PROGRESS IN REACTOR AND ACCELERATOR BASED BNCT AT KYOTO UNIVERSITY RESEARCH REACTOR INSTITUTE

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Kyoto University Research Reactor Institute



Introduction



Boron Neutron Capture Therapy



- Abbreviated to BNCT.
- A noninvasive therapeutic modality for treating locally invasive malignant tumors.
- Two step procedure: (1) injection with a tumor-localizing drug containing boron. (2) irradiation with thermal or epi-thermal neutrons.
- The above reactions are utilized. The ranges of the α and Li-7 particles are approximately 8 and 5 μm , respectively.



Introduction (1)

 The world's first clinical irradiation for boron neutron capture therapy (BNCT) was carried out using a neutron irradiation field for BNCT, installed at a research nuclear reactor in USA in 1951





From "http://www.bnl.gov/bgrr/"



Introduction (2)

- In early 2009, the world's first accelerator-based system for BNCT clinical irradiation, "Cyclotron-Based Epi-thermal Neutron Source (C-BENS)" was completed at Kyoto **University Research Reactor** Institute (KURRI).
- The clinical trial using C-BENS was started in 2012.





C-BENS at KURRI



Introduction (3)

 At present, the development of the accelerator-based irradiation system for **BNCT** is energetically performed by various groups in the world. It is the time when BNCT is shifting from a special particle therapy to a general therapy, now.



Russian system



Argentina system



Introduction (4)

 The history and recent advances in BNCT at KURRI are reported focusing on the topics for physical engineering and medical physics.



Reactor-based facility (KUR-HWNIF)



Accelerator-based facility (C-BENS)

History of BNCT at KURRI



Kyoto University Research Reactor Institute



- Abbreviated to KURRI.
- Established in 1968.
- Located in the south part of Osaka.
 - 80km distant from Kyoto. 7,700km distant from Adelaide.
- Two neutron irradiation facility for BNCT: **KUR-HWNIF** and **C-BENS**.





History of BNCT at KURRI (1) 1974-1995

- The first clinical study for BNCT at the Heavy Water Facility installed in Kyoto University Reactor (KUR) was performed in May 1974.
- The BNCT clinical irradiation at this facility regularly started in February 1990.



Only thermal neutron irradiation could be available, so BNCT was applied to malignant melanoma and brain tumors with craniotomy.



History of BNCT at KURRI (2) 1995-2001

- From 1995 to 1996, the reactor-based facility was remodeled.
- The BNCT clinical study was restarted in November 1996.



BNCT was applied to malignant melanoma using thermal neutron irradiation, and brain tumors with craniotomy mainly using the mixed irradiation.



History of BNCT at KURRI (3) 2001-2006

- In December 2001, the first BNCT for oral cancer in the world was carried out using epi-thermal neutrons.
- In June 2002, BNCT for brain tumors without craniotomy was started.
- During five years until the rector-operation was stopped for the fuel change, one hundred and ninety-three BNCTs were carried out.



In 2005, the wider application was promoted for the cancers of **body parts such as liver, lung**, etc..



History of BNCT at KURRI (4) 2006-2010

- During the reactor-operation stop, some minorchanges of Heavy Water Facility were carried out.
- In 2009, the world-first cyclotron-based irradiation system (C-BENS) practical for BNCT was installed at KURRI.

Fuel low-enrichment

	New fuel	Old fuel
Kind	Uranium silicide-aluminum dispersion fuel material	Uranium-aluminum fuel
Composition	U ₃ Si ₂ -Al	UAl
Uranium enrichment	20 (%)	93 (%)
Uranium density	3.2 (g/cm ³)	0.58(g/cm ³)
²³⁵ U content (for one fuel plate)	12 (g)	10 (g)
²³⁵ U content (for one fuel element)	213 (g)	180 (g)
Size of fuel element	80×75×870 (mm)	80×75×870 (mm)
Number of fuel plate for one fuel element	18	18
Gap between fuel plates	3(mm)	3(mm)





History of BNCT at KURRI (5) 2010-

- In May 2010, the BNCT clinical irradiation was restarted simultaneously with the restart of the reactor-operation.
- After the restart, two hundreds and thirty five BNCT irradiations have already been carried out as of September 2016.



Neutron Irradiation Systems



Reactor-based BNCT Facility at KURRI





KUR Heavy Water Neutron Irradiation Facility



Epi-thermal Neutron Moderator

 It consists of aluminum and heavy water (80%/20%). It reduces the high-energy neutrons generated due to the U-235 fission reaction in the reactor core, and increases the ratio of epi-thermal neutron component.

Spectrum Shifter

 It consists of four small "heavy water" tanks. It adjusts the ratios of thermal and epi-thermal.

Thermal Neutron Filter

• It is made of cadmium. It adjusts the ratio of thermal neutrons.

The neutron irradiations are available for the various energy spectra, using the spectrum shifter and thermal neutron filter.



Irradiation characteristics of KUR-HWNIF

Beam quality

Irradiation mode	Thermal	Epi- thermal	Mix
Heavy water thickness (cm)	30	0	0
Cadmium ratio	150	1	11
Thermal neutron flux (cm ⁻² s ⁻¹)	1.8E+09	3.7E+07	6.1E+09
Epi-thermal neutron flux (cm ⁻² s ⁻¹)	1.9E+07	9.1E+08	9.2E+08
Fast neutron flux (cm ⁻² s ⁻¹)	3.5E+06	5.1E+07	5.1E+07
Gamma-ray dose rate (cGy/h)	160	70	340



Neutron energy spectrum

The irradiation characteristics were a little changed after the fuel lowenrichment.

This change hardly influences on the BNCT clinical irradiation.



Reactor-based system to accelerator-based system

- For the irradiation system using accelerator, only the neutron source changes from reactor core to accelerator target.
- The basic concept is almost the same between reactor-based system and accelerator-based one.
- The selection for the target parts, such as nuclear reaction, kinds of accelerated particle, accelerated energy, etc. is the most important key-point.







Targets and reactions

Nuclear reaction	Q-value (MeV)	Threshold energy (MeV)	Accelerated particle	Accelerated energy (MeV)	Neutron yield (s ⁻¹ /mA)	Maximum neutron energy (MeV)
⁷ Li(p,n) ⁷ Be	-1.64	1.88	proton	~ 2.5	9×10^{11}	0.8
⁹ Be(p,n) ⁹ B	-1.85	2.06	proton	~ 4.0	9×10^{11}	2.2
⁹ Be(p,xn) ⁹ B			proton	~ 30	2×10 ¹⁴	30
² D(d,n) ³ He	+3.27		deuteron	~ 0.15	7×10^{8}	2.4
³ T(d,n) ⁴ He	+17.59		deuteron	~ 0.15	5×10^{10}	14
² D(x,n) ¹ H x: bremsstrahlung from W target	-2.23		electron	~ 6.0	$\sim 6 \times 10^{11}$	~ 1.2
Spallation W target			proton	\sim 70	1×10^{15}	72



Accelerator-based BNCT Facility at KURRI

- In 2008, Cyclotron-Based Epi-thermal Neutron Source (C-BENS) was installed at KURRI.
- This system is placed on the first floor in Innovation Research Laboratory.







Cyclotron-Based Epi-thermal Neutron Source (C-BENS)



- Sumitomo Heavy Industries:HM30
- Accelerated particle : -H
- Proton energy:30MeV
- Beam current: 1mA
- Pb : used as a breeder and a reflector for high energy neutrons
- Fe : used as a moderator
- Al and CaF2 : used as a shaper for epi-thermal region
- Polyethylene : used as a shielding for high energy neutrons





Irradiation characteristics of C-BENS



- The energy spectrum of the neutron beam from C-BENS is harder.
- The quality is a little better.
- The epi-thermal neutron intensity is over 2-times larger.



Comparison between KUR-HWNIF and C-BENS

Facility	KUR-HWNIF	C-BENS
Facility type	Reactor-based	Accelerator-based
Neutron beam	Thermal - epi-thermal	Epi-thermal only
Purpose	Research and study	Clinical use only
BNCT-application	New challenge Wider application	For tumors with the sufficient experiments and achievements at KUR-HWNIF
Tumor type	Brain tumors Head & neck tumors Skin cancers Lung tumors Liver tumors Others	Recurrent brain tumors Recurrent head & neck tumors

Beam Characterization



Neutron energy spectrum (1)

- Neutron energy spectrum is estimated by multi activation foil method.
- The activation foils are small, and the irradiation field is hardly disturbed.
- The nuclear reactions can be selected according to the neutron energy range.





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Neutron energy spectrum (2)

- Bonner's ball method is used for the supplement of multi activation foil method.
- The moderation material and wall thickness can be chosen for the neutron energy range.
- Activation foils (mainly for thermal neutron range) and/or He-3 counter, etc. are used as the detector.
- The disturbance should be considered.
- The response function should be determined by simulation calculation.







Primary gamma ray

- Similarly to the estimation for neutron energy spectrum, the estimation at "a certain point" is necessary.
- The estimation method using small detector is better, by which the irradiation field is hardly disturbed.
- Thermo luminescent dosimeter (TLD) and/or glass detector are used.
- Normally, TLD has sensitivity to neutrons, so the correction for the neutron response is needed.
- In KURRI, we use a special TLD of BeO enclosed in quartz glass capsule.







Neutron and gamma-ray dose rates

- Ionization chambers are also used for the measurement of neutron and gamma-ray dose rates, as an online system.
- Four components, such as thermal neutrons (below 0.5 eV), epi-thermal neutrons (0.5 eV – 10 keV), fast neutrons (above 10 keV) and gamma rays, are separately measured.
- Chambers are selected in considering the neutron energy spectrum and the mixing ratio of gamma ray. The wall material, wall thickness and ionization gas are changed.
- For example, the wall materials are Si₃N₄, polyethylene, graphite, magnesium, etc.. As needed, a cover of Li-6-enriched LiF is prepared. The ionization gasses are CO₂, N₂, tissue equivalent gas, CH₄, Ar, etc..
- For neutrons, the disturbance should be considered.







Multi ionization chamber system (MICS)

- "Multi ionization chamber system (MICS) " is under development.
- The wall material, wall thickness and ionization gas are selected specially for each component.
 - (1) Thermal neutron : Si_3N_4 wall and N_2 gas.
 - (2) Epi-thermal neutron : Si_3N_4 wall covered with enriched ⁶LiF cover, and N_2 gas.

(3) Fast neutron

: Polyethylene wall and CH₄ gas.

(4) Gamma ray

: Graphite wall and Ar gas.

(C1)

C2

C3

C4

Four signals from the four chambers are arithmetically operated using a formula of Cramer.



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Dose distribution in a phantom

- For the estimation of dose distribution in a phantom, activation foil method and TLD method are also utilized, conventionally.
- Au foil with and without Cd cover, used for thermal and epi-thermal neutrons.
- In, Ni, Al, etc. are used for fast neutrons.
- TLD cannot be placed near the activation foils, which generates much gamma rays.
- Recently, some online system using ionization chambers, scintillation optical fiber (SOF) detector, etc. are studied.





Monitoring under irradiation



Beam monitoring by MICS





Monitoring on patient surface

- On the patient surface, the incident epithermal neutron and the thermal neutron moderated in the patient are mixed.
- The separative measurement is necessary for the monitor of the incident epi-thermal neutron intensity.
- Activation foil method using Au and Mn, and TLD method are utilized, conventionally.
- Recently, an online system using SOF detector is studied.







Estimation for B-10 concentration

- The B-10 concentration is changed according to the elapsed time. The change of concentration is larger for the patients. Then, the estimation of B-10 concentration under irradiation is necessary.
- At present, prompt gamma-ray analysis (PGA) is used. The blood samples are obtained from the patient at some points after the injection. Then, the average B-10 concentration is estimated.





Online estimation system for B-10 concentration (1)

- Some online estimation system for B-10 concentration has been studied.
- For example, prompt gamma-ray SPECT (PG-SPECT) system is studied.
- In this system, the many gamma-ray detectors of high energy resolution, strong neutron shield, and collimator of high position resolution.
- The development of this system is very difficult, at present.





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Online estimation system for B-10 concentration (2)

- For the other example, gamma-ray telescope system is studied.
- A gamma-ray telescope system is installed at KUR-HWNIF.
- In our telescope system, two units are installed. One is focused mainly on tumor part, and the other is only on normal part.
- This system is used for the liver-tumor BNCT at KURRI.



Monitor

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MCA

MΠ

Semiconductor detector

ight source

Irradiation room

1000

limator system Conclusion



Conclusion (1)

- The recent advances in BNCT at KURRI were reported focusing on the topics for physical engineering and medical physics.
- Two BNCT neutron irradiation facilities in KURRI, such as KUR-HWNIF and C-BENS were introduced.
- Some topics for the beam characterization and online monitoring were introduced. For the more advance of BNCT, the development of the online systems are expected.



Conclusion (2)

- Many plans of accelerator-based BNCT systems are taking shape, but it is the situation that these haven't got going yet.
- Recently, the shut down of the research reactor occurs successively. In the while, there is little possibility that a new research reactor is installed.
- At the present, BNCT is performed at only three institutes, such as KURRI in Japan, CNEA in Argentina, and NTHU in Taiwan. At the two latter institutes, only reactor-based systems are used.
- Shifting from reactor-based BNCT to acceleratorbased BNCT, is needed to be promoted as soon as possible.



BNCT network in Japan





BNCT network in Japan



Thank you for Your Attention



o KURRI Tokushima

Univ.

