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An intra-operative positron probe with background rejection capability for FDG-guided surgery

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For radio-guided surgery on tumors using F-18-FDG, detection of annihilation gamma photons emanating from other parts of the body produces background radiation counts and limits its use in clinical situations. To overcome this limitation, we have developed an intra-operative positron probe with background-rejection capability. The positron probe uses a phoswich detector composed of a plastic scintillator and a bismuth germinate (BGO). A positron from a positron emitter such as F-18 is detected by the plastic scintillator and emits annihilation photons. The BGO detects one of the annihilation photons while a photo-multiplier tube (PMT) detects scintillation photons from both scintillators. The decay time differences of these two scintillators are used to distinguish whether the event is a true event where a positron and a following annihilation photon are detected simultaneously, or a background event. In this configuration, only positrons can be selectively detected, even in an environment of high background gamma photon flux. Spatial resolution was 11-mm full width at half maximum (FWHM) 5 mm from the detector surface. Measured sensitivity for the F-18 point source was 2.6 cps/kBq 5 mm from the detector surface. The background count rate was less than 0.5 cps for a 20-cm diameter cylindrical phantom containing 37 MBq of F-18 solution measured on the phantom surface, while the positron count rate was almost linear over a range of approximately 6 kcps. These results indicate that our developed intra-operative positron probe is valuable for radio-guided surgery on tumors using F-18-FDG in a high flux of background annihilation gamma photons.

Key words: positron, intra-operative probe, background, FDG

INTRODUCTION

INTRA-OPERATIVE PROBES have recently become important instruments in nuclear medicine.[1] The most frequently used are gamma probes that detect gamma photons from single photon emitters such as Tc-99m (141-keV).[2] Recently, these gamma probes have become widely used for sentinel lymph node localization. The other application of the intra-operative probe is tumor detection for surgery. After a radiopharmaceutical that accumulates in the tumor has been administered to a patient, the surgeon detects the tumor with the intra-operative probe and resects it during the surgery. Using an intra-operative probe, the surgeon can also confirm that the removed parts really do contain tumorous tissue, or that the tumor has been completely removed. In this application, the radiopharmaceutical F-18-fluorodeoxyglucose (FDG) is promising for this purpose.[1,3–5]

The positron emitter (FDG) can be detected by two methods in the intra-operative period.[6–12] One is detection of beta particles and the other is detection of annihilation gamma photons. In both methods, it is difficult to distinguish the beta particles or gamma photons from the

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background gamma photons because the background gamma photons have a high energy level (511 keV) that is similar to that of F-18 positrons. Detection of background gamma photons decreases the tumor to normal ratio making it difficult to use them in the clinical setting.

Several attempts have been made to overcome these limitations. One method uses stacked detectors for intra-operative beta probes.[10,11] The authors stacked two silicon detectors or plastic scintillation detectors and detected beta particles and gamma photons on the front surface of the first detector, while the second detector inside the detector system detected only gamma photons. They subtracted the counts of the second detector from the first detector to obtain the true beta counts. Levin et al. proposed a phoswich imaging detector composed of CaF_2(Eu) coupled to a Gd_2SiO_5:Ce (GSO) to eliminate the background gamma photons.[13,14] They detected beta particles emitted by the CaF_2(Eu) and gamma photons emitted by the GSO, and employed a type of coincidence method to obtain the true events.

We propose a phoswich positron detector similar to that of Levin et al. The detector uses a plastic scintillator for detecting the beta particles, while the BGO detects gamma photons. This configuration has already been applied to a continuous blood sampling system by some of the authors and showed sensitivity improvement over the conventional beta detector.[15] In that paper we also showed possibility of detecting low energy positrons from F-18. Thus we applied this detector configuration to an intra-operative positron probe for FDG and tested its performance.

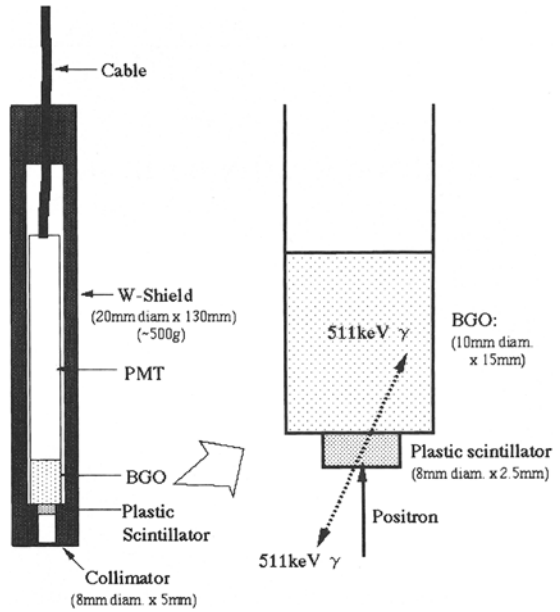

Fig. 1 Schematic diagram of the detector component of the position intra-operative probe.

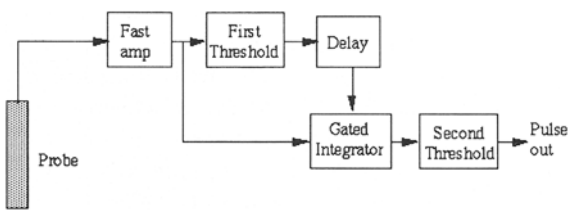

Fig. 2 Schematic diagram of the electronic circuit of the intra-operative positron probe.

MATERIALS AND METHODS

(1) System description

A schematic diagram of the intra-operative positron probe is shown in Figure 1. The probe consists of a plastic scintillator, a BGO, and a photo-multiplier tube (PMT). A positron from F-18 enters the shield via the hole in the collimator and is detected by the plastic scintillator. The positron loses its energy in the plastic scintillator (optically coupled to the BGO) and emits two annihilation photons in opposite directions. Though one of the photons escapes from the detector, the other is redirected to the BGO where it is detected. In this case, a fast component of the plastic scintillator and a slow component of the BGO can be observed. When the background annihilation photon is detected by the plastic scintillator, only the fast component is observed. When the background annihilation photon is detected by the BGO, only the slow component is observed. By using the pulse shape information, these two types of background events can be rejected and it is possible to selectively detect positrons by the probe.

Plastic scintillator was selected as the first scintillator for the positron detector because it is sensitive to beta particles but relatively insensitive to gamma photons because of its low atomic number and low density. BGO was selected as the second scintillator for gamma photon detector because it has high stopping power for the high energy gamma photons. In addition, the BGO has a slow decay time (300 ns) compared with that of the plastic scintillator (less than 10 ns) making it easy to use pulse shape analysis to distinguish true events from noise events.

The plastic scintillator used for the probe is an NE-102: 8 mm in diameter and 2.5 mm high. The 2.5 mm thickness of the plastic scintillator was determined because 2.5 mm is slightly thicker than the positron range of F-18 in water. The BGO is 10 mm in diameter and 15 mm in height; a 15 mm high BGO can stop more than 70% of the 511-keV gamma photons. The reason why the diameter of BGO is larger than that of the plastic scintillator is to keep the solid angle of annihilation photons produced in the plastic scintillator looking for the BGO large. These two scintillators are optically coupled to a 10 mm diameter head-on type PMT (Hamamatsu H3161-10). Optical cement (Saint-Gobain, BC600) was used for this optical coupling, ensuring long term stability. The detector was encased in a 4 mm thick tungsten shield to decrease the

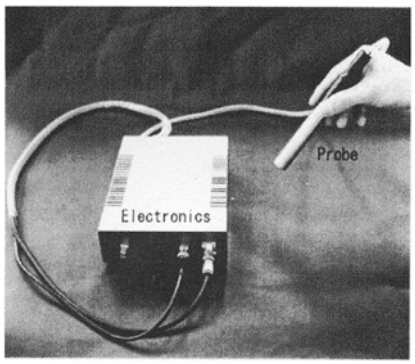

Fig. 3 Photograph of the developed intra-operative positron probe.

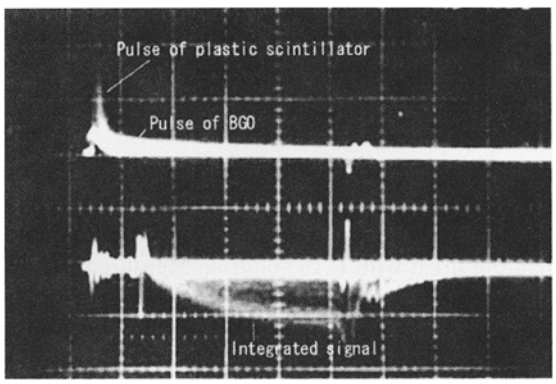

Fig. 4 Pulse shape of the output of the fast amplifier (*upper signal*) and the integrated signal (*lower signal*).

background gamma photons that impinge on the BGO. A tungsten collimator is mounted at the tip of the probe. The diameter of the collimator's hole is 8 mm, and its length is 5 mm.

In Figure 2, we show a schematic diagram of the intra-operative positron probe's electrical circuit. It is similar to the electrical circuit that was used for the phoswich blood sampling system for pulse processing.[15] The pulse from the PMT is amplified by the fast amplifier and fed to the first threshold. The first threshold level is set at 30% of the peak amplitude of the plastic scintillator signal. When the signal amplitude is higher than the first threshold, the gated integrator starts integration after the fast signal has decayed. If this integrated pulse is within the 511-keV energy window, the pulse is recognized as a true signal. The lower threshold level for the second one was set at 75% of the peak amplitude of the BGO signal. These threshold levels were determined to minimize the background counts due to the scattered gamma photons in the scintillator while keeping the system sensitivity reasonable.[16]

A photograph of the developed intra-operative positron probe is shown in Figure 3. The diameter of the detector part is 20 mm, the length is 130 mm, and the weight is

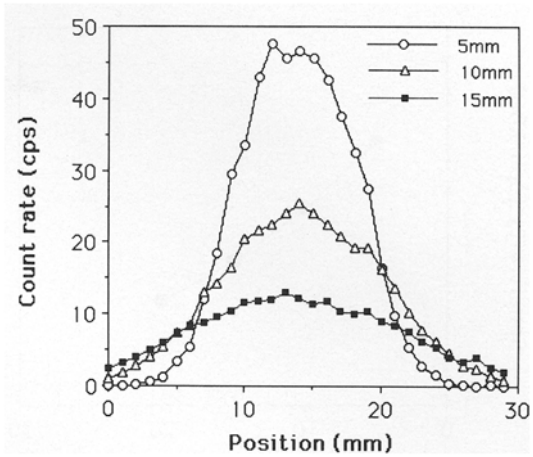

Fig. 5 Point spread function of the positron probe for F-18 point source.

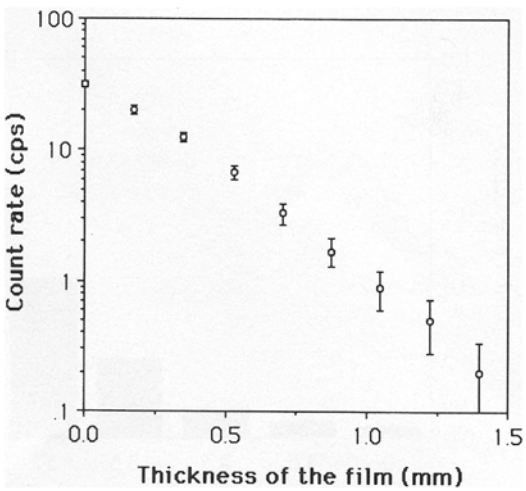

Fig. 6 Depth response of the intra-operative positron probe.

approximately 500 g. The output of the detector is connected to the electronics housing that contains a pulse shape analysis circuit and a high voltage power supply for the detector's PMT. The electronics output is connected to a rate meter, which includes a buzzer to aurally display the count rate. Figure 4 shows a photograph of the pulse shapes of the fast and the delayed integrated signal outputs. Here, the fast signal from the plastic scintillator and the slow signal from the BGO in the fast amplifier's output signal can be seen. The fast signal's decay time is approximately 20 ns and that of the slow signal is 300 ns. The decay time of the fast signal from plastic scintillator was slightly smoothed by the limited speed of the amplifier. The delay time for the delayed gated integrator was set at 150 ns. Also visible in the integrated signal is a photopeak (thicker part of the pulse) of 511-keV gamma photons.

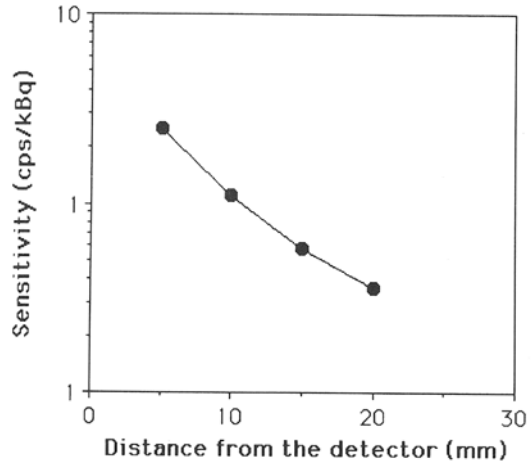

Fig. 7 Sensitivity as a function of the distance from the collimator surface.

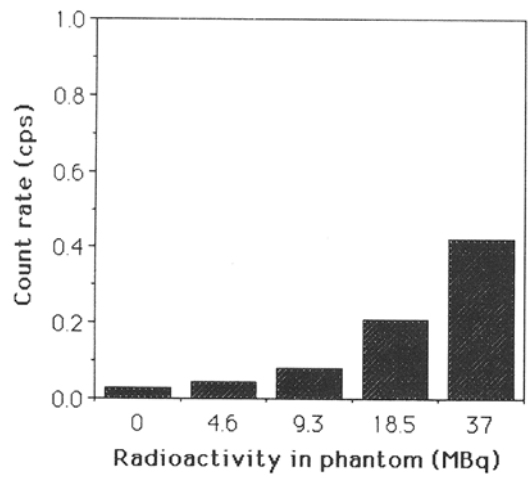

Fig. 8 Background count rate with and without background phantom.

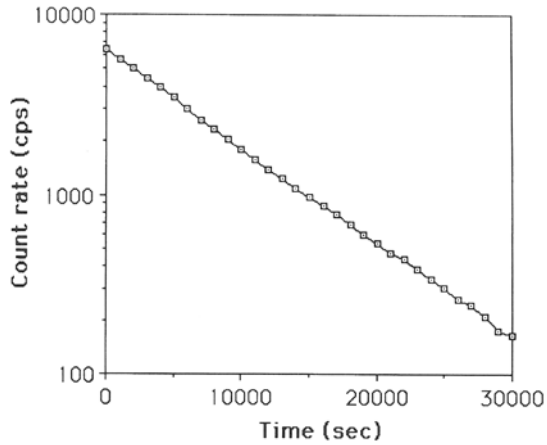

Fig. 9 Count rate characteristic of the probe.

(2) Performance evaluation

1) Spatial resolution

To estimate the spatial resolution, point spread functions (PSFs) for the F-18 point source were measured. An F-18 point source of approximately 0.1 MBq, 1 mm in diameter was positioned 5 mm, 10 mm, and 15 mm from the collimator surface, the probe was moved in 1-mm steps and the count rate was measured. Measurements were performed without any background gamma sources.

2) Depth response

It is important to measure the depth response of the probe because surgeons need to know the depth of the tumor during surgery. Plastic films of different thickness were inserted between the probe and an F-18 point source, and the count rate for each depth was measured.

3) Sensitivity

We measured sensitivity as a function of the distance from the collimator using an F-18 point source as a function of the distance from the detector surface.

4) Background counts

To observe the background counts of 511-keV gamma photons, the positron probe was positioned on the flat surface of the 20 cm diameter 20 cm high cylindrical phantom filled with F-18 solution. Measurements were made at 4 radioactivity levels: from 4.6 MBq to 37 MBq. The count rate was measured with the phantom and compared to the control case without the phantom. Because the thickness of the phantom was more than 5 mm, only 511-keV gamma photons were emitted from the phantom.

5) Count rate characteristic

The count rate characteristic must not be too low because surgeons need to roughly know the positron concentration from the count rate of the probe. The count rate was measured using an F-18 point source by following the rate of decay.

RESULTS

1) Spatial resolution

Measured PSFs are shown in Figure 5. The spatial resolution of the probe was 11 mm FWHM, 1 mm from the collimator surface.

2) Depth response

The depth response is shown in Figure 6. As the thickness of the plastic film stack was increased, the count rate decreased almost exponentially. The depth response curve is clearly quite steep and the probe can measure only the surface area of the tissue. The addition of a 0.25 mm thick plastic film decreased the count rate to half of that without film.

3) Sensitivity

Measured sensitivity is shown in Figure 7. The measured sensitivity was 2.6 cps/kBq at 5 mm from the detector surface and decreased as the distance from the collimator increased.

4) Background counts

The background counts with and without the phantom are shown in Figure 8. In the case with the phantom even with 37 MBq radioactivity, the background count rate was less than 0.5 cps.

5) Count rate characteristic

The count rate characteristic is shown in Figure 9. The count rate of the probe was linear over a range of more than 6 kcps.

DISCUSSION AND CONCLUSION

In this type of detector, which uses a collimator, the spatial resolution and the sensitivity are inversely proportionally related. We can improve the spatial resolution with some loss of sensitivity by reducing the size of the hole or increasing the length of the collimator or vice versa. The count rate for tumor in FDG-guided surgery will be an important factor to consider. Because the injected dose for human use is limited, the count rate of this probe during surgery will also be limited. For the low count rate situation, the sensitivity of the probe should be increased by reducing the collimator depth and/or increasing the size of the scintillators. In addition, animal experiments and phantom studies that simulate more realistic conditions will be needed to see whether the performance of the probe meets the requirements of the clinical situation before the probe is used for human studies.

It is difficult to evaluate whether the depth response of the probe should be steep in clinical situations. If the depth response of the probe is steep, surgeons can detect the rough location of the tumor without suffering interference from the counts from deeper parts of the tissue; however, it will be difficult to accurately locate a tumor surrounded by normal tissue in this case. In addition, the probe will usually be used with a covering material such as a surgical glove that decreases the sensitivity. From Figure 6, it is estimated that the sensitivity loss with the 0.2 mm thick covering material will be around 40% if the material is similar to plastic.

On the other hand, if the depth response is not steep, the surgeons will suffer interference from radiation counts originating from deeper in the tissue than the actual location of the tumor. The advantage, though, is that surgeons can get information about deeper tissue from a distance.

The probe diameter (20 mm) seems large compared with other commercial intra-operative gamma probes. The diameter of our probe was determined by the diameters of the BGO and the PMT, and the thickness of the tungsten shield. Reducing the diameter of the BGO reduces the sensitivity of the probe. It may be possible to reduce the thickness of the tungsten shield because the positron probe can essentially eliminate the background gamma photons electrically and does not need any gamma shield. Reducing the thickness of the tungsten shield will also reduce the weight of the detector part. However, without any gamma shield, accidental background counts may occur, in which an individual pulse from the plastic scintillator and an individual pulse from BGO occur simultaneously, resulting in a higher background count rate. Thus, we have to accept some increase in background counts if the thickness of the gamma shield is to be reduced.

The advantage of the positron probe over the conventional intra-operative beta probe is the higher sensitivity and smaller background count rate because the maximum energy of F-18 positrons is 635-keV and the pulse height of the scintillator for the positrons are similar to those of 511-keV gamma photons. Therefore, if one needs to decrease the background count rate of 511-keV gamma photons, a higher threshold level has to be set that reduces the sensitivity. Conversely, if higher sensitivity is called for, a lower threshold will have be set, which increases background counts. In our positron probe, it is possible to set the threshold level lower to 30% of the 511-keV gamma signal of the plastic scintillator thereby increasing the sensitivity and minimizing the background noise.

The advantage of the positron probe over the conventional intra-operative gamma probe is the lower background count rate and the lower weight. The gamma probe usually suffers interference from 511-keV gamma photons due to their higher penetration. To reduce the background counts that penetrate the gamma shield, one can increase the thickness of the gamma shield; however, to reject 95% of the gamma photons, for example, a 10 mm thick tungsten or 15 mm thick lead shield is required. These have the disadvantages of increased probe weight and diameter. The developed positron probe has a higher sensitivity and lower background count rate over the conventional beta probe or gamma probe.

Because the FDG is widely used for cancer diagnosis, we believe that it will not be long before the FDG is used for radio-guided surgery. One possible approach is the use of the PET or PET/CT to detect tumors. During surgery, the positron probe will be used for both detecting the tumor and for resection. After the operation, PET or PET/CT will be also used to confirm whether the tumor is completely removed. In FDG- and PET-guided surgery applications, our positron probe will be useful.

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