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ARTICLE

Feasibility study on BNCT-SPECT using a CdTe detector

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There is no doubt that boron neutron capture therapy (BNCT) is a promising cancer therapy in the near future. At present, one of the severest problems to solve is monitoring of the treatment effect during neutron irradiation. It is known to be difficult in real time. So far, activation foils, small detectors and so on were used to measure the thermal neutron fluence in a certain place of the tumor. The dose distribution is thus estimated from the measured result and prediction with a transport code. In the present study, 478keV gamma-rays emitted from the excited state of ^{7}Li produced by ^{10}B(n,α)^{7}Li reaction are directly measured to realize real time monitoring of the treatment effect of BNCT. In this paper, the result of the feasibility study carried out using a Monte Carlo transport code is summarized. We used CdTe detectors with a quite narrow collimator to obtain a BNCT image keeping good spatial resolution. The intensity of capture gamma-rays of 2223keV produced by ^{1}H(n,γ)^{2}H reaction is very much higher than that of 478keV. We thus adjusted the detector efficiency by selecting an appropriate thickness so as to optimize the efficiency ratio between 478 and 2223keV. From the result of the detector response calculation, in case of 20 mm thick CdTe detector with the collimator of 2 mm in diameter, sufficient net count of ~1000 for 478 keV in 30 min. was realized. It means an efficient and high-resolution BNCT-SPECT image could be obtained.

KEYWORDS: BNCT, SPECT, CdTe, gamma-ray, thermal neutron

I. Introduction

As is well known, cancer is ranked first in the cause of humans' death in Japan. There are three cancer therapies available, i.e., operation, chemotherapy and radiotherapy. The radiotherapy is known as a less-invasive treatment keeping a high quality of life (QOL). Up to now, gamma-rays were often utilized for this purpose. Recently charged-particle beam like proton, carbon and so on started to be applied. And more recently, a strong cancer therapy became available, named boron neutron capture therapy (BNCT).

Gamma-rays can affect normal tissues not a little, because the treatment effect can be expressed in a form of exponential function of the depth from the human body surface. Around the surface the damage induced by gamma-rays becomes always large. Charged-particles have a Bragg peak at the end of its range, where the kinetic energy is released dominantly. The energy release can be focused on the tumor location, if the incident charged-particle energy is adjusted appropriately. However, even with the charged-particle treatment, it is a little difficult to kill only the tumor if the tumor does not have a simple massive shape or the tumor is a complicated mixture of normal and cancer cells. BNCT is a quite new cancer treatment which can kill only the tumor by charged-particles produced by ^{10}B(n,α)^{7}Li reaction. The effect to normal tissues could be suppressed substantially, if ^{10}B could be concentrated only in the tumor, as shown in Fig. 1.

The treatment effect of BNCT is large as mentioned above. The treatment effect is estimated by making a product of ^{10}B concentration and thermal neutron flux intensity. The distribution of ^{10}B concentration can be estimated by using positron emission tomography (PET) just before an actual BNCT.[1] However, the ^{10}B concentration is changing gradually, meaning the estimated distribution by the PET is just a reference. The thermal neutron flux intensity can be estimated by simulation calculation with a calculation code system like JCDS[2] developed by JAEA. Under these predicted conditions, the irradiation schedule is made prior to BNCT. After starting irradiation, with help of supplemented means like activation foils, small neutron detectors and so on, the ending time of irradiation is determined. However, by this procedure it was reported that the convalescence did not follow the expectation before. Also, there were different convalescences observed at KUR and JRR-4 even by BNCT with an equal protocol.[3] This fact indicates the current irradiation scheduling can give a reference plan for BNCT neutron irradiation but could not estimate the real treatment effect. The key issue is that it is

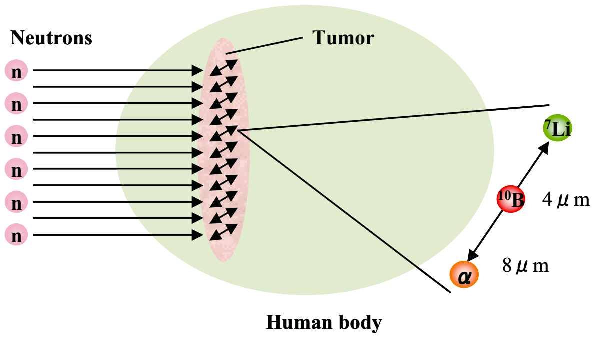

Fig. 1 Conceptual figure of BNCT. ^{10}B is accumulated in the tumor by a suitable DDS agent.

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not possible to know the real treatment effect during irradiation in real time. For spreading of BNCT, the issue is to be solved as soon as possible.

In the present study, to develop a new SPECT to monitor 3-dimensional treatment effect of BNCT in real time by determining the intensity distribution of $^{10}B(n,\alpha)^{7}Li$ reaction distribution directly showing the treatment effect by measuring 478 keV gamma-rays emitted from the residual ^{7}Li nuclide, a feasibility study is carried out to establish a technique to measure the 478 keV gamma-rays in an environment filled with a lot of background gamma-rays.

II. Measurement

1. Principle of Measurement

The principle of the present real-time measuring technique is as follows. As well known, the next nuclear reaction is utilized for BNCT.

$$^{10}B + n \rightarrow \alpha + {}^{7}Li + 2.79\ MeV$$
$$\rightarrow \alpha + {}^{7}Li^{*} + 2.31\ MeV + \gamma\ (478\ keV) \qquad (1)$$

Out of produced ^{7}Li, 94 % of it is in an excited state, from which 478 keV gamma-ray is emitted by a transition from the second excited state to the ground state almost simultaneously. This gamma-ray is measured in this technique. If the position and intensity of the gamma-ray emission is measured, it is equivalent to the reaction rate distribution of $^{10}B(n,\alpha)^{7}Li$ reaction, and is the 3-dimensional treatment effect of BNCT. The measurement could be realized by a so-called SPECT system. And using one-by-one estimation based on the Bayes' theorem, 3-dimensional visualization of the treatment effect of BNCT might become possible in real time.

2. Difficulty in Measurement

In reality, however, it is not so straightforward to realize the 478 keV gamma-ray measurement in BNCT. In case of a normal SPECT measurement, no radiations exist except those used for acquiring its tomography image. Near-ideal measurement can be accomplished. However, in the case of BNCT-SPECT, the thermal neutron intensity used reaches ~1×10^{9}n/sec/cm^{2} around the tumor. The cross section of $^{10}B(n,\alpha)^{7}Li$ is surely quite large, i.e., ~3800 b. However the ^{10}B concentration is just about 10 ppm in the tumor. Hence, the intensity of 478 keV gamma-rays emitted from $^{10}B(n,\alpha)^{7}Li$ reaction becomes much smaller than that of secondary gamma-rays emitted by various (n,γ) reactions and direct signal due to neutrons induced inside the CdTe detector by incident neutrons. Thus it becomes quite hard to selectively measure 478 keV gamma-rays out of a strong radiation field including a lot of background gamma-rays by using a normal SPECT.

Backgrounds to be removed in the present measurement include as in the following.

(1) 2223 keV gamma-rays produced by $^{1}H(n,\gamma)^{2}H$ reaction at around the tumor.

(2) Direct signal due to neutrons produced by scattering of incident neutrons and capture gamma-rays except from ^{1}H at around the tumor.

(3) Direct signal due to neutrons produced by scattering of incident neutrons and capture gamma-rays at around the structural materials and wall surrounding the target.

(4) Annihilation gamma-rays.

Especially, (1) and (4) are known to be very severe. The point is to measure the photopeak of 478 keV gamma-ray precisely even in a very bad S/N-ratio field, i.e., the peak might be hiding in or be overlapped with a dominantly existing Compton continuum and 511 keV peak. On the other hand, direct contribution from neutrons of (2) and (3) is not high in case of using nuclear reactors.

3. Prospect So Far

The above discussion is the reason why the present technique could not be realized in the past. As its earliest stage research, Verbakel et al.[4] proposed a telescope for on-line measurement of boron concentration in the tumor using an HpGe detector. Later, for example, Per Munck af Rosenschoeld et al.[5] investigated an on-line prompt gamma-ray tomography during BNCT by an HpGe with a pin-hole collimator. They reported the spatial resolution could be achieved to be around 2 cm. On the other hand, as for scintillators, as is well known, scintillation detectors are used as an elemental detection device for PET, it is commonly thought to be difficult to use for measuring single photons unlike PET. However, more recently, Minsky et al.[6] reported the latest result of the experimental feasibility study using a $LaBr_3(Ce)$ scintillator to realize a SPECT for BNCT. For semiconductor detectors, there is a paper including CdTe and HpGe detectors by Kobayashi et al.[7] Especially CdTe detectors are promising because quite a small one can be produced and the energy resolution is excellent. Kobayashi investigated possibility of SPECT for BNCT with HpGe and CdTe detectors. Both detectors have an enough ability to measure gamma-rays of interest. However, the system becomes a little too large in case of HpGe detectors. And it was concluded that the device should be more improved in case of using CdTe detectors because of its low efficiency. They pointed out that about 100 counts are needed to detect from 1 cm^{3} tumor located in the deepest place.

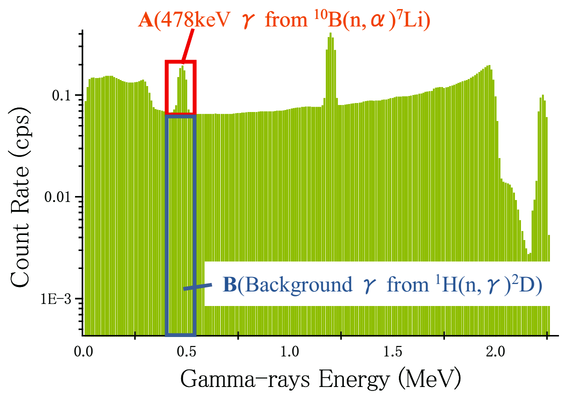

Fig. 2 Expected PHS obtained by a 20 mm thick CdTe detector. Clear 478 keV photopeak is seen on the Compton continuum formed by 2223 keV gamma-ray emitted via $^{1}H(n,\gamma)$ reaction.

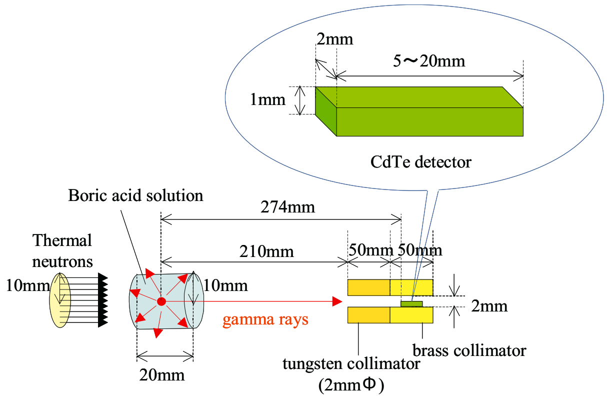

Fig. 3 PHS calculation model by MCNP.

At present, however, one must consider that the background intensity becomes quite large as pointed out in the previous sections and even in this case one detector should have around 1000 counts to achieve an acceptable statistical accuracy, in order to realize a good spatial resolution of about mm order. This is however not so easy.

4. Measuring Technique

The requirements assumed for the measurement by BNCT-SPECT are summarized as follows:

(1) Spatial resolution should be less than several mm. (We aim at ~ 2 mm.)

(2) Statistical accuracy should be less than several %. (We aim at integral count of ~ 1000 per detector. in 30 min.)

The presently proposed measuring technique is as in the following:

To improve the spatial resolution, the detector should be small and thus should have an enough large sensitivity. We employ a CdTe device for this purpose. To make the sensitivity large the detector should be thick. In the present study, a CdTe detector having a small area of 1 x 2 mm^2 and a large thickness of up to 20 mm is selected. In the current technology, a high-energy resolution detector (Schottky type) can be utilized. The statistical accuracy can thus be improved. As for the thickness, a wide (2 mm x up to 20 mm) and thin (1mm) detector available on the market is so used that gamma-rays enter from the side surface. The incidence area is therefore 1 x 2 mm^2 and the thickness can be increased up to 20 mm. In this way, the efficiency of 478 keV gamma-rays can be improved, simultaneously suppressing the count of 2223 keV gamma-rays emitted from $^{1}H(n,\gamma)^{2}H$ reaction. As a result, the obtained spectrum is like Fig. 2 from the calculation to be detailed in Chap. 3, in which the photopeak of 478 keV is overlapped with the Compton continuum formed by 2223 keV gamma-rays. From these kinds of pulse height spectra, the net count of 478 keV should be extracted with an acceptably small statistical error.

III. Analysis

1. Calculation Conditions

In the analysis, nuclear reaction of boron with neutron is precisely modeled as detailed in the next section. Here,

Table 1 Feasibility calculation results for five cases. A/(A+B) is the ratio of the net count for 478 keV (A) to the background count formed by 2223 keV gamma-ray (B), as shown in Fig. 2.

Case.	^{10}B [ppm]	Neutron flux [/cm²/sec]	Detector thickness [mm]	0.478MeV ($^{10}B(n,\alpha)^{7}Li$) [cps]	A/(A+B)
1	10	10^9	20	0.580	0.575
2	10	10^9	15	0.499	0.561
3	10	10^9	10	0.387	0.578
4	10	10^9	5	0.221	0.580
5	100	10^8	20	0.569	0.930

treatment of backgrounds introduced in Sec. II.2. is precisely described. As pointed out in Sec. II.2., the effect of background contributions (1) and (4) is dominant compared to other two. At first, contribution (1) was dealt with accurately in the analysis. Among other three, background contribution (3) was neglected because the intensity and spectrum is largely depending on the irradiation conditions. Background contribution (2) was also not considered by taking into account the following assumption.

a) The neutron beam is so collimated that neutrons are incident only to the tumor.

b) The CdTe detector is heavily shielded and collimated so that it can view just the tumor.

In the simulation calculation, a model shown in Fig. 3 was thus used meeting the conditions above. For background contribution (4), also the intensity strongly depends on the irradiation circumstances and was therefore not taken into account in the analysis, because the CdTe detector employed in the present study has an excellent energy resolution so that it is expected that it could distinguish the signals of 478 keV and 511 keV basically.

2. Calculation Method

Simulation calculations are performed with MCNP-4C[8]. Fig. 3 shows the calculation model. The tumor is modeled as a cylindrical phantom of 2 cm in diameter and 2 cm long, filled with boric acid solution including 10~100 ppm ^{10}B. The thermal neutron flux intensity is $10^9 n/sec/cm^2$ for 10 ppm and $10^8 n/sec/cm^2$ for 100 ppm, because it is assumed in the present study that the irradiation time is fixed to be 30 min. The distance between the tumor and the front edge of the collimator is 21 cm. The pulse height spectra are calculated with F8 tally of MCNP. We adopted two-step calculations as follows. In the first step, the gamma-ray source term was calculated with the tumor phantom to which neutrons are incident. In the second step, with the obtained source of the phantom, gamma-ray transport calculation was carried out with the phantom and detector model with a tungsten collimator of 2 mm in diameter. Also, separate calculations for 478 and 2222 keV gamma-rays were performed and the results are summed up to make the real spectrum to be observed in an actual BNCT. Fig. 2 shows an example of the pulse height spectrum for the case of 20 mm thick CdTe detector.

3. Discussion on Feasibility

Table 1 shows the calculation results. The count rate for the case of 5 mm thickness seems to be a little small. On the other hand, it is enhanced up to 0.58 cps if using a thicker one of 20 mm. One thousand counts per 30 min. could be accomplished. It is remarkably pointed out that the ratio of 478 to 2223 keV (A/(A+B) values) is not going up even if the thickness of the detector increases. The reason is in the following. The cross section of photoelectric effect of 2223 keV gamma-ray with CdTe is very small, however, the Compton scattering cross section is relatively large and in addition more-or-less the same as the photoelectric effect cross section of 478 keV. The behavior of increment of the count rates for 478 keV photopeak and the Compton continuum of 2223 keV becomes quite similar to each other in case that the detector thickness increases. This means the effect of increase of the detector thickness is large and very effective. In the above case, the statistical error is suppressed within 5 %. If the ^{10}B concentration can be increased, the thermal neutron flux intensity can be decreased. As a result, the intensity of 2223 keV gamma-rays is decreased relatively. As shown in the table (Case 5), this effect is remarkable and the accuracy is improved down to 3 %. In conclusion, from the present series calculations, the feasibility is confirmed especially in the case of 20 mm thick CdTe detector with the collimator of 2 mm in diameter. However, it should be noted that in an actual case there exist a lot of other backgrounds caused by incident neutrons. We need to check up the background contribution in a real BNCT case.

IV. Future Work

Now we are developing two detector systems. One is a line sensor with 64-CdTe array device. A tungsten collimator having 32 holes, the diameter of which is 0.5 mm, is used together. The other ones are CdTe detectors of 1 x 2 mm^2 and 5~20 mm in thickness. By the former one, image reproduction from the measured pulse height spectrum is planned to be confirmed through one-by-one estimation based on the Bayes' theorem. For the latter, through a neutron irradiation experiment with a boric acid solution phantom, possibility of high accuracy measurement of 478 keV gamma-rays under a strong background environment by 2223 keV gamma-rays will be confirmed. Then finally, we will carry out gamma-ray spectrum measurement including all of possible backgrounds in a real clinical situation to confirm the feasibility of the BNCT-SPECT with the presently proposed CdTe device.

V. Conclusion

In the present study, a feasibility study was carried out for development of a new BNCT-SPECT using a Monte Carlo transport code. 478 keV gamma-rays emitted from the excited state of ^{7}Li produced by ^{10}B(n,α)^{7}Li reaction were directly measured to realize real time monitoring of the treatment effect of BNCT. We used CdTe detectors with a quite narrow collimator to obtain a BNCT image keeping good spatial resolution. As well known, the intensity of capture gamma-rays of 2223 keV produced by ^{1}H(n,γ)^{2}H reaction was very much higher than that of 478 keV. We thus adjusted the detector efficiency by selecting an appropriate thickness so as to optimize the efficiency ratio between 478 and 2223 keV. From the result of the detector response calculation, in case of 20 mm thick CdTe detector with the collimator of 2 mm in diameter, sufficient net count of 1000 for 478 keV in 30 min. could be obtained. It means an efficient and high-resolution SPECT image would be realized. Now we are developing two detector systems aiming at real applications. One is a line sensor with 64 array CdTe devices. The other one is CdTe detectors of 1 x 2 mm^2 and 5~20 mm in thickness. After test measurements, we will carry out gamma-ray spectrum measurement including all the possible background in a real clinical situation to confirm the feasibility of BNCT-SPECT with the presently proposed CdTe device.

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