UCANS-II, Indiana Univ., 5-8 Jul, 2011

Neutronic study on a epithermal moderator system for the boron neutron capture therapy based on a small proton accelerator

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Contents

- BNCT project to built a facility in Ibaraki prefecture
- Neutronic design for a moderator-reflector system

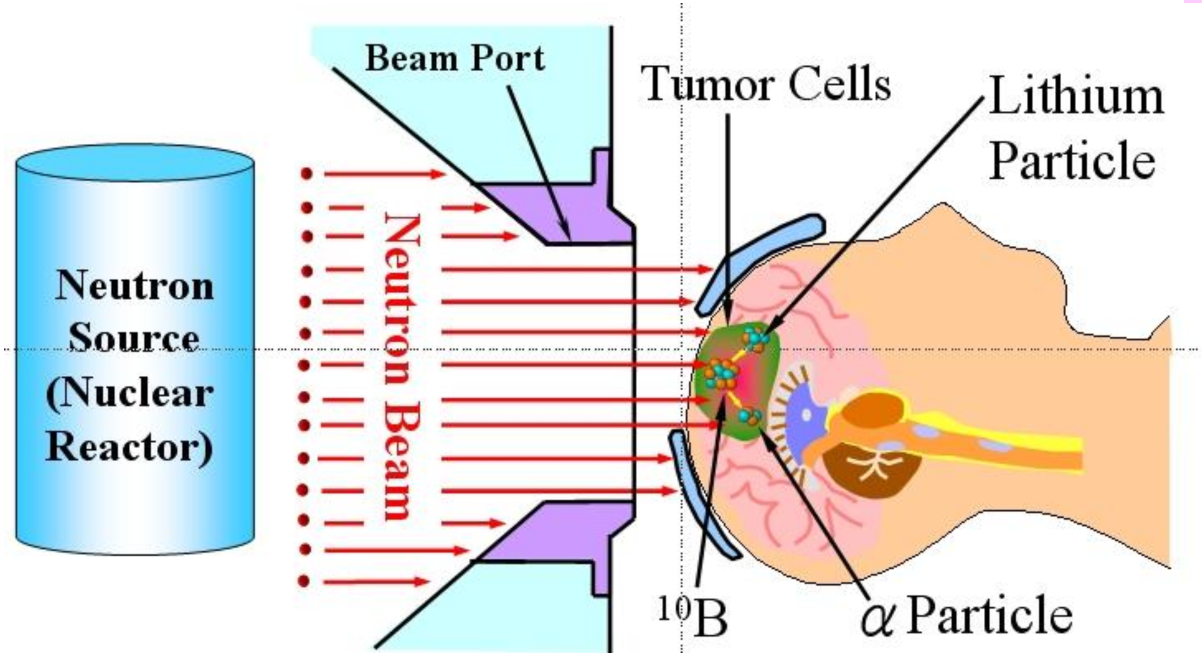
BNCT project to built a facility in Ibaraki prefecture

Boron Neutron Capture Therapy (BNCT)
～ A next-gen Cancer Therapy ～

Principle of BNCT

①Inject boron compound which can accumulate in cancer cells selectively.
②Irradiation thermal neutrons to focal site.
③Alpha particle and Li particle are released by the reaction with B-10 and the thermal neutron, and then the particles break DNA of the cancer cells.
④Finally, the particles destroy cancer cells selectively.

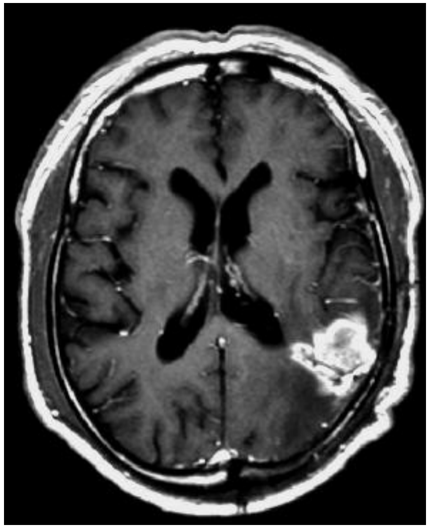
Principle



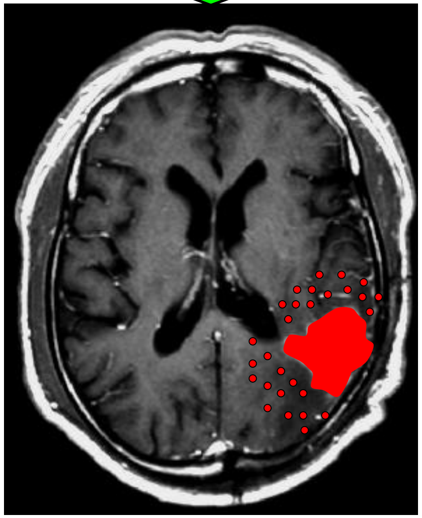
Feature

- ● High LET treatment by the particles
- ● Treatment finish with a single irradiation
- ● BNCT can treat intractable cancer such as invasive cancer, multiple cancer and recurrent cancer
- ● Prediction of effect of the therapy by using PET diagnosis in advance

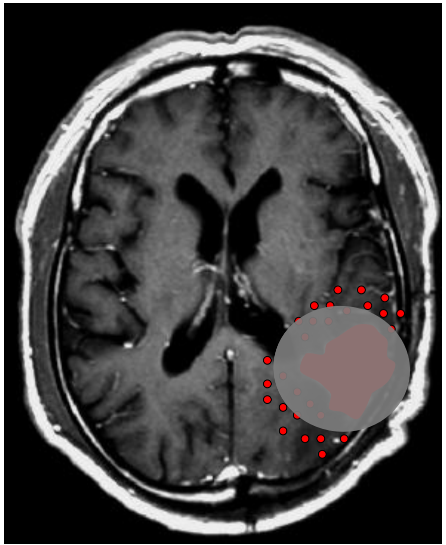
BNCT can treat intractable cancer：Invasive Cancer



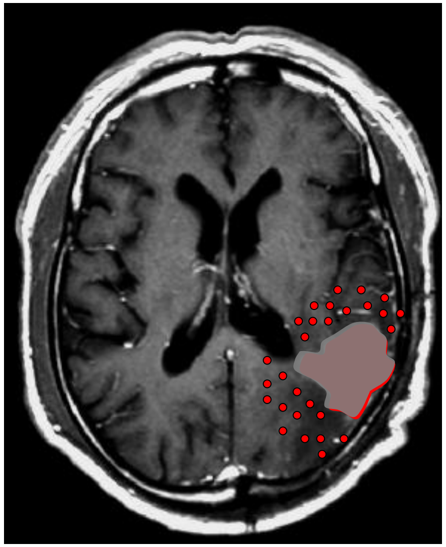
Malignant Brain Tumor



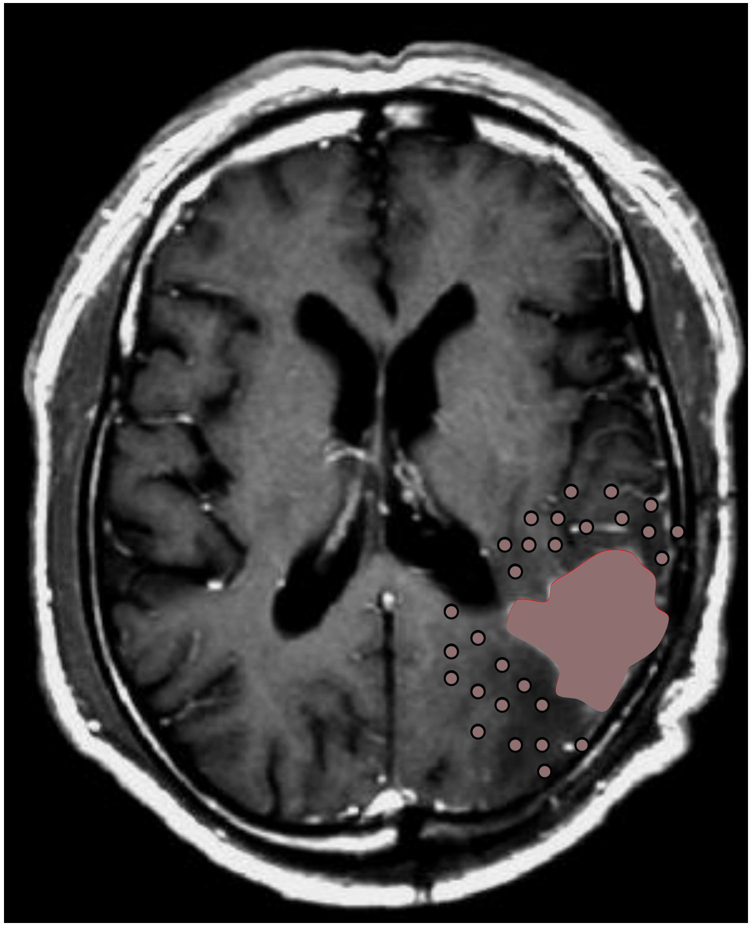
Need for cell level treatment



X-ray therapy



Particle therapy

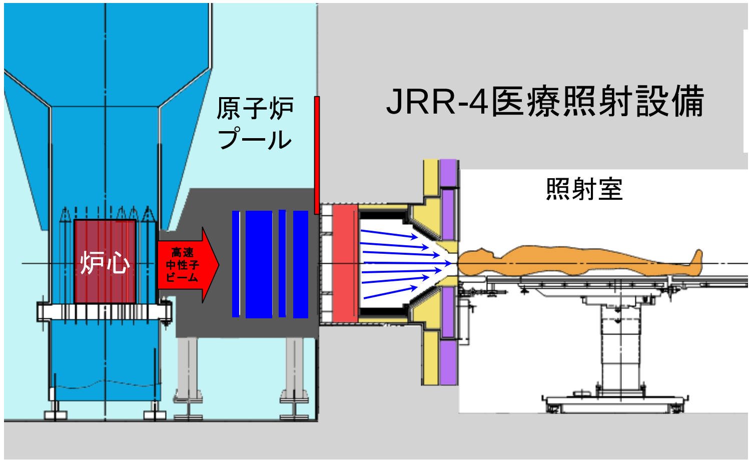


BNCT

Cancer cells are targeted with boron compound, and then the cancer cells can be destroyed by neutron irradiation.

Future Perspective of BNCT

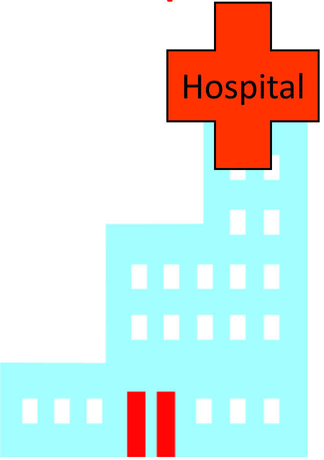
Reactor(JRR−4)　1999～



- ●Can’t establish for Medical Services（Clinical trial only）！
- ●Reactor must stop a few month per year due to relative regulation
- ● In Japan, JRR-4 and KUR (only 2 Facilities) Can not build new reactor for BNCT
- ●JRR-4 has been stopped by the Great Earthquake.

Need for an another neutron source device

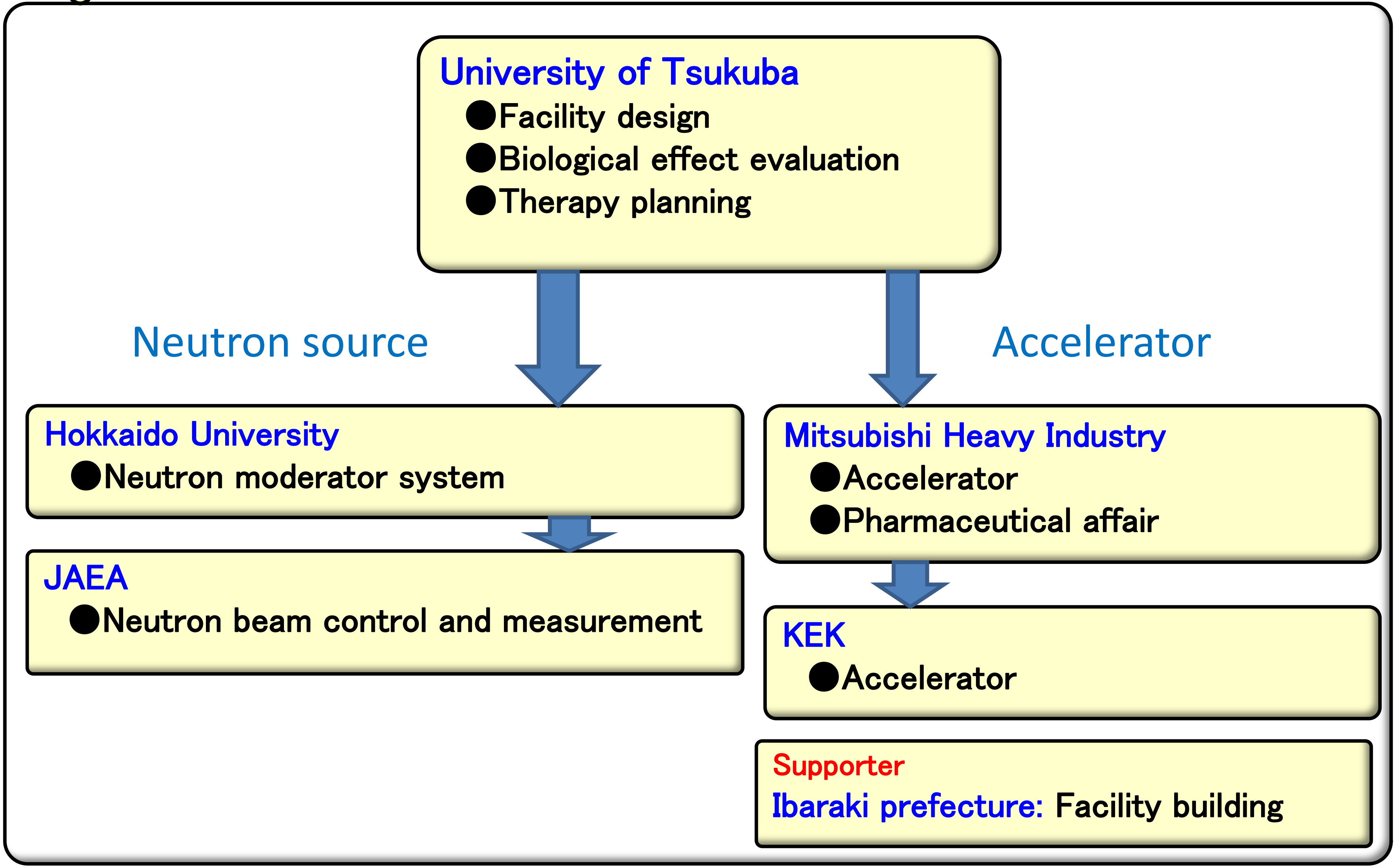
Compact accelerator based neutron source which can be installed to hospital



- ●We can perform the treatment throughout a year in a hospital
- ●BNCT can be step-up to advance medical and health -care in the near future
- ●In hospital, BNCT can combined with several method such as fractionated irradiation or intra-operative irradiation.

BNCT project team for Ibaraki prefecture BNCT facility

Budget for accelerator development has been approved.



University of Tsukuba

- Facility design
- Biological effect evaluation
- Therapy planning

Neutron source

Hokkaido University

- Neutron moderator system

JAEA

- Neutron beam control and measurement

Accelerator

Mitsubishi Heavy Industry

- Accelerator
- Pharmaceutical affair

KEK

- Accelerator

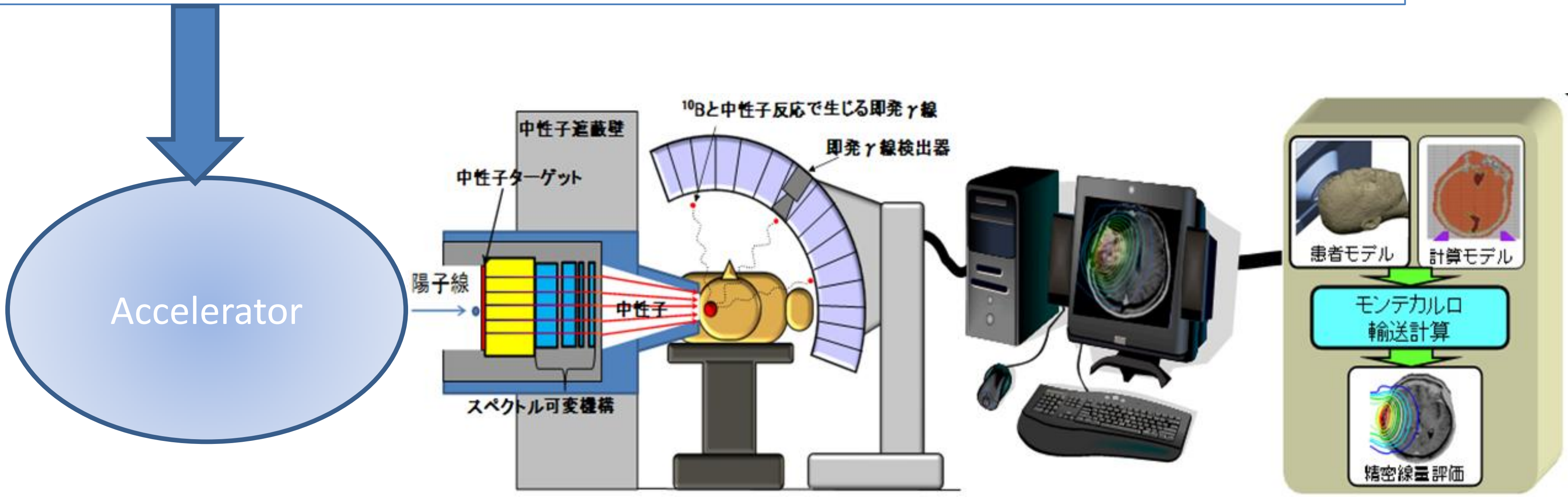
Supporter

Ibaraki prefecture: Facility building

Accelerator design

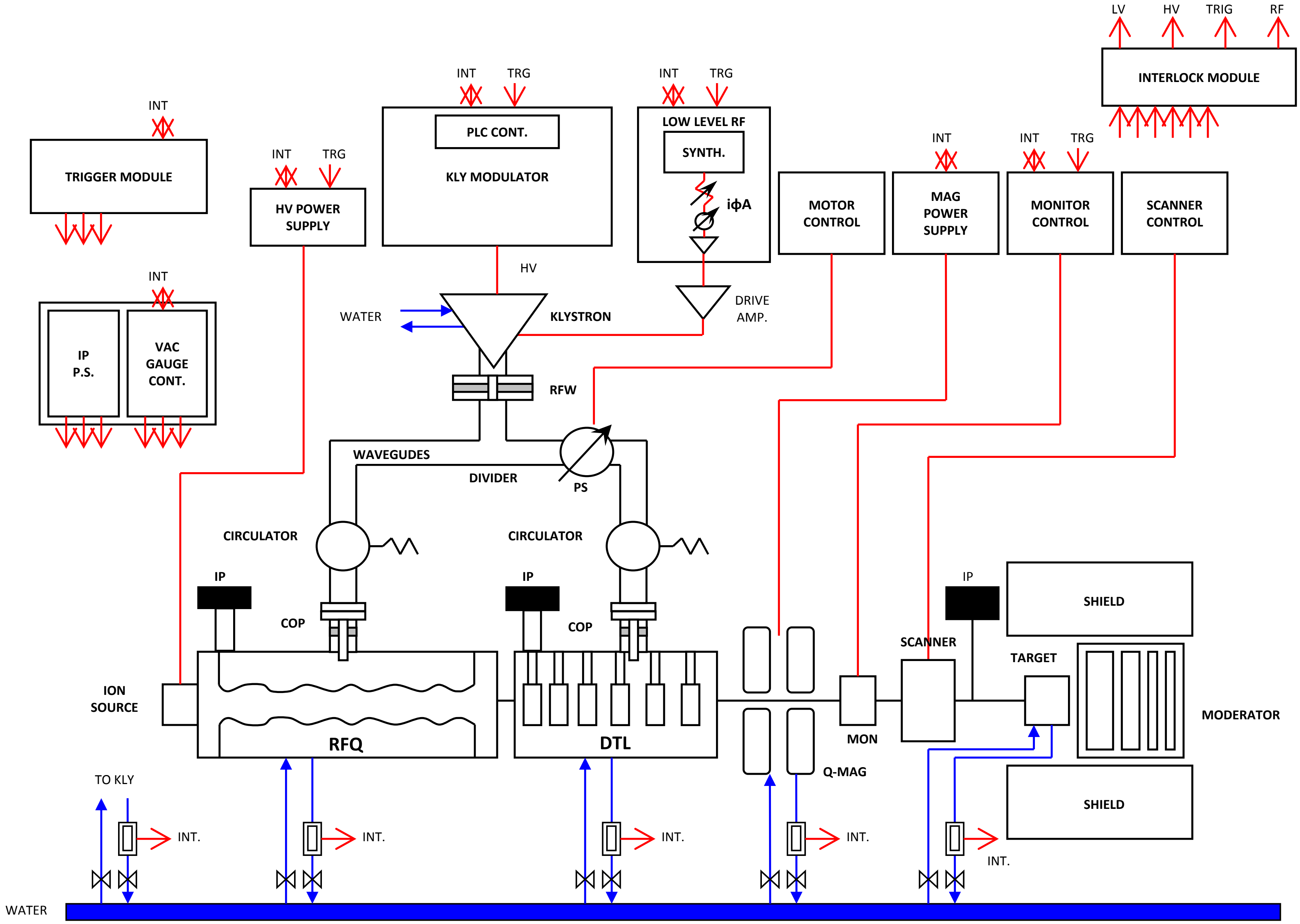
Basic strategy 1: specifications of the accelerator should be based on the target-technology
Basic strategy 2: Our goal is to realize the facility to install in hospitals

- ➔ Reasonably low cost, good maintainability, easy radiation shielding
- ➔ Long lifetime ➔ anti-blistering
- ➔ Low radioactivity ➔ beam energy should be below nuclear reaction threshold energy
- ➔ 8 MeV
- ● Epi-thermal neutron flux $> 1.0 \times 10^{9}$ /sec/cm^{2}
- ● Fast neutron contamination $< 1.0 \times 10^{-12}$ Gy·cm^{2}
- ● Necessary beam power ➔ ~80kW
- ● Necessary average beam current ➔ 10mA
- ● Technology choice is Linac based facility ➔ J-PARC front-end Linac (RFQ+DTL)
- ● Peak current: 50mA, duty factor: 20%
  - ➔ overcome space charge effect, a new issue is design of water cooling system
- ● Simplify fabrication method (this application is not the injector of synchrotron)

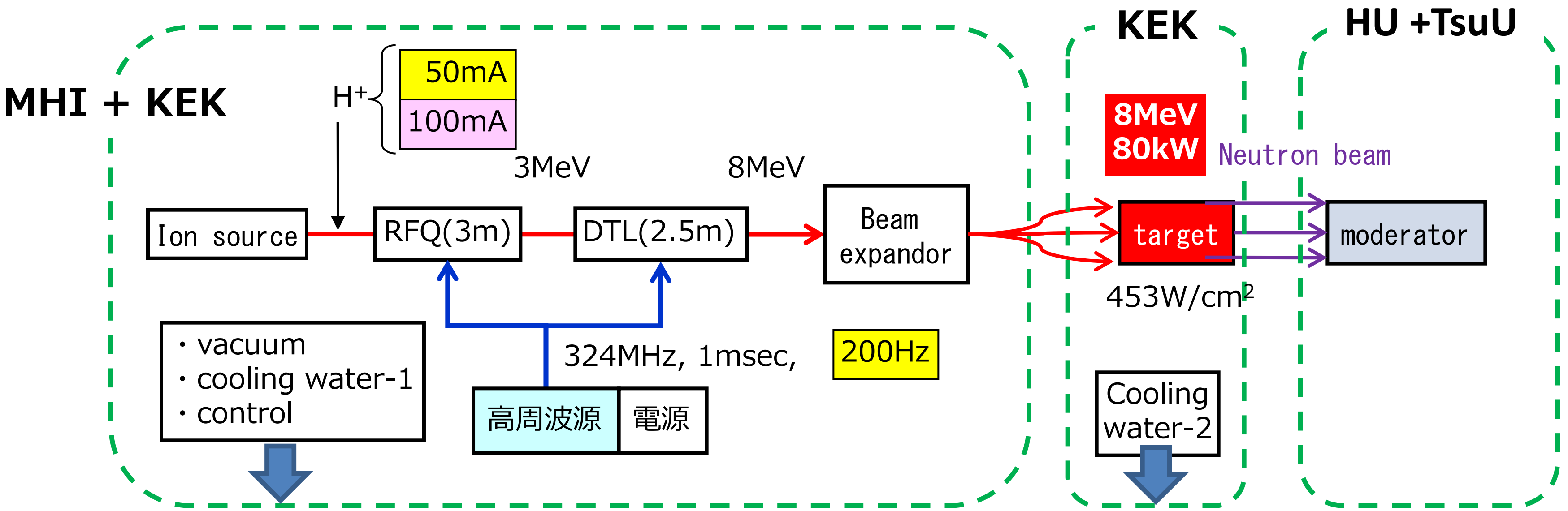


(1) Optimization of neutron source **(2) Real time monitoring** **(3) Therapy planning**

A block diagram of the system

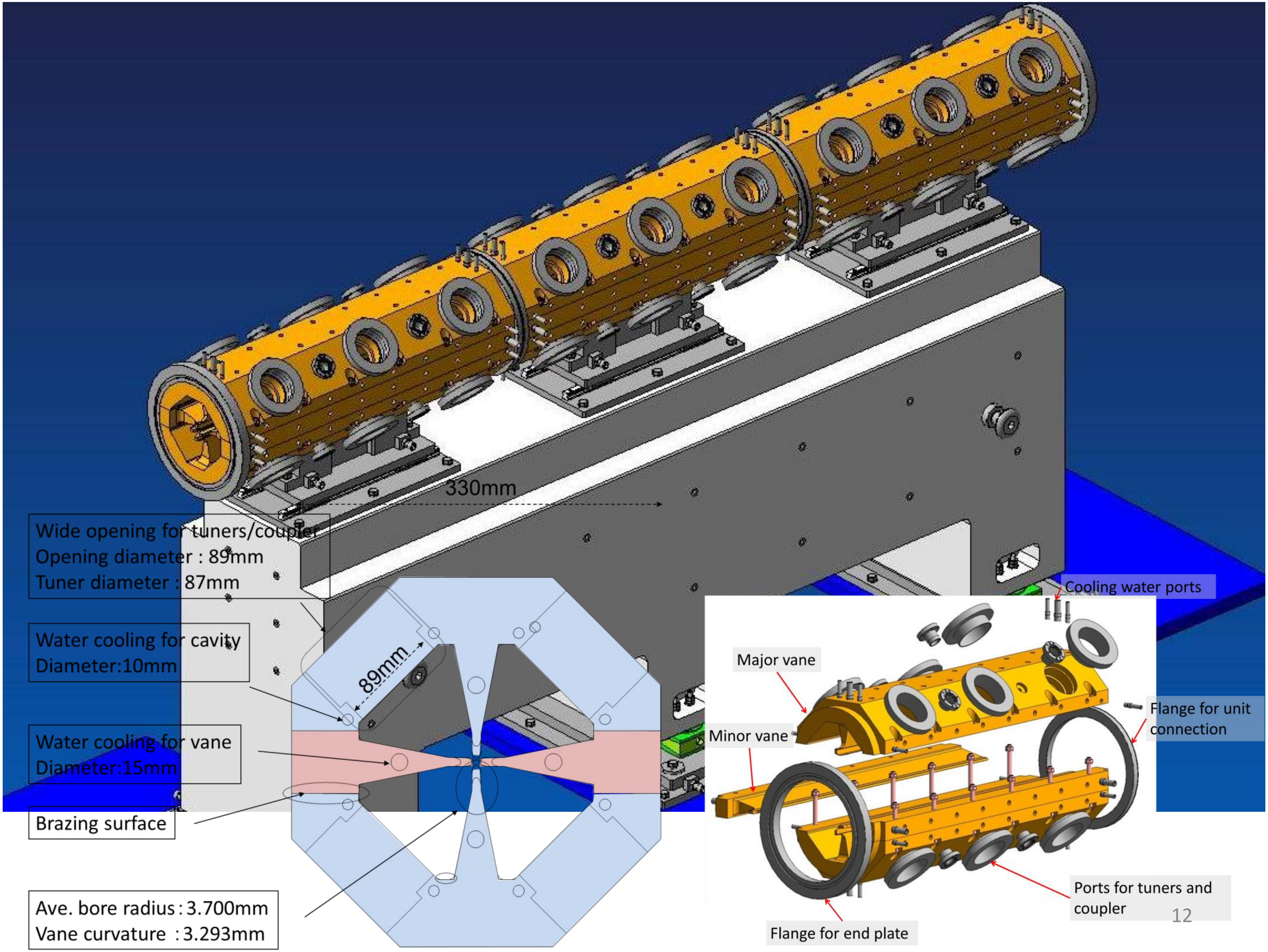


LINAC OPERATION PARAMETERS



item	H⁺: 50mA, Rep.: 200Hz
① RF source	Klystron
② RF frequency	324 MHz
③ Duty Factor	20% (200kW)
④ peak output	1.0 MW
⑤ pulse width	1 msec
⑥ repetition rate	200 Hz
⑦ phase stability	<±2degrees
⑧ efficiency	> 50%
⑨ gain	> 50 dB
⑩ operation temperature	60℃

hroshi.matsumoto@kek.jp/masakazu.yoshioka@kek.jp/hitoshi.kobayashi@kek.jp



Wide opening for tuners/coupler
Opening diameter : 89mm
Tuner diameter : 87mm

Water cooling for cavity
Diameter:10mm

Water cooling for vane
Diameter:15mm

Brazing surface

Ave. bore radius : 3.700mm
Vane curvature : 3.293mm

Cooling water ports

Major vane

Minor vane

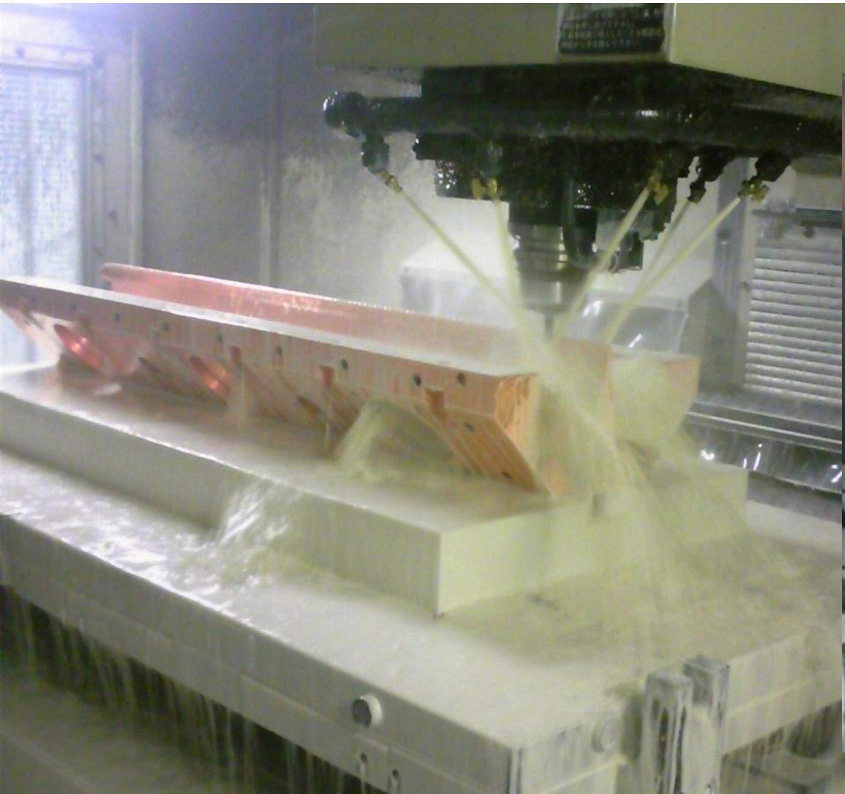
Flange for unit connection

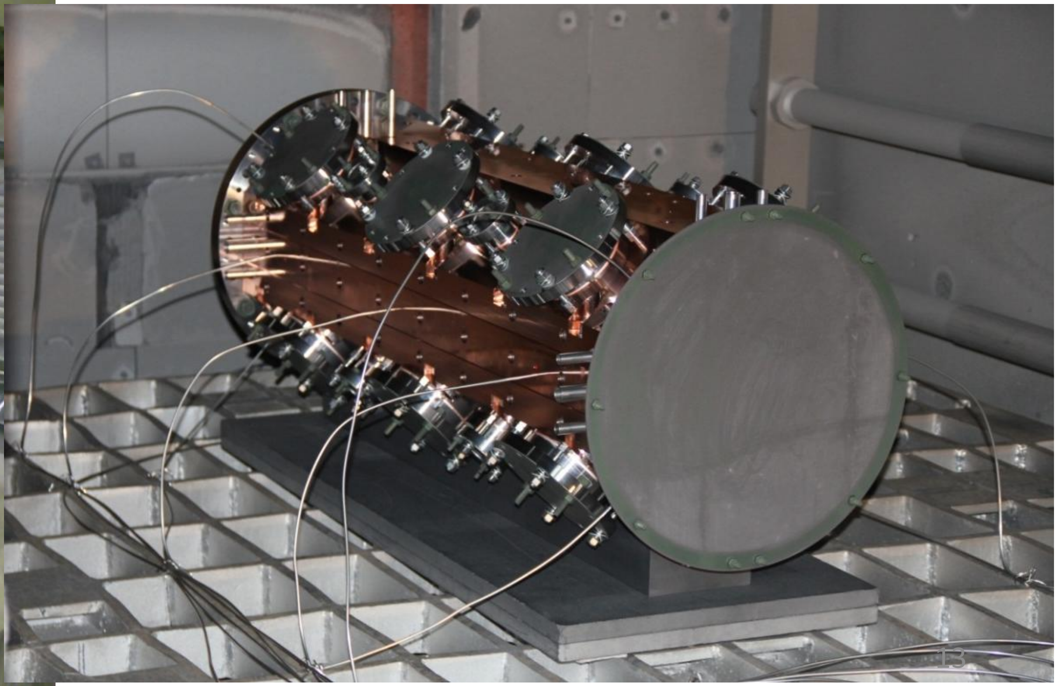
Ports for tuners and coupler

Flange for end plate

Technical choice for fabrication	
Material	High-purity oxygen-free copper with HIP (Hot Isostatic Pressing)
Drilled hole plugging	Electron beam welding (EBW)
Annealing	600 degree C in a vacuum furnace
Vane machining	Numerical-controlled machining with ball-end mill
Surface treatment	Chemical polishing (3-5μm)
Vane integration	Vanes and ports are jointed in one step brazing
Unit cavities connection	Welding for vacuum seal, bolting for mechanical alignment

RFQ parameters	
Frequency [MHz]	324
Acceleration energy [MeV]	0.05 to 3
Vane length [mm]	3172.114
Inter-vane voltage[kV]	82.9
Max. surface field [MV/m]	31.6(1.77 Kilpatrick)
Ave. bore radius [mm]	3.7
Vane-tip curvature [mm]	0.89r0 (3.293mm)
Number of cells	294 + (transition cell, FFS)
RF Power [kW]	361
RF duty [%]	3
Dipole tuner	DSRs





Neutronic design of a moderator-reflector system

Moderator-Reflector system for BNCT

Conditions for the epithermal neutron source for BNCT

①Thermal neutron flux : $<5.0 \times 10^{7}$ (1/sec/cm^2)
②Epithermal neutron flux : $>1.0 \times 10^{9}$ (1/sec/cm^2)
③Fast neutron dose/ϕ_{epi} $<1.0 \times 10^{-12}$ (Gy・cm^2)
(Ratio of fast neutron)

(Conditions at KURRI)

Energy ranges

Thermal neutron : <0.5eV

(Reactor based ones)

Epithermal neutron : 0.5eV～10keV

Fast neutron : >10keV

(Cyclotron based source at KURRI)

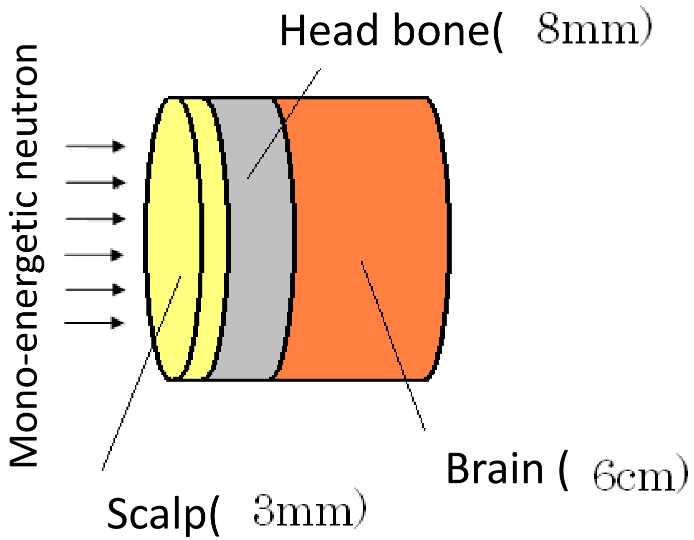
Epithermal neutron : 0.5eV～40keV

Fast neutron : >40keV

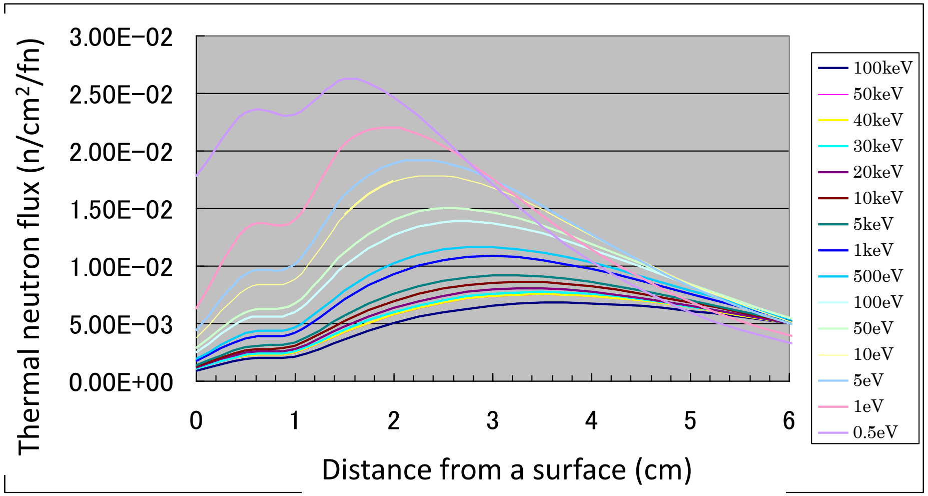
Choice of upper energy of the epithermal region is one of issues.

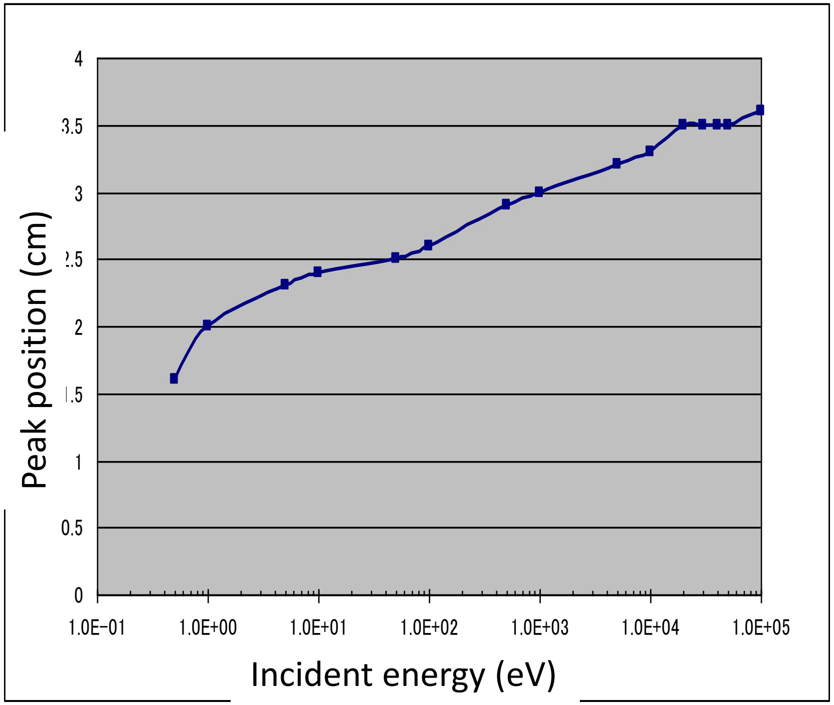
Consideration on upper energy (1)

Incident neutron energy dependence of the thermal neutron distribution



*Higher energy over 10 keV is not so effective to get to deep part.



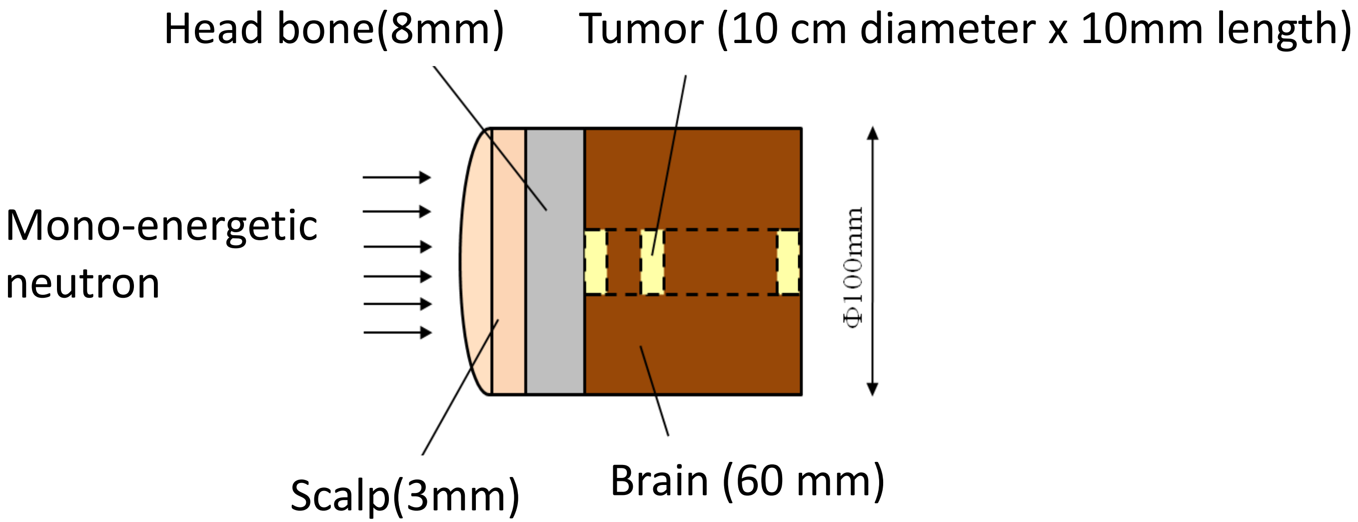


Thermal neutron distribution in a brain

Peak position of thermal neutron flux

Consideration on upper energy (2)

Absorbed dose



Head bone(8mm)

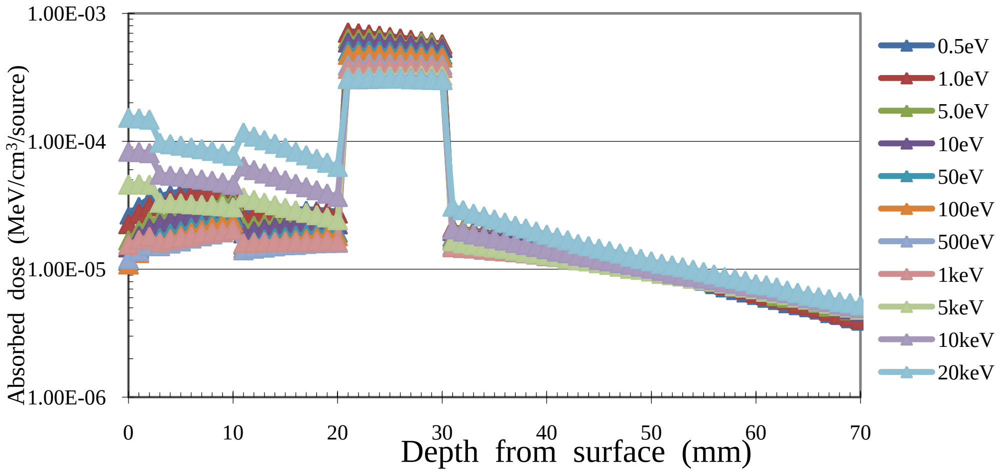
Tumor (10 cm diameter x 10mm length)

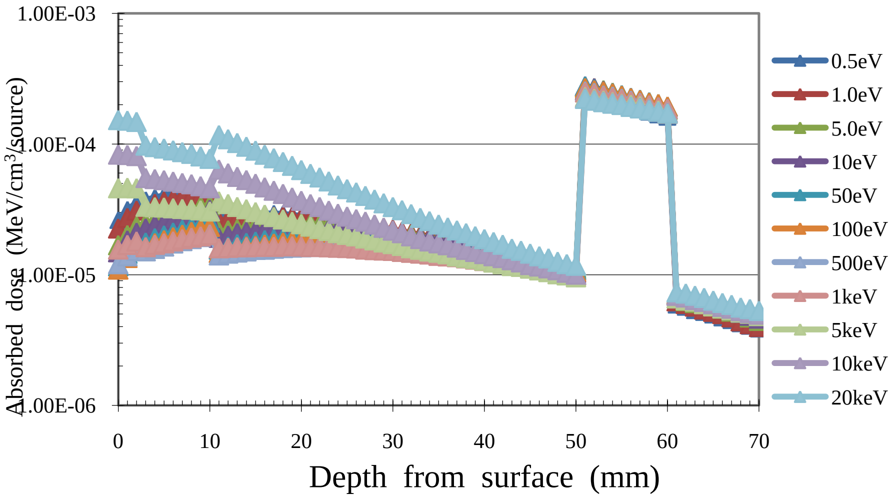
Mono-energetic neutron

Φ100mm

Scalp(3mm)

Brain (60 mm)





Upper energy should not be raised since skin dose increases with energy.

Consideration on moderator-reflector system

Choice of reactions (Preliminary optimization of a moderator)

- Li(p,n) reaction

Method ①: Direct use of neutrons produced by 1.9MeV proton

➡ The energy of the produced neutrons is low enough to use the neutron for BNCT

Method ②: Use of the moderated neutrons produced by 2.5-3.0MeV protons

➡ The energy of the produced neutrons is little bit higher but the intensity is also higher. The required moderation will be not so severe, so reduction is not so much.

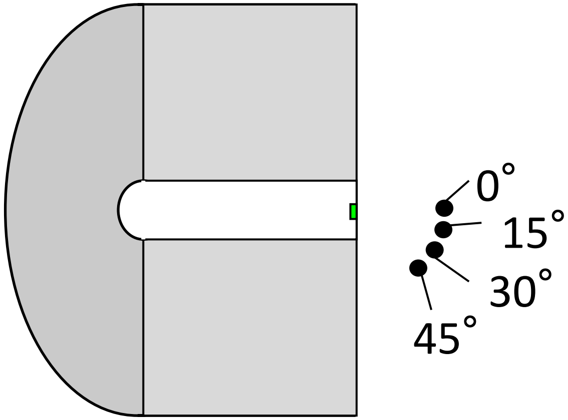
- Be(p,n) reaction

Method ③: Use of the moderated neutrons produced by 11MeV protons

➡ The neutron energy is much higher than Li(p,n) reaction, but the intensity is about 15 times higher. So, we will get enough intensity even after moderation.

	Ep	Neutron intensity	Neutron energy	
Li(p,n)	1.9MeV	1.5×10^{10} (n/sec/mA)	Max. 90 keV	Ave. 38keV
	2.5MeV	8.8×10^{11} (n/sec/mA)	Max. 787keV	Ave. 326keV
Be(p,n)	11MeV	2.15×10^{13} (n/sec/mA)	Max. 8.55MeV	Ave. 2.37MeV

①Direct use of Li(p,n) neutrons



The emitted neutron energy spectrum of Li(p,n) reaction depend on the angular and higher energy neutron will produced in forward direction. Therefore, we study angular dependence.

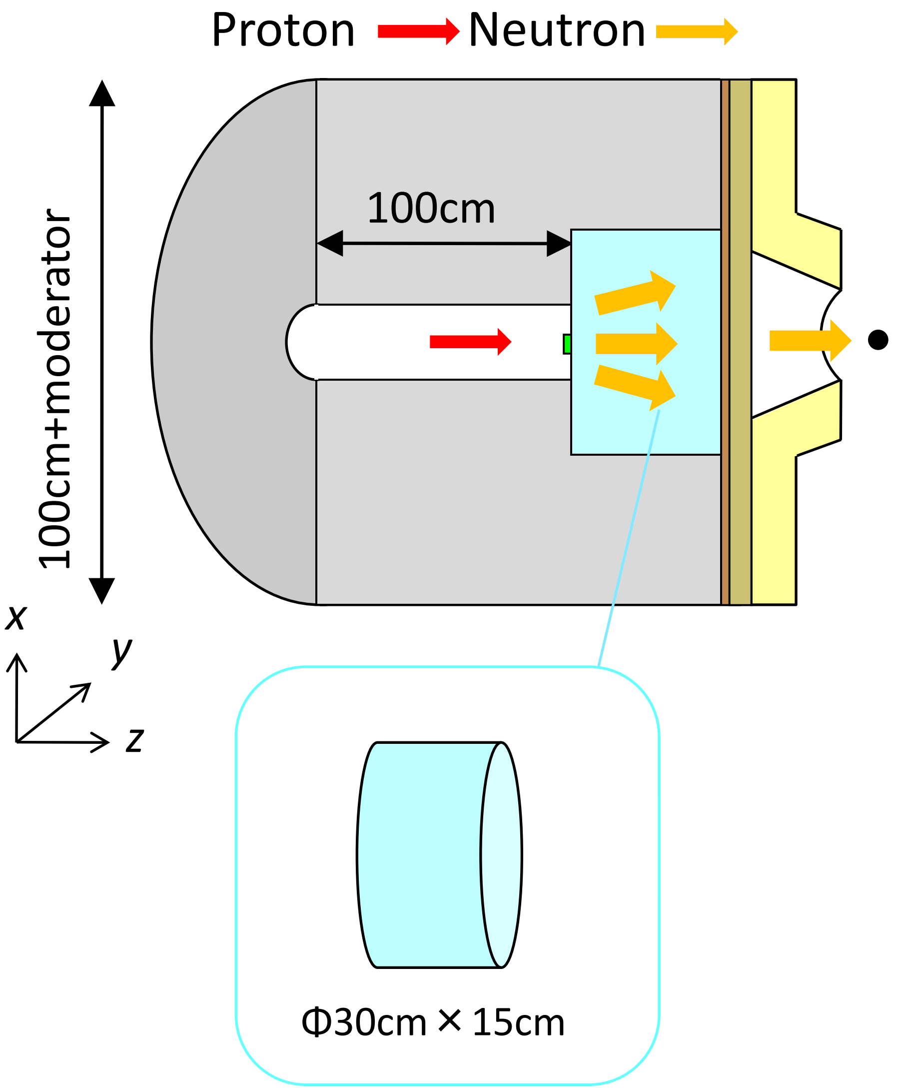
Fast Neutron dose/ϕ_{epi} $<1.0\times10^{-12}$ (Gy・cm^2)

Angle (degree)	Thermal Flux (1/sec/cm^2/mA)	Epithermal Flux (1/sec/cm^2/mA)	Fast Neutron dose/ϕ_{epi} (Gy・cm^2)
0	2.11×10^{3}	1.29×10^{8}	3.63×10^{-12}
15	2.05×10^{3}	1.17×10^{8}	3.40×10^{-12}
30	1.67×10^{3}	9.39×10^{7}	2.59×10^{-12}
45	6.82×10^{2}	3.70×10^{7}	1.33×10^{-12}

It will be difficult to use 1.9 MeV protons directly since this method cannot fulfill the fast neutron dose rate.

Moderator use of ②Li(p,n) reaction, and ③Be(p,n) reaction —Slab type—

- Simulation code : MCNPX



🟩 Target (Li or Be)

🟦 Moderator

⬜ Reflector (Pb)

🟫 Thermal neutron shield (Cd)

🟨 Gamma-rays shield (Bi)

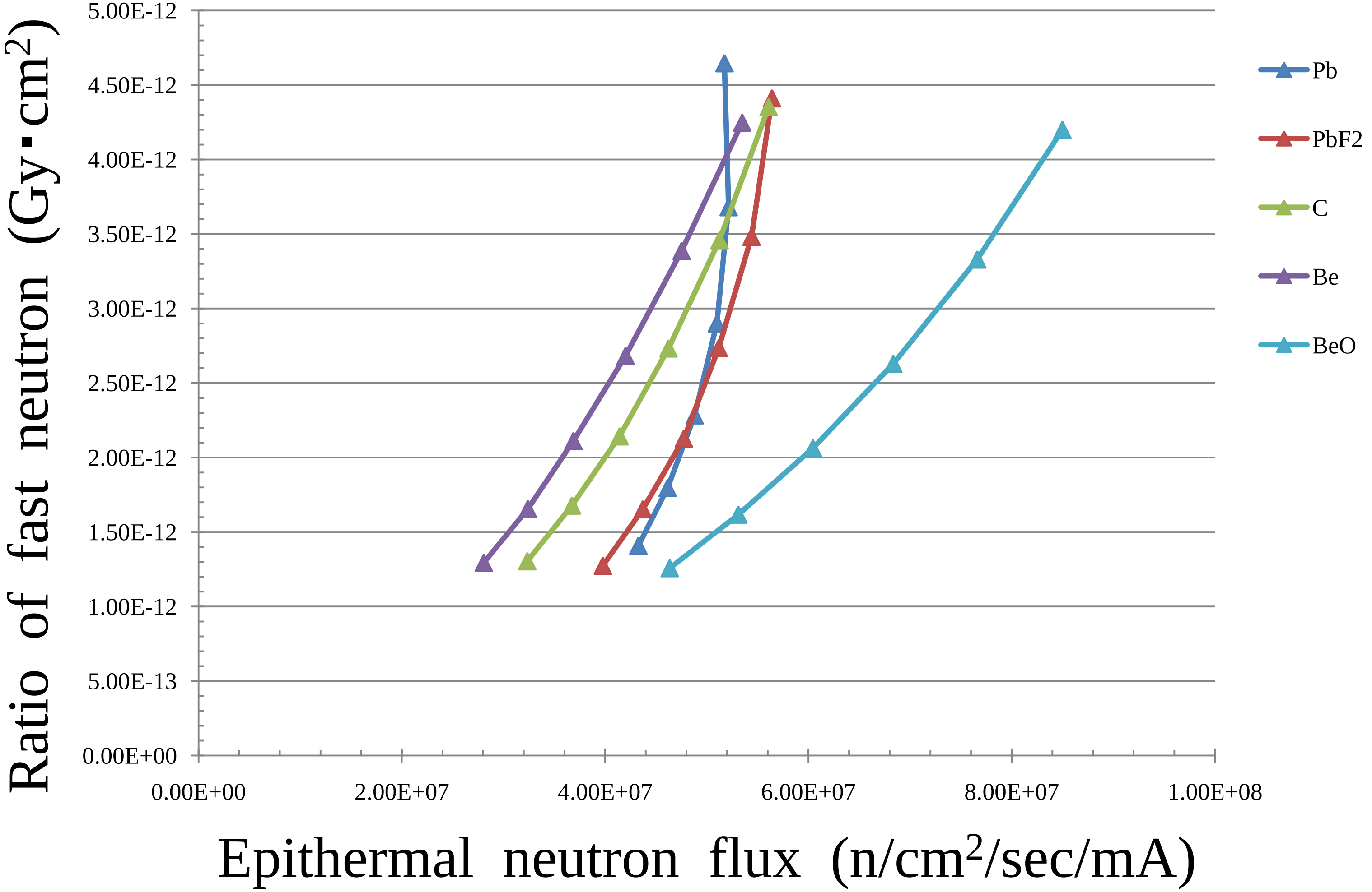
🟨 Collimator (B_4C)

● Detector

Tally : exit of the collimator

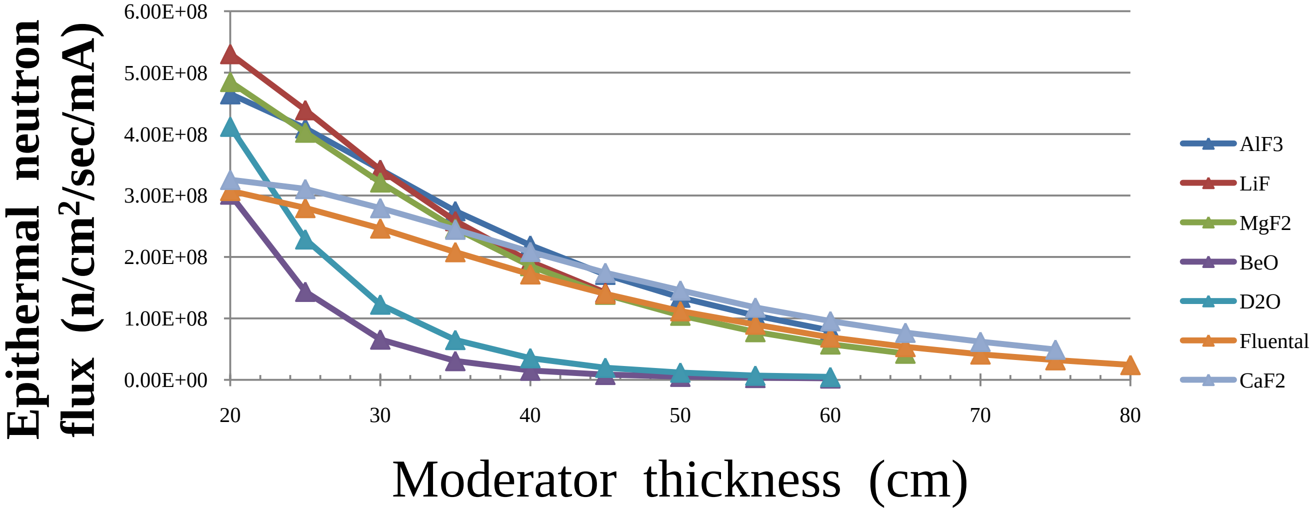
Change of the epithermal neutron flux and the fast neutron dose rate depending on the reflector materials

Slab type

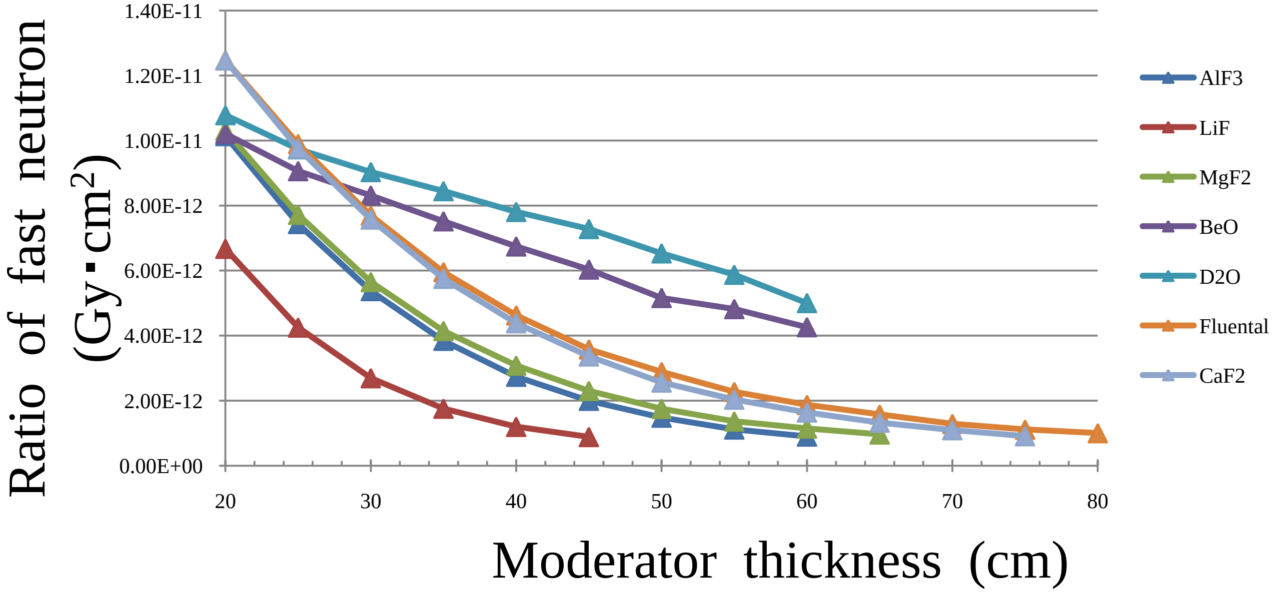


Choice of moderator materials

Epithermal neutron intensity depending on moderator thickness



Ratio of fast neutron depending on the moderator thickness



Moderated neutron case —Slab type—

Ep (MeV)	Moderator size	Thermal n (1/sec/cm^2/mA)	Epi-thermal n (1/sec/cm^2/mA)	Rtio of fast n dose/ϕ_{epi} (Gy・cm^2)
2.5	Φ36cm × 21cm	3.29×10^3	2.79×10^7	1.00×10^{-12}
2.6	Φ38cm × 22cm	4.81×10^3	3.09×10^7	1.00×10^{-12}
2.7	Φ30cm × 24cm	3.75×10^3	3.16×10^7	9.96×10^{-13}
2.8	Φ36cm × 25cm	6.36×10^3	3.17×10^7	9.84×10^{-13}
2.9	Φ40cm × 26cm	9.11×10^3	3.19×10^7	9.96×10^{-13}
3.0	Φ40cm × 27cm	9.25×10^3	3.23×10^7	1.00×10^{-12}
11	Φ50cm × 40cm	9.10×10^5	1.63×10^8	1.00×10^{-12}

①Thermal n<5.0×10^7 (1/sec/cm^2)
②Epi-thermal n> 1.0×10^9 (1/sec/cm^2)
③Fast n dose/ϕ_{epi}<1.0×10^{-12} (Gy・cm^2)

(Thermal n< 0.5eV　Epi-thermal 0.5eV～10keV　Fast n >10keV)

Minimum current of the accelerators
Li(p,n): 30.96mA (Ep=3.0MeV), Be(p,n): 6.13mA (11MeV)

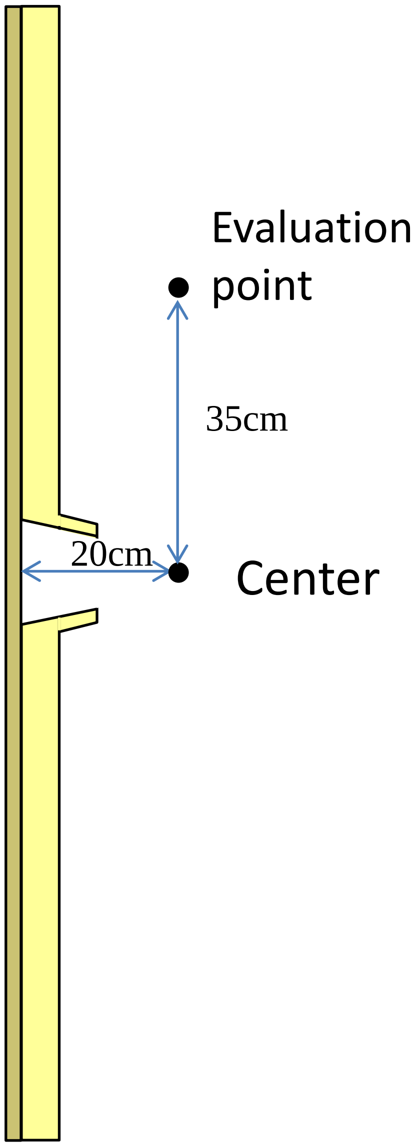
Consideration on radiation dose around the beam extraction area

Guide line of shield for BNCT

Based on the guide line at KURRI

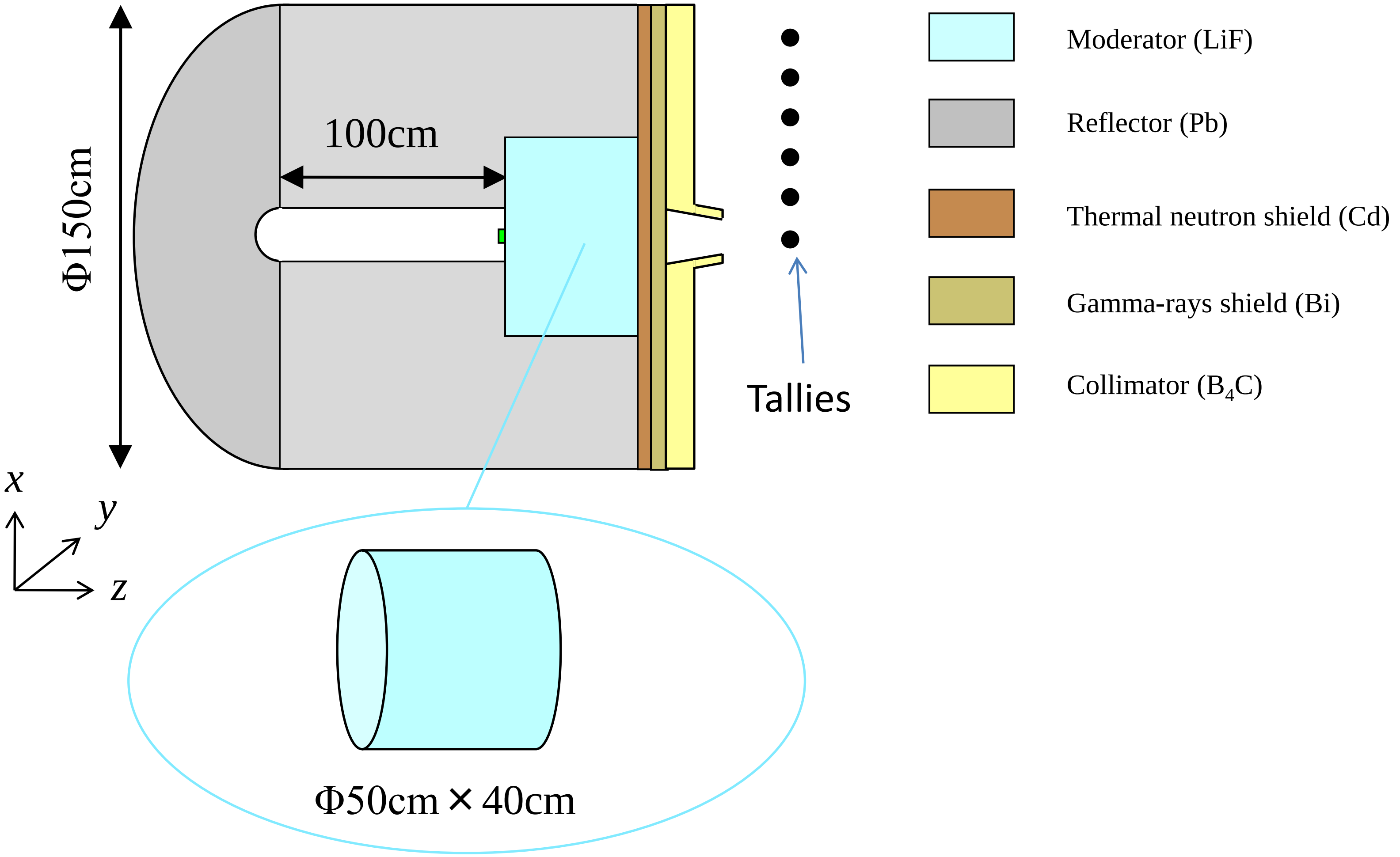
Guide line for shield

- Free-in-air without patient
- 30 cm outside of the collimator edge
- Less than 1/20 of thermal, epithermal, fast neutron fluxes at the beam center
- Less than 1Sv/h under the condition of 1×10^9n/cm^2/sec epithermal neutron flux at the



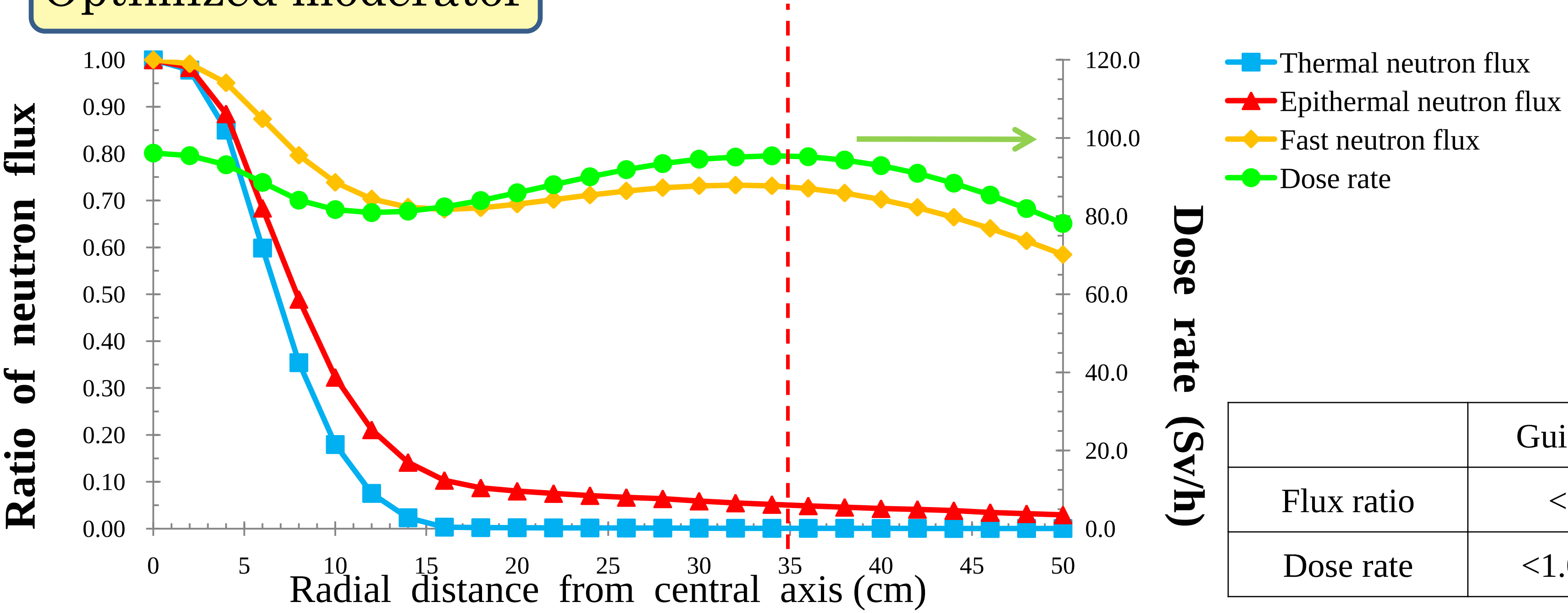
Simulation system (Be(p,n) reaction-Slab type)

- Simulation code：MCNPX
- Proton energy：11MeV



Ratio of each neutron flux between center and outside of center, and dose rate

Optimized moderator



	Guide line
Flux ratio	<0.05
Dose rate	<1.0 Sv/h

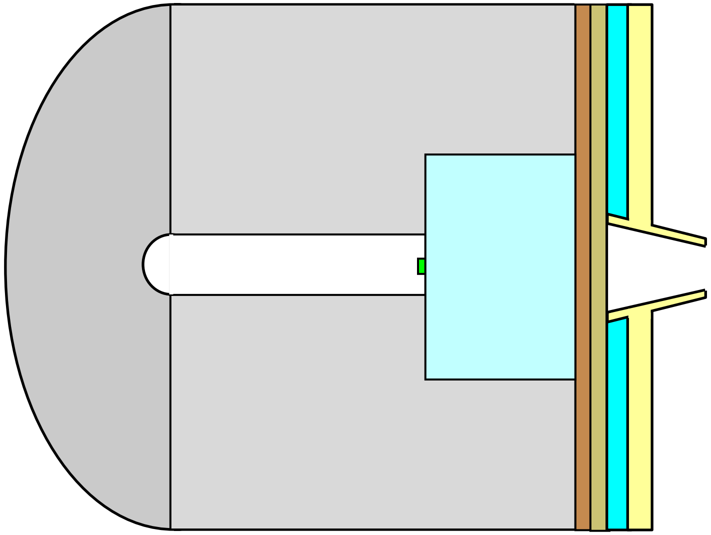
	Thermal neutron (n/cm^2/sec/mA)	Epithermal neutron (n/cm^2/sec/mA)	Fast neutron (n/cm^2/sec/mA)	Dose rate (Sv/h)
Center	9.15×10^5	1.62×10^8	3.75×10^7	—
Evaluation point	7.24×10^2	8.40×10^6	2.74×10^7	95.44
Ratio	0.001	0.052	0.731	—

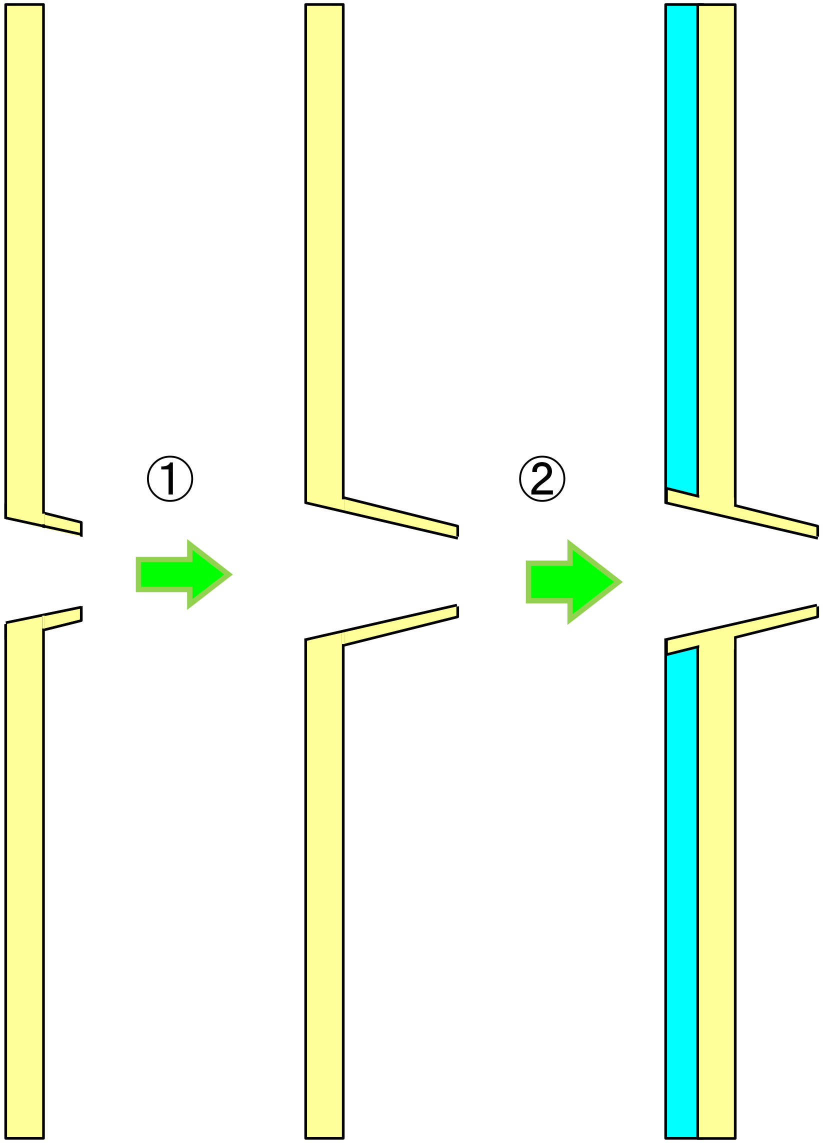
➡ The ratios of thermal and epithermal neutron flux es and the dose rate do not fulfill the guide line.

Improvement of shielding performance

① We lengthen the collimator from 10 cm to 20 cm to get more concentrated beam

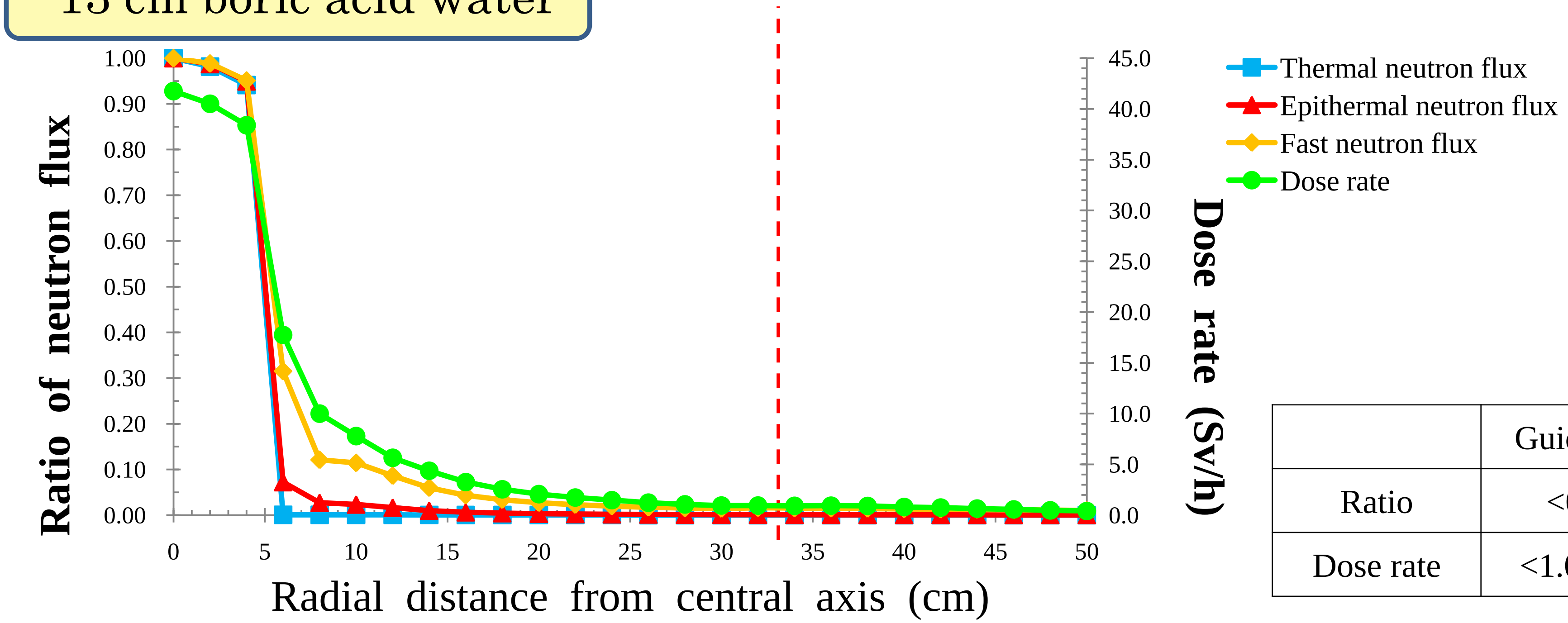
② We put a shielding material of boric-acid water to reduce the fast neutron flux





Revised value of ratio of each neutron flux between center and outside of center, and dose rate

13 cm boric acid water



	Guide line
Ratio	<0.05
Dose rate	<1.0 Sv/h

	Thermal neutron ($n/cm^2/sec/mA$)	Epithermal neutron ($n/cm^2/sec/mA$)	Fast neutron ($n/cm^2/sec/mA$)	Dose rate (Sv/h)
Center	1.60×10^6	2.79×10^8	3.84×10^7	—
Evaluation point	3.05×10^2	1.38×10^5	2.54×10^5	0.92
Ratio	0.0002	0.0005	0.007	—

➡ The guide line was fulfilled by adding the fast neutron shield.

Summary

- Preliminary simulations have been performed and further detailed simulations are needed taking into account realistic configuration.
- The guide line other than the irradiation area has been fulfilled. Further study for optimization is required.

Present results for the optimized system

	Thermal neutron $(\mathrm{n/sec/cm^2})$	Epithermal neutron $(\mathrm{n/sec/cm^2})$	Ratio of fast neutron $(\mathrm{Gy \cdot cm^2})$	Accelerator power	
				Ip (mA)	Power (kW)
Be(p,n), Slab type	5.73×10^{6}	1.00×10^{9}	7.36×10^{-13}	3.58	39.4
Irradiation condition	$<5.00 \times 10^{7}$	$<1.00 \times 10^{9}$	$<1.00 \times 10^{-12}$		

After this simulation the required accelerator power was reduced to 39.4kW

We have just started the development of the accelerator as well as target and moderator-reflector systems.