The accelerator BNCT System for Sustainable Quality of Life

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Thursday Oct. 24, 2024

Agenda

1) Quality of life after Cancer treatment

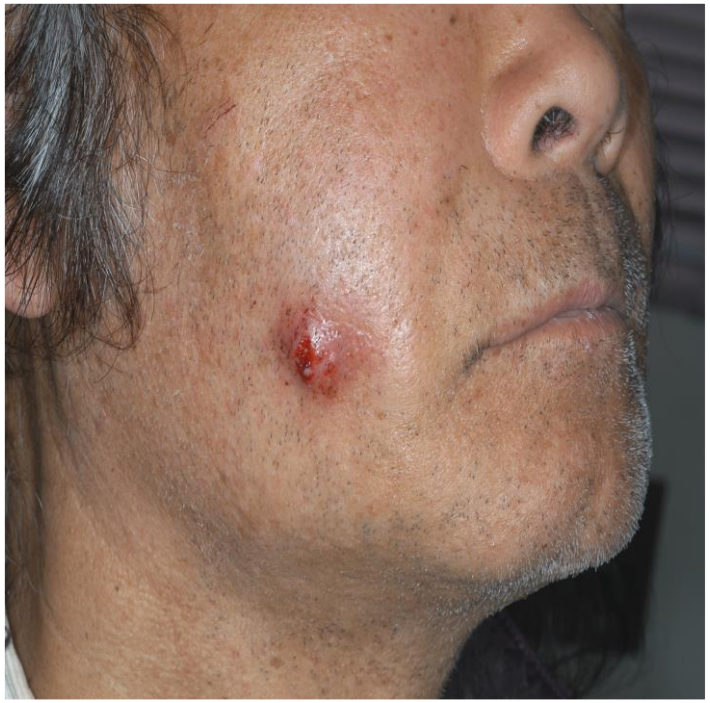
2) Boron Neutron Capture Therapy for cancer

3) The Accelerator BNCT System

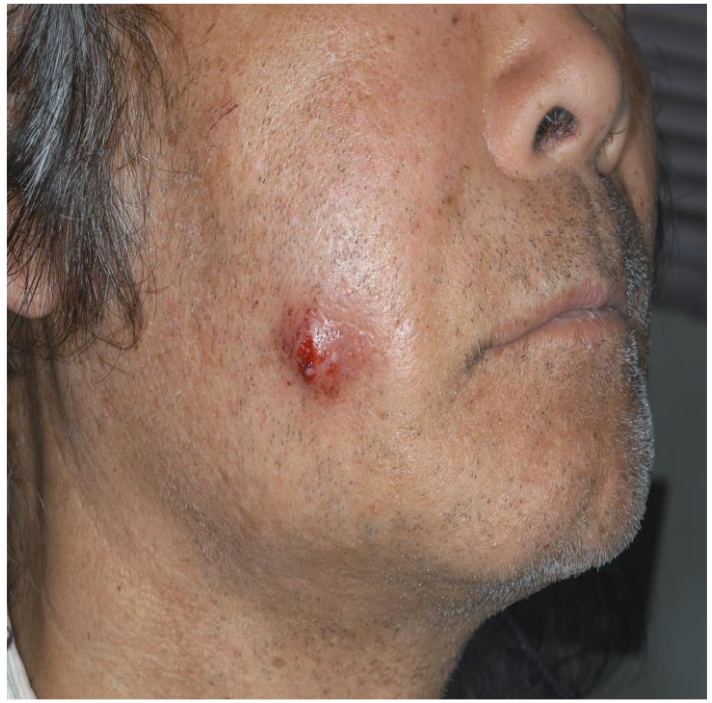
1) Quality of life after Cancer therapy

https://www160.statcan.gc.ca/index-eng.htm

Something’s wrong?

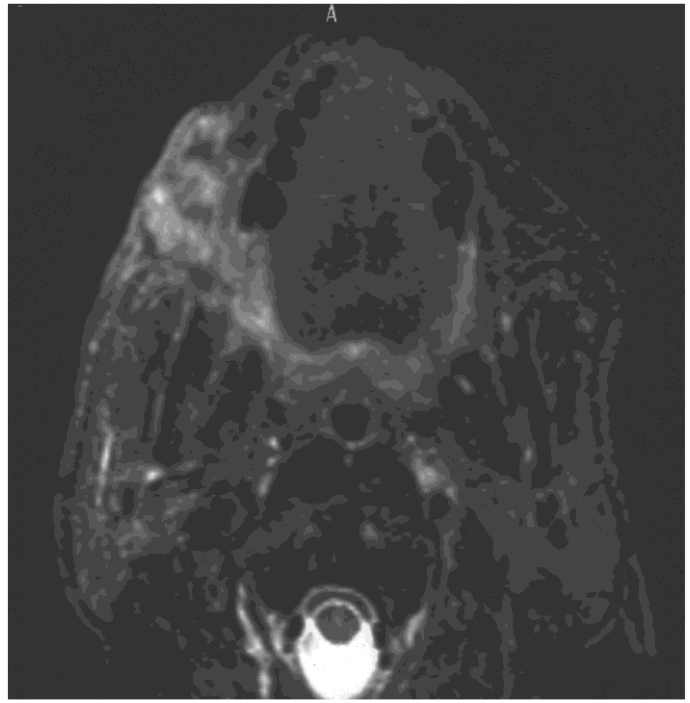


Diagnosis Buccal mucosa SCC, cT4aN0, Stage Ⅳ A



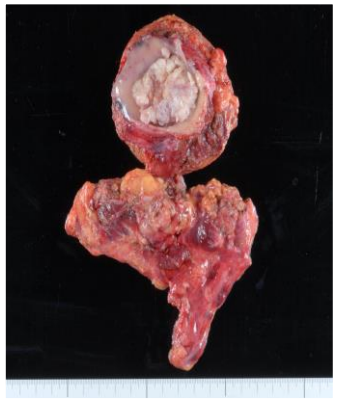
Oral examination

Image diagnosis



Histological diagnosis: SCC

Cancer treatment ~Surgery~

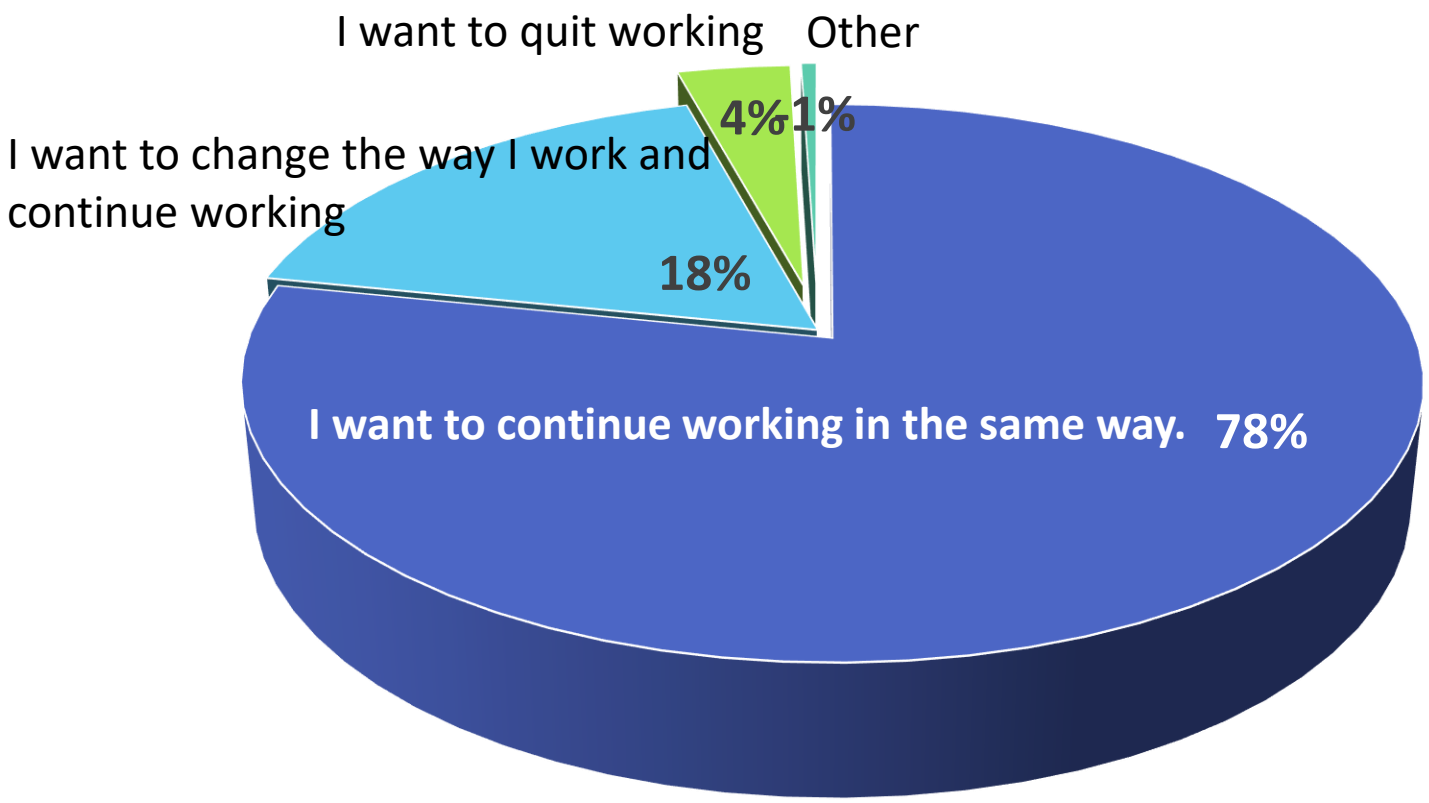


The cancer has been cured!
But…

This is not what I expected

The patient still need to do rehabilitation.

Willingness to work after cancer in Japan



Reason for wanting to continue working : 96 %

- Maintenance of livelihood; 81.7 %
- Fulfillment and purpose in life; 35.3 %
- Treatment cost; 28.6%

*Multiple answers

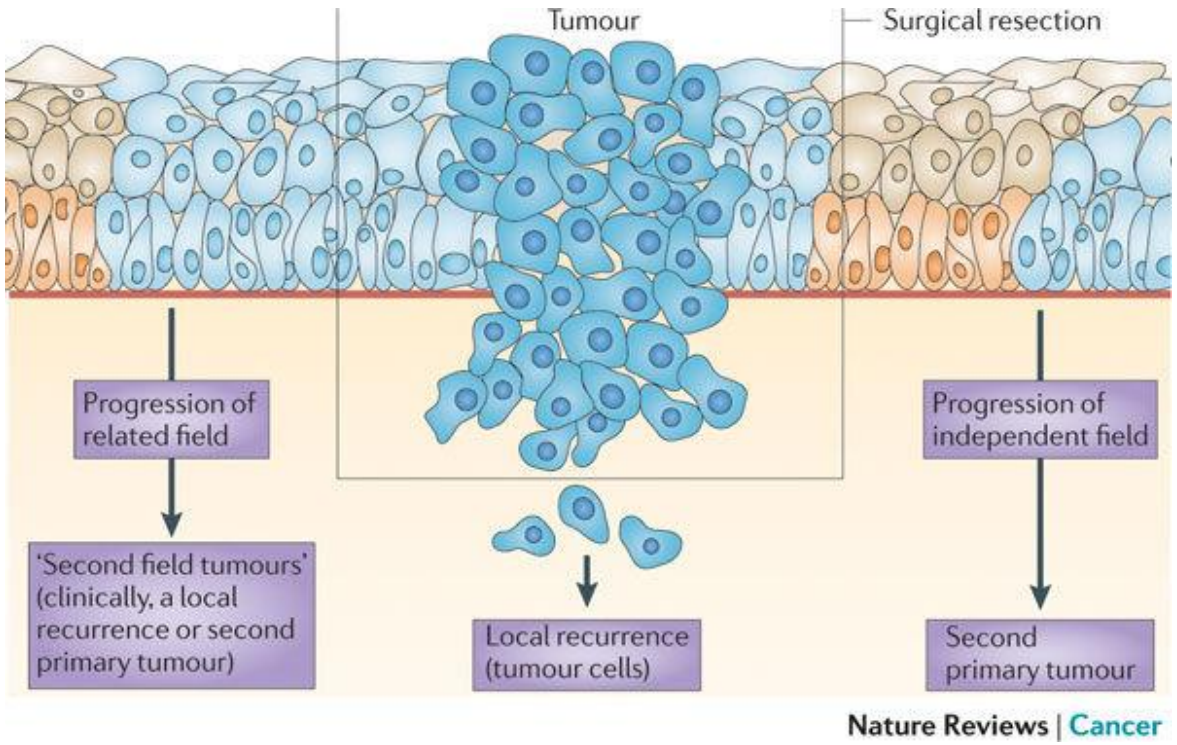
The cancer patients who are working while receiving treatment: 53.6 %

出典1：東京都福祉保健局「東京都がん医療等に係る実態調査結果（がん患者の就労等に関する実態調査）（平成31年3月）」よりメットライフ生命にて作成

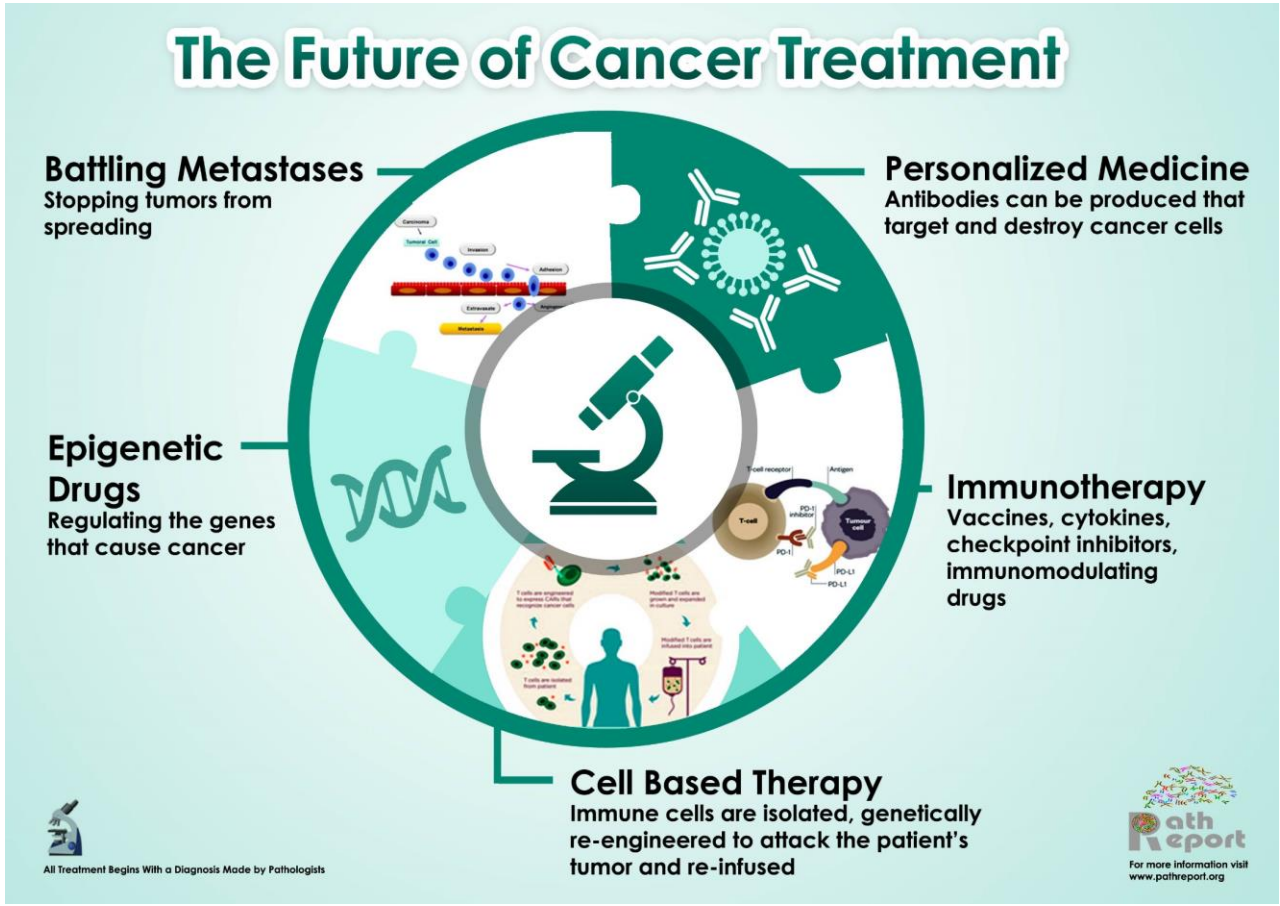
出典2：メットライフ生命調べ「特定疾病に関するインターネット調査（2021年11月）」より作成。調査対象者は「ガン罹患者およびガン罹患経験者」です。

From Anatomy based to Biology based cancer treatment

Anatomy based therapy



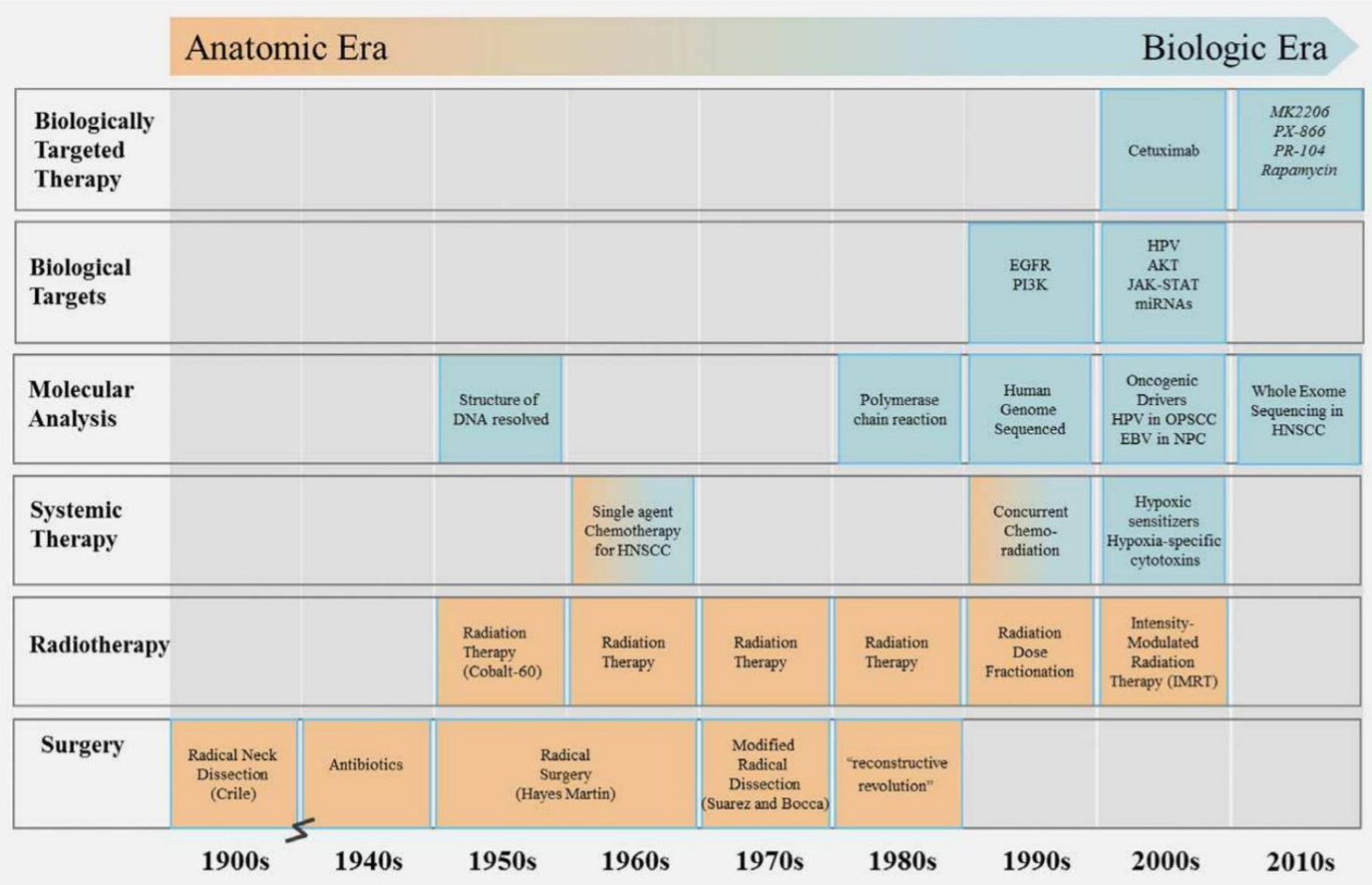
Biology based therapy



Function-Sparing Therapy

Nature Reviews Cancer **vol11**, 2011

Management of head and neck cancer



Insurance medial treatment in Japan

2012：Cetuximab (EXTREME trial)
Immune checkpoint inhibitor
2017：Nivolumab (Checkmate 141 clinical trial)
2019：Pembrolizumab (KEYNOTE-048)
Chemical surgery
2020：BNCT system (JHN002 study)
2020：ASP-1929 photoimmunotherapy (NCT02422979)

Int. J. Cancer 2013

2）Boron Neutron Capture Therapy for Cancer

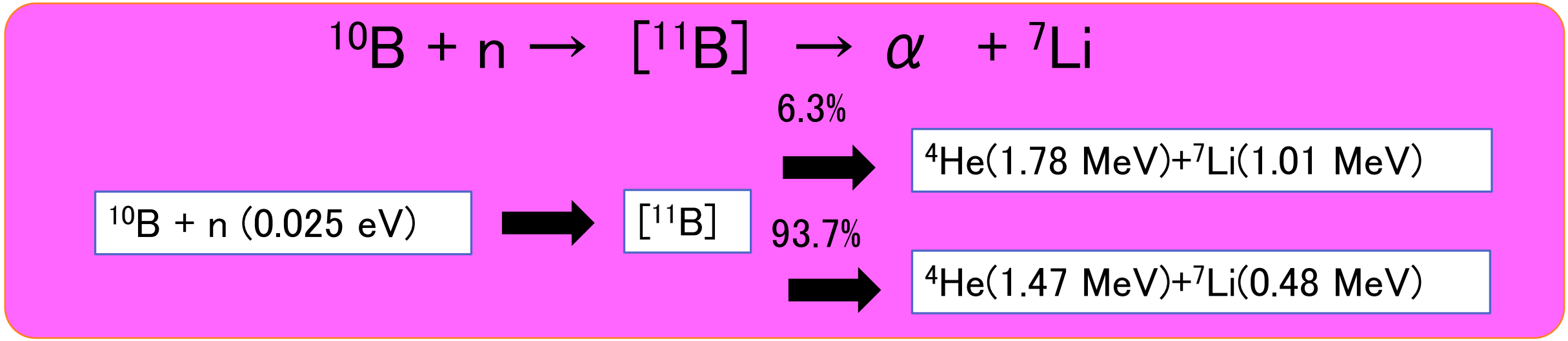
B：Boron
N：Neutron
C：Capture
T：Therapy

History of BNCT

1932: J. Chadwick discovers the neutron

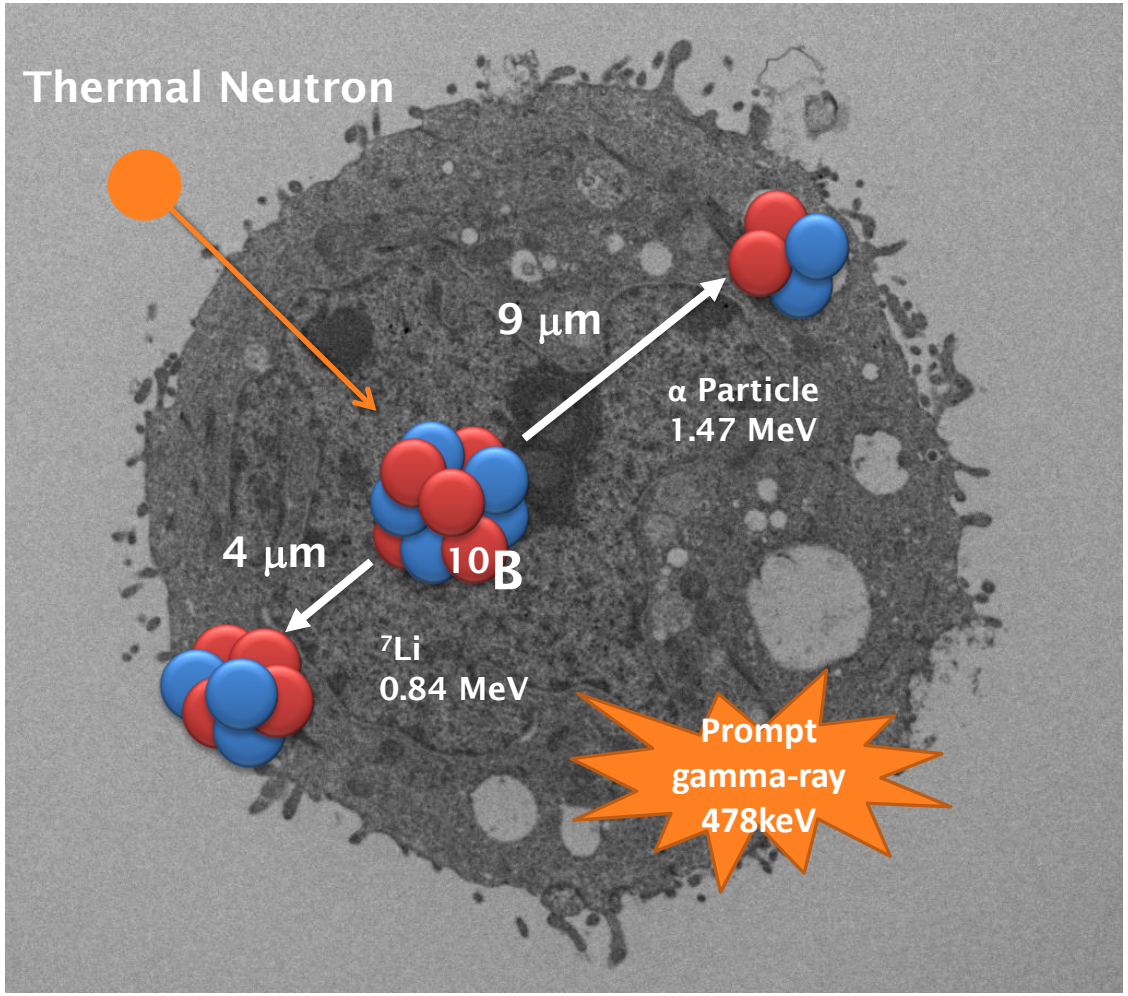
1936:G.L. Locher proposes BNCT as a cancer therapy

1951: W. Sweet initiates BNCT clinical trial



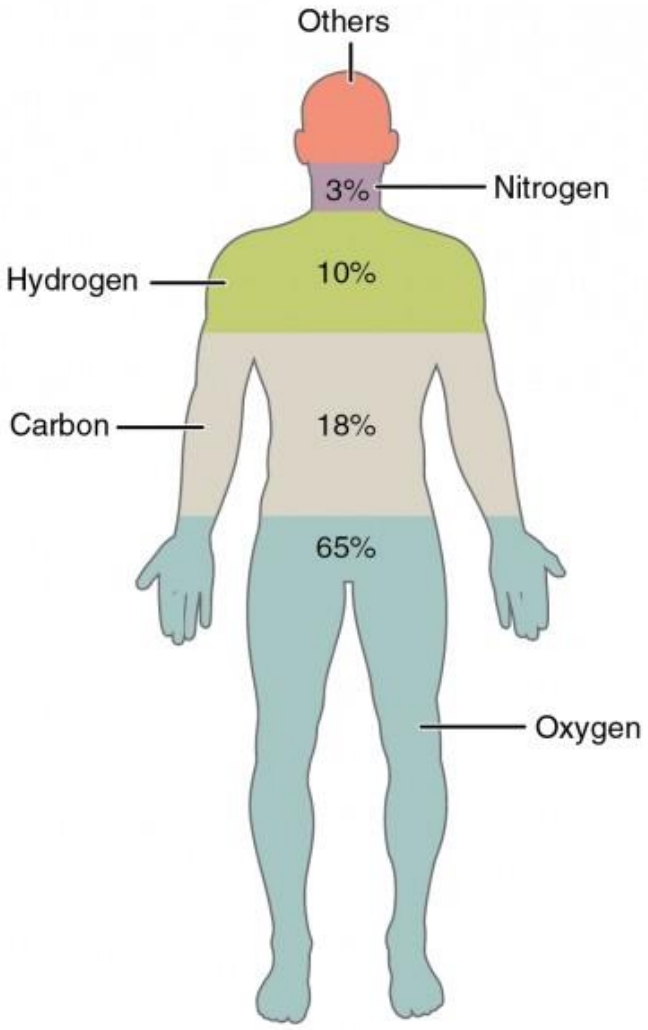
Targeted Boron-10 Therapy for Cancer

$^{10}B\ (n,\ \alpha)\ ^{7}Li$ capture reaction



No damage to surrounding tissue
→ High quality of Life

Non-Boron-10 in human body



Atomic Composition of a Man

(70 kg)

Element	Mass [%]	Mass [mol]	Mass 70 [kg]	Atoms 7×10^{27} atoms	Nuclide	Ratio [%]	Neutron cross sections [barn] *
Oxygen	61	2700	43 kg	1.61×10^{27}	^{16}O	99.757	<0.0002
Carbon	23	1300	16 kg	8.33×10^{26}	^{12}C	98.93	0.0037
Hydrogen	10	6900	7 kg	4.22×10^{27}	^{1}H	99.989	0.332
Nitrogen	2.5	129	1.8 kg	3.9×10^{25}	^{14}N	99.632	1.75
Calcium	1.4	25	1.0 kg	1.6×10^{25}	^{40}Ca	96.941	3.4
Phosphate	1.1	25	780 g	9.6×10^{24}	^{31}P	100	0.19
Boron	-	-	18mg	2×10^{20}	^{11}B	80	0.0055
					^{10}B	20	3835

＊ thermal neutron(En=0.025eV), 1 [barn]= $1X10^{-24}$ cm^2

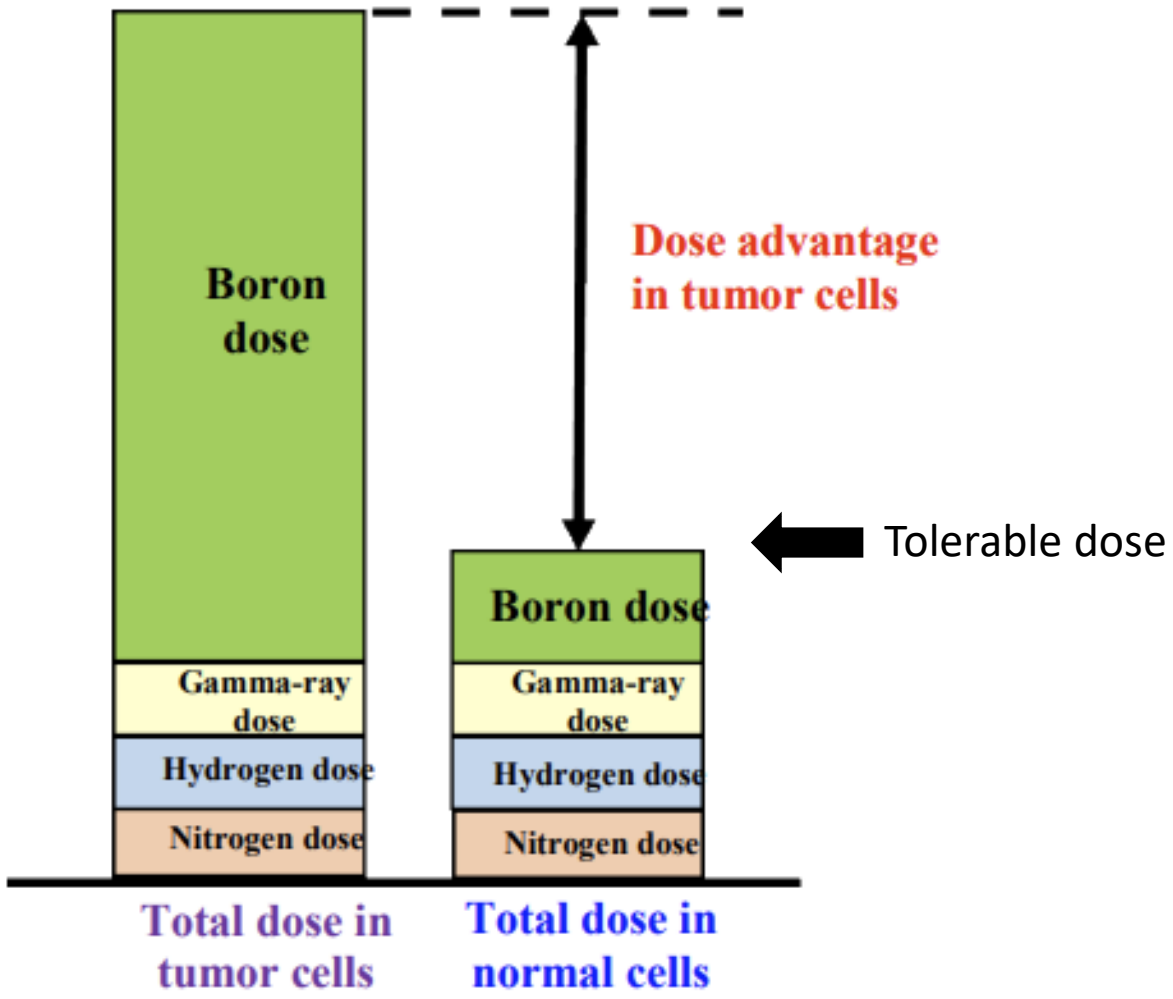
Reference: Emsley, John, The Elements, 3rd ed., Clarendon Press, Oxford, 1998
http://www.foresight.org/Nanomedicine/index.html, 2006.
https://wwwndc.jaea.go.jp/NuC/index.html

https://courses.lumenlearning.com/nemcc-ap/chapter/elements-and-atoms-the-building-blocks-of-matter/

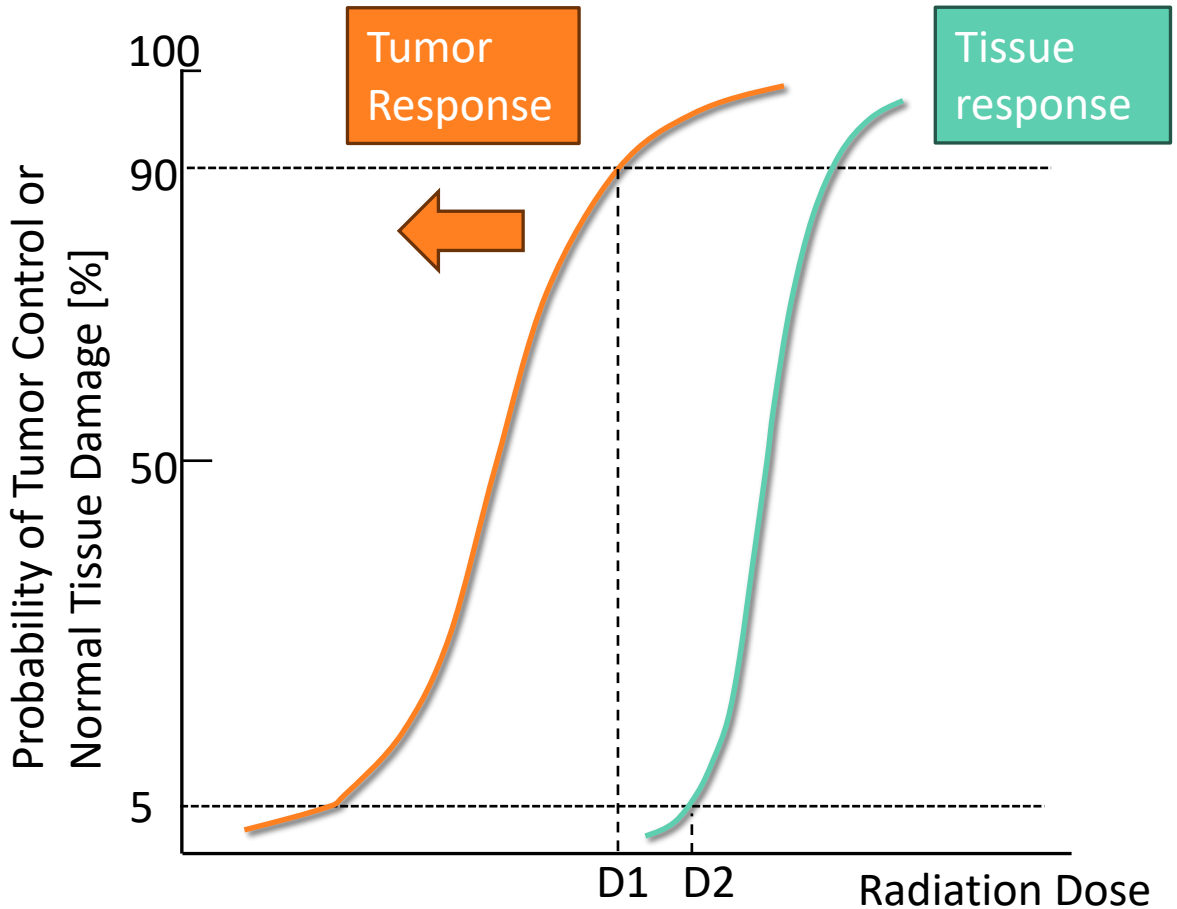
＊人間は約70%が水（H_2O）。

A single irradiation of BNCT

Biological dose of BNCT



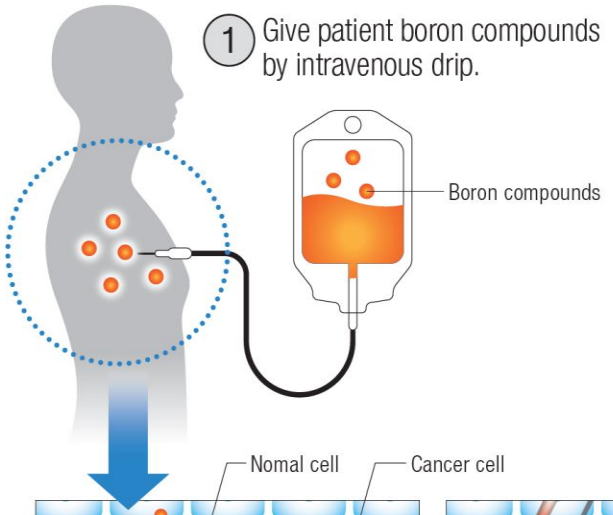
Therapeutic ratio (TR) = D2/D1: TR>1



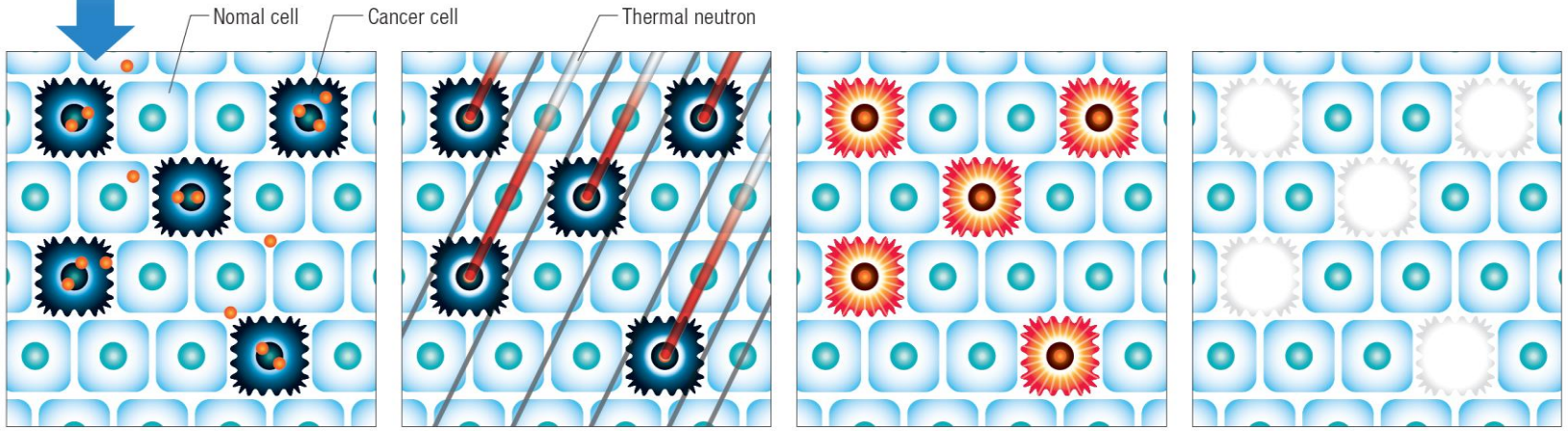
1 time treatment
→ Early return to society

BNCT Procedures

BNCT procedures



Before commencing BNCT, the accumulation of boron compounds in the cancer is checked by marking boron agents with a radioactive nuclide and administering a PET inspection. After determining that a sufficient level of boron can accumulate in the cancer, the patient receives a dose of boron compound and is irradiated with an epithermal neutron taken from a nuclear reactor or an accelerator. Neutron thermalization of the epithermal neutron then takes place in the body and the boron reacts with the cancer to selectively destroy the cancer in an effective manner.



http://www.pref.osaka.lg.jp/jigyochosei/bnct-jituyouka/

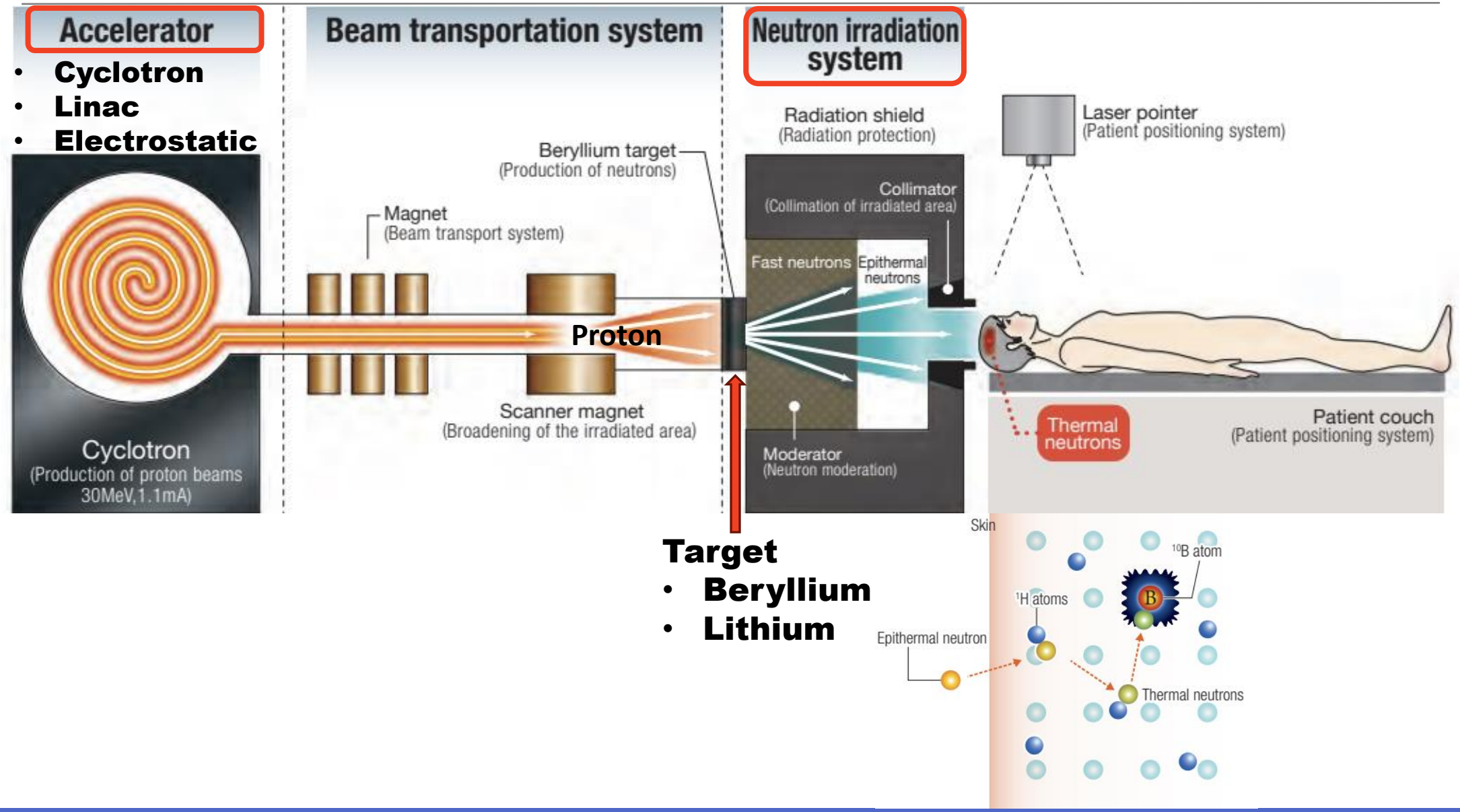
3) Accelerator based BNCT system

Country	Institute/Hospital	Accelerator type	Target material	Beam energy (MeV)	Beam current (mA)	Status
Japan	Southern Tohoku Hospital	Cyclotron	Be	30	1.0	Treatment
	Kansai BNCT Research Center	Cyclotron	Be	30	1.0	Treatment
	Kyoto University	Cyclotron	Be	30	1.0	Research
	National Cancer Center Hospital	Linac	Li	2.5	12	*1
	Edogawa Hospital	Linac	Li	2.5	12	*1
	University of Tsukuba	Linac	Be	8	2.1	*2
	Nagoya University	Electrostatic	Li	2.8	15	*3
	Shonan Kamakura Hospital	Electrostatic	Li	2.6	12	*3
Finland	Helsinki University Hospital	Electrostatic	Li	2.6	12	*2
China	Xiamen Humanity Hospital	Electrostatic	Li	2.5	10	*1
	IHEP	Linac	Li	3.5, 2.8	2.9, 20	*3
	China Institute of Atomic Energy	Cyclotron	Be	14	1	*5
	Lanzhou University	Electrostatic	Li	2.6	15	*5
Italy	CNAO	Electrostatic	Li	2.5	10	*5
	INFN	Linac	Be	5	30	*4
S. Korea	Gil Hospital	Linac	Be	10	8	*1
U.K.	Birmingham University	Electrostatic	Li	2.6	12	*4
Russia	Budker Institute	Electrostatic	Li	2.0-2.3	10	Research
Argentina	CNEA (deuteron)	Electrostatic	Be, C	1.45	30	*4
Spain	University of Granada	Electrostatic	Li	2.1	30	*5

*1: Clinical study, *2: Preparation of clinical study, *3: Commissioned, *4: Under development, *5: In planning

EPJ Techniques and Instrumentation volume 10, Article number: 18 (2023)
https://doi.org/10.1140/epjti/s40485-023-00105-5

Accelerator BNCT system



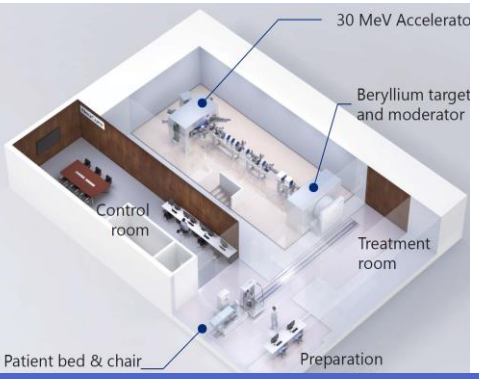
https://www.pref.osaka.lg.jp/o020050/jigyochosei/bnct-jituyouka/bnctnikansurujyouhou.html

Accelerator based BNCT hospitals in Japan

住友重機械工業 **Cyclotron & Be target (30 MeV, 1mA)**

Southern Tohoku General Hospital (Cancer treatment by health insurance from 2020)

Kansai BNCT Medical Center (Cancer treatment by health insurance from 2020)

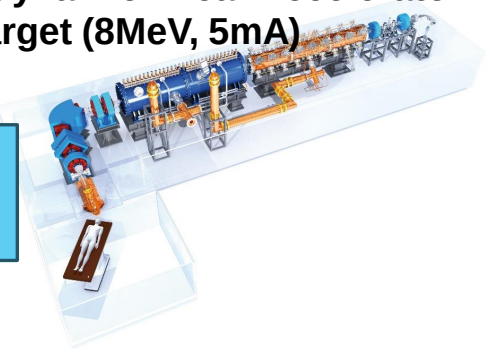


BNCT hospitals: 6
Patient treatments: 2
Clinical trials:3
Comimissioning:1

BPA

株式会社ｉＢＮＣｔ **Electrodynamic linear Accelerator & Be target (8MeV, 5mA)**

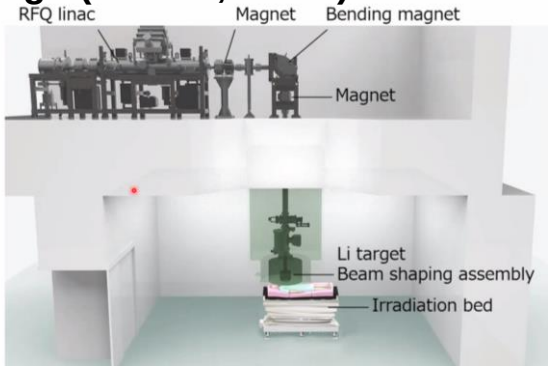
Tsukuba University (Clinical trials)



CICS **Electrodynamic linear Accelerator & Li target(2.5MeV, 20mA)**

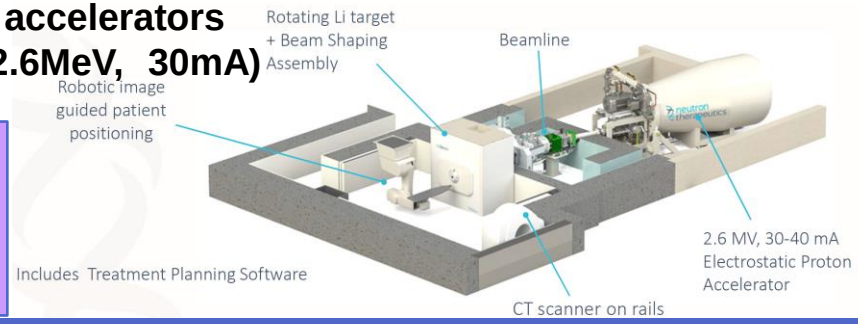
National Cancer Center (Clinical trials)

Edogawa Hospital (Clinical study)



neutron therapeutics **Electrostatic accelerators & Li target (2.6MeV, 30mA)**

Shonan Kamakura General Hospital (Preclinical Study)



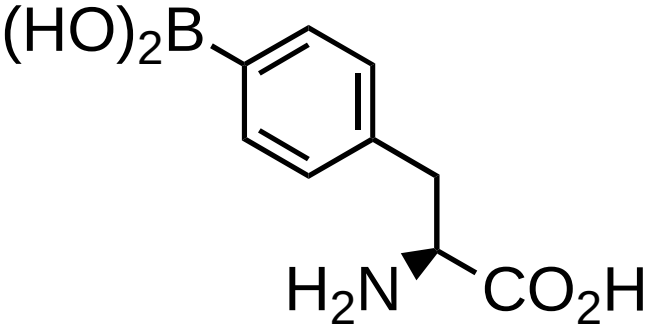
ISBN978-4-9913228-0-8

NTRC Neutron Therapy Research Center

Japan. Committed to SDGs

Boron-10 for BNCT in Japan

Product Name	Steboronine® intravenous drip bag 9000 mg/300 mL
Generic Name	Borofalan [10B]
Indications	Locally unresectable recurrent or unresectable advanced head and neck cancer
Dosage & Administration	For adult patients, Borofalan [10B] is administered intravenous infusion at approximately 500 mg/kg. In particular, for the first two (2) hours, the amount of Borofalan [10B] per hour is adjusted for 200 mg/kg (i.e. total amount for 2 hours: 400 mg/kg). After that 2 hours, neutron irradiation to the cancer lesion begins, and at the same time, Borofalan [10B] is administered at 100 mg/kg for one (1) hour until the neutron irradiation is completed.
NHI Price	JPY 444,215 (per 300mL bag)
Manufactured by	Stella Pharma Corporation



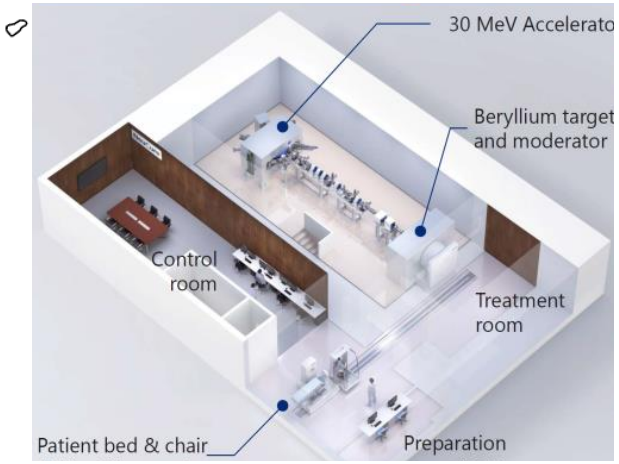
https://stella-pharma.co.jp/cp-bin/wordpress5/wp-content/uploads/2020/05/Steboronine-launched_ENG.pdf

Accelerator based BNCT systems

住友重機械工業

住友重機械工業 **Cyclotron & Be target**
（30 MeV, 1mA)

Southern Tohoku BNCT Research Center
Feb. 2016 - June 2018 Phase Ⅱ Clinical Trials; Recurrent high-grade glioma
July 2016- Feb.2018 Phase Ⅱ Clinical Trials; Head and neck cancer
June 2020~ Medical treatment covered by health insurance; **locally advanced or locally recurrent head and neck cancer**



***Pengbo (Hinan) Medical Technology in China (2025-planned)**

Kansai BNCT Medical Center
June 2020 ~ Medical treatment covered by health insurance; **locally advanced or locally recurrent head and neck cancer**
2022~ Clinical study; Recurrent malignant glioma

Kyoto University (prototype)
Oct.2012-April 2015 Phase Ⅰ Clinical trials; Brain tumor
Jan. 2016 Jan.- June 2018 Phase Ⅱ Clinical Trials; Brain tumor
Feb.2014- Jan. 2016 Phase Ⅰ Clinical Trials; Head and Neck Cancer

NTRC Neutron Therapy Research Center
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Southern TOHOKU BNCT Research Center

一般財団法人 脳神経疾患研究所 附属
南東北BNCT研究センター
Southern Tohoku BNCT Research Center

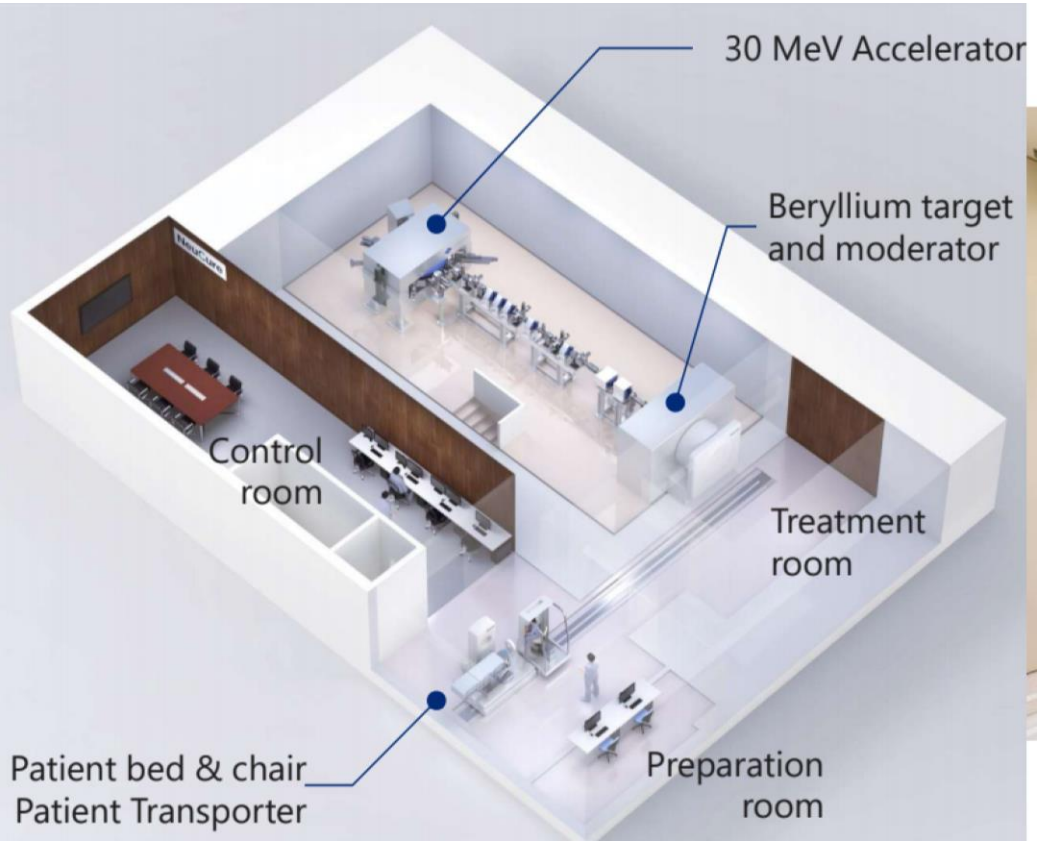
https://youtu.be/NrGtA2Cd3_k

NTRC Neutron Therapy Research Center

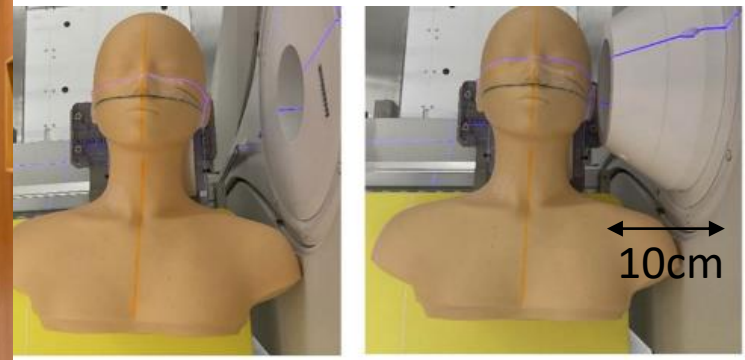
Japan. Committed to SDGs

Kansai BNCT Medical Center

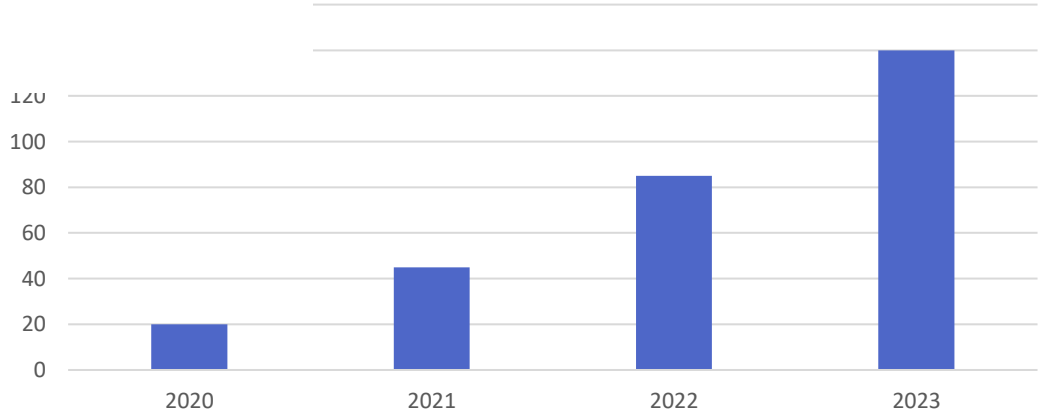
Pharmaceutical University



Development of extended collimator



2020~ BNCT for head and neck cancer
290 cases (until 2024 March)



https://www.nature.com/articles/s41598-022-17974-7
https://www.osaka-med.ac.jp/kbmc/bnct/consultation.html

2020 ~ BNCT for locally advanced or locally recurrent head and neck cancer

BPA (Steboronin ®) for BNCT: 558 head and neck cancer cases (~2024 March)

335 patients registered*
between 20 May, 2020 and 24 March, 2023

179 early treatment cases in 162 patients
covered by CRF survey until 31 January, 2022

17 cases excluded due to second registration for treatment to relapse after BNCT

162 first treatment cases in the safety analysis set

7 cases excluded from efficacy analysis
- 4 with inadequate neutron irradiation
- 2 with uncollected CRF after 6 months
- 2 with unsatisfactory tumor response
- 1 with off-label use

155 cases in the efficacy analysis set

Patients
- Prior conventional radiotherapy : 93 %
- Prior chemoradiotherapy: 79%

	SCCHN (*n* = 137)	NSCCHN (*n* = 17)
ORR, % (95% CI)	72.3 (64.0–79.6)	64.7 (38.3–85.8)
Best overall response		
CR, *n* (%)	63 (46.0)	8 (47.1)
PR, *n* (%)	36 (26.3)	3 (17.7)
SD, *n* (%)	31 (22.6)	5 (29.4)
PD, *n* (%)	6 (4.4)	0
NE, *n* (%)	1 (0.7)	1 (5.9)

Abbreviations: SCCHN, squamous cell carcinoma of the head and neck; NSCCHN, non-squamous cell carcinoma of the head and neck; ORR, overall response rate; CI, confidence interval; CR, complete response; partial response; SD, stable disease; PD, progressive disease; NE, not evaluated.

一般財団法人 脳神経疾患研究所 附属
南東北BNCT研究センター
Southern Tohoku BNCT Research Center

DOI: 10.3390/cancers16050869

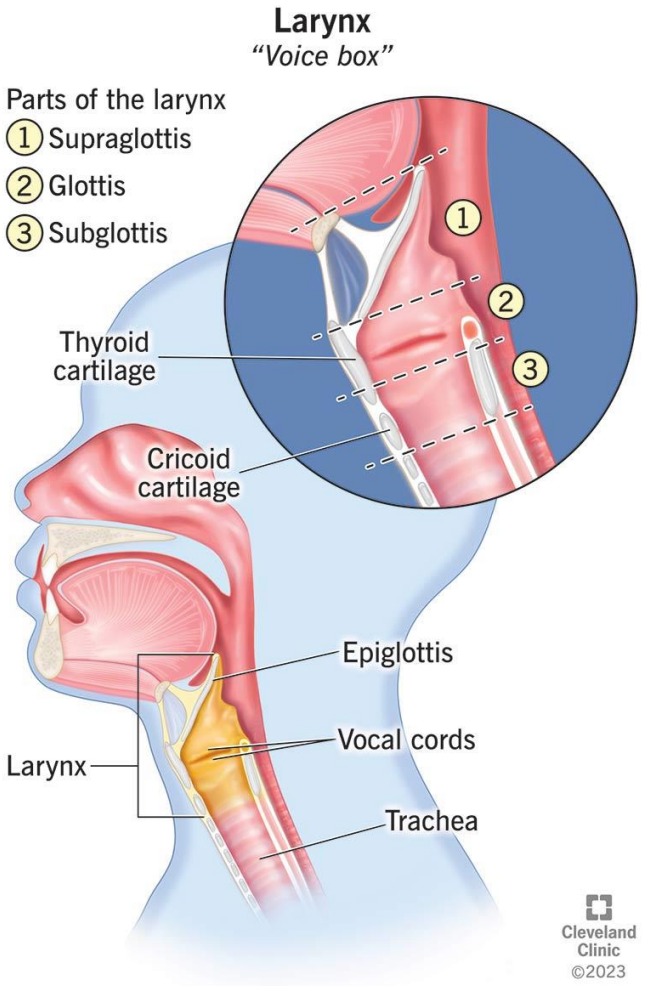
NTRC Neutron Therapy Research Center

Japan. Committed to SDGs

BNCT for Recurrent laryngeal carcinoma

Function of Larynx

- Respiratory “breathing”: to provide an open airway
- Phonatory “Speaking”: to provide a mechanism for sound production
- Protective: to prevent food or drink from accidentally entering the trachea

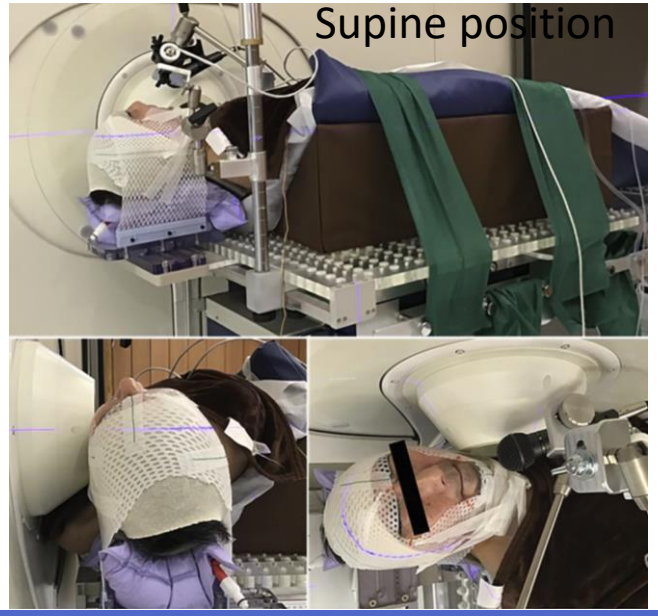


15 patients, median age 74 years

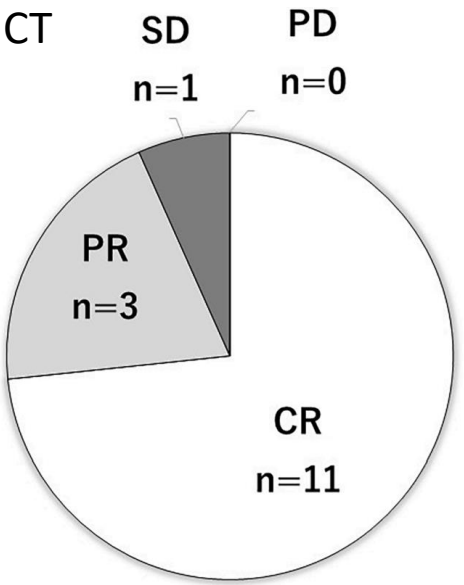
Patient and tumor characteristics and treatments administered.

Patient	Age (y), Gender	Subsite	TNM	Initial therapy	Time from initial RT to BNCT (m)	rTNM	Recurrent tumor diameter (mm)
1	53/M	glottic	T1aN0M0	RT 70Gy	9	rT1aN0	8
2	64/M	glottic	T2N0M0	CRT(CDDP) 70Gy	82	rT2N0	14
3	74/M	glottic	T1aN0M0	RT 66 Gy, TOLS	44	rT2N0	14
4	55/F	glottic	unknown	CRT(CDGP) 66Gy	107	rT2N0	15
5	81/M	glottic	T2N0M0	BRT(Cetuximab)70 Gy, SOHND	76	rT2N0	16
6	84/M	subglottic	T2N0M0	CRT(CDDP) 70Gy	87	rT2N0	17
7	84/M	glottic	unknown	RT (dose unknown)	150	rT2N0	18
8	81/M	glottic	T2N0M0	RT 67 Gy, TOLS × 4	45	rT2N1	9
9	74/M	glottic	T3N0M0	CRT(CDDP) 67 Gy, TOLS,S-1	28	rT3N0	12
10	85/M	glottic	T3N0M0	RT 70Gy	10	rT3N0	15
11	61/M	glottic	T3N0M0	CRT(CDDP) 70Gy	6	rT3N0	20
12	74/F	glottic	T3N1M0	TPF, CRT(CDDP) 16Gy	12	rT3N1	11
13	87/F	glottic	T2N0M0	RT 64.8Gy	47	rT4aN0	15
14	69/M	glottic	T1aN0M0	RT63Gy, TOLS, PIT	95	rT4aN0	20
15	74/M	glottic	T1aN0M0	RT 70 Gy, Partial laryngectomy	139	rT4aN0	22

RT: radiation therapy, CRT: concurrent chemoradiotherapy, TOLS: Transoral laser surgery,.
CDDP: cis-diamminedichloroplatinum, CDGP: cis-diammineglycolatoplatinum.
SOHND: supra omohyoid neck dissection, PIT: Photoimmunotherapy.



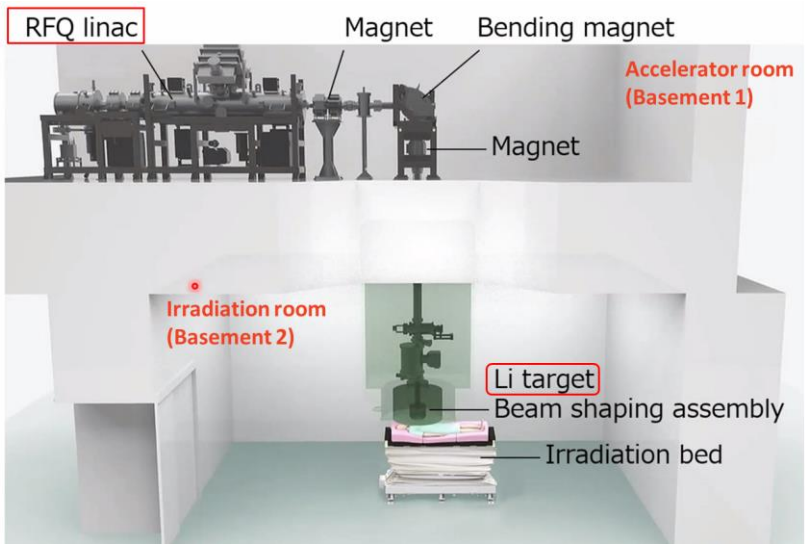
Tumor response at three months after BNCT



https://doi.org/10.1016/j.anl.2024.06.007

Accelerator based BNCT systems

Electrodynamic linear Accelerator
& Li target (2.5MeV, 20mA)



国立がん研究センター
中央病院
National Cancer Center Hospital

National Cancer Center Hospital
November 2019 ~ 2022 Phase 1 Clinical Trial; **Malignant Melanoma & Angiosarcoma**
November 2022~ Phase 2 Clinical Trial; **Angiosarcoma**
September 2024 ~Phase 1/2 Clinical Trial; **FBPA-PET positive recurrent thoracic solid malignant tumor**

社会福祉法人 仁生社
江戸川病院

Edogawa Hospital
July 2023 ~ March 2024 Clinical study; **Recurrent breast cancer** after radiation therapy
August 2024 ~ Clinical study; **FDG-PET positive tumors**

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2019~ BNCT for scalp angiosarcoma

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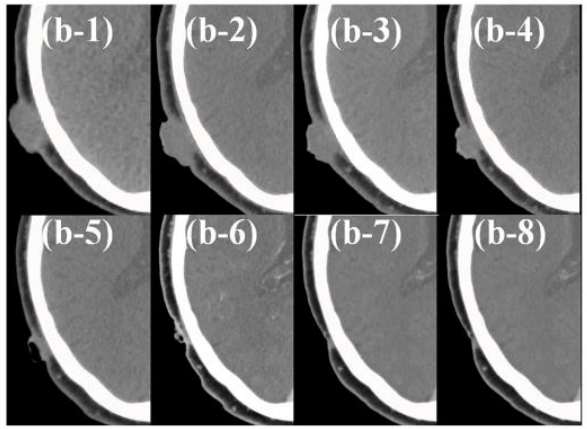
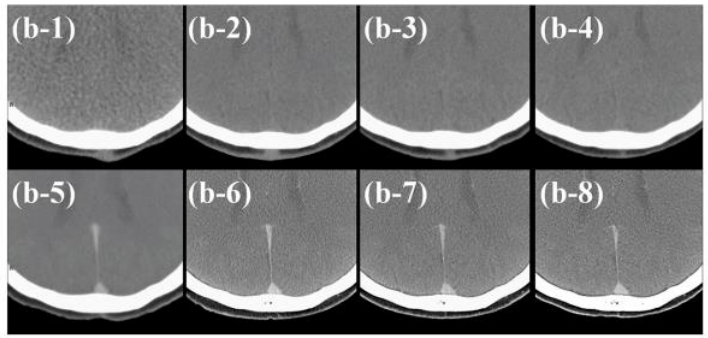
Phase 1 clinical trials; maximum dose to skin 12 Gy-Eq

68-year-old female,
Right temporodorsal scalp mass; 35 × 28 mm and 22 mm
Blood boron concentration; 42.2 ppm
Proton charge; 9526 mC
Irradiation time; 17mins
Epithermal neutron; 5.3×10^{11} cm-2



- High QOL
- Complete Response (CR)

66-year-old female,
Dorsal scalp mass; 29 × 23 mm and 10 mm
Blood boron concentration; 36.5ppm
Proton charge; 11636 mC
Irradiation time; 20 mins
Epithermal neutron; 6.3×10^{11} cm-2



https://doi.org/10.1016/j.ctro.2022.02.006

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2022~ BNCT for cutaneous malignant melanoma

Check for updates

OPEN ACCESS

EDITED BY
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Kyoto University, Japan

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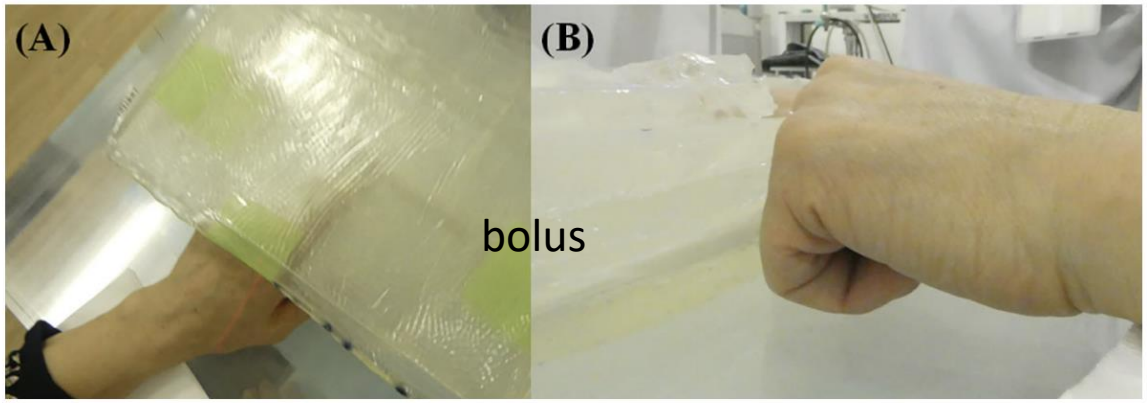
Hokkaido University, Japan
Shintaro Shiba,
Shonan Kamakura General Hospital, Japan

Acral cutaneous malignant melanoma treated with linear accelerator-based boron neutron capture therapy system: a case report of first patient

国立がん研究センター
中央病院
National Cancer Center Hospital

72-year-old female, malignant melanoma on a second finger of the left hand, Tumor size; 20 × 12 mm



Maximum dose of the skin; 18 Gy-Eq
Blood boron concentration; 33.7 ppm
Proton charge; 18230 mC
Irradiation time; 30.4 mins
Epithermal neutron; 9.7×10^{11} cm-2

- High QOL
- Complete Response (CR)

Before BNCT

DOI 10.3389/fonc.2023.1272507

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2023~ BNCT for recurrent breast cancer

社会福祉法人 仁生社
江戸川病院

June 2023 ~ March 2024 Specific Clinical Research; Recurrent breast cancer after radiation therapy

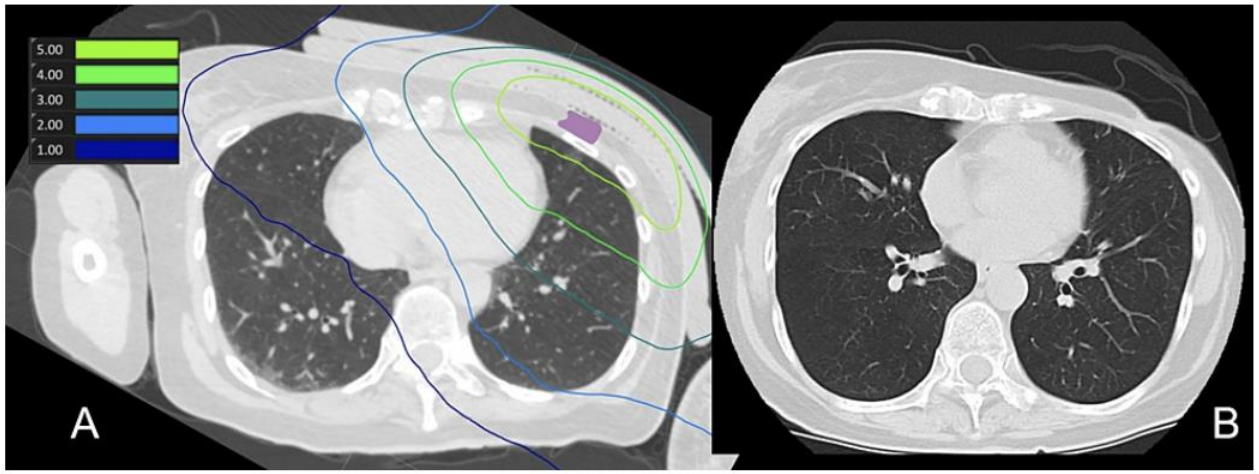
Cureus
Part of SPRINGER NATURE
Open Access Case Report
DOI: 10.7759/cureus.57417

The Effects of Boron Neutron Capture Therapy on the Lungs in Recurrent Breast Cancer Treatment

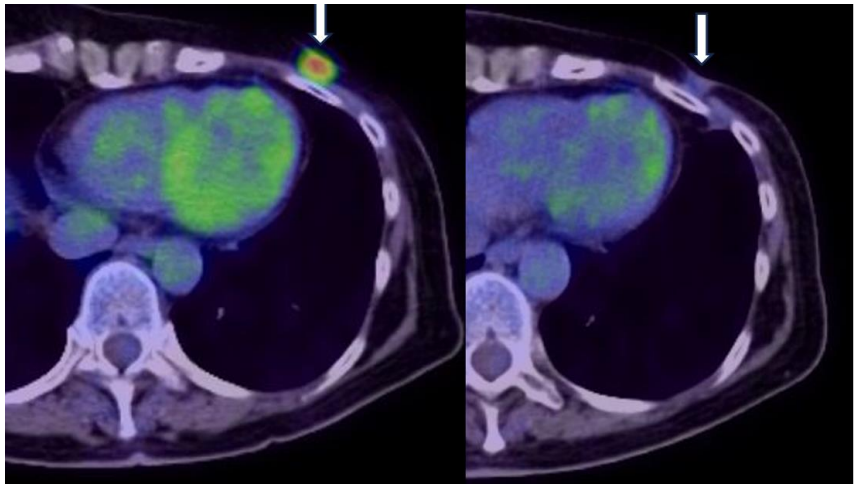
61-year-old woman

Left breast cancer ; Chemotherapy , mastectomy (ypT2N1M0), and radiotherapy with 54 Gy in 30 fractions
The recurrence in the left chest ; Surgery ,radiotherapy with 50.4 Gy in 28 fractions and chemotherapy for 3 years
The further recurrence on the left chest wall; BNCT

Dose distribution map for BNCT　　90 days post-treatment



Before BNCT　　6 months post-BNCT



The prescribed dose of ipsilateral lung;
Minimum dose; 23.6 Gy-Eq, Average dose ; 2.7
CT scans after BNCT showed no evidence of radiation pneumonitis.

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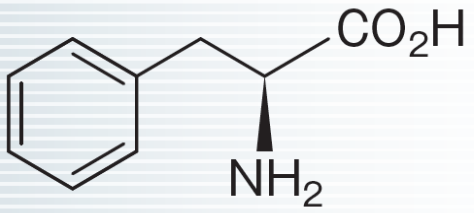
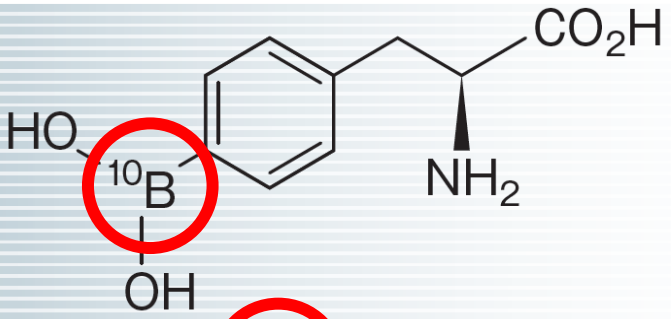
2024 ~ BNCT for FBPA-PET positive recurrent solid thoracic malignant tumor

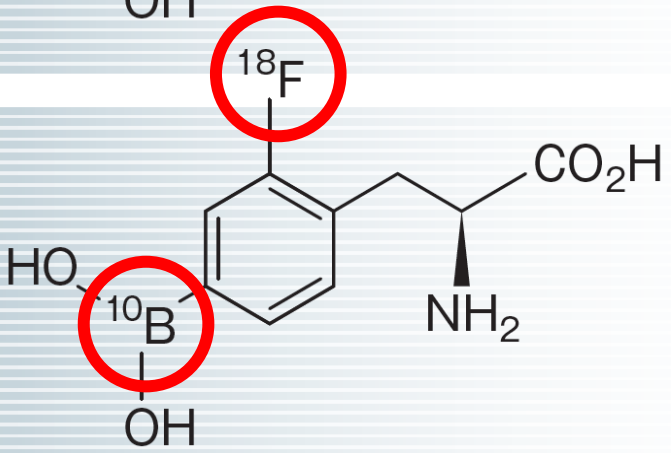
L-phenylalanine



L-BPA

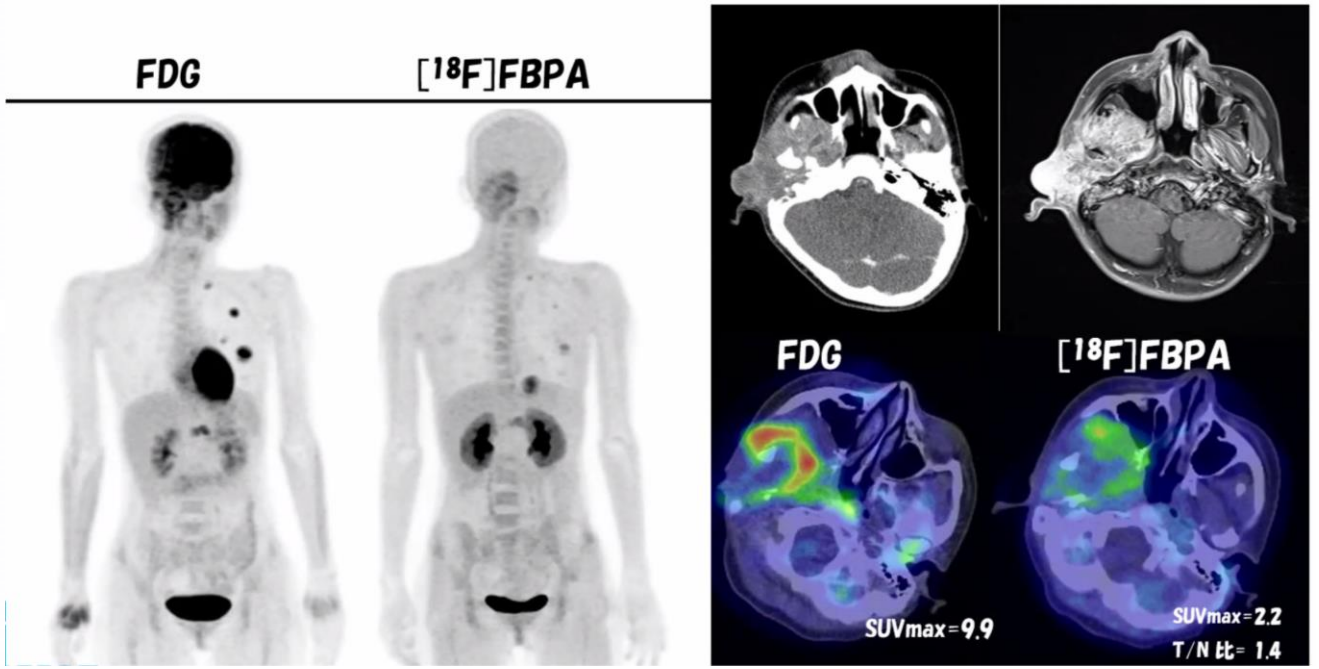


L-FBPA



Recurrent Adenoid Cystic Cancer of rt. Parotis

国立がん研究センター
中央病院
National Cancer Center Hospital



- Imaging of tumor site boron accumulation
  ➡ Indication of BNCT
- Tumor tissue/normal tissue (T/N ratio)
  ➡ BNCT Dose Calculation

http://www.jsnct.jp/about_nct/pet.html

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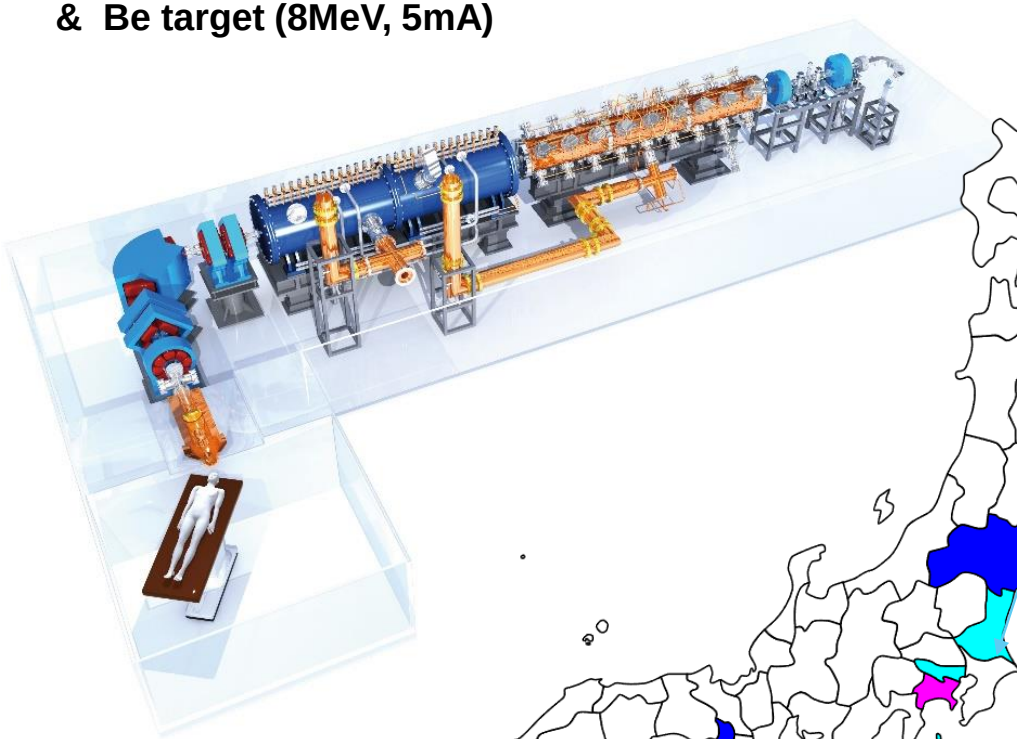
Accelerator based clinical BNCT systems

筑波大学 University of Tsukuba

株式会社ｉＢＮＣｔ

Electrodynamic linear Accelerator
& Be target (8MeV, 5mA)

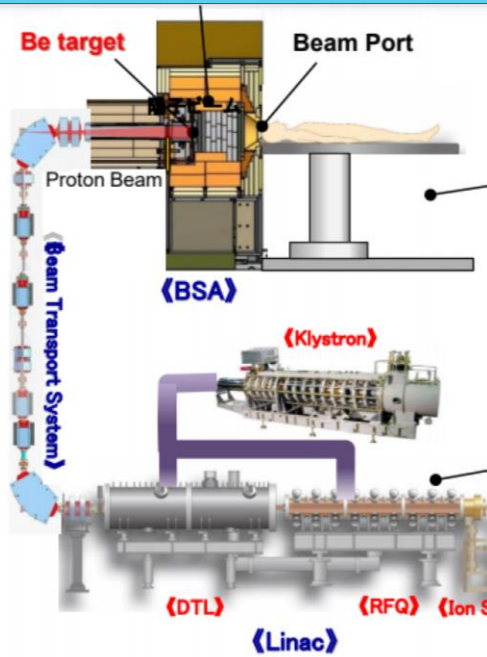


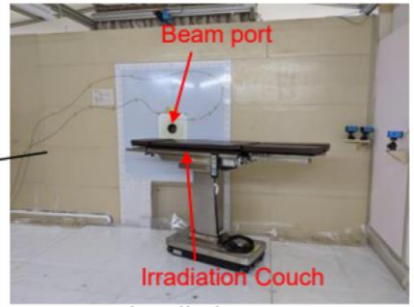
BPA

Tsukuba University
February 2024~ Phase 1　Clinical Trial ; Newly diagnosed glioblastoma

Facility building

Biological Experimental Room





Irradiation room

Accelerator room

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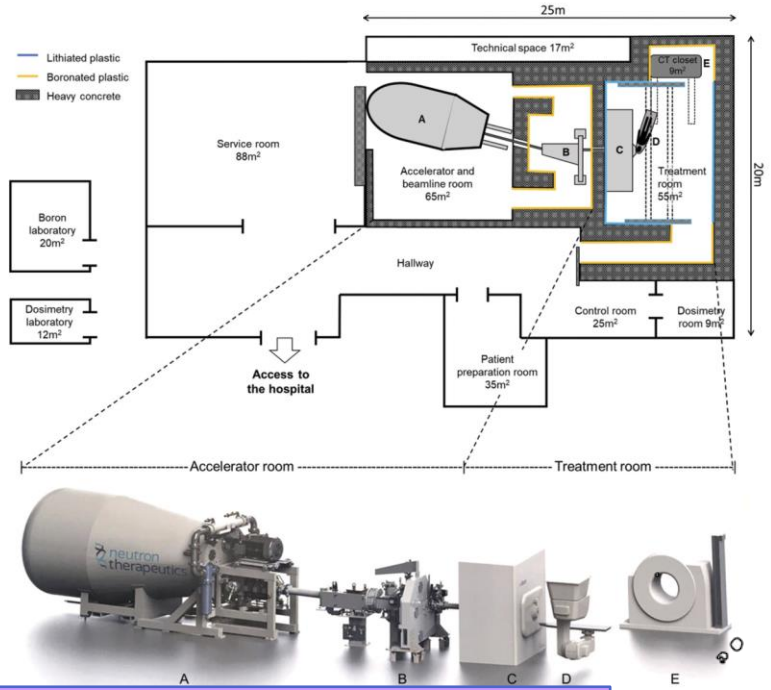
Accelerator based clinical BNCT systems

neutron therapeutics

Electrostatic accelerators
& Li target (2.6MeV, 30mA)



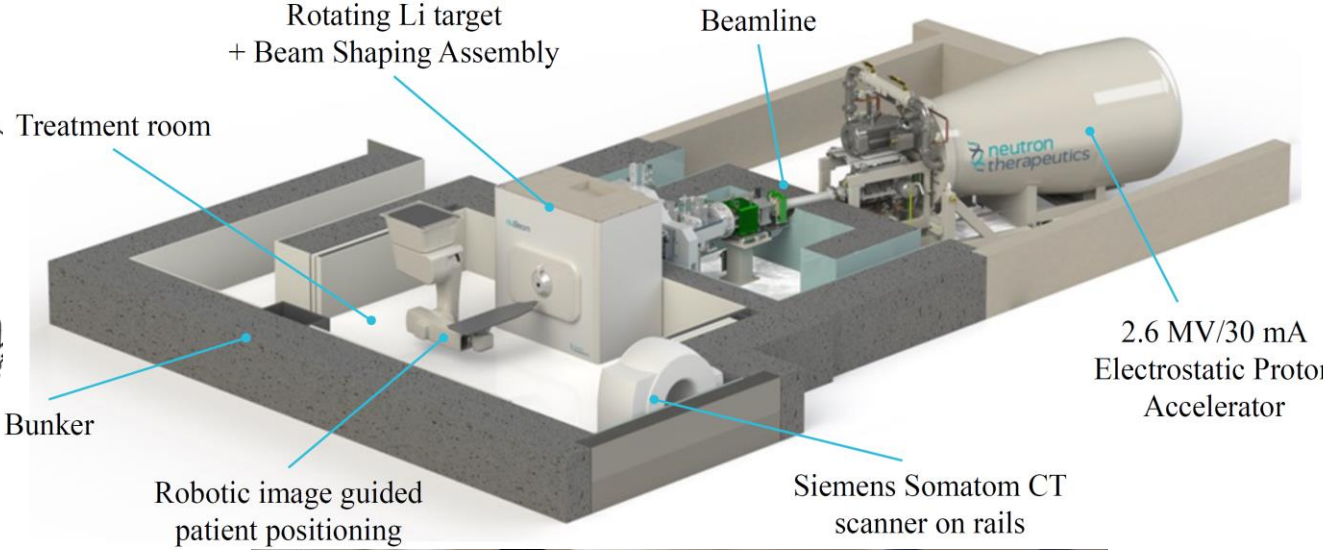
Leo Cancer Care Upright Patient Positioning System.

医療法人 徳洲会
湘南鎌倉総合病院
SHONAN KAMAKURA GENERAL HOSPITAL

Rotating Li target
+ Beam Shaping Assembly

Beamline

Treatment room



Bunker

Robotic image guided patient positioning

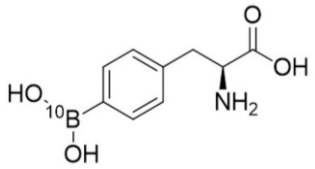
2.6 MV/30 mA Electrostatic Protor Accelerator

Siemens Somatom CT scanner on rails

Helsinki University Hospital, Finland
(Preparation of clinical trials)

INTERPHARMA PRAHA, a.s.

4-(Borono 10B) -L-phenylalanine
Molecular Formula: C9H12BNO4
C.A.S. No.: [80994-59-8]



Shonan Kamakura General Hospital
(Preparation of clinical study)

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Development of Accelerator based clinical BNCT (~ Sep. 2024)

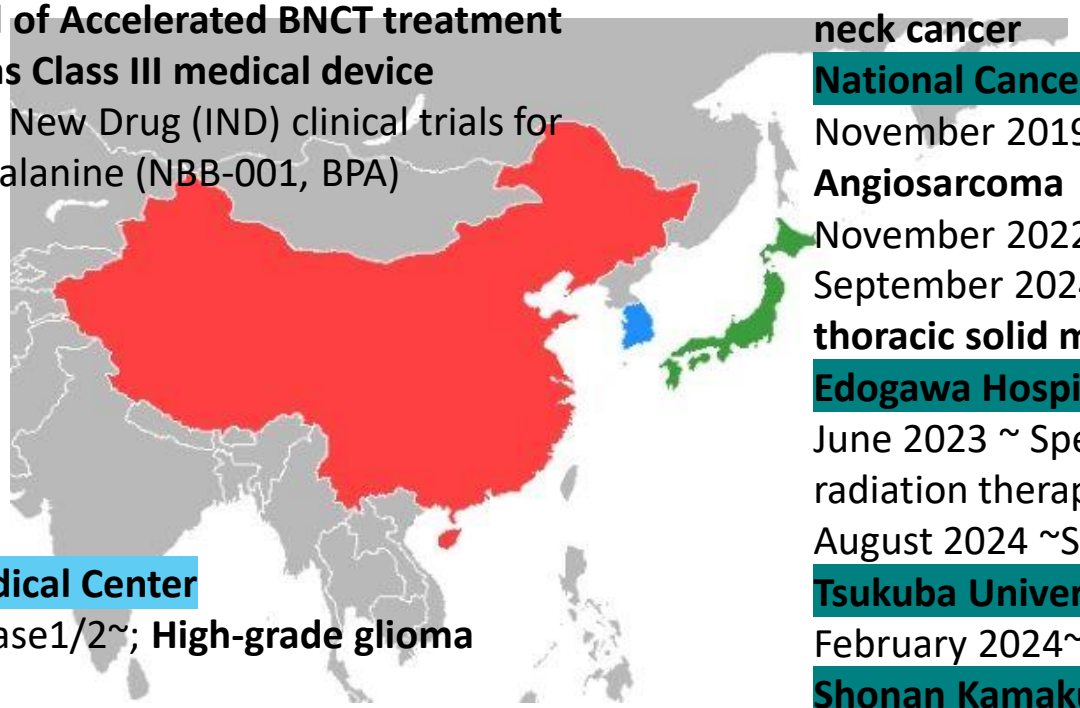
China

Xiamen Humanity Hospital (XHH) BNCT Center

October 2022~ clinical study; **Recurrent head and neck cancer, High-grade glioma, Melanoma**

March 2024 **The approval of Accelerated BNCT treatment system (NeuPEX Block-I) as Class III medical device**

May 2024~ Investigational New Drug (IND) clinical trials for Neuboron's boronophenylalanine (NBB-001, BPA)



Korea

Gachon University Gil Medical Center

June 2022 clinical trials phase1/2~; **High-grade glioma**

Japan

South Tohoku BNCT Research Center

2016-2019 Phase 2 Clinical Trial**; Head and neck cancer**

June 2020~ Medical treatment covered by health insurance; **Head and neck cancer**

Kansai BNCT Medical Center

June 2020 ~ Medical treatment covered by health insurance; **Head and neck cancer**

National Cancer Center Hospital

November 2019 ~ 2022 Phase 1 Clinical Trial; **Malignant Melanoma & Angiosarcoma**

November 2022~ Phase 2 Clinical Trial; **Angiosarcoma**

September 2024~ Phase1/2 Clinical Trials; **FBPA-PET positive recurrent thoracic solid malignant tumor**

Edogawa Hospital BNCT

June 2023 ~ Specific Clinical Research; **Recurrent breast cancer** after radiation therapy

August 2024 ~Specific Clinical Research; **FDG-positive tumors**

Tsukuba University

February 2024~ Phase 1 Clinical Trial ; **Newly Diagnosed Glioblastoma**

Shonan Kamakura Hospital

2025 ~ Clinical Study (Planned)

Ximen Humanity Hospital-Neuboron BNCT Center

NEUBORON

Tandem & Li target
(2.35MeV, 10mA)

NeuPex Block-I uses a tandem electrostatic accelerator to provide a low-energy proton beam at a relatively high beam current. Electrostatic accelerators are well-known as a power-efficient, stable machines. Figure III-4 shows the main vessels of the accelerator system.

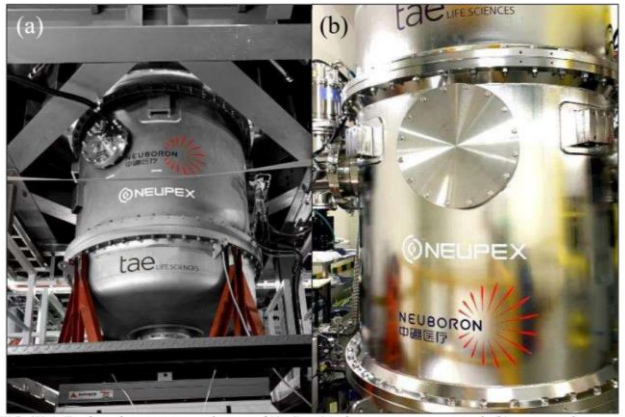
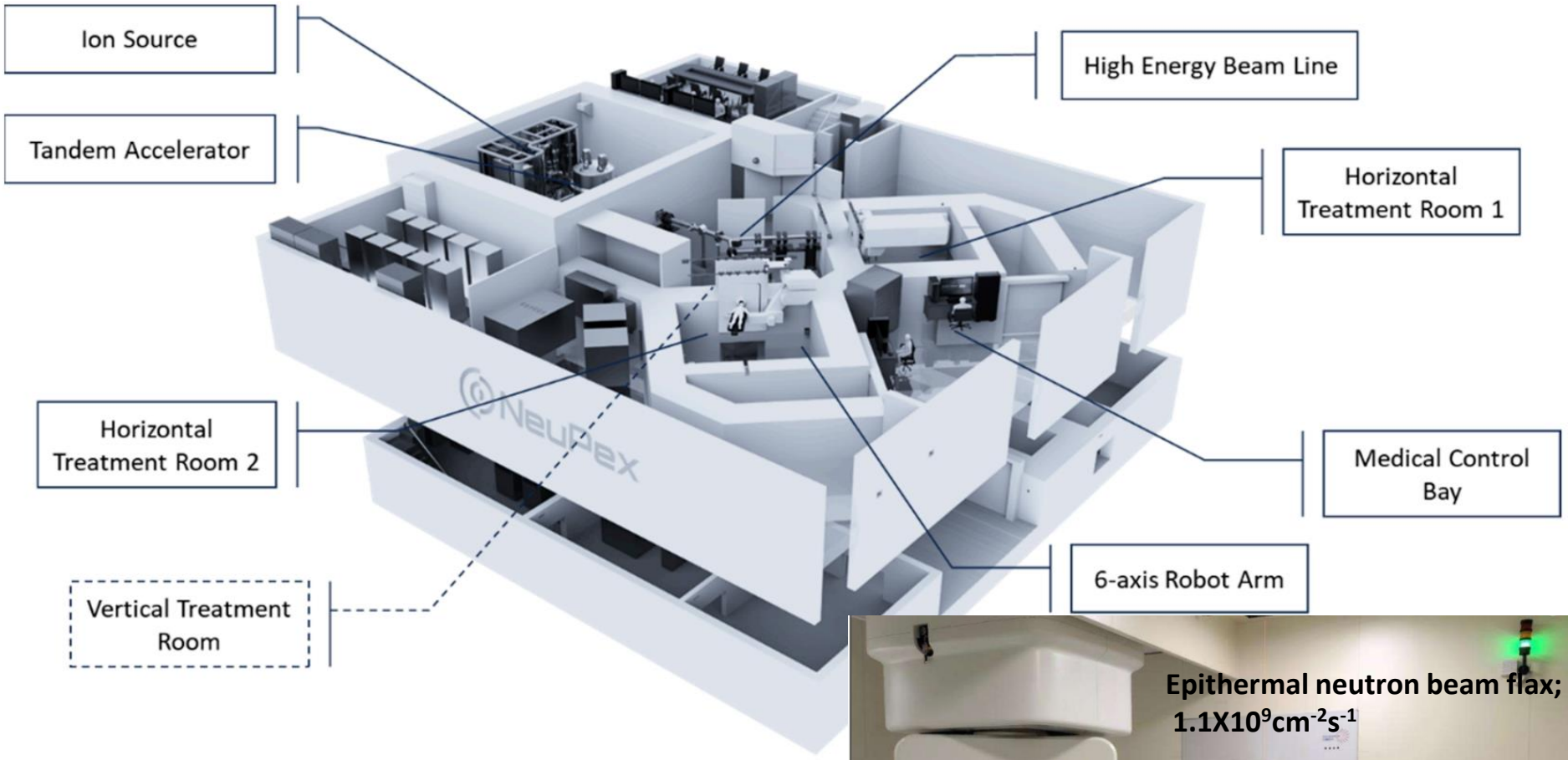
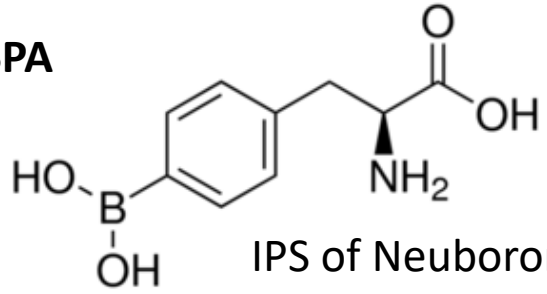


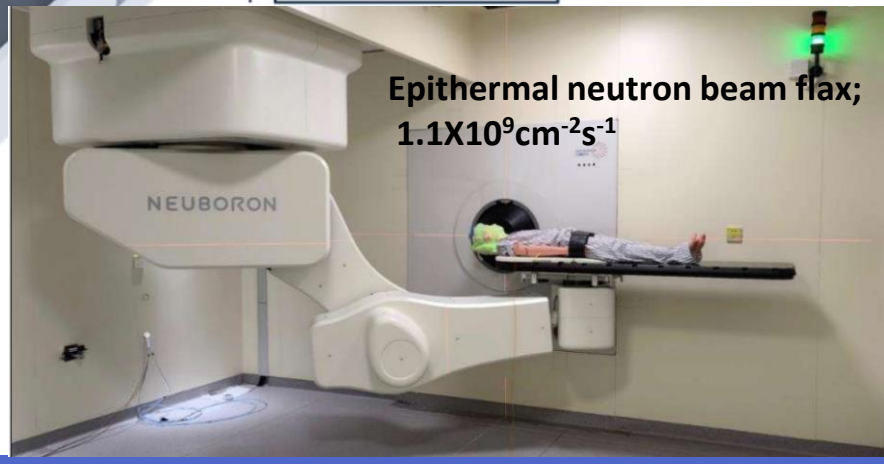
FIG. III-4. Tandem electrostatic accelerator of NeuPex (a) electrostatic power vessel, (b) main accelerator vessel.



BPA



IPS of Neuboron Medical Group



Epithermal neutron beam flax;
$1.1X10^{9}cm^{-2}s^{-1}$

https://en.neuboron.com/products
https://taelifesciences.com/360/treatment.html

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2022 ~ BNCT for advanced refractory Malignant Tumors

October 2022 ~ June 2024, 24 patients

Investigator-initiated trial (IIT)

- IIT-001(Chinese Clinical Trial Registration Number: ChiCTR2200066473),

"A Single-center, Single-arm Clinical Trial of the Safety and Efficacy of Boron Neutron Capture Therapy (BNCT) for Advanced Refractory Malignant Tumors"

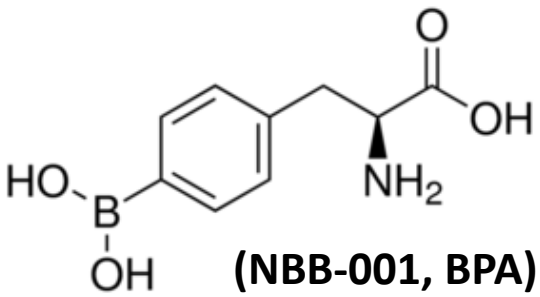
3 month follow up

High QOL, Patients satisfaction and Tumor regression

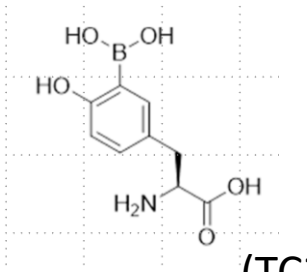
- IIT-002 on going, 5 patients

Head and neck cancer and brain tumor (glioma)

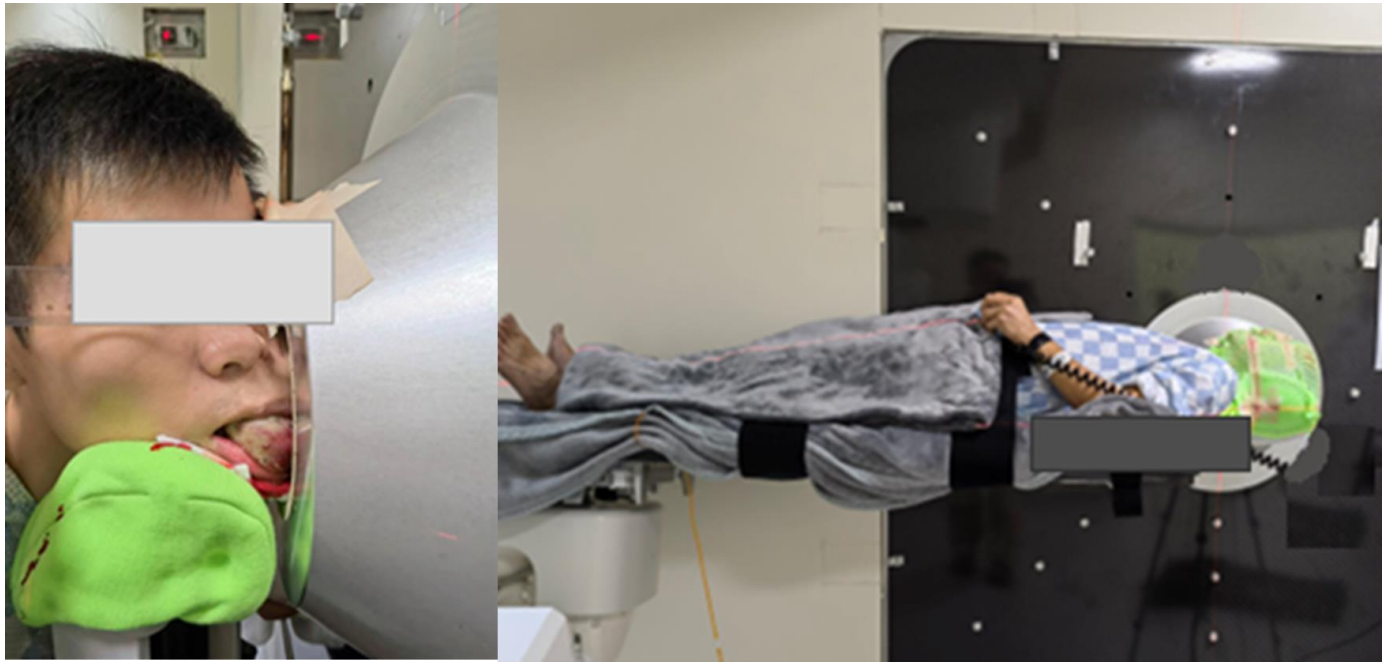
- IIT-003 LAT-1 and/or 18F-BPA positive tumors



(NBB-001, BPA)



(TC220)



March 2024 The approval of Accelerated BNCT treatment system (NeuPEX Block-I) as Class III medical device

May 2024~ Investigational New Drug (IND) clinical trials for Neuboron's boronophenylalanine (NBB-001, BPA)

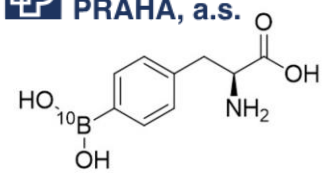
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10452212/

Accelerator-BNCT Clinical Research Center, Korea

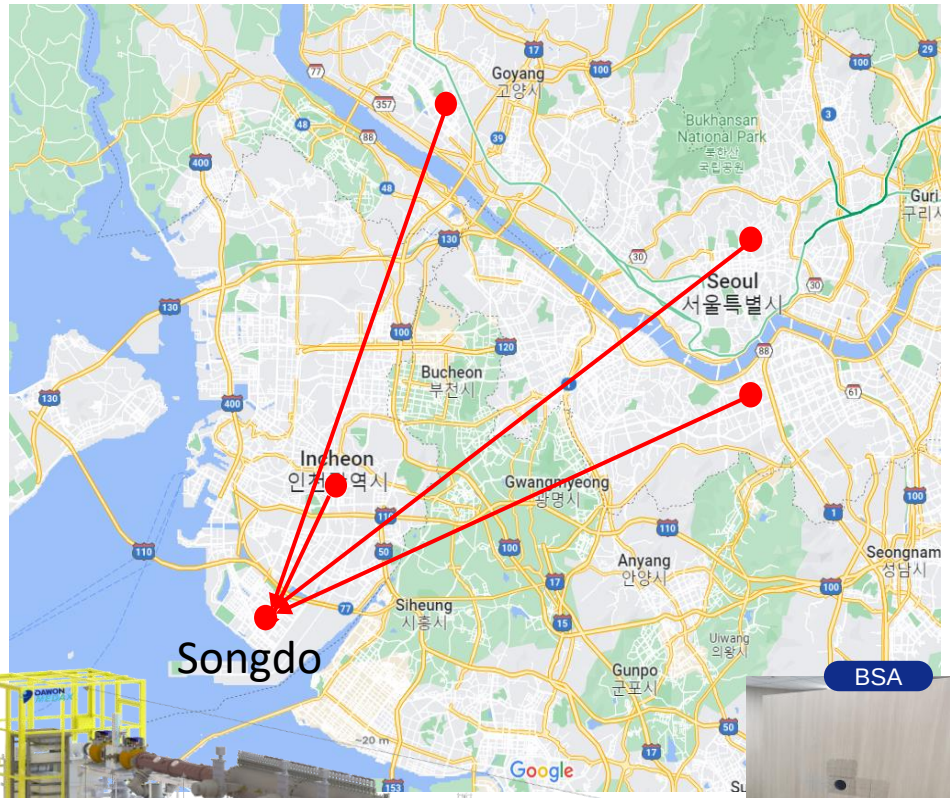
DAWON MEDAX

LINAC & Be target (10MeV, 2mA)

INTERPHARMA PRAHA, a.s.



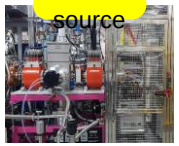
4-(Borono 10B) -L-phenylalanine
Molecular Formula: C9H12BNO4
C.A.S. No.: [80994-59-8]

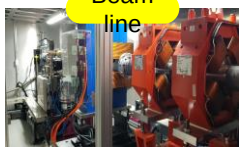


10MeV, 2mA LINAC

10cm X10cm
Be target (inside BSA)

Epithermal neutron beam flax; $1.0X10^{9}cm^{-2}s^{-1}$





June 2022~ High-grade glioma
2023 ~ Head and neck cancer

Gachon University Gil Medical Center

National Cancer Center

The Catholic University of Korea Seoul St. Mary's Hospital

Seoul National University Hospital

Courtesy of Dr. Hyo Jung Seo

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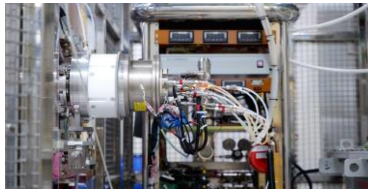
DawonMedax A-BNCT Center





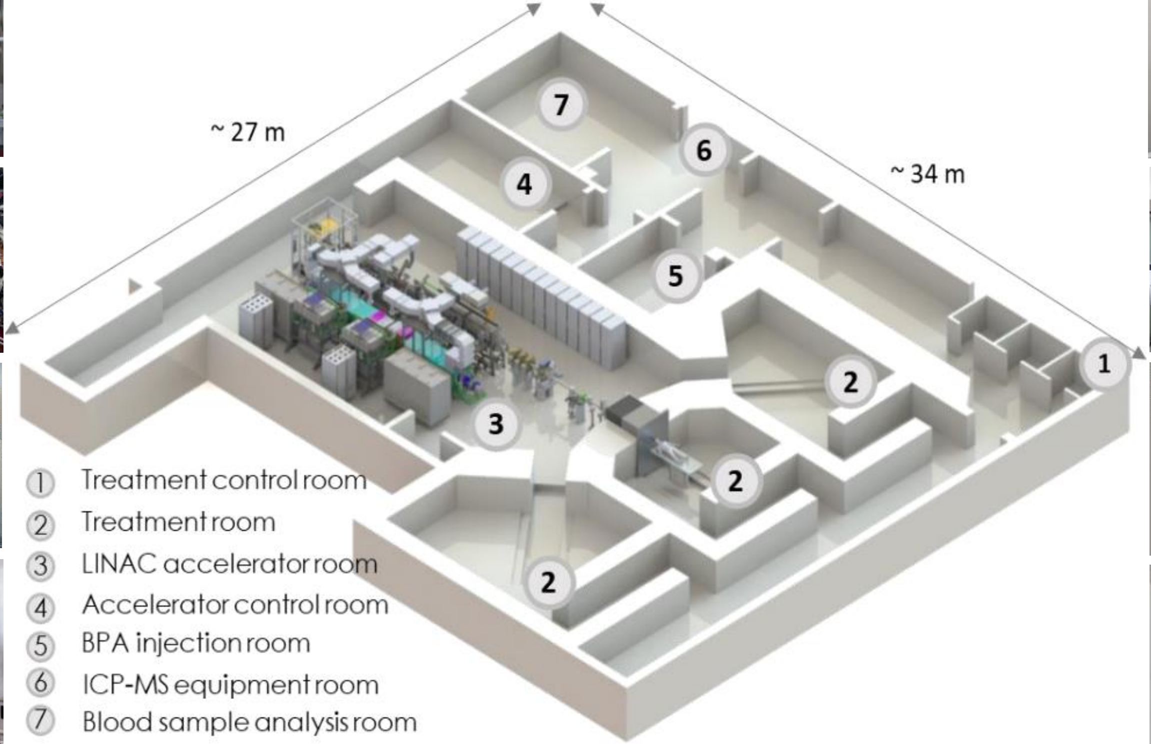












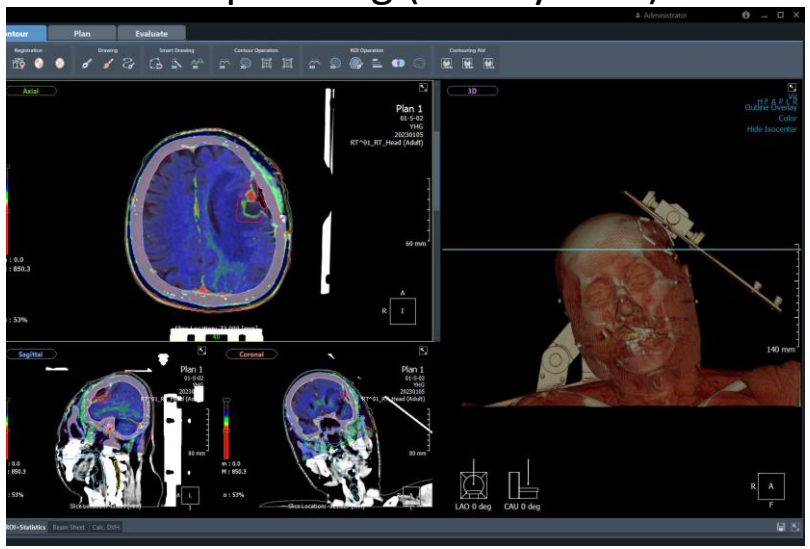
Courtesy of Dr. Hyo Jung Seo

https://doi.org/10.1007/s43673-022-00063-2

BNCT for Recurrent Glioblastoma

June 2022~2023 11 High-grade glioma patients (6 clinical trials, 5 compassionate cases)

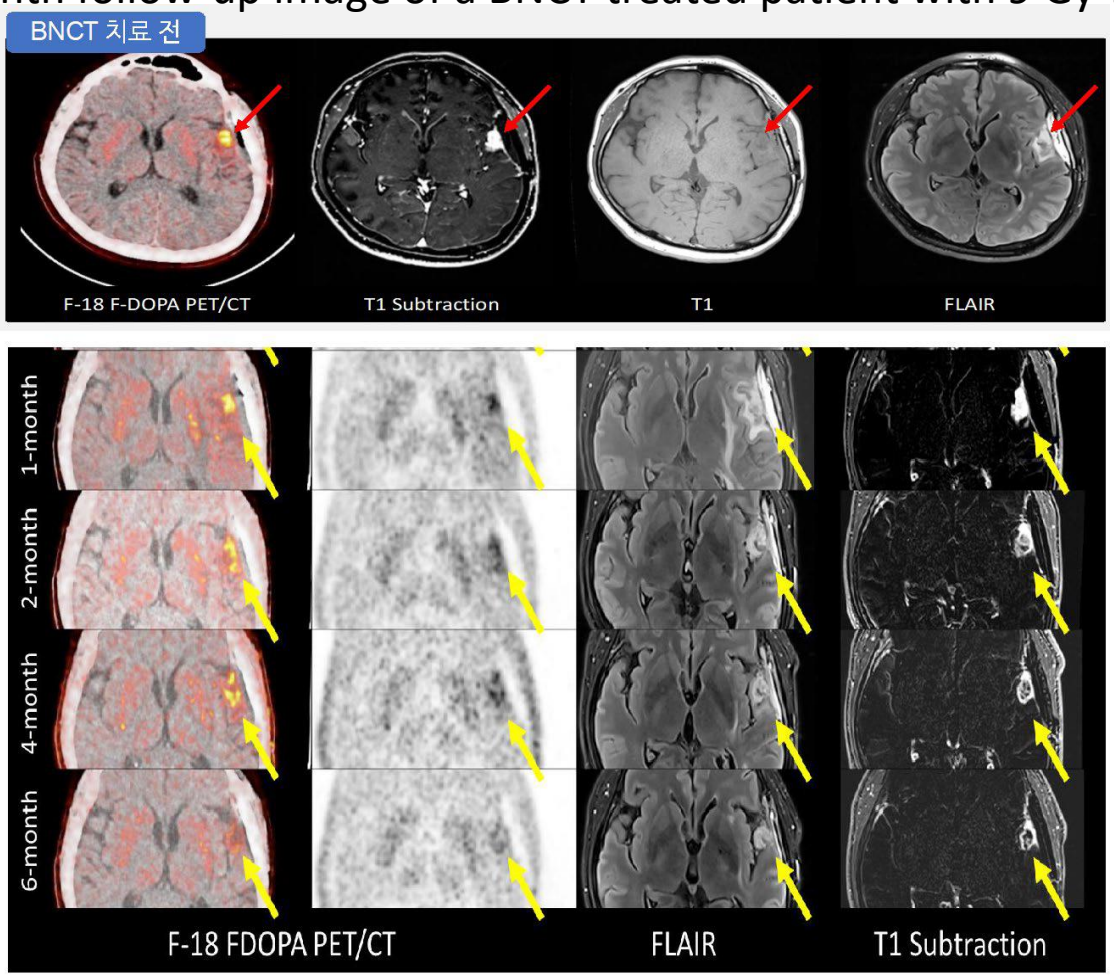
Treatment planning (TPS system)



BPA (Interpharma, Czech) administration

Neutron irradiation

6-month follow-up image of a BNCT treated patient with 9 Gy-Eq DLT



- 6 month “progress-free survival”
- Stable disease (SD) or “complete response”

Courtesy of Dr. Young-soon Bae, UCANS10

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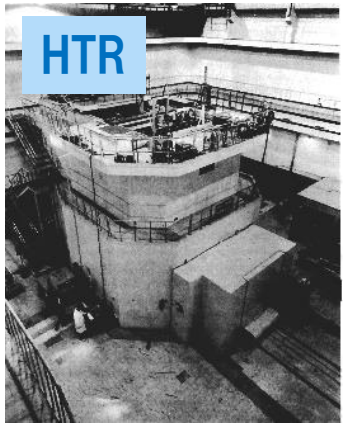
Summary

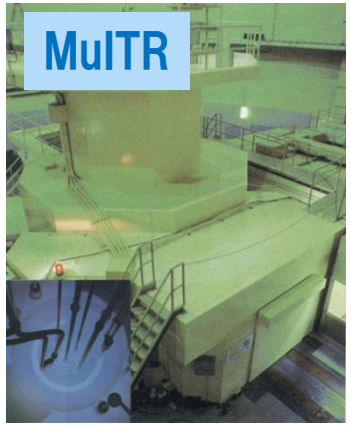
- **BNCT is a cancer therapy that uses a nuclear reaction between neutrons and boron to selectively destroy cancer cells with little damage to normal cells.**
- **BNCT usually is treated with a single irradiation. Therefore, early return to society is possible.**
- **With the development of the accelerator BNCT system, hospital-based treatment has started in Japan from 2020.**
- **BNCT has a high level of patient satisfaction, with improvement in post-treatment QOL observed.**

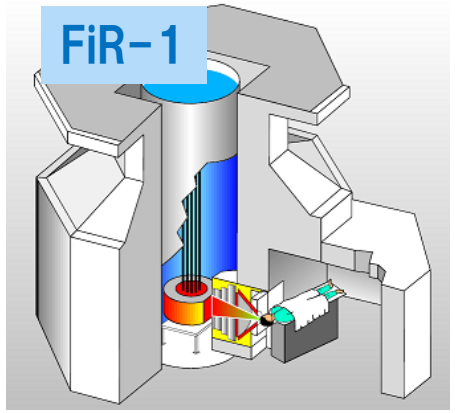
Thank you for listening!

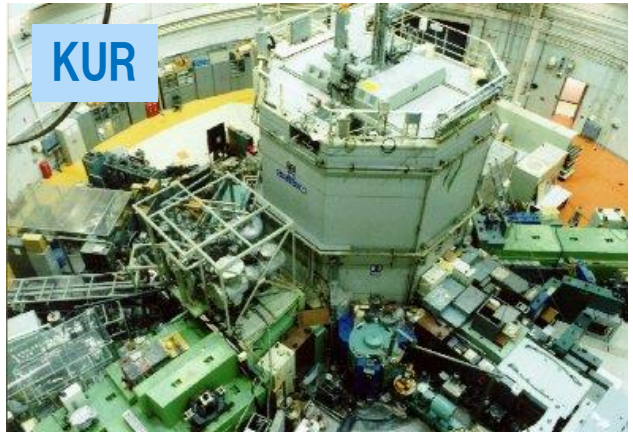
https://iaea-collaborating-centre.studio.site/

The development of reactor-based BNCT





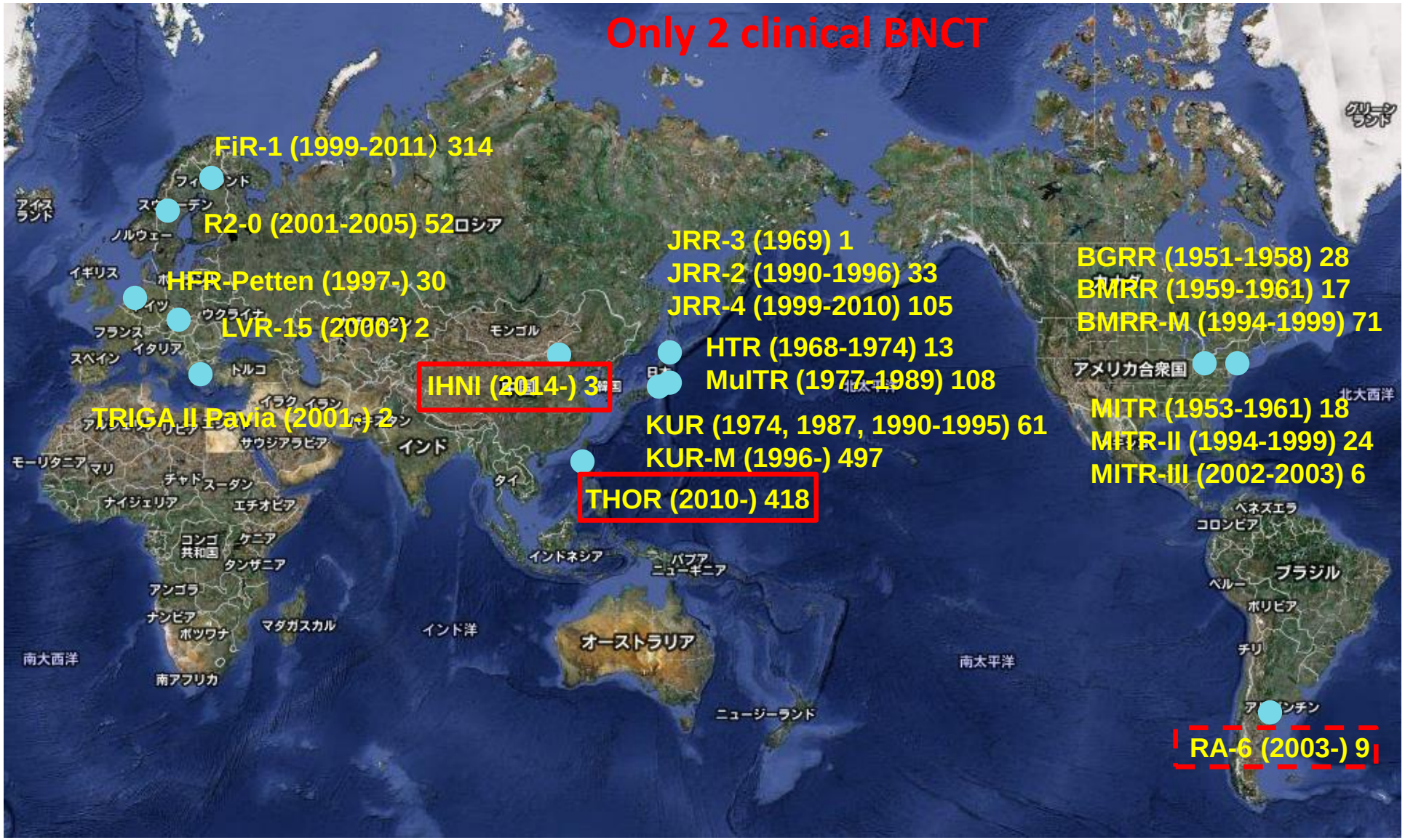




Courtesy of Prof. Sakurai, Kyoto Univ.

Reactor-based neutron sources in the world

>1400 until 2014, majority after 2001



USA	Brain Tumor※	135
	Skin※	6
Netherlands	Brain Tumor※	22
Finland	Brain Tumor※	150
	Head & Neck※※	29
Czech Republic	Brain Tumor※	2
Sweden	Brain Tumor※	52
Italy	Liver Cancer※	2
Argentina	Skin※	7
Taiwan, China	Head & Neck※※	10
Japan	Malignant Brain Tumor※※	393
	Head and Neck Cancer※※	186
	Malignant Melanoma※※	42
	Lung Cancer※※	14
	Liver Cancer※※	7
	Mesothelioma※※	23
	Others※※	10

※ ~ Jan., 2009
※※~ March, 2012

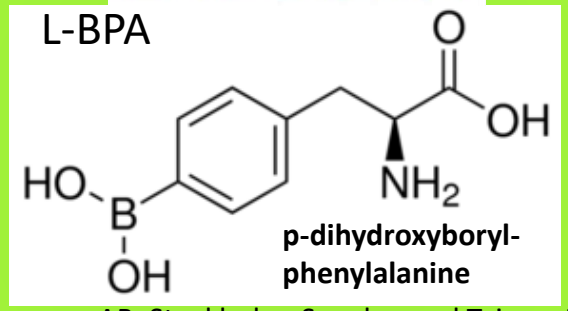
Courtesy of Prof. Sakurai, Kyoto Univ.

2010 ~ Reactor-based BNCT in Taiwan

Boron

信東生技股份有限公司 TAIWAN BIOTECH CO., LTD.

L-BPA



p-dihydroxyboryl-phenylalanine

(Hammercap AB, Stockholm, Sweden and Taiwan Biotech Co. Ltd, Taiwan, China)

(BPA-Fructose, 500 mg/kg)

Neutron

國立清華大學 NATIONAL TSING HUA UNIVERSITY

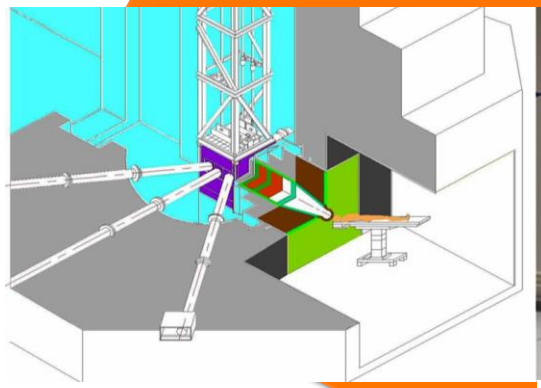
Epithermal neutron flux for 1 MW power is 1.7 × 109 n cm−2 s−1 in air at the beam exit

2023~ Medical device approval from Taiwan Food and Drug Administration

Tsing **H**ua **O**pen-pool **R**eactor

Therapy

Brain tumor
Head and neck cancer



臺北榮民總醫院 Taipei Veterans General Hospital

2010~ Head and neck cancer
2017~ salvage BNCT as emergent / compassionate use for recurrent malignant brain tumors

The treatment of foreign patients, including patients from America, Japan, Brazil, Australia, Spain, Swiss, Italy, Singapore and China (~34 patients till Aug.2023)

Dr. Yi-Wei Chen

THOR status	Clinical intent	Indication	Case number	Execution period	Clinical outcome
Not-approved medical facilities by TFDA (2010-2023.5)	Phase I trial	Recurrent H&N cancers	17	2010-2013	Improved patients' QOL, with 6 patients CR and 6 patients with tumor volume reduced by more than 30% (PR)
	Phase II trial	Recurrent H&N cancers	11	2014-2020	Similar as phase I
	Salvage	Recurrent **brain** and H&N cancers	> 400	2017-	Effective in palliating the disease and improving the patients' QOL; to be evaluated
Approved medical device (2023.6-)	Phase I/II trial	Recurrent **glioblastoma** after CCRT and Avastin	55	2023.12.01-2026.04.30	To be evaluated

Cancer Conqueror, Precision Medical Technology: Current Status and Future Prospects of THOR-BNCT Development in Taiwan, Sep 2023

Courtesy of Dr. Yi-Wei- Chen

Current BNCT status in Taiwan

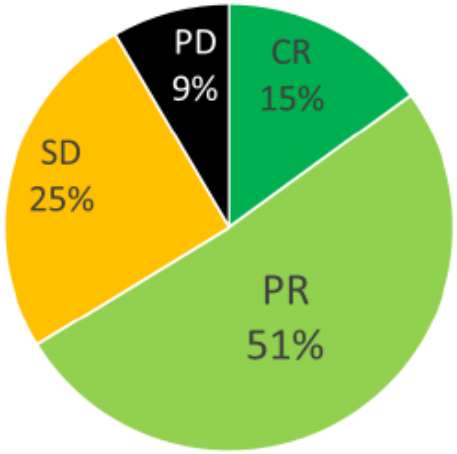
Item	Brain	H&N	Others	Total	P1	P2	P3	E
Irradiation times	264	197	7	468	33	14	3	418

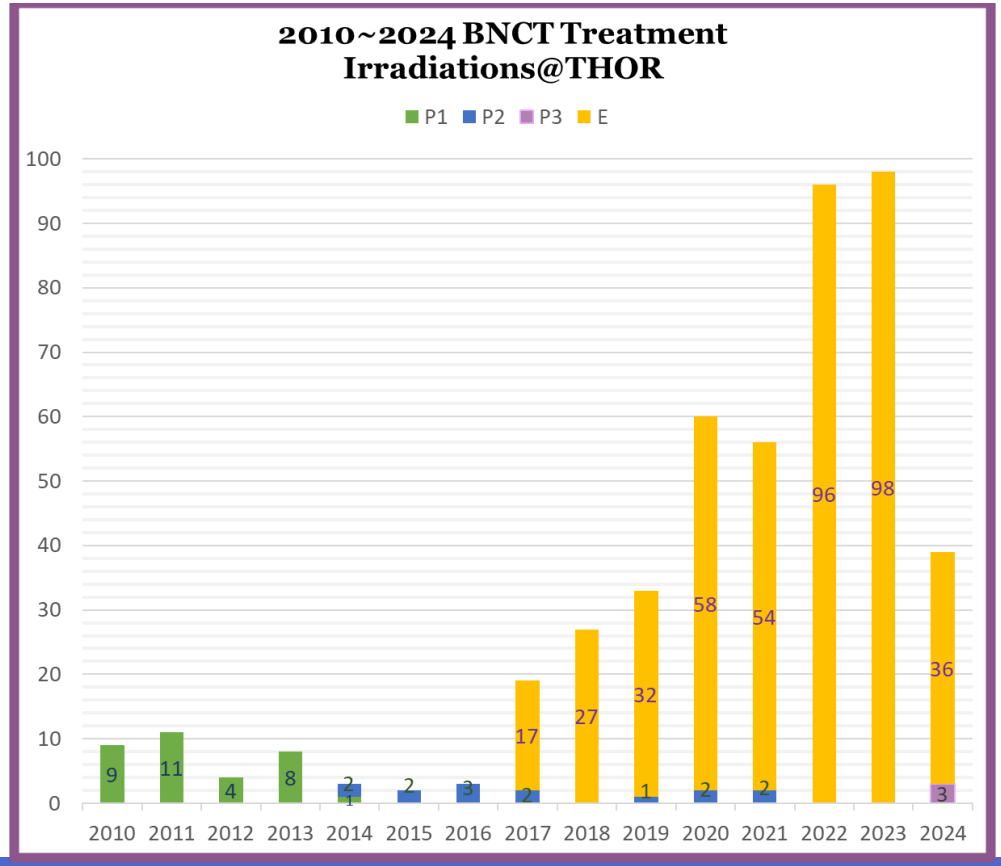
2010.08.11~ 2024.04.19 by JJP

Median follow-up time is 7.5 months.

Longest survival is 17.9 months

Shortest survival period after BNCT is 1.1 month.





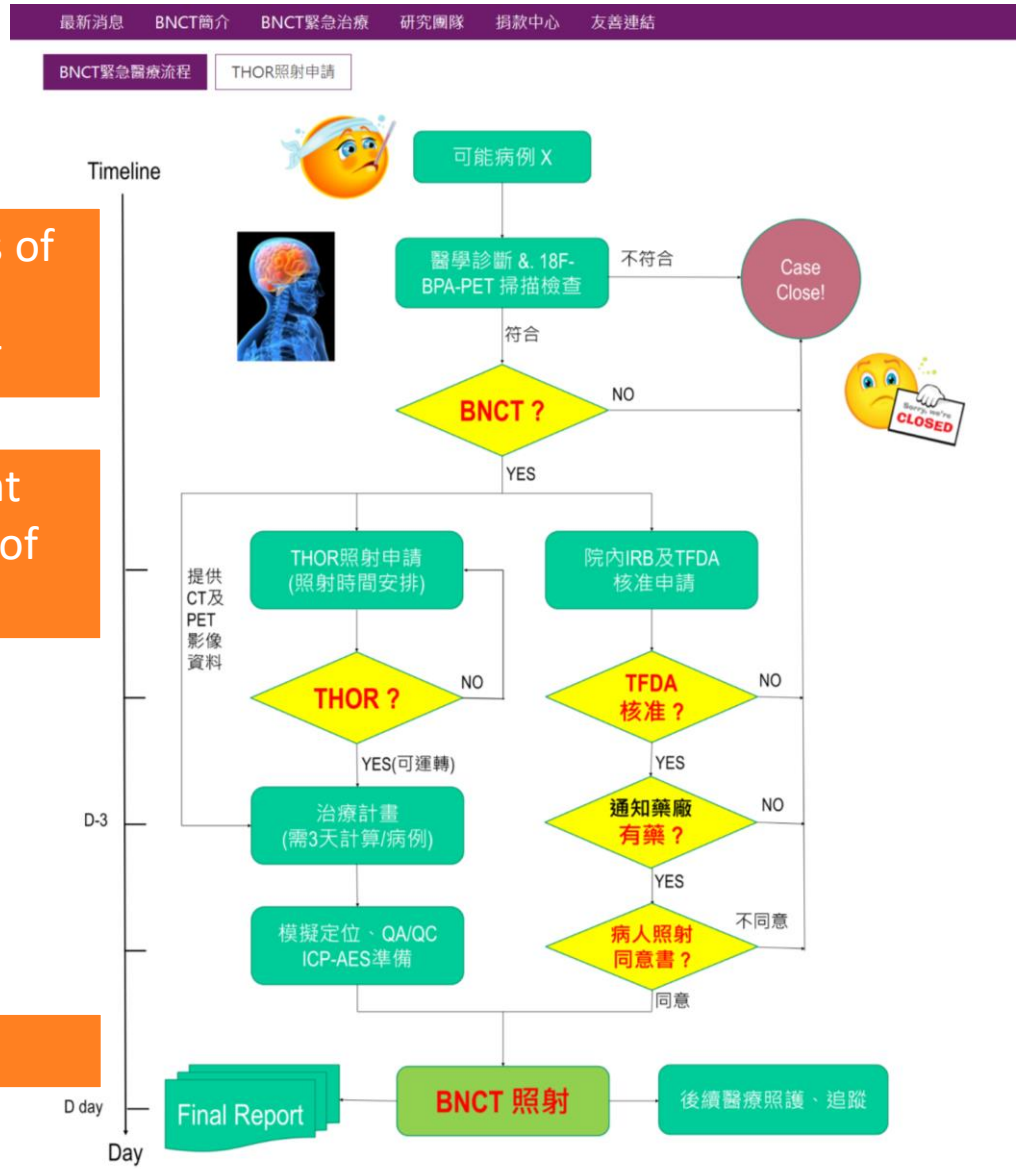
Courtesy of Dr. Yi-Wei- Chen

BNCT in Taiwan

Diagnosis of BNCT by FBPA-PET

Treatment planning of BNCT

BNCT



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以單次申請BNCT醫療服務計算，為新台幣**壹拾貳萬元**整，若採計畫性照射，第二次及以後之照射則每次收費新台幣**壹拾萬元**整。 (1st NT$ 120,000, 2nd NT$ 100,000)

•聯絡人： 王雅亭小姐，
電話： (03) 5742884，傳真：(03) 5725974
email : ytwang@mx.nthu.edu.tw / reactor@my.nthu.edu.tw

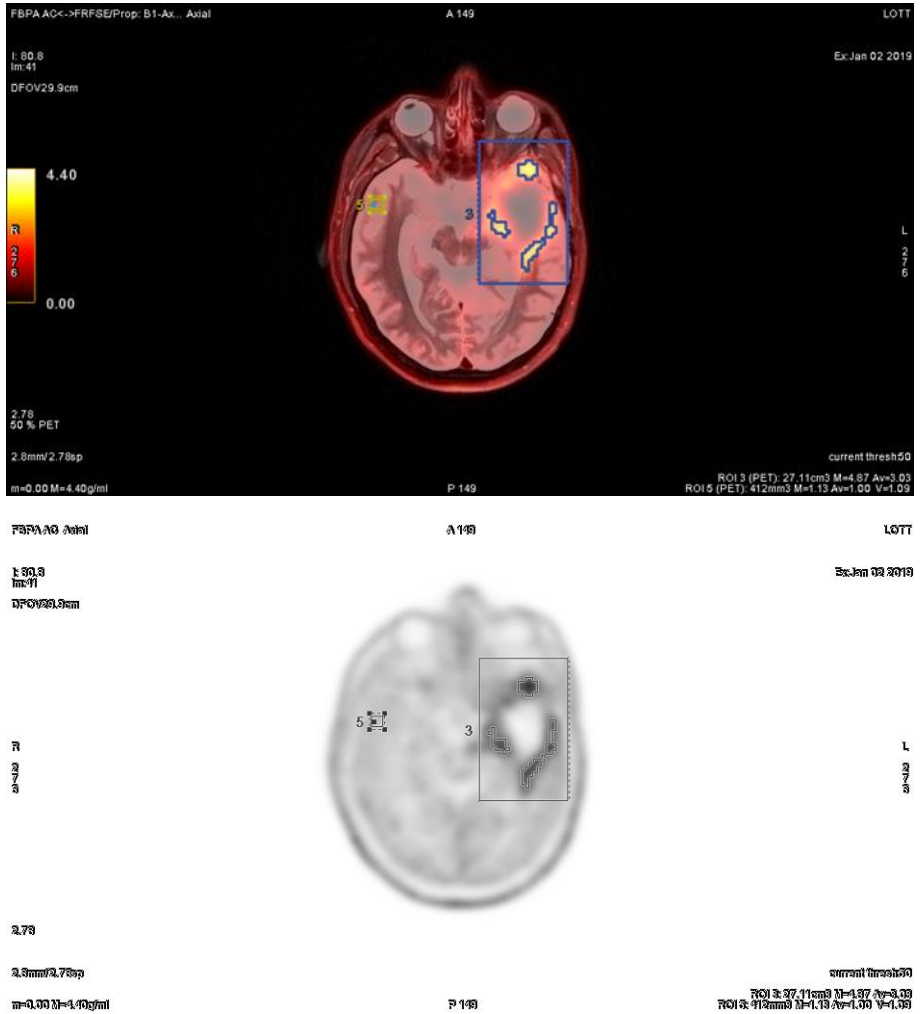
https://bnct.site.nthu.edu.tw/p/426-1197-5.php?Lang=zh-tw

NTRC Neutron Therapy Research Center

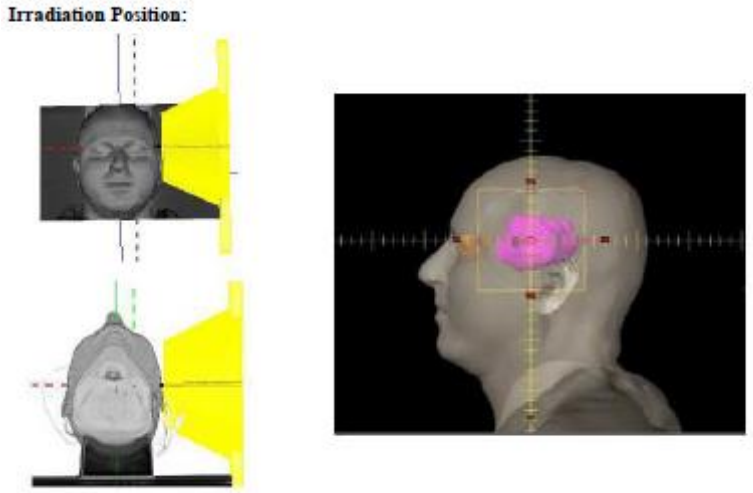
Japan. Committed to SDGs

BNCT for Recurrent glioblastoma (Australian patient)

FBPA-PET Imaging before BNCT

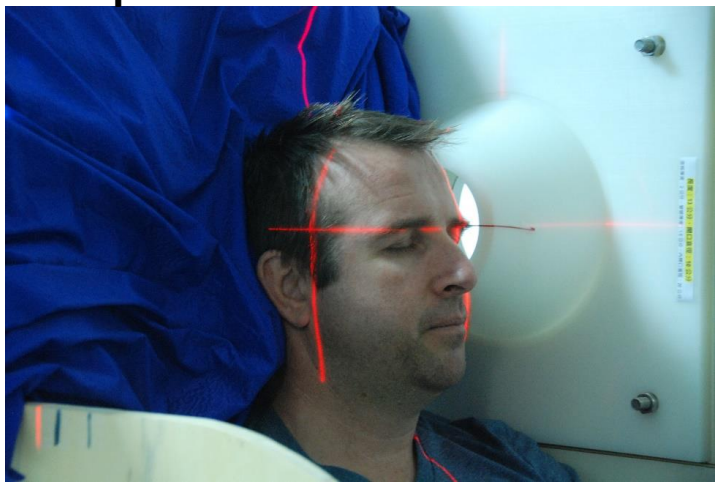


Simulation before BNCT



BNCT

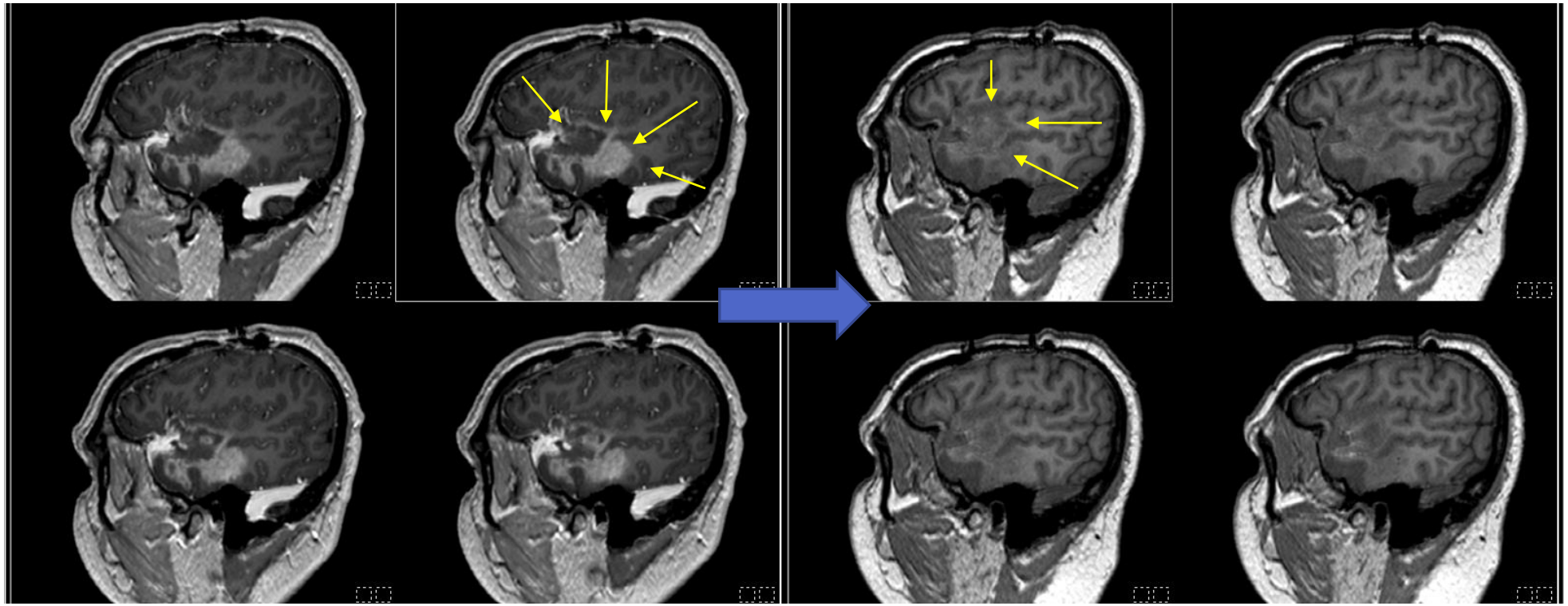
Set up



Boron administration

Courtesy of Dr. Yi-Wei- Chen

BNCT for Recurrent glioblastoma (Australian patient)



Before BNCT
(2019-01-16)

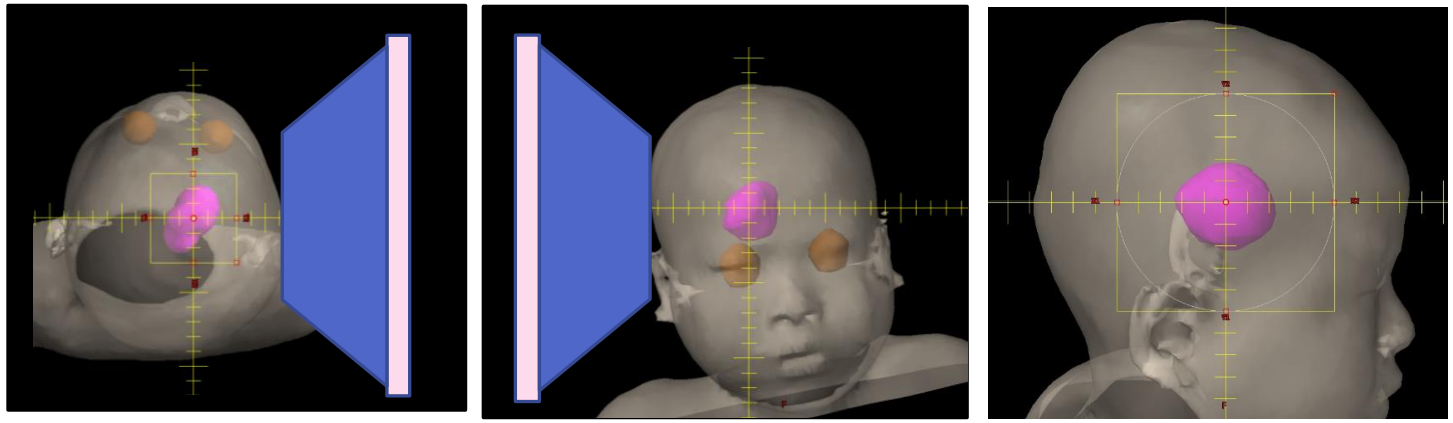
BNCT on
201901-30

After BNCT
(2019-02-26)

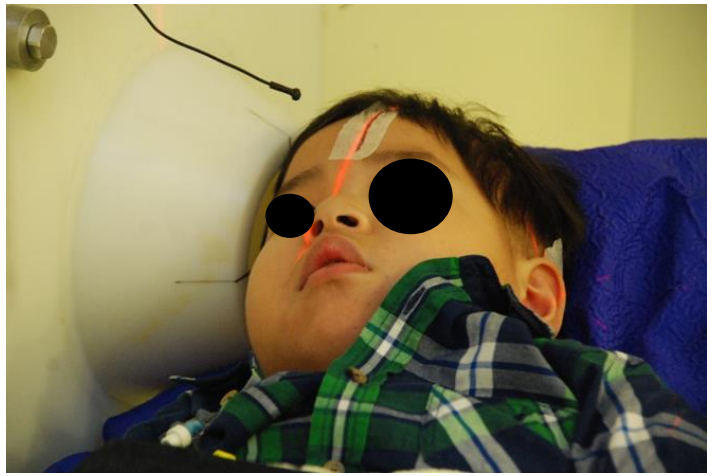
Courtesy of Dr. Yi-Wei- Chen

BNCT for brain tumor (8-year-old kid)

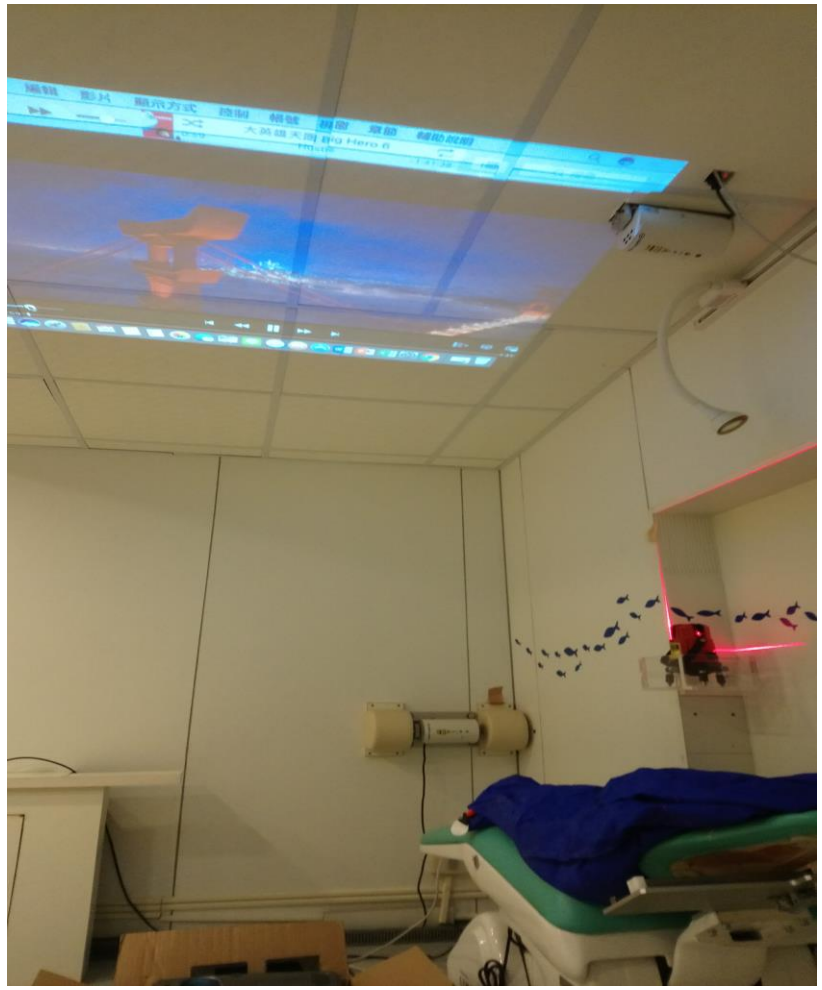
Simulation before epithermal neutron irradiation



- Collimator length 10 cm, diameter of opening 10 cm
- Neutron source to tumor center distance 18 cm

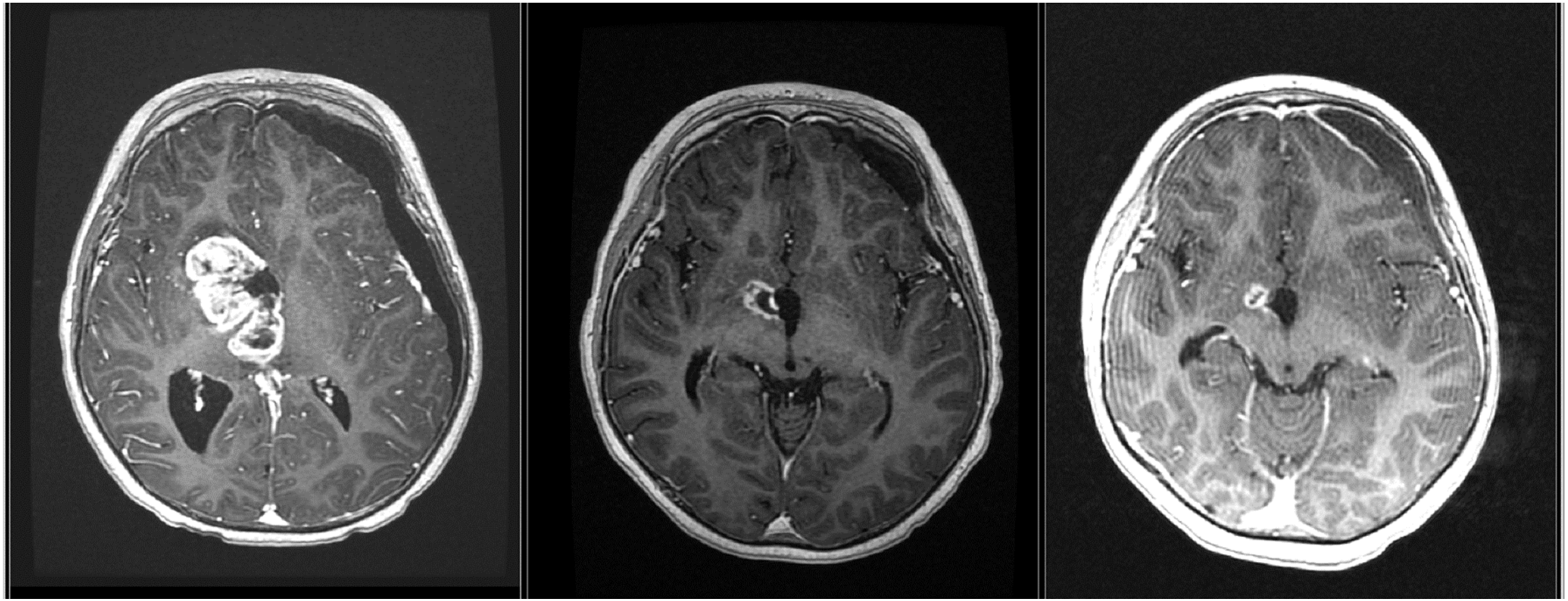


Treatment room



Courtesy of Dr. Yi-Wei- Chen

BNCT for brain tumor (8-year-old kid)



After 40 Gy X-ray RT

After BNCT 20.7 Gy-E

Courtesy of Dr. Yi-Wei- Chen

Development of salvage BNCT system for recurrent malignant glioma patients in Taiwan

biology

MDPI

Article

Salvage Boron Neutron Capture Therapy for Malignant Brain Tumor Patients in Compliance with Emergency and Compassionate Use: Evaluation of 34 Cases in Taiwan

Survivals after BNCT

	OS			CSS			RFS	
	Median Survival (Months)	6 Months	12 Months	Median Survival (Months)	6 Months	12 Months	Median Survival (Months)	6 Months
All cases	7.25	52%	29%	7.80	58%	38%	4.18	32%
CR	17.43	100%	64%	28.00	100%	50%	9.23	65%
PR	15.47	73%	62%	15.47	73%	62%	8.21	55%
SD	6.00	14%	0%	6.00	33%	0%	3.00	0%
PD	4.83	0%	0%	4.83	40%	0%	1.50	0%
ORR	15.65	82%	61%	17.11	82%	73%	8.44	59%
DCR	8.10	62%	35%	9.07	62%	41%	4.57	39%

OS, overall survival; CSS, cancer-specific survival; RFS, relapse-free survival;

Treatment Response after BNCT

Response	N (%)	95% CI
CR	6 (17.6%)	0.05–0.30
PR	11 (32.4%)	0.17–0.48
SD	12 (35.3%)	0.19–0.51
PD	5 (14.7%)	0.03–0.27
ORR	50.0%	0.33–0.66
DCR	85.3%	0.73–0.97

ORR, objective response rate (ORR = CR + PR); DCR, disease control rate (DCR = CR + PR + SD).

Biology 2021, 10, 334. https://doi.org/10.3390/biology10040334

NTRC Neutron Therapy Research Center

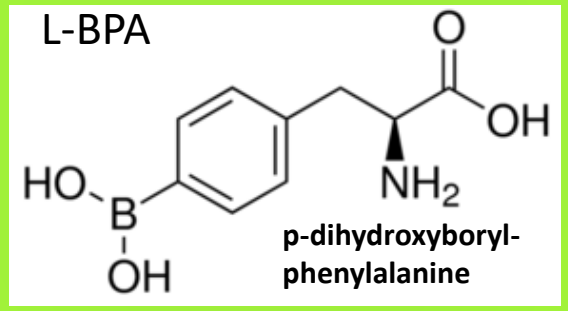
Japan. Committed to SDGs

2014 ~ Reactor-based BNCT in the hospital, China

In-Hospital Neutron Irradiator (IHNI-1) in China, Beijing Capture Technology Limited Co. (BCTC)

Boron

L-BPA



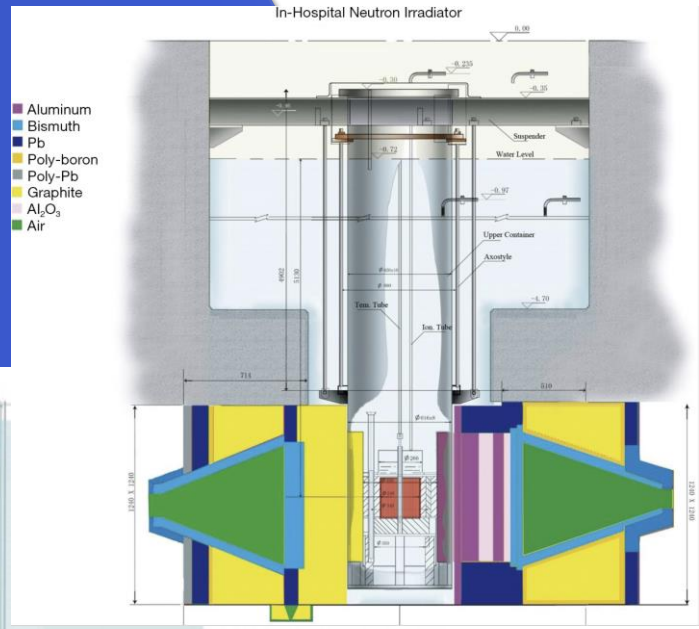
p-dihydroxyboryl-phenylalanine

(BPA-Fructose)

Neutron

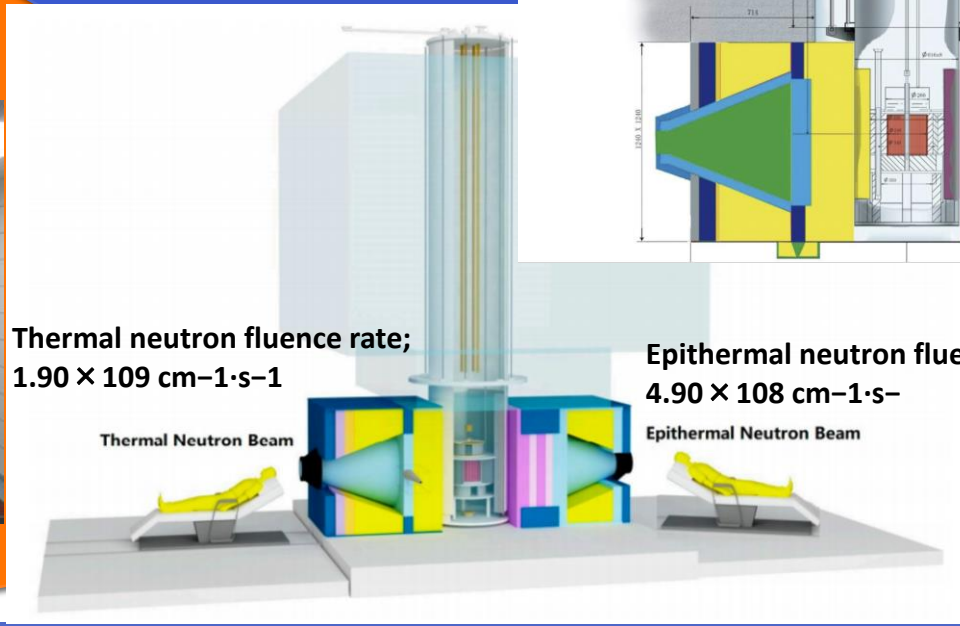
In-Hospital Neutron Irradiator (IHNI-1)

- **Thermal Neutron (<0.4eV)**
- **Epithermal neutron (0.4 eV – 10keV)**



Therapy

Melanoma



Thermal neutron fluence rate; 1.90 × 109 cm−1·s−1

Epithermal neutron fluence rate ; 4.90 × 108 cm−1·s−

自主创新 造福人类

世界首台医院中子照射器

The First In-Hospital Neutron Irradiator (IHNI-1) in the World

二元靶向放疗治癌的新技术：中子俘获疗法

doi: 10.3390/cancers15164060

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2014~ BNCT for melanoma @ IHNI-1

Third Xiangya Hospital of Central South University
ClinicalTrials.gov (No. NCT02759536)

Case Report

Boron neutron capture therapy for malignant melanoma: first clinical case report in China

Zhong Yong[1*], Zewen Song[2*], Yongmao Zhou[3], Tong Liu[4], Zizhu Zhang[4], Yanzhong Zhao[5], Yang Chen[4], Congjun Jin[4], Xiang Chen[6], Jianyun Lu[7], Rui Han[8], Pengzhou Li[9], Xulong Sun[9], Guohui Wang[9], Guangqing Shi[1], Shaihong Zhu[9]

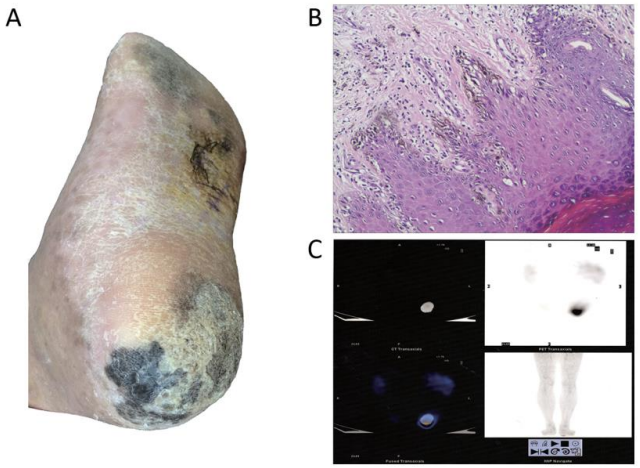

Figure 1 Gross examination, pathological analysis and PET/CT scan of the patient before BNCT. (A) Gross examination of the skin lesions in the patient's left foot before BNCT; (B) Pathological analysis before BNCT; (C) PET/CT before BNCT. BNCT, boron neutron capture therapy; PET, positron emission tomography; CT, computed tomography.

BNCT

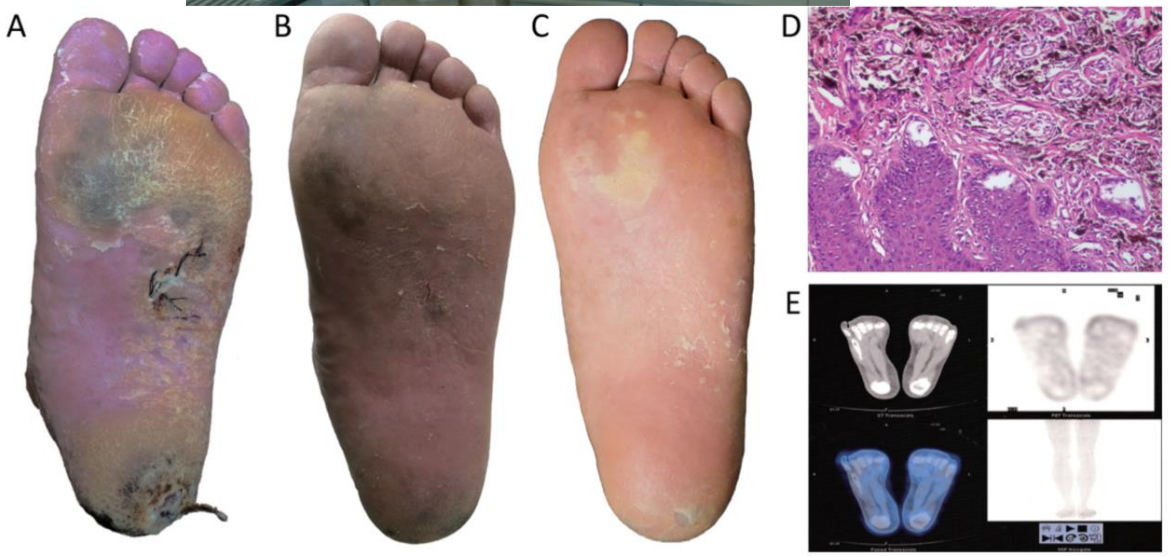

Figure 4 Gross examination, pathological analysis and PET/CT scan of the patient after BNCT. (A–C) Gross examination of the skin lesions in the patient's left foot 2 weeks (A), 5 weeks (B) and 24 months (C) after BNCT; (D) Pathological analysis after BNCT; (E) PET/CT scan after BNCT. BNCT, boron neutron capture therapy; PET, positron emission tomography; CT, computed tomography.

Clinical Trials.gov.No. NCT02759536

NTRC Neutron Therapy Research Center

Japan. Committed to SDGs

Latest reactor-based BNCT development all over the world

Ca. 2000 patients underwent BNCT all over the world.

1951: 1st clinical trial of BNCT for recurrent glioblastomas in U.S.

2001: 1st BNCT clinical trial for head and neck cancer in Japan

Up to now clinical trails using reactor based BNCT

- Japan: more than 1000 cases
- Finland: 311 cases for both clinical trials and compassionate use
- Taiwan: more than 450 cases for both clinical trials and compassionate use

2014: Reactor based BNCT in the hospital in China

2023: The approval of reactor based BNCT system as medical device in Taiwan