Characteristics of neutron irradiation facility and dose estimation method for neutron capture therapy at Kyoto University research reactor institute

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Abstract. The neutron irradiation characteristics of the Heavy Water Neutron Irradiation Facility (HWNIF) at the Kyoto University Research Reactor Institute (KIJRRI) for boron neutron capture therapy (BNCT), were described. The present method of dose measurement and its evaluation at the KURRI, were explained. Especially, the special feature and noticeable matters were expound for the BNCT with craniotomy, which was applied at present only in Japan.

1. INTRODUCTION

The updating construction of the HWNJF of the Kyoto University Research Reactor (KUR, full power: *5* MW) had been performed from November *1995* to March 1996 mainly for the improvement in neutron capture therapy (NCT) [1,2]. The main aims were (i) improvement in the safety and maintainability of the facility, (ii) improvement in the performance for NCT in the application of both thermal and epi-thermal neutrons, and (iii) the improvement in the utility such as NCT clinical irradiation during the full-power continuous KUR operation, etc.. The KUR Advanced Irradiation System for NCT was organized. The first NCT clinical irradiation at the HWNIF was performed for a brain-tumour patient with the thermal neutron irradiation mode in November 1996. Fourteen NCT clinical irradiation; four with the thermal neutron irradiation mode and ten with the mix irradiation mode of thermal and epi-thermal neutrons, were already performed as of June 1999. Solo-irradiation of epi-thermal neutrons is planning to start in near future. The knowledge and experiences obtained from sixty-one NCT trials before the updating and fourteen trials after that, were reported in the viewpoint of radiation medical physics.

2. THE KUR ADVANCED CLINICAL NEUTRON IRRADIATION SYSTEM

Figure 1 shows the layout of the KIJR advanced clinical irradiation system. This system consists of the HWNIF, the radiation shielding system and the remote carrying system. In the HWNIF, the epi-thermal neutron moderator to increase the epi-thermal neutron component, the neutron energy spectrum shifter and heavy water shutter to control the neutron energy spectrum, are installed inside of the heavy water tank in order from the core side. The thermal neutron filters of cadmium and boral to control the thermal neutron component, and the bismuth layer as a gamma ray filter, are installed outside of the heavy water tank. The neutron irradiation with several neutron energy spectra from almost pure thermal neutrons to epi-thermal neutrons are available at the HWNIF.

The radiation shielding system consists of (i) the heavy water shutter and the neutron energy spectrum shifter against fast neutrons, (ii) the thermal neutron filters of cadmium and boral against thermal neutrons, and (iii) the beam shutter and the entrance shield door for the irradiation room against both neutrons and gamma rays. An open-or-close operation of the radiation shielding system can be done by remote control, and it takes about five minutes. In the standing point of the safety for radiation exposure, the operations of the entrance shield door and the beam shutter are interlocked. As the total dose equivalent rate of neutrons and gamma rays is a little less than *250* kt Sv/hr at the normal working area in the irradiation room

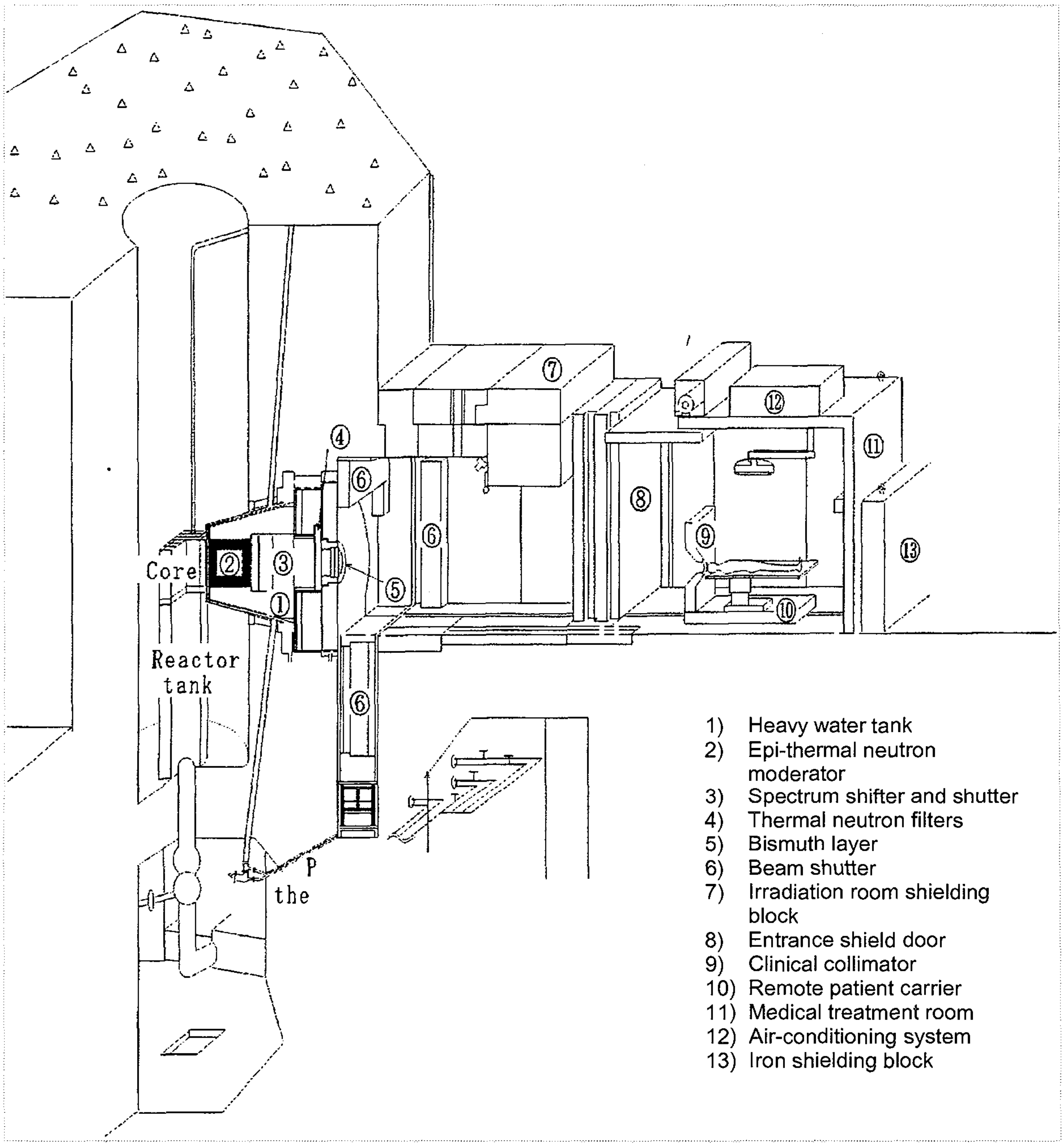


FIG.1. Layout of the KUR advanced clinical irradiation system.

under a continuous KUR operation, the admittance time to the irradiation room should be limited within four hours per a week.

Employing the Remote Carrying System together with the Radiation Shielding System, the clinical irradiation are possible under a continuous KUR operation. The setting and positioning for a patient and the regulation of the monitoring equipment, etc., can be performed outside of the irradiation room. Patient Carrier, employing the X-Y laser pointers, etc. A clinical collimator system and a manual X-Y table are settled on the Remote The positioning of the patient to the collimator aperture is easily possible table, a clinical bed with position-control mechanism for up-down and rotation, Thus, the utility and application of the facility for NCT is remarkably improved.

3. THE IRRADIATION CHARACTERISTICS AT THE NORMAL IRRADIATION POSITION

3.1. Characterization methods

The boundary energies between thermal and epi-thermal neutrons, and between epi-thermal and fast neutrons, are usually fixed to 0.6 eV and 10 keV, respectively, for biomedical uses at the KURRI. Gold foil of 5011 m thickness and 3 mm diameter, and cadmium cover of 0.7 mm thickness are used in the measurement of thermal neutron flux and cadmium ratio. For the estimation of epithermal neutron flux, its energy region is represented by 4.9 eV, which corresponds to the main resonance peak of ^{197}Au (n, γ) ^{198}Au cross section. The epi-thermal neutron flux is calculated as the integrated neutron flux from 0.6 eV to 10 keV, on the assumption that the neutron energy spectrum accorded to a l/E spectrum for the energy range.

Table I.: Measured values of the neutron fluxes and gamma ray dose equivalent rates at the bismuth surface during the full-power (5MW) KUR operation.

Irradiation mode	$D_2$0 thickness (cm)	Cadmium ratio	Thermal neutron flux (n/cm^2/s)	Epi-thermal neutron flux* (n/cm^2/s)	Gamma ray dose equivalent Rate (cSv/hr)	D~ / ~ (cSvI(nlcm ^{2}))
00-0111-F	60	700	*5.9E+08*	1.7E+06	40	1.9E-11
00-0110-F	50	650	7.7E+08	2.4E+06	50	1.8E-11
00-0101-F	40	400	1.OE+09	5.IE+06	60	1.7E-11
00-0011-F	30	160	2.OE+09	2.5E+07	100	1.4E-11
00-0010-F	20	51	2.3E+09	9.3E+07	110	1.3E-11
00-0001-F	10	22	3.3E+09	3.2E+08	180	1.5E-11
00-0000-F	0	9.4	*5.OE+09*	1.2E+09	330	1.9E-11
CO-0000-F	0	Almost 1	Not estimable	1.1 E+09	60	1 .6E-11
OB-0000-F	0	Almost 1	Not estimable	4.OE+08	50	3.5E-11

Measurements were carried out using the “irradiation rail device”.
Neutron fluxes were estimated with gold activation foils, and gamma ray doses were measured with TLD (BeO).
*It is assumed that the epi-thermal neutrons have a pure 1/E spectrum.
For the CO-0000-F and OB-0000-F modes, Dγ/$\varnothing$epi

In the measurement of gamma ray dose rate, thermo-luminescent dosimeter (TLD) of BeO is used. For the TLD on the commercial base (TLD-170L produced by Matsushita Electric Industrial Co., Ltd.), the BeG powder is encapsulated with borosilicate glass. The sensitivity of the TLD-170L is about I cSv per 10 x 10^{10} n/cm^2 thermal neutron fluence due to the (n, α) reactions of ^{10}B contained in the borosilicate glass. So, we ordered the special TLD encapsulated with quartz glass, which does not contain ‘^{0}B. Incidentally, the BeO powder for the TLD-170L also has a little sensitivity to low-energy neutrons, because of the ^{6}Li impurity. The thermal neutron fluence of 8 x 1012 n/cm^2 is approximately comparable to 1 cSv gamma ray dose. Though the sensitivity of the special-ordered TLD is improved, we usually use the TLD together with gold foil for the neutron-sensitivity correction.

3.2. Irradiation characteristics for the irradiation modes

The "irradiation mode" means an irradiation condition of the facility. The first and second characters in the symbol defining the irradiation mode, as shown in Table 1, represent the open-close conditions of the cadmium and boral filters, respectively. The character "0" means the filter "opened (not full-closed)", and the character "C" and "B" mean the cadmium and boral filters "full-closed", respectively. The four numbers represent the conditions of the heavy water shutter and spectrum shifter tanks, in order from the irradiation-room side. The number "0" and "1" mean "empty" and "full", respectively. The last character represents the center thickness of the bismuth layer, which is optional among 0 cm, 5 cm, 18.4 cm and 23.4 cm. Usually, the bismuth layer thickness is set to be 18.4 cm, namely in the "F" condition.

The measured irradiation characteristics at the normal irradiation position for the several "irradiation modes" are tabulated in Table 1. The thermal neutron flux at the normal irradiation position is influenced about ±10% by the KUR power, the reactor-core arrangement of the fuels and the reflectors, and the control-rod positions, etc.. The epi-thermal neutron flux is more affected by the reactor-core arrangement than the thermal neutron flux, and the flux fluctuation is empirically thought to be about ± 20%. The estimation of the gamma ray dose rate has the error of ± 20%.

As shown in Table 1, both thermal neutron flux and epi-thermal neutron flux decrease according to the increase of the heavy water thickness. For the standpoint of biomedical uses, we defined three groups of the irradiation modes as follows: (1) thermal neutron irradiation group; the cadmium ratio is over 100, (2) mixed neutron irradiation group; the cadmium ratio is below 100, and (3) epi-thermal neutron irradiation group; the cadmium or boral filters are fully closed. Especially, "00-0011-F", "00-0000-F" and "CO-0000-F" modes, whose available neutron fluxes are the largest in the respective groups, are defined as the standard irradiation modes, and called "standard thermal neutron irradiation mode", "standard mixed neutron irradiation mode" and "standard epi-thermal neutron irradiation mode", respectively.

Figure 2 shows the relative intensities of thermal neutrons, epi-thermal neutrons and gamma rays, and the measured values of the cadmium ratio at the normal irradiation position as functions of the cadmium filter aperture. The epi-thermal neutron intensity hardly changes according to the cadmium filter aperture. On the other hand, the thermal neutron intensity, the gamma ray dose rate and the cadmium ratio decrease as the aperture decreases. It is found that the cadmium ratio can be controlled from approximately I to the maximum value of the respective irradiation mode by changing the cadmium filter aperture. As the gamma ray intensity changes according to the same tendency as the thermal neutron intensity, it is thought that the gamma rays at the normal irradiation position are almost generated from the (n, ~) reactions of the bismuth with thermal neutrons. For the cadmium aperture smaller than about 50 mm, the gamma ray intensity increases as the aperture decreases. The reason is thought to be that the gamma rays generated from the cadmium filter and the component from the reactor core exceed the secondary gamma rays from the bismuth layer for the filter aperture of about 50 mm.

Figure 3 shows the comparison of the neutron energy spectra at the normal irradiation position among the 00-0000-F, CO-0000-F and OB-0000-F modes. These neutron energy spectra were estimated mainly by multi-foil activation method with an adjusting code "NEUPAC" [3], and the estimation error was about 20%. The difference of the energy spectra between the CO-0000-F and OB-0000-F modes, is dependent on the difference of the energy characteristics for the neutron penetration between the cadmium and boral filters.

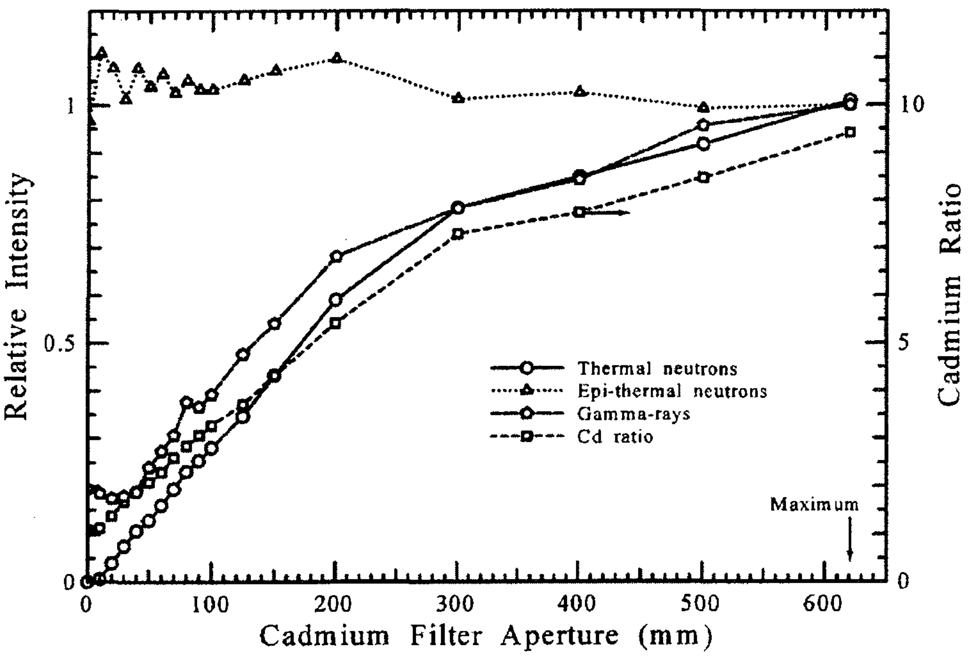


FIG. 2. Measured relative intensities of neutrons and gamma rays, and cadmium ratio at the normal irradiation position depended on the cadmium filter aperture (0 mm: the CO-0000-F mode, 620 mm; the 00-0000-F mode).

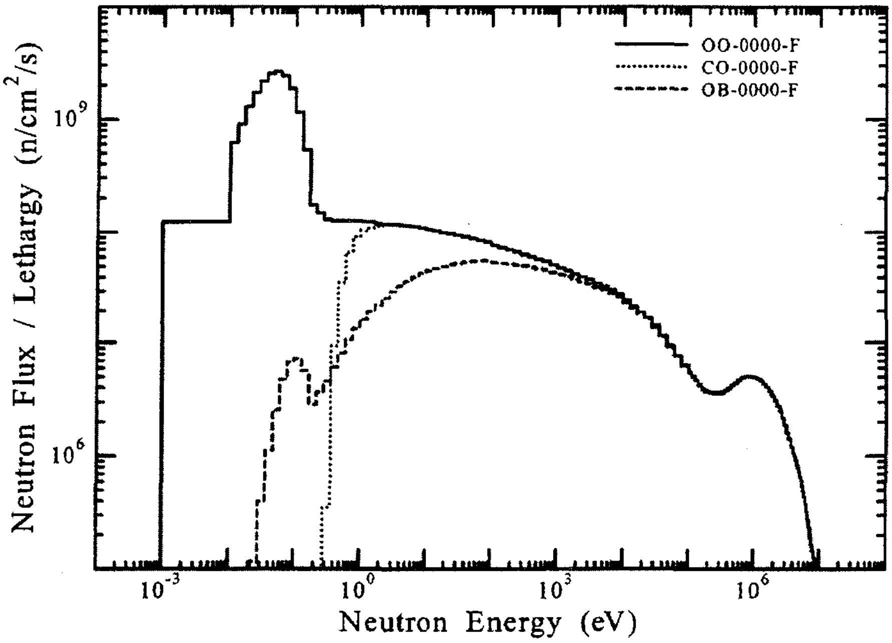


FIG. 3. Neutron energy spectra at the normal irradiation position for the 00-0000-F, CO-0000-F and OB-0000-F modes, estimated by multi-foil activation method

3.3. The dose distribution characteristics for nct clinical irradiation

3.4. Dose distribution in a head phantom

Figures 4 (a) and (b) show the measured depth distributions of thermal neutron flux and gamma ray dose rate in a head phantom for the three standard irradiation modes of 00-0011-F, 00-0000-F and CO-0000-F using the clinical collimator system shown in Fig. 5. The measured data of the old facility is also shown. The used phantom is a water-filled case made with acrylic resin of about 3 ruin thickness, modified a human head. The irradiation field size is 10 cm in diameter.

In the comparison between the 00-0000-F and CO-0000-F modes, the latter thermal neutron flux at the 5 cm depth is 30% of the former one. As the difference between the both modes is mainly generated from whether the thermal neutrons are incident or not, about 30 % of the thermal neutron flux at the 5 cm depth for the 00-0000-F mode is contributed from the moderated thermal neutrons. As the cadmium ratio of the incident neutron beam is smaller, the distribution shape is gentler, the distribution peak position is deeper, and the thermal neutron flux at the deeper part is relatively larger. For example, the depths where the thermal neutron flux becomes 20% of that at the peak position, are about 3.7 cm for the old facility, about 4.5 cm for the 00-0011-F mode, about 5.3 cm for the 00-0000-F mode, and about 8 cm for the CO-0000-F mode. Not only the depth distributions but also the radial distributions are expected to be improved. For the gamma ray dose distributions, the more gamma rays are generated in the phantom according as the thermal neutron flux at the deeper part relatively increases.

3.4. Whole-body exposure dose

Figure 5 shows the measured whole-body distributions of thermal neutron flux and gamma ray dose equivalent rate under an NCT clinical irradiation for the 00-00 1 1-F, 00-0000-F and CO0000-F modes. Three kinds of clinical collimators are provided for thermal, mixed and epi-thermal neutron irradiation. The maximum aperture sizes are 190 mm. The irradiation field sizes were set to be 10 cm in diameter, using the thermal neutron irradiation collimator with a plastic sheet containing ^{6}LiF at 30% in weight for the 00-0011-F mode, and using the mixed neutron irradiation collimator with an inner collimator of polyethylene containing natural LiF at 50% in weight for the 00-0000-F and CO-0000-F modes. On the assumption of the same thermal neutron fluence at the head top, the gamma ray dose equivalents at the respective parts of the human body for the 00-0011-F and 00-0000-F modes, have been applied for NCT, are about one fourth to one third of those for the old

4. THE DOSE MEASUREMENT AND ESTIMATION UNDER BNCT CLINICAL IRRADIATION AT THE KURRI

4.1. Feature of BNCT clinical irradiation with craniotomy

The thermal neutron irradiation is suitable for tumour seated near the surface such as melanoma, but its application is limited for deep-seated tumour, because thermal neutron flux in human body monotonously decreases depended on the depth from the body surface The

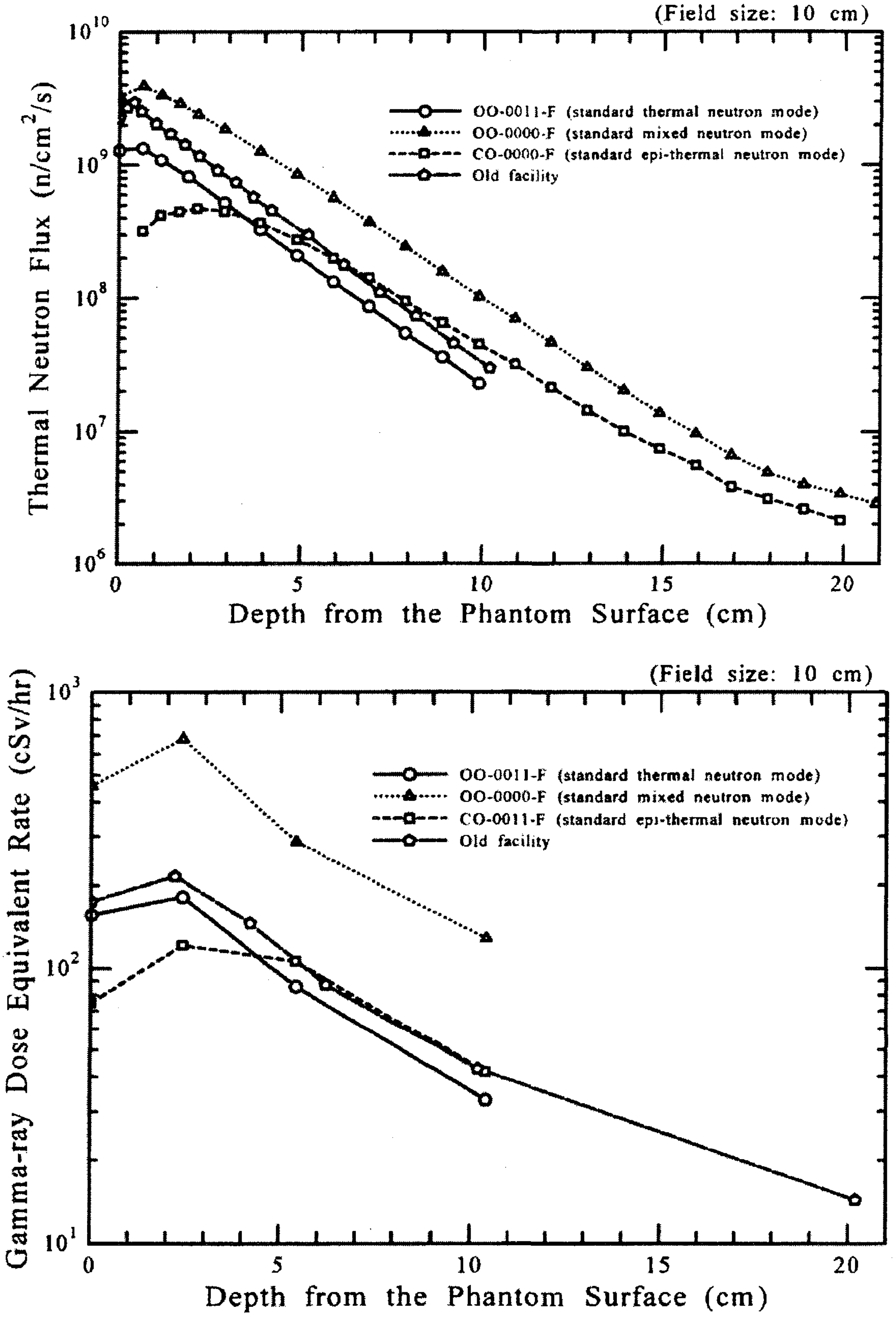
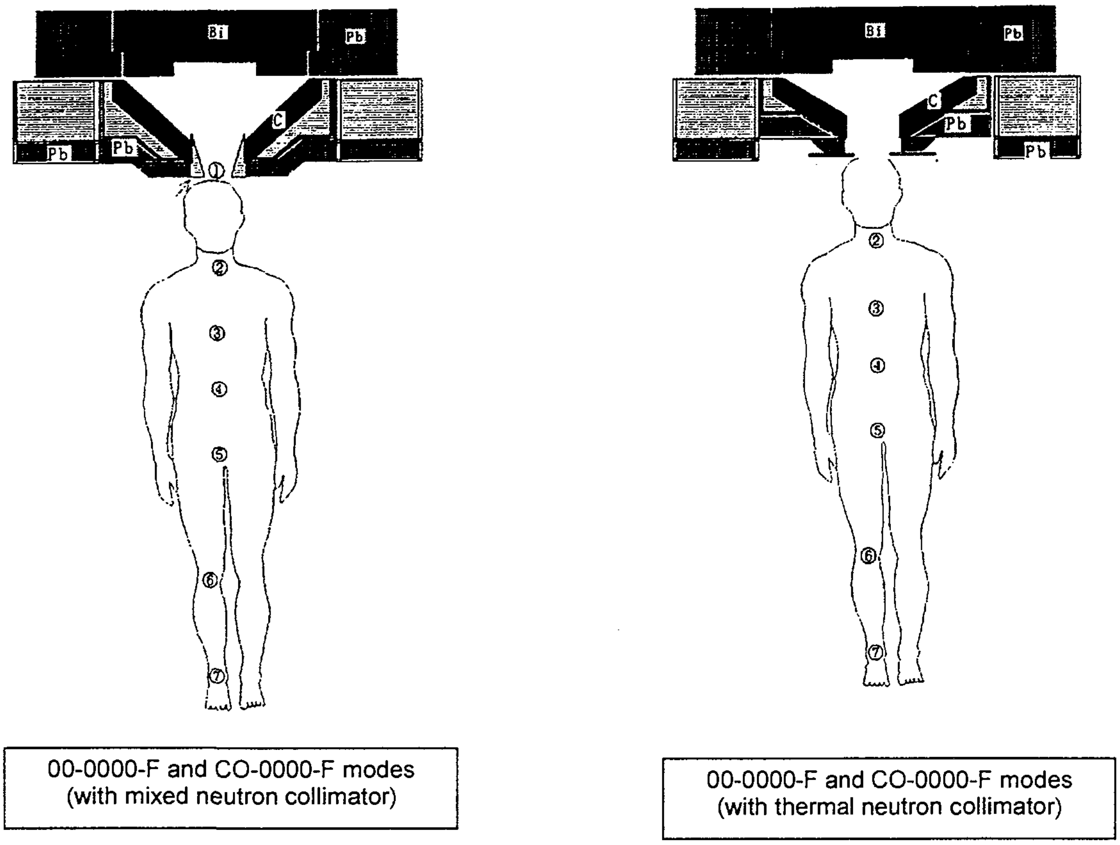


FIG. 4AB. Measured depth distributions along the central axis in a head phantom. a) thermal neutron flux, b) gamma ray dose equivalent rate.



00-0000-F and CO-0000-F modes (with mixed neutron collimator)

00-0000-F and CO-0000-F modes (with thermal neutron collimator)

FIG. 5. Measured whole-body distributions of gamma ray dose equivalent rate and thermal neutron flux under NCT clinical irradiation.

BNCT for brain tumour in Japan has been performed together with craniotomy as so-called "under-surgery irradiation", and the demerit of thermal neutron irradiation has been somewhat covered up. From the clinical experiences, the treatable depth for thermal neutron irradiation is thought to be about 5 cm depth from the surface [4]. The other hand, solo-irradiation of epi-thermal neutrons has a characteristic to lower the thermal neutron flux near the surface and relatively increase the flux at the deeper part. This characteristic is a merit for treatment of deep-seated tumour, and it makes the BNCT without craniotomy possible. However, for the case of under-surgery irradiation, the treated part is practically near the surface, and then the shallow part may not be sufficiently irradiated by thermal neutrons with the solo-irradiation of epi-thermal neutrons.

We have been proposing the application of the mix irradiation of thermal and epi-thermal neutrons to NCT, from the viewpoint of the dose-distribution control in human body [5]. Figure 6 shows calculated depth distributions along the central axis in a head phantom for the BNCT with craniotomy using the solo-irradiation of thermal neutrons and epi-thermal neutrons, the mixirradiation of 0.24 and 2 in $\varnothing/_{\mathrm{epi}}/\varnothing_{\mathrm{th}}$.. The distributions are normalised to be unity at the respective peak positions. In this case, the size of the removed part by craniotomy is S cm in diameter and 3 cm in depth. It is thought that the application of the mix neutron irradiation can cover up the respective demerits of thermal and epi-thermal neutron irradiation. Its application to the actual BNCT has already started using the mix irradiation modes at the updated FWNIF. Moreover, as shown in Fig. 2, the mixing ratio of thermal neutrons to epi-thermal neutrons can be continuously controlled by adjusting the aperture of the cadmium thermal neutron filter at the updated facility. Then, the intermediate distribution of thermal neutron flux can be tailored between the 00-0000-F mode and CO-0000-F mode shown in Fig.4.

4.2. Dose measurement method

At the KURRI, the dose measurements under BNCT clinical irradiation are performed according to activation method using gold wires for the thermal neutrons, and using TLDs for the gamma rays. The TLD of Mg_2SiO_4(Tb) powder (produced by Kasei Optonix, Ltd.) is enclosed in polyethylene tube in order to put on the irradiated surface. For the whole-body exposure, the commercial-base ThD of BeO (ThD- 1 70L) is used, covered with ^{6}LiF thermal-neutron shielding case.

A process of the dose estimation for the clinical irradiation is as follows;

(1) Before a clinical irradiation, the dose rate distributions of neutrons and gamma rays in a body are estimated by phantom experiments and/or simulation calculations.
(2) Thermal neutron flux is directly monitored at some interested points in the irradiated part using gold wires during the first 15–30 minutes of the clinical irradiation, and the thermal neutron flux distribution in the tumour part is estimated in the reference to the results in (1).
(3) The ^{10}B concentrations in the samples of the patient blood and tissue are measured by prompt gamma ray analysis (PGA) [6], and the concentrations in the tumour part and normal tissue are estimated using the data obtained from the basic experiments and the former clinical irradiation.
(4) Using the data from (2) and (3), the absorbed doses at the interested parts are estimated and the whole irradiation time is decided.

This estimation process is completed about 40–55 minutes after the start of the clinical irradiation.

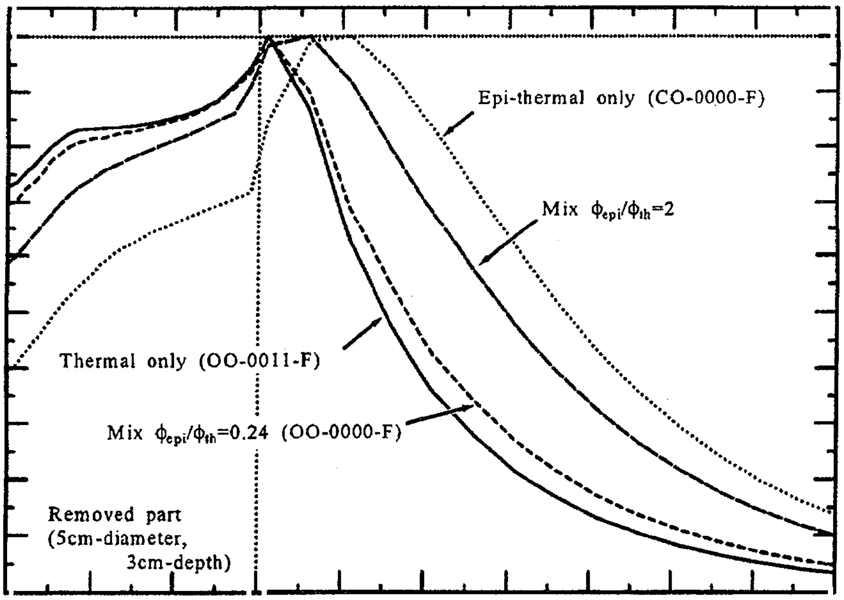


FIG. 6. Calculated depth distributions along the central axis in a head phantom for the BNCT with craniotomy. (The removed part size is S cm in diameter and 3 cm in depth.)

4.3. Dose evaluation methods

The standpoints on the dose estimation in tumour part and normal tissue are different between for brain tumour and melanoma. For brain tumour, the medical doctors attach importance on the total physical absorbed dose, PD (Gy), which almost corresponds to the sum of the physical absorbed doses of ^{14}N(n,p)’^{4}C and ‘^{0}B(n, a)^{7}Li reactions mainly with thermal neutrons, and ‘H(n,n)’H reactions mainly with epi-thermal and fast neutrons.

$$PD = (K_N N + K_B B) \Phi_{th} + D_f \qquad \text{(eq. 1)}$$

Here, (F ~, is thermal neutron fluence (n/cm^2), D_f is physical absorbed dose due to epi-thermal and fast neutrons (Gy), N is concentration of ^{14}N (%), B is concentration of ^{10}B (ppm), and K_n and K_B are kerma factors of ^{14}N(n,p)^{14}C and ^{10}B(n, *a*)^{7}Li reactions (Gy cm^2), respectively. In usual, the D_f is estimated by phantom experiments and/or simulation calculations. Incidentally, it is assumed that the composition of tumour and normal tissue is H:11.1%, C:12.6%, N:2% and O:74.3%. One of the current criteria for the clinical dose is that the PD is over 15 Gy at the deepest tumour part and under 10 Gy at the surface [7]. The dose estimation for the gamma rays is not included in the equation 1, but the above mentioned dose criterion is decided on the consideration of the gamma ray contribution.

For the case of melanoma, the RBE absorbed dose, RD (RBE Gy) is used.

$$RD = (R_N K_N N + R_B K_B B + G) \Phi_{th} \qquad \text{(eq. 2)}$$

Here, R_N and R_B correspond to the RBEs of ^{14}N(n,p)^{14}C and ^{10}B(n, α)^{7}Li reactions, respectively, and the both RBEs are assumed to be 2.5 [8]. G is the ratio of gamma ray dose to thermal neutron fluence (RB_E Gy)/(n/cm^2), and this is previously estimated by phantom experiments and/or simulation calculations. As the BNCT clinical irradiation for melanoma is performed normally using the thermal neutron irradiation modes, the dose estimations about epi-thermal and fast neutrons are not included. A current clinical dose criterion is that the dose is over 25 RBE Gy for the tumour part and under 18 RBE Gy for the normal skin tissue.

5. CONCLUSION

In the dose report for an BNCT clinical irradiation, the following two data are mainly required; (i) the dose information for the estimation of the therapeutic efficacy, and (ii) the dose report for the estimation of the harmful side-effect. For the data (ii), only the whole-body dose exposure is measured at present time. The dose-exposure estimation both for normal tissue near the irradiated part and for the internal organs, is one of the subjects to be solved near future. For the data (i), the following matters are pointed out at the KURRI;

(1) It takes at least 40 minutes for the dose estimation.
(2) For the BNCT with craniotomy, it is difficult to complete the simulation calculations in a short time just before the start of the clinical irradiation. Because the irradiation geometry becomes fixed just before the irradiation, so the final confirmation for the irradiation condition is difficult.
(3) The thermal neutron flux distribution near the surface is easily affected by the surrounding conditions such as the geometry, etc., especially for the BNCT with craniotomy.
(4) The present estimation method of ‘^{0}B concentration by PGA is based on the assumption that the concentrations at tumour part and normal tissue are homogeneously equal.

At present, we are considering about the introduction of an on-line dose estimation method using small semiconductor detectors for neutron dose and, a telescope system for gamma ray dose [9]. Also, we are researching the possibility of a PO-SPECT system, which is one of direct, real time and 3-D dose estimation techniques for ‘^{0}B(n, a y)^{7}Li reaction distribution in tissue [10].

The three standard irradiation modes of the HWNIF for NCT are summarized as follows;

(1) the standard thermal neutron irradiation mode, 00-00 1 1-F: tumour seated near the surface, such as melanoma (within a few cm depth).
(2) the standard mixed neutron irradiation mode, 00-0000-F: tumour seated at comparatively deeper part (depth from a few cm to almost 5 cm).
(3) the standard epi-thermal neutron irradiation mode, CO-OOOOF: BNCT for deep-seated tumour with out craniotomy.

The standard mixed neutron irradiation mode is the main current, and its effectiveness is being confirmed for BNCT.

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[10] KOBAYASHI, T., SAKURAI, Y., “A non-invasive dose estimation system for boron neutron capture therapy under a clinical irradiation by PG-SPECT -conceptual study and fundamental experiments using HPGe and CdTe semiconductor detectors - Med. Phys. (submitted in 1998). part is estimated in the reference to the results in (1).