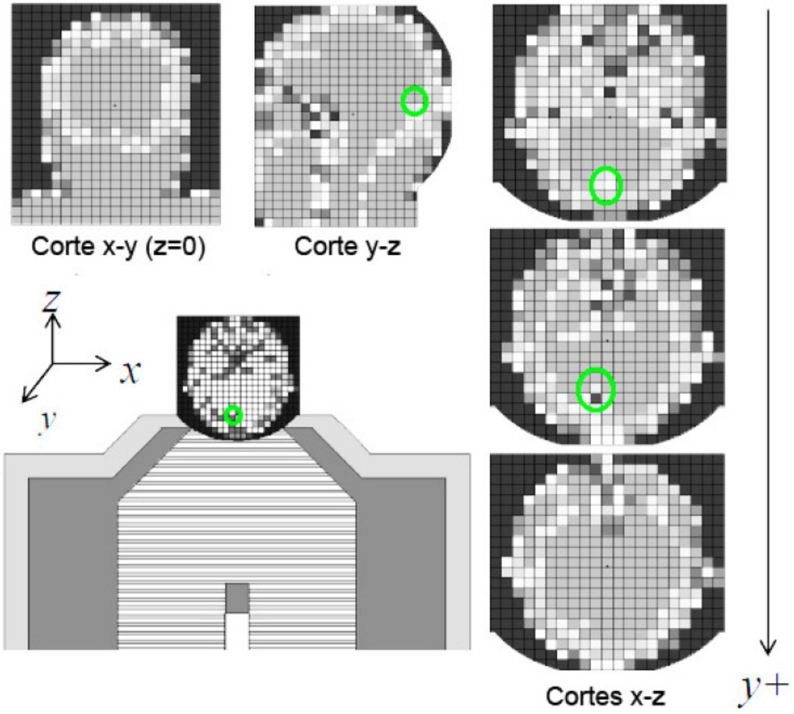
Preliminary results

Herrera, M. et al., PoS XLASNPA (2014)

- NCTPlan (MCNP-Based Treatment Planning Tool)
- Voxel model of a patient's head (11025 voxels of 1 cm^3)
- Diagnostic: Glioblastoma Multiforme (GBM)
- Size and localization: 4.2 cm^3, Occipital Lobe
- Irradiation conditions: Single Field, posterior-anterior direction (not optimized)
- Dose prescription: 11.0 Gy-Eq (Peak dose normal brain)

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

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



Tissue	RBE		CBE	^{10}B
	Gamma	Thermal/Fast	Boron	uptake
Skin	1	3.0	2.5	1.5
Brain	1	3.2	1.3	1.0
Tumor	1	3.2	3.8	3.5

Table 1: Adopted Radiobiological Effectivenesses (RBE), Compound Biological Effectiveness (CBE) and ^{10}B concentration in different tissues (relative to blood) Boron uptake in blood was taken as 15 ppm.

A more realistic case …

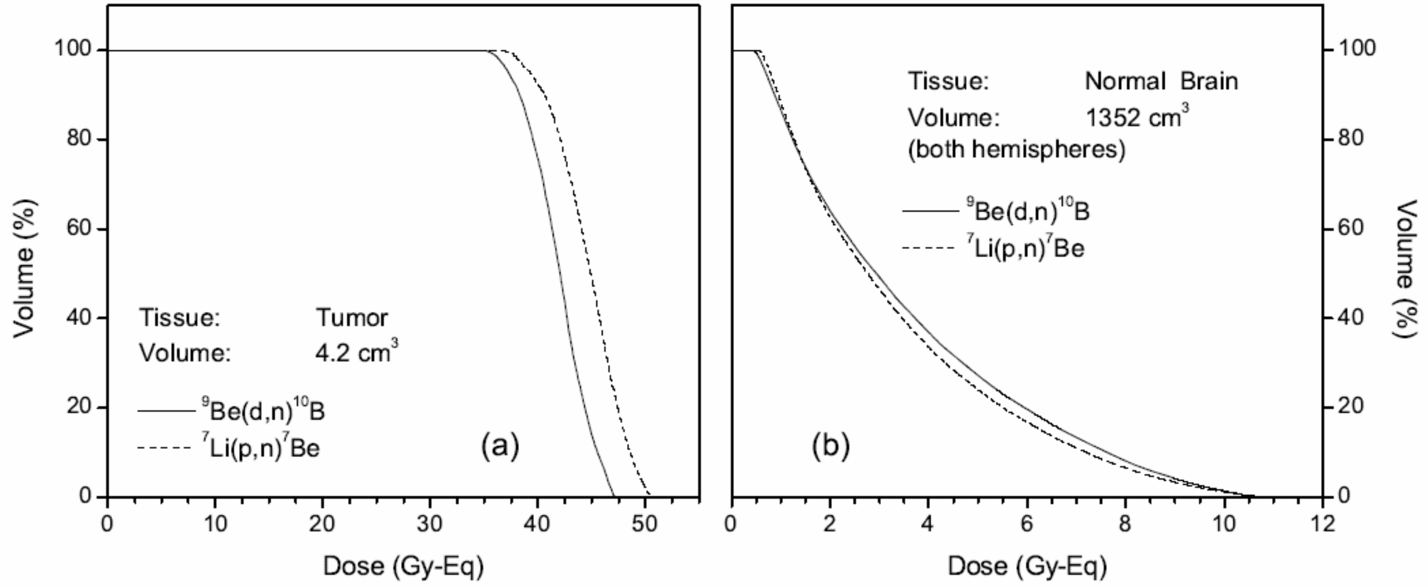
Preliminary results

Herrera, M. et al., PoS XLASNPA (2014)

Beam	Time (min.)	Tumor (Gy-Eq)			Normal Brain (Gy-Eq)			Skin (Gy-Eq)		
		min.	mean	max.	min.	mean	max.	min.	mean	max.
Beryllium	60.4	31.5	42.0	47.2	0.4	3.6	11.0	0.1	3.0	15.4
Lithium	35.1	37.0	45.0	51.8	0.5	3.4	11.0	0.2	2.3	13.0
Reference *	45-65	19.8-32.3	----	47.6-64.4	----	1.9-2.6	10.5-13.8	----	----	10-16

** Clinical trials at Brookhaven Medical Research Reactor (10 GBM patients) (Chadha, Int. J. Radiat. Oncol. Phys.,1998)*

Dose Volume Histograms



A more realistic case …

Preliminary results

Beam	Time (min.)	Tumor (Gy-Eq)			Normal Brain (Gy-Eq)			Skin (Gy-Eq)		
		min.	mean	max.	min.	mean	max.	min.	mean	max.
Beryllium	60.4	31.5	42.0	47.2	0.4	3.6	11.0	0.1	3.0	15.4
Lithium	35.1	37.0	45.0	51.8	0.5	3.4	11.0	0.2	2.3	13.0
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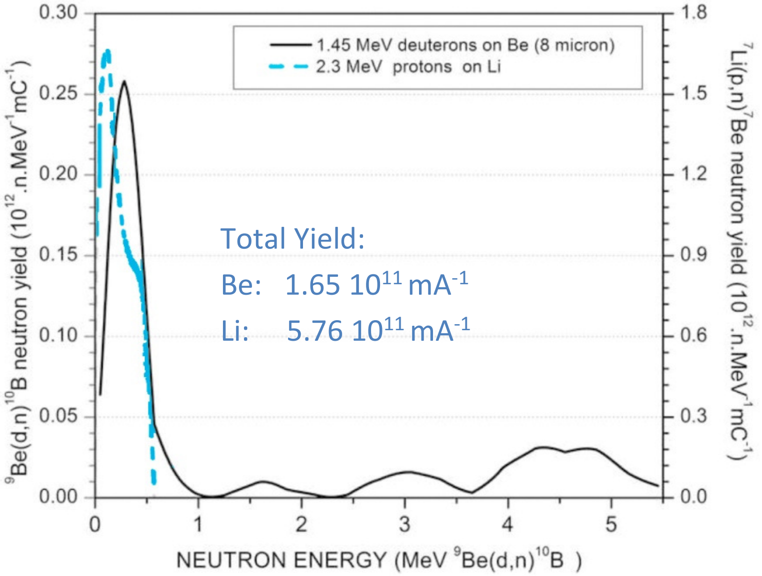
Primary neutron spectra

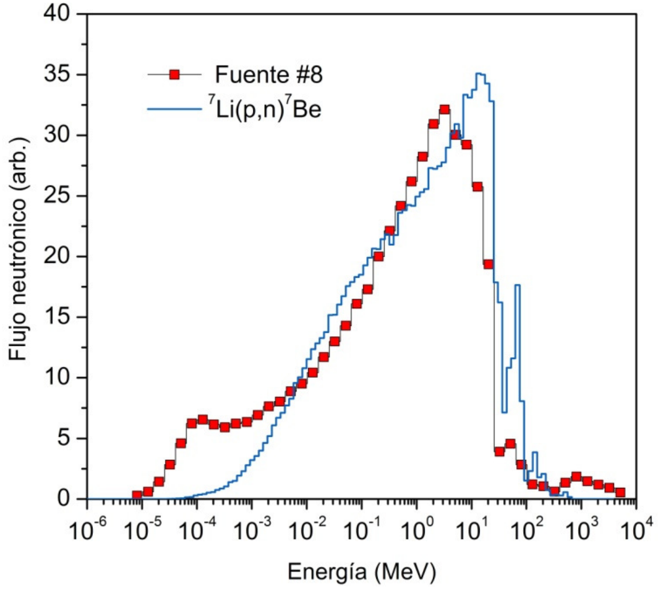


Total Yield:

Be: 1.65 10^{11} mA^{-1}

Li: 5.76 10^{11} mA^{-1}

Neutron spectra at the beam port



Final remarks

- A neutron source based on the ^{9}Be(d,n)^{10}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}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).