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Research article

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A double photon coincidence detection method for medical gamma-ray imaging

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Abstract: Cascade nuclides emit two or more gamma rays successively through an intermediate state. The coincidence detection of cascade gamma rays provides several advantages in gamma-ray imaging. In this review article, three applications of the double photon coincidence method are reviewed. Double-photon emission imaging with mechanical collimators and Compton double-photon emission imaging can identify radioactive source positions with their angular-resolving detectors, and reduce the crosstalk between nuclides. In addition, a novel method of coincidence Compton imaging is proposed by taking coincidence detection between a Compton event and a photopeak events. Although this type of coincidence Compton imaging cannot specify the location, it can be useful in multi-nuclide Compton imaging.

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Introduction

In recent decades, nuclear medicine technology has made a significant contribution to the improvement of medical diagnoses. This is particularly true for the diagnosis of early-stage cancer. Typically, a molecular probe labeled with a radionuclide is injected into the body, and its internal dynamics imaging, achieved by detecting radiation, provides the functional or metabolic information. Visualization of the radionuclide accumulation in the body requires estimation of the incident direction of the photons. Two types of nuclear medicine imaging systems have been used in clinical settings. Positron emission tomography (PET) simultaneously detects annihilation gamma-rays with energies of 511 keV [1,2]. The emission directions of two photons produced after the annihilation of a positron and an electron are opposite; thus, the coincidence detection can electrically estimate the annihilation position along a line (Figure 1 (a)). Another imaging system is single photon emission computed tomography (SPECT) [3,4]. SPECT physically limits the direction of incoming photons using mechanical collimators (Figure 1 (c)). Whereas PET scans are only able to use a probe labelled with a positron, SPECT can utilize various radionuclides that emit low-energy photons (typically up to approximately 400 keV).

However, specifying the radionuclide position at a single point using conventional PET and SPECT imaging is difficult because these imaging methods can estimate it only on a line. An imaging method that specifies the radionuclide location is ideal because it would lead to a reduction in artifacts in an image and would not require any reconstruction methods. Recently, the time-of-flight (TOF) PET has been developed; its high time resolution enables the estimation of a positron position at a higher resolution, and not only along a line [5-8]. The flight time difference between the detection of

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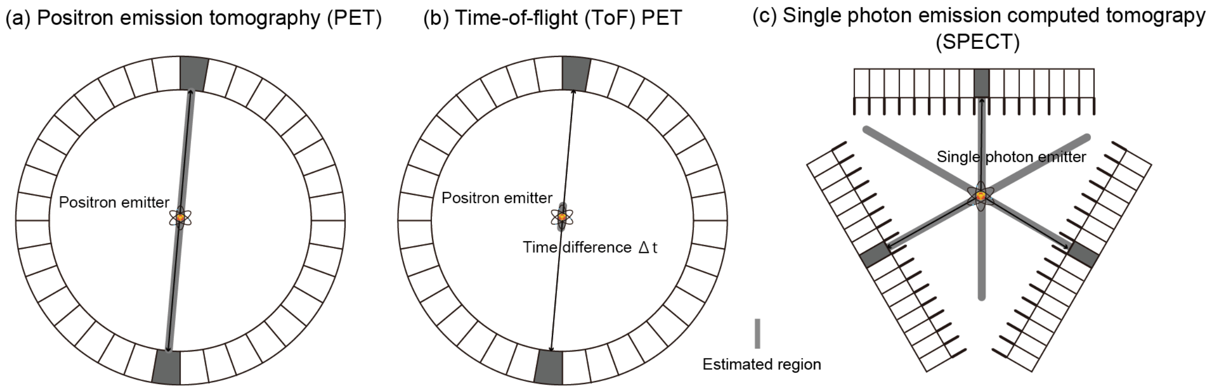

Figure 1: Schematic drawings of conventional nuclear medicine imaging technologies. (a) Positron emission tomography (PET). Annihilation gamma-rays with energies of 511 keV yielded after a positron and an electron annihilation are detected simultaneously. The position of a positron emitter can be estimated on a line connecting two detectors as the direction of annihilation gamma rays is opposite. (b) Time-of-flight PET. The time difference Δt corresponds to a position on a line. (c) Single photon emission computed tomography. The direction of incident gamma-rays is limited by mechanical collimators.

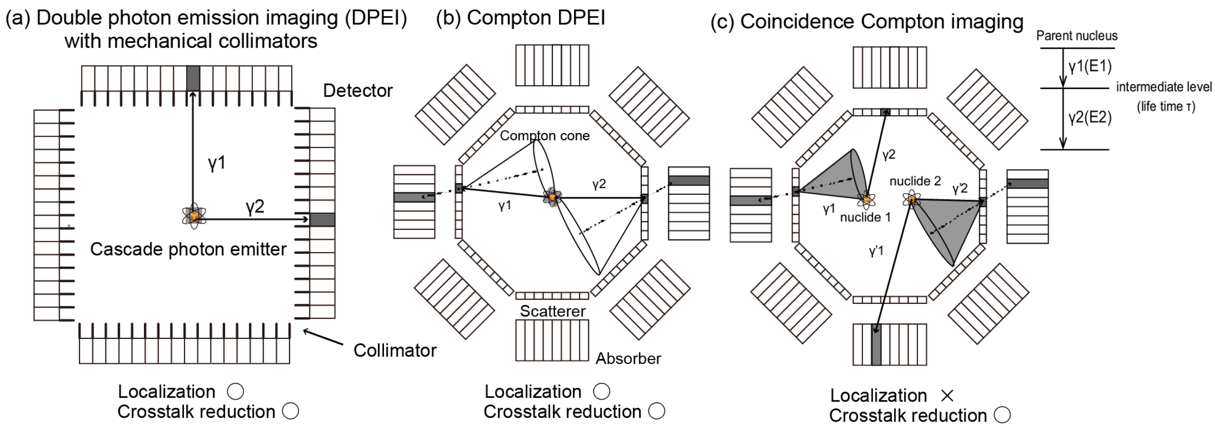

Figure 2: Concepts of applications of the double-photon coincidence method. (a) Double photon emission imaging (DPEI) with mechanical collimators. The radionuclide position can be specified at the intersection point of lines determined by coincidence cascade gamma rays events. (b) Compton DPEI. The radionuclide position can be estimated at the intersection area of Compton cones determined by the coincidence detection of cascade gamma rays Compton events. (c) Coincidence Compton imaging. The coincidence detection between a Compton event and a photopeak event of cascade gamma rays is useful to reduce crosstalk reduction in multi-nuclide Compton event although the localization cannot be performed.

annihilation photons corresponds to a position on a line connecting the two detection points (Figure 1 (b)). For example, a time resolution of 500 picoseconds (ps) correlates with a spatial resolution of 7.5 cm [7]. Recently, a commercial TOF-PET system achieved a high time resolution of 214 ps [9]. Moreover, a demonstration of reconstruction-free PET with a timing precision of 32 ps has also been reported [10].

Gamma-gamma coincidence imaging with mechanical collimators was proposed around 1980 [11-15]. This method localizes the radionuclide position at an intersection determined by the incident directions of multiple gamma rays from a cascade nuclide (Figure 2(a)). For example, ^{111}In, which is a SPECT nuclide, emits 171 keV and 245 keV gamma-rays successively through an intermediate state with a half-life of 85 nanoseconds (ns). In coincidence detection with a time window, these gamma rays are thus considered to be emitted from the same nucleus. The coincidence detection of cascade gamma rays specifies the radionuclide position at one point using mechanical collimators. Whereas the conventional SPECT system requires rotating detectors for three-dimensional (3D) imaging, gamma-gamma coincidence imaging provides 3D imaging without any rotation, in principle. However, since this concept was introduced, few research on gamma-gamma coincidence imaging had been carried out.

Recently, we illustrated the gamma-gamma coincidence imaging (referred to as "double photon emission imaging (DPEI)" in this paper) with parallelhole collimators [16,17]. Other groups have also reported similar concept imaging results using a Monte Carlo simulation for ^{111}In [18] or have demonstrated ^{177}Lu DPEI with parallel hole and slit hole collimators [19]. Double-photon coincidence detection has many potential applications in gamma-ray imaging. Figure 2 outlines three novel applications for double-photon coincidence detection. Herein, we review studies on these applications.

Double photon emission imaging with mechanical collimators

One of the double-photon coincidence detection applications is DPEI with mechanical collimators, as previously discussed. Unlike the annihilation gamma rays from PET nuclides, which are always emitted in opposite directions, cascade gamma rays are emitted in various directions. Therefore, the radionuclide position can be localized at the intersection point when the emission angle for the coincidence event of the cascade gamma rays is not 180°.

First, we demonstrated the ^{111}In DPEI with two scintillator detectors and parallel-hole collimators [16]. The scintillator detector consists of an 8×8 array of high-resolution-type $Ce:Gd_3Al_2Ga_3O_{12}$ (HR-GAGG) scintillators [20,21] and an 8×8 array of silicon photomultipliers (SiPM: Hamamatsu MPPC S13361-3050). The crystal size was 2.5 mm × 2.5mm × 4 mm. The pitch sizes of the HR-GAGG and SiPM array were 3.2 mm × 3.2 mm. An 8×8 array of parallel-hole collimators was attached to the scintillator detector. The pitch size of the collimator was 3.2 mm × 3.2 mm and the diameter of hole was 2 mm. The 64-channel signals from the SiPM array were processed by the dynamic time over threshold method (dToT) [22,23] in parallel, and were then acquired by the field-programmable gate array (FPGA)-based ToT data acquisition (DAQ) system in the form of list-mode data consisting of the pixel number, ToT width, and time stamp. The energy resolution was approximately 10.2% at 245 keV. Two parallel-hole collimator detectors were placed at 90° (Figure 3 (a)). The radioactive source of the ^{111}In solution was dispensed into a syringe of diameter 4 mm and placed at the center of the detector. A DPEI image of ^{111}In was successfully obtained without any rotation. In addition, we demonstrated the simultaneous multi cascade nuclide DPEI [17]. ^{177}Lu is another cascade nuclide that is used in nuclear medicine. ^{177}Lu emits beta rays; therefore, it has been used for the treatment of neuroendocrine tumors [24-26]. Cascade gamma-rays with energies of 113 keV and 208 keV as well as beta rays are also mainly emitted. These energies are also suitable for mechanical collimation imaging. In simultaneous ^{111}In and ^{177}Lu imaging with mechanical collimators, the crosstalk caused by different gamma rays affects the reconstructed SPECT image. The scattered photon and photopeak events in the energy-overlapped peak contribute to crosstalk events. Although scatter correction methods, such as the dual-energy window [27,28] and triple-energy window [29,30] subtraction methods, are applied to reduce artifacts caused by crosstalk in the SPECT reconstruction method, they cannot eliminate crosstalk events directly. Another advantage of double-photon coincidence detection is the potential to discriminate between nuclide types. Although a photopeak of a first gamma ray includes scattered photon events from gamma-rays with higher energies as well as energy-overlapped events, some of crosstalk events can be reduced directly by coincidence detection with a second gamma ray. In a previous study [17], we succeeded in demonstrating the crosstalk reduction capability of double-photon coincidence detection, as well as to its ability to visualize 3D images without rotating detectors. Whereas artifacts were appeared at the position of other nuclides in both ^{111}In and ^{177}Lu back-projection SPECT images, they were reduced in the double-photon coincidence images. The signal-to-background ratio (SBR) was also improved by a factor of more than 3 using double-photon coincidence detection.

However, the disadvantage of coincidence method is limited by its lower detection efficiency. The absolute detection efficiency of DPEI with parallel hole collimators was decreased by a magnitude of 10^{-4} [17]. Recently, we developed a second prototype DPEI system with parallel- and slit-hole collimators. A slit-hole collimator only limits the radioactive source position on the plane; however, the combination of parallel- and slit-hole collimators can restrict it to the intersection of a line and plane (figure 3 (b)). The demonstration result of the ^{111}In imaging with the second prototype system showed that the detection efficiency improved by a factor of approximately 5.3 compared with the first prototype DPEI

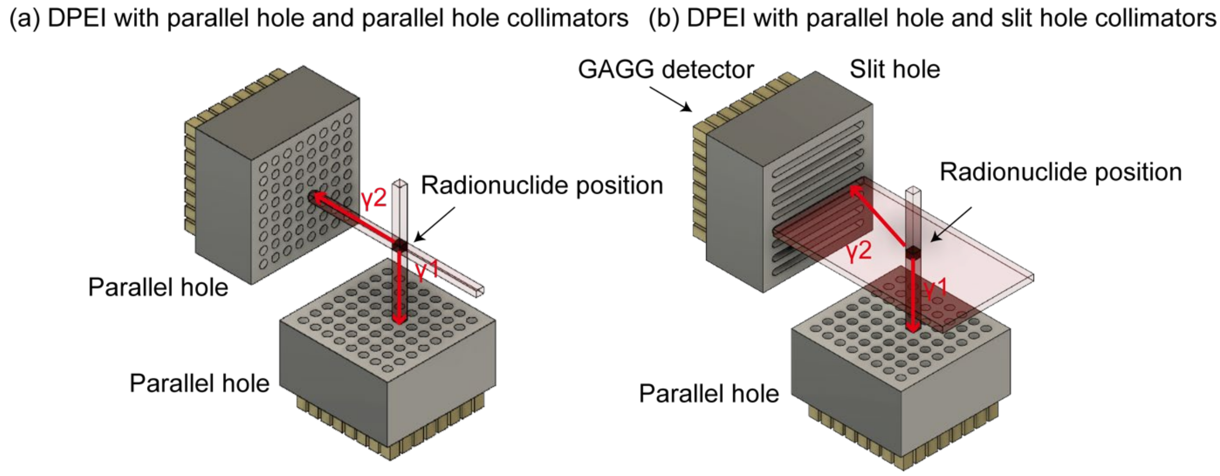

Figure 3: Schematic drawings of DPEI with mechanical collimators. (a) DPEI with parallel hole collimators. The radionuclide position can be specified at the intersection point of two lines. (b) DPEI with parallel hole and slit hole collimators. The radionuclide position can be identified at the intersection point of a plane and a line.

system with parallel-hole collimators. In addition, Liu et al. [19] compared the detection efficiency of a conventional SPECT and a stationary cascade gamma-ray coincidence imager (SCGCI), which consists of multi slit and multi pinhole collimators. The detection efficiency of the SCGCI was 3.85×10^{-6}, which was 10^2 times smaller than that of a conventional SPECT. They also reported the simulation results that showed that SCGCI provided higher quality images than conventional SPECT images reconstructed by the filtered back projection method.

Compton double photon emission imaging

Recently, Compton cameras have been actively developed for medical applications in nuclear medicine and proton/ion therapy [31-36]. Compton imaging is a promising gamma ray imaging method that utilizes Compton scattering kinematics [37]. The Compton camera can resolve the angle θ of the incident photons using equation (1):

$$\cos\theta = 1 - m_e c^2 \left(\frac{1}{E_2} - \frac{1}{E_1 + E_2} \right) \qquad (1)$$

where E_1 and E_2 are the recoil electron and scattered photon energies, respectively, m_e is the electron's rest mass, and c is the light velocity. The position of the radioactive source is estimated on a conical surface with an angle θ centered on the line connecting a Compton scattering detection point in the scatterer and a scattered photon detection point in the absorber. The distribution image is technically generated by drawing Compton cones. The low SBR is one of the disadvantages of this method, although there are excellent features, such as a wide target energy range and wide field of view. Double-photon coincidence detection can be applied to Compton imaging owing to its angler-resolving capabilities. Coincidence detection of the cascade gamma-rays' Compton event (typically a Compton event consisting of a scatterer event and an absorber event) can be used to limit the radionuclide location to intersections of two Compton cones (Figure 2 (b)). Multiphoton coincidence Compton imaging was proposed in the 2010s by Andreyev et al. [38,39]. They simulated triple-photon coincidence Compton imaging; however, the experimental results have not been reported. Recently, we reported the simulated and experimental results of Compton DPEI with two Compton cameras [40-42]. We succeeded in experimentally demonstrating a drastic SBR improvement in the Compton DPEI. The results of ^{134}Cs DPEI with HR-GAGG scintillator detector-based Compton cameras showed a SBR improvement of more than twofold [41]. In addition, the artifacts caused by ^{137}Cs 662 keV gamma-ray backgrounds in the ^{134}Cs 605 keV gamma-ray's Compton imaging were eliminated in the DPEI. The demonstration of ^{111}In DPEI with Si/CdTe Compton cameras succussed in generating the clearer images of three ^{111}In point sources using DPEI [42]. However, the detection efficiency of the DPEI was decreased by an order of 10^3 [40,41]. The detection efficiency can be improved by increasing the number of camera and devising the arrangement of the cameras. DPEI also requires the ability of the Compton camera to properly perform Compton imaging for each energy level of the cascade gamma ray.

Crosstalk reduction in multi-nuclide Compton imaging

As mentioned earlier, coincidence detection of Compton DPEI reduces the detection efficiency significantly compared with that of conventional Compton imaging, whereas DPEI identifies the location in a narrower area and reduces the crosstalk artifact. Focusing on the potential for a reduction in the amount of crosstalk, the double-photon coincidence detection can be used in different ways. Compton DPEI must consider coincidence events of the cascade gamma-rays Compton event. In contrast, double-photon coincidence detection can extract the coincidence events of cascade gamma rays Compton events and photopeak events (Figure 2 (c)). Although Compton events provides angle information for incoming gamma rays, photopeak events does not generate any direction or angle information. Therefore, these coincidence events cannot identify the radioactive source location although they can distinguish the types of nuclides. This method contributes to reducing the crosstalk backgrounds in multi-nuclide Compton imaging. We demonstrated the feasibility of this coincidence Compton imaging for simultaneous ^{111}In and ^{177}Lu Compton imaging with eight HR-GAGG scintillator detector-based Compton cameras [43]. The coincidence events between a 245 keV Compton event and a 171 keV photopeak event for ^{111}In or a 208 keV Compton event and a 113 keV photopeak event for ^{177}Lu were extracted as coincidence Compton events. The artifact caused by crosstalk backgrounds between nuclides was reduced and the SBR of the coincidence Compton imaging was improved by 1.1-1.7 times. The detection efficiency of coincidence Compton imaging decreased by a factor of 10^2 compared with that of conventional Compton imaging. As the detection efficiency of photopeak events is larger than that of Compton events, the decrease in the detection efficiency of coincidence Compton imaging can be suppressed to a greater extent than that of DPEI.

Conclusions

In this review article, we introduced three applications for the double-photon coincidence detection method. Although coincidence detection decreases the detection efficiency compared with the conventional method, it has the potentials to localize the radionuclide positions and directly reduce the crosstalk. Cascade nuclides not only improve gamma-ray imaging, but also have the potential to provide more advanced information. The chemical state of the cascade nuclide can be extracted using the angular correlation of cascade photons, which are perturbed by external electric and magnetic fields [44,45]. We succeeded in simultaneous chemical sensing and accumulation imaging of 111In solutions [44]. Recently, Moskal et al have proposed a positronium imaging, which can sense the chemical environment of a radionuclide [46,47]. They experimentally demonstrated this novel imaging by detecting mean lifetimes of parapositronium and orthopositronium [46] or by detecting three-photon annihilations of ortho positronium atoms based on the trilateration method [47]. Moreover, the detection of three photons enables to perform simultaneous double-isotope PET imaging [48]. It is anticipated that this kind of research will lead to innovative changes in nuclear medicine.

Acknowledgements

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