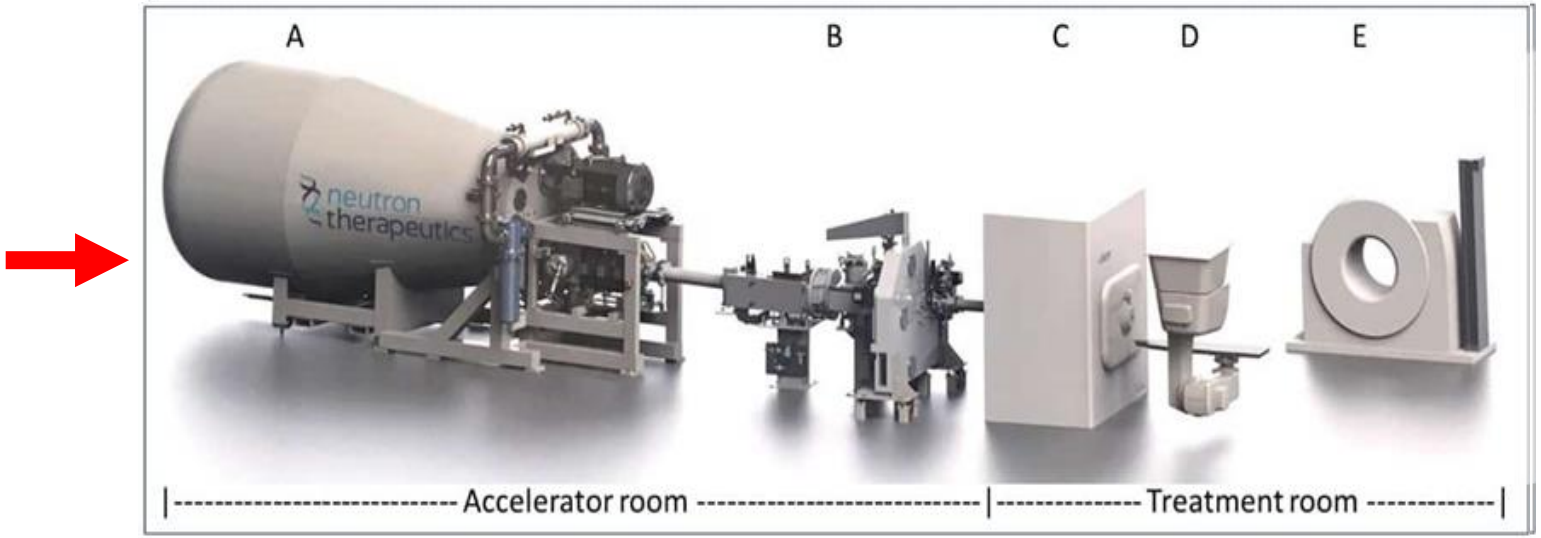
Accelerator Based Boron Neutron Capture Therapy

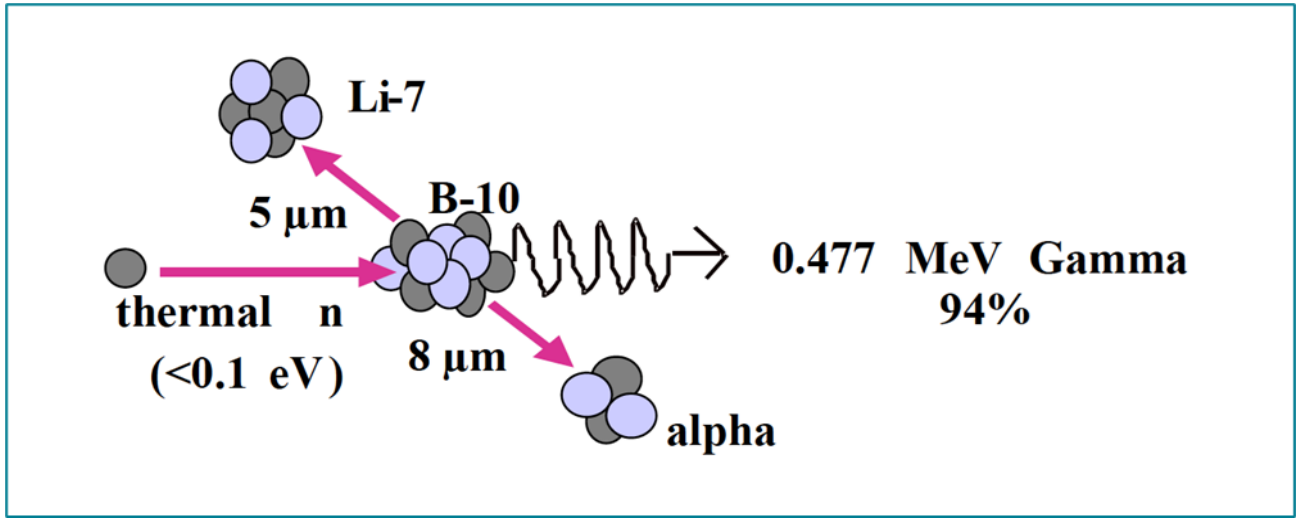
Paweł Olko

Institute of Nuclear Physics Polish Academy of Sciences



Rationale for Boron Neutron Capture Therapy (BNCT)

- Boron accumulates in the tumor and in other areas of the body
- Tumor area is irradiated with epithermal neutrons and interacts with boron producing short range alpha-particles

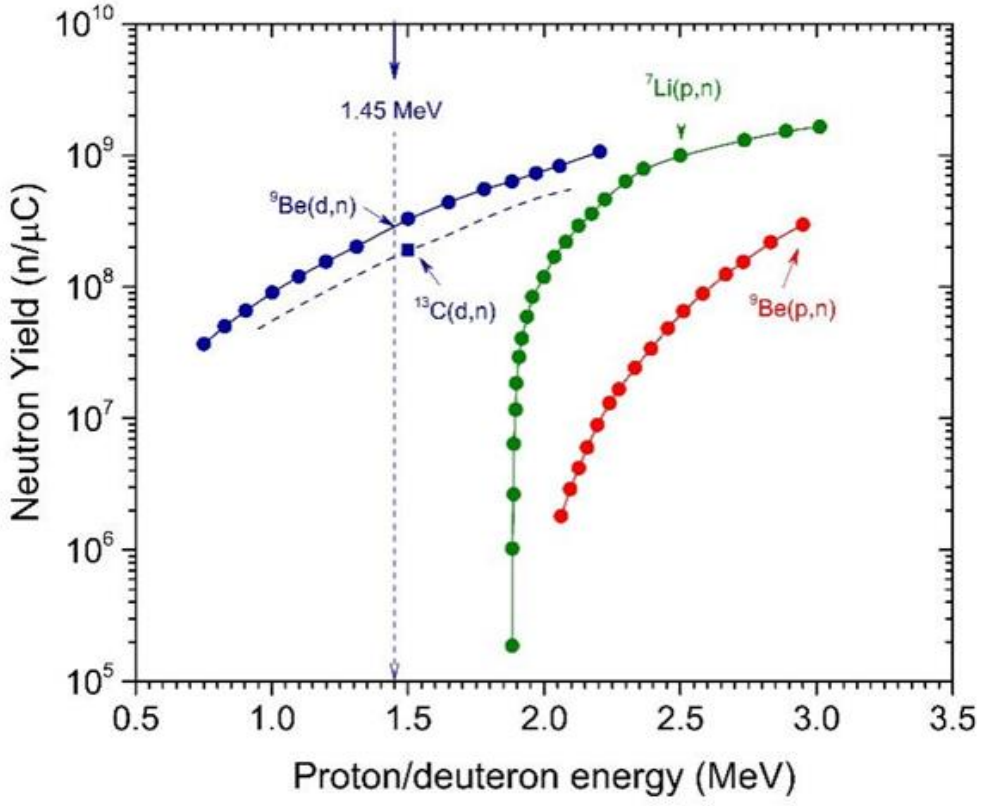


High fluence) neutron source needed : reactor or accelerator with high current

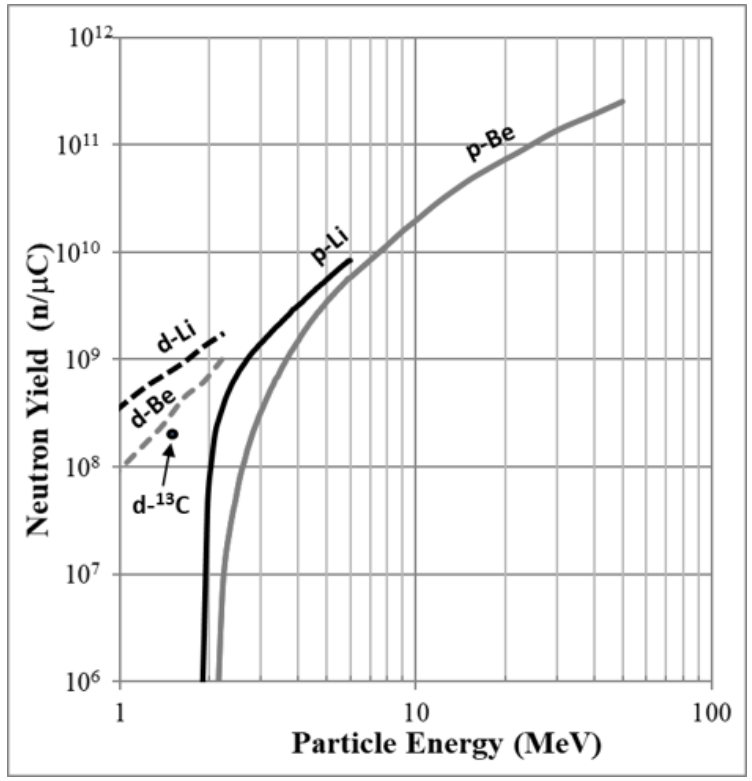
Neutron energy at the patient's entrance (epithermal) 0.5 eV to 10 keV

Epithermal neutron flux > 10^9n/cm^{2}s.

Thick target yields for the neutron-producing reactions considered for AB-BNCT.



Kononov VN et al. , NIMA: 2006 doi:10.1016/j.nima.2006.03.043

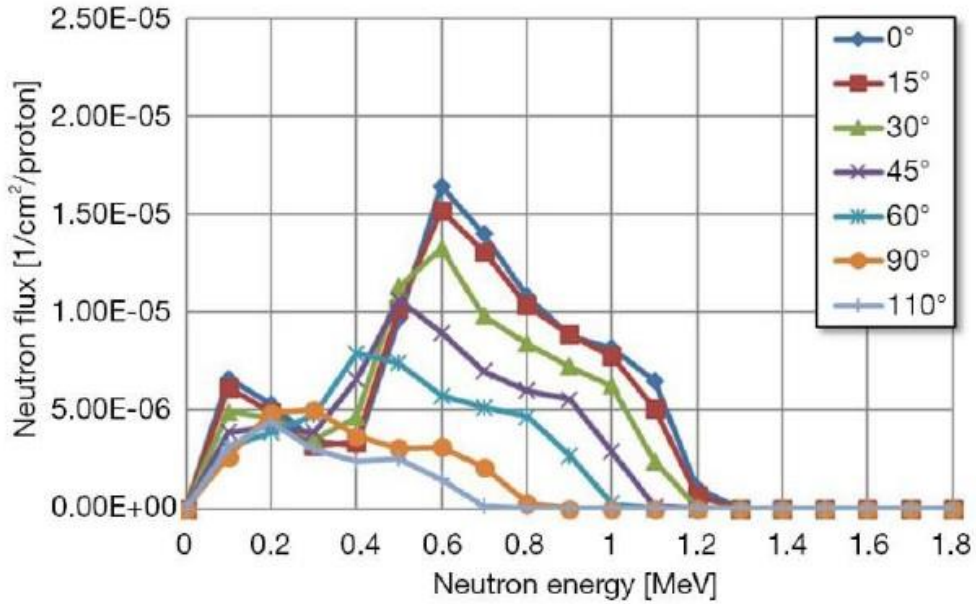


Colonna N, Medical Physics. 1999 doi:10.1118/1.598599

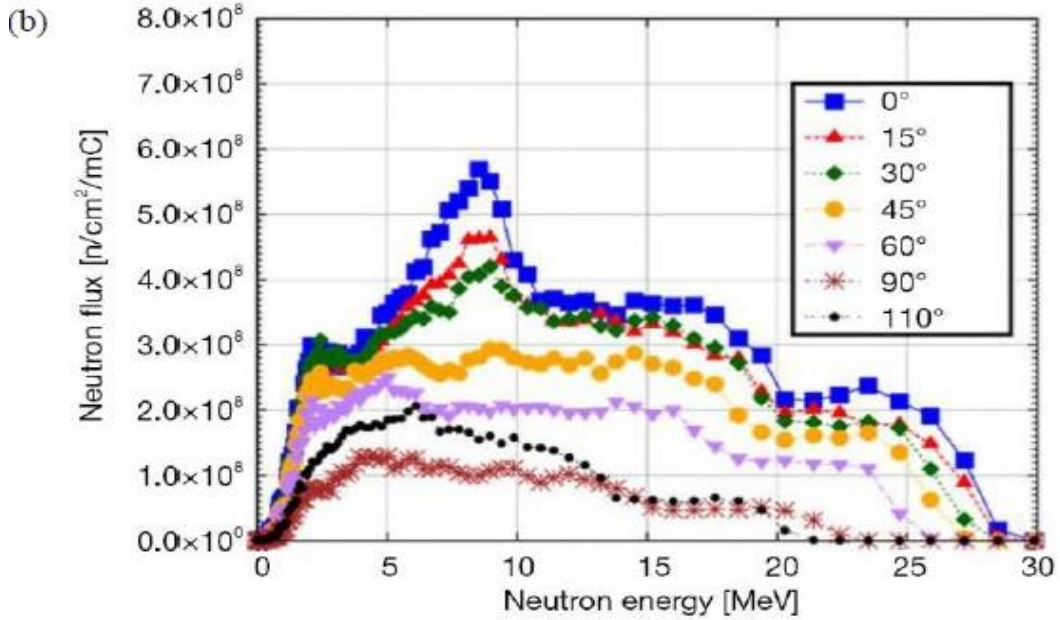
The minimal energy to produce neutrons with acceptable yield is about 2 MeV (D) – 2.5 MeV (p)

Neutron spectra produced in reactions used for AB-BNCT

Kiyanagi Y. Accelerator-based neutron source for boron neutron capture therapy. *Therapeutic Radiology and Oncology*. 2018;2:55-55. doi:10.21037/tro.2018.10.05



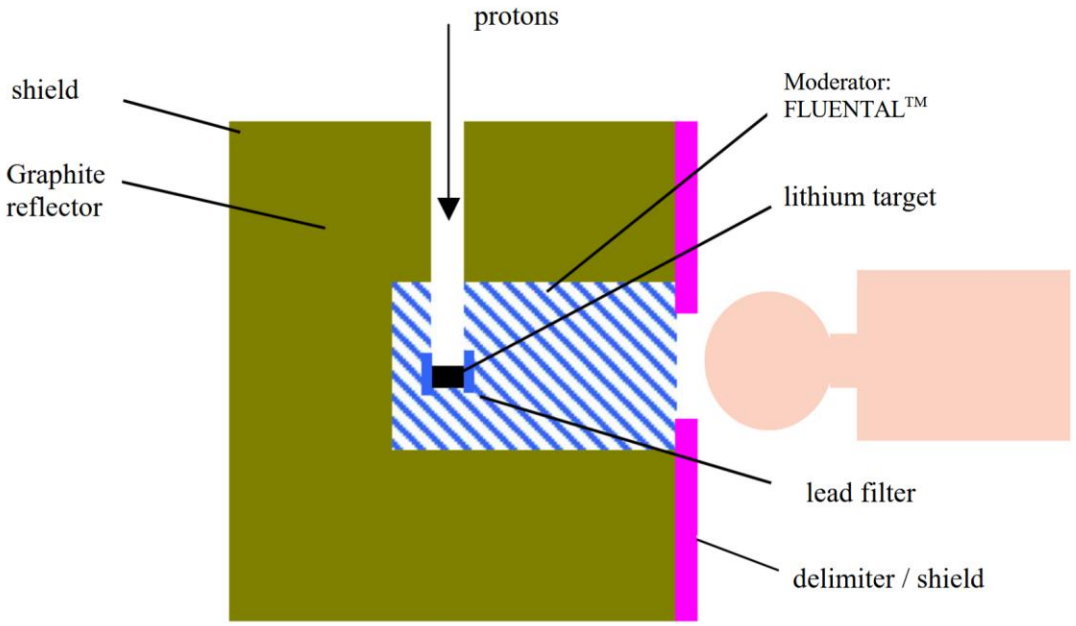
Neutron energy spectra at various emission angles for the p-Li reaction at a proton energy of 2.8 MeV

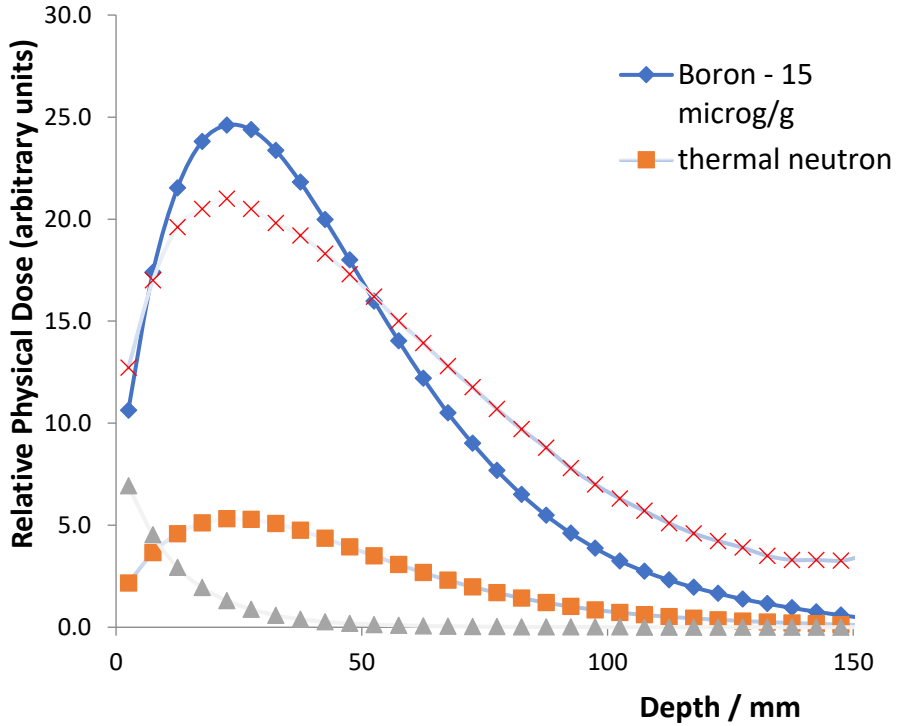


Neutron energy spectra at various emission angles for the p-Be reaction at a proton energy of 30 MeV

The fast neutron component adds unwanted dose to tissue.
The optimal spectrum is composed mainly from epithermal neutrons

Depth dose distribution for the AB-BNCT neutron beam





Culbertson et al. 2004doi:10.1016/j.apradiso.2004.05.057

Simulation of depth dose distribution in water phantom for the neutron beam at the Birmingham Accelerator-Generated epithermal Neutron Source (BAGINS) BNCT facility

Low energy accelarators for BNCT

Cyclotrons

Electrodynamic linear accelarators

Electrostatic accelarators

20 TABLE 5. CURRENT STATUS AND PERFORMANCE OF ACCELERATORS INTENDED FOR AB-BNCT FACILITIES

Institute/location	Machine status	Target reaction	Beam energy (MeV)	Current goal (mA)	Final power (kW)	Refs
		CYCLOTRONS				
Kyoto University, Japan	Clinical trials and research	5.5 mm ^{9}Be(p,n)	30	1	30	[7, 28]
Southern Tohoku Hospital, Japan	Treatments covered by insurance	5.5 mm ^{9}Be(p,n)	30	1	30	[7, 28, 53]
Kansai BNCT Research Center, Japan	Treatments covered by insurance	5.5 mm ^{9}Be(p,n)	30	1	30	[7, 28, 30]
Pengbo Hainan BNCT Center, China	Project planning	5.5 mm ^{9}Be(p,n)	30	1	30	
		ELECTRODYNAMIC LINEAR ACCELERATORS				
A-BNCT, Dawon Medax, Rep. Korea	RFQ-DTL: Preclinical	Thick ^{9}Be(p,n)	10	8	80	[54]
Tsukuba, Japan	RFQ-DTL: Preclinical	0.5 mm ^{9}Be(p,n)	8	10	80	[31, 55]
SARAF, Soreq, Israel*	RFQ-DTL: Under development	Liquid jet Li(p,n)	2.5	20	50	[33]
INFN, Legnaro, Italy*	RFQ: Under development	Solid ^{9}Be(p,n)	5	30	150	[56]
IHEP, BNCT-01, Dongguan, China	RFQ: Operational	Solid ^{7}Li(p,n)	3.5	5	17.5	[57]
IHEP, BNCT-02, Dongguan, China	RFQ: Under construction	Solid ^{7}Li(p,n)	2.8	20	56	[57]
National Cancer Center, Tokyo, Japan	RFQ: Clinical trial	Solid ^{7}Li(p,n)	2.5	20	50	[32, 36–37, 58]
Edogawa Hospital, Japan	RFQ: Commissioning	Solid ^{7}Li(p,n)	2.5	20	50	[7]
		ELECTROSTATIC ACCELERATORS				
Budker Institute, Novosibirsk, Russia*	VITA: Operational	Solid ^{7}Li(p,n)	2.0–2.3	10	23	[45]
Blokhin Cancer Center, Moscow, Russia	VITA: Under construction	Solid ^{7}Li(p,n)	2.3	7	20	[59]
Xiamen Humanity Hospital, Neuboron BNCT Center, China	VITA: Clinical study and research	Solid ^{7}Li(p,n)	2.5	10	25	[45, 60–61]
CNAO, Pavia, Italy	VITA: Under construction	Solid ^{7}Li(p,n)	2.5	10	25	[45]
Nagoya University, Japan	Dynamitron: Commissioning	Solid ^{7}Li(p,n)	2.8	15	42	[62–63]
University of Birmingham, UK*	Single ended: Under installation	Solid ^{7}Li(p,n)	2.6	30	78	[64–65]
Helsinki University Hospital, Finland	Single ended: Commissioning	Solid ^{7}Li(p,n)	2.6	30	78	[66]
Shonan Kamakura Hospital, Japan	Single ended: Under installation	Solid ^{7}Li(p,n)	2.6	30	78	[67]
University Hospital of Brussels, Belgium	Single-ended: Project planning	Solid ^{7}Li(p,n)	2.6	30	78	[68]
University of Granada, Spain	Single-ended: Under development	Solid ^{7}Li(p,n)	2.1	30	63	[69–70]
CNEA, Buenos Aires, Argentina	ESQ: Under development	^{9}Be(d,n) thin 8 μm, ^{13}C(d,n) thick	1.45	30	43	[7–9]
KIRAMS, Rep. Korea	ESQ: Under development	^{9}Be(d,n) thin 8 μm, ^{13}C(d,n) thick	1.45	30	43	[7–9]

Note: The KIRAMS project is within a collaborative agreement with CNEA, Argentina. Facilities denoted with * are non-clinical facilities.

IAEA , 2023

Less-expensive, small footprint – good for hospitals

BNCT becomes a hot topic

Japan:
- 5 BNCT centers
- BNCT reimbursed for some head&neck cancers
- officially approved and covered by national health insurance- unresectable, locally advanced or locally recurrent head and neck cancers

Taiwan:
- Long experience in reactor based BNCT
- New AB-BNCT at Taipei Veterans General Hospital (TVGH), cyclotron based

China:
- In 2018, the BNCT Center at Xiamen Humanity Hospital (XHH), the first AB-BNCT center in China
- 10 BNCT centers under construction



TAE Life Sciences



BNCT in Europe – the resurection

The Netherlands:

Petten recator, 1st patient 1997

Decommisioning 2013

Finland:

Otaniemi TRIGA Mark II reactor:

249 patient treated 1999–2012

The reactor closed at 2012

Finland:

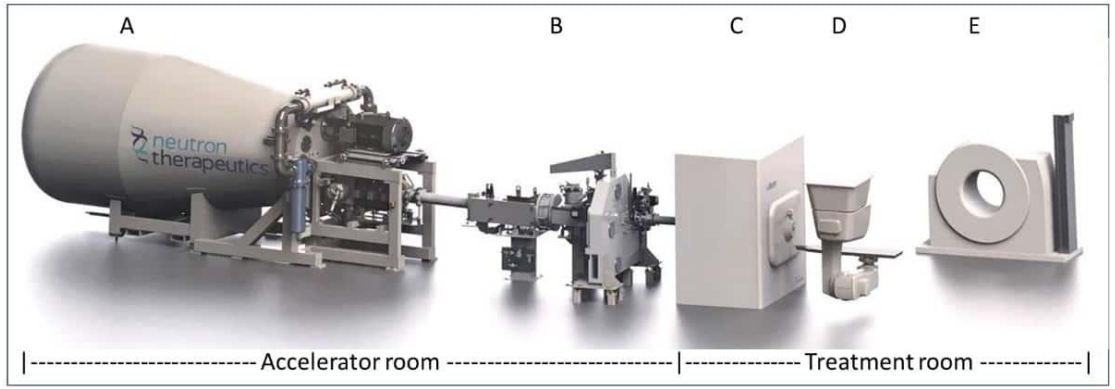
NuBeam facility at the University Hospital Helsinki **first patient 2026**

Italy:

CNAO and TEA Life Science build a facility at Pavia, **start in 2027**



BNCT treatment room at the UH Helsinki



https://physicsworld.com/

AB- BNCT Procedure

1. Administration of BPA (before or during the treatment)
2. Patient positioning using Computed Tomography
3. Measurements of BPA concentration in blood.
4. Irradiation (about 30 minutes)
5. Typically 1 field, max. two fields



https://www.skgh.jp/news/142841/

nuBeam facility in Kamakura, Kanagawa, Japan.

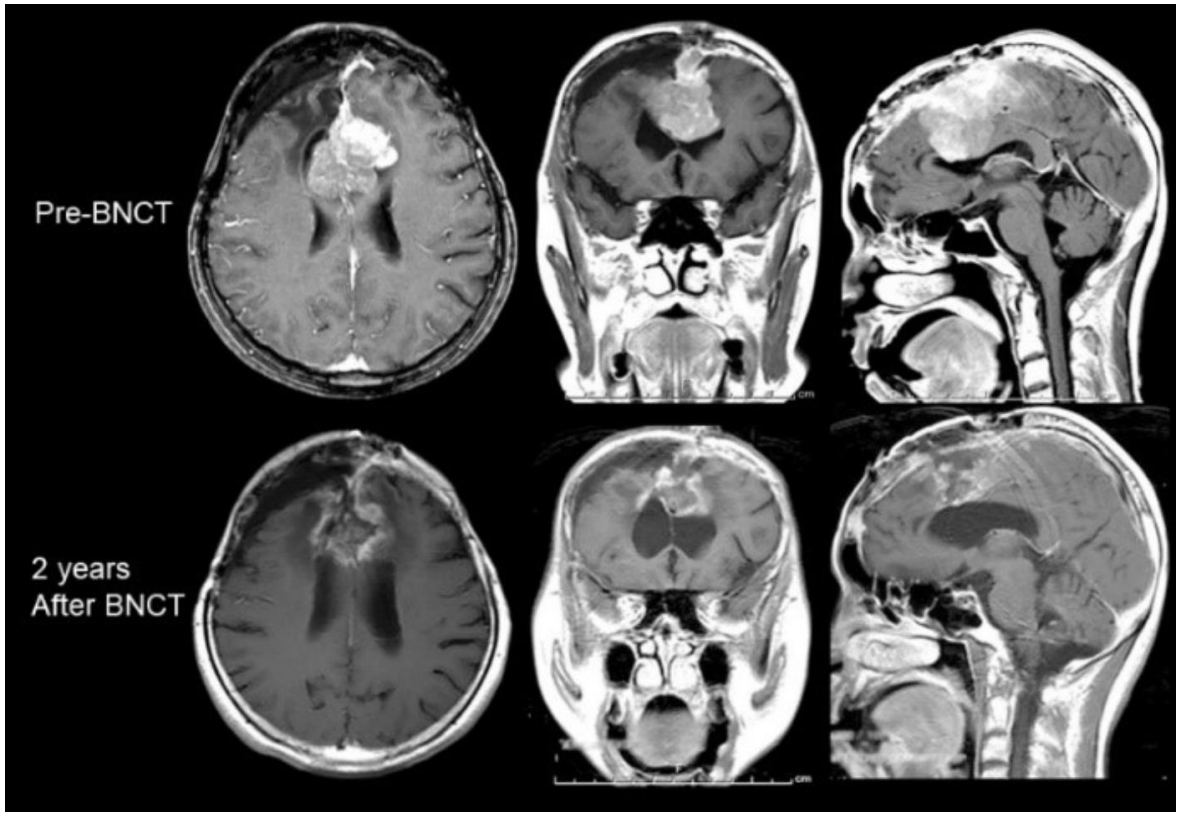
Tandem electrostatic accelerator , 2.6 MeV protons, 30 mA

What cancers are treated in BNCT?

In Japan, Boron Neutron Capture Therapy (BNCT) is officially approved and covered by national health insurance for unresectable, **locally advanced or locally recurrent head and neck cancers**

Several clinical trials were performed for **malignant melanoma, breast cancer, lung cancer, and liver cancer**

The biggest expectations were for treatment of **glioblastoma and gliomas** – for which the conventional external beam radiotherapy is mostly unsuccessful. Up to now without spectacular success.



courtesy of S. Miyatake, Osaka Medical College

AB-BNCT versus Targeted Alpha Therapy

1. Boron-containing compound
2. Neutron capture reaction
3. α- particles
4. **Range 5-10 μm**
5. LET: 50-200 keV/μm
6. External neutron beam needed
7. **Dose distribution depends on B concentration and neutron beam**
8. **Defined irradiation period**

1. Radiolabeled targeting molecule
2. Radioactive decay
3. α- particles
4. **Range: 40-100 mm**
5. LET: 50- 150 keV.um
6. Beam not needed
7. **Depends on radionuclide distribution**
8. **Governed by physical decay and biological clearance**

THE HENRYK
INSTITUTE
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BNCT can be regarded conceptually as externally activated, targeted high-LET particle therapy

BNCT in Poland – our current activities

1. BNCT research facility at Maria reactor, Świerk
2. Intention letter Bydgoszcz Centre of Oncology with TAE Life Sciences
3. Polish Consortium for BNCT
4. Cooperation with the European Radiation Dosimetry Group EURADOS
5. Report of International Commission on Radiation Units and Measurements on BNCT



Special channel and beam shutter prepared, experimental and control room

Facility waits for approval of the National Atomic Energy authority (PAA)

BNCT –like neutron source at the linear accelarator at IFJ PAN – research opportunities

1. Dosimetry and spectrometry methods for BNCT beams:
   - testing Tissue Equivalent ionization chambers,
   - development of TL/OSL dosimetry methods
   - development of spectrometry using activation foils

2. Neutron shaping devices:
   - experimental verification of Monte Carlo calculations

3. Testing of the new pharmaceuticals with boron
   - collaboration with chemistry laboratories

4. Calibration beams for radiation protection
   - testing different targets and phantoms



Summary and Conclusions

1. Boron Neutron Capture Therapy is again consider as an interesting method for radiation therapy because the new accelerators are able to produce high intensity neutron beams

2. New Accelerator-Based BNCT centers are put in operation in Japan, Taiwan, China, Finland and Italy.

3. The planned in IFJ PAN linear accelerator offers opportunities to produce neutron beam, which allows for many R&D in AB-BNCT, including dosimetry, spectrometry, construction of targets and beam shaping devices, radiobiology and chemistry of boron compounds.

4. This research can be of interest for Polish Consortium of BNCT and for the growing interest of BNCT users and developers around the world.