

Construction of a CZT-SPECT system based on Large-Sized Pixelated CZT Crystal and Performance Evaluation for in-vivo Multi-Radionuclides Distribution Measurement

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Abstract

Single photon emission computed tomography (SPECT) is the commonly used imaging modality in clinical nuclear medicine for disease diagnosis. However, traditional SPECT systems have several disadvantages when monitoring the distribution of radiopharmaceuticals labeled various radionuclides. A cadmium zinc telluride (CZT) SPECT system based on a 15 mm thick, three-dimensional (3D) pixelated CZT crystal is developed. The performance of this CZT-SPECT system in detecting the distribution of different radiopharmaceuticals are analyzed through mouse phantom experiments. The results show that for ^{99m}Tc (141 keV), ^{177}Lu (208 keV), and ^{18}F (511 keV), the energy resolution of the CZT-SPECT system is 2.38%, 1.94%, and 1.47%, respectively. The depth of interact (DOI) of gamma rays emitted by different radionuclides in the CZT crystal are recorded, that is, for 141 keV, 208 keV and 511 keV gamma rays, the DOI ranges are approximately 2.17-5.85 mm, 2-9 mm, and 1-11 mm, respectively. Both qualitative and quantitative results indicate that the CZT-SPECT system can achieve spatial distribution detection and reconstruction, even when a single radionuclide or multiple radionuclides coexist. The full width at half maximum (FWHM) of each kidney reconstructed is almost less than 5 mm for these radionuclides. Due to the excellent energy resolution and the large size of the 3D-CZT crystal, the CZT-SPECT system developed can effectively measure the in-vivo distribution of various diagnostic and therapeutic radiopharmaceuticals labeled with different radionuclides. The results of this study can also provide technical support for the future development of more radiopharmaceuticals.

Full Text

Preamble

Construction of a CZT-SPECT System Based on Large-Sized Pixelated CZT Crystal and Performance Evaluation for in-vivo Multi-Radionuclides Distribution Measurement

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Abstract

Single photon emission computed tomography (SPECT) is a widely used imaging modality in clinical nuclear medicine for disease diagnosis. However, traditional SPECT systems exhibit several limitations when monitoring the distribution of radiopharmaceuticals labeled with various radionuclides. To address this, we developed a cadmium zinc telluride (CZT) SPECT system based on a 15 mm thick, three-dimensional (3D) pixelated CZT crystal and analyzed its performance in detecting different radiopharmaceuticals through mouse phantom experiments. The results demonstrate that for ⁹⁹Tc (141 keV), ¹⁷⁷Lu (208 keV), and ¹⁸F (511 keV), the energy resolution of the CZT-SPECT system is 2.38%, 1.94%, and 1.47%, respectively. The depth of interaction (DOI) of gamma rays emitted by different radionuclides in the CZT crystal was recorded; specifically, for 141 keV, 208 keV, and 511 keV gamma rays, the DOI ranges are approximately 2.17-5.85 mm, 2-9 mm, and 1-11 mm, respectively. Both qualitative and quantitative results indicate that the CZT-SPECT system can achieve spatial distribution detection and reconstruction, even when a single radionuclide or multiple radionuclides coexist. The full width at half maximum (FWHM) of each reconstructed kidney is less than 5 mm for all radionuclides tested. Due to the excellent energy resolution and large size of the 3D-CZT crystal, the developed CZT-SPECT system can effectively measure the in-vivo

distribution of various diagnostic and therapeutic radiopharmaceuticals labeled with different radionuclides. These findings provide technical support for the future development of additional radiopharmaceuticals.

Keywords: Single photon emission computed tomography; Cadmium zinc telluride; Mouse phantom; Kidney; Depth of interaction; Three-dimensional reconstruction.

Introduction

Single photon emission computed tomography (SPECT) is a cornerstone imaging modality in clinical nuclear medicine and serves as an essential tool for disease diagnosis and management [1,2]. A SPECT system primarily comprises radiation detectors, mechanical collimators, and back-end electronics [3,4]. Collimators shield and restrict gamma rays such that only those from specific directions are detected [5,6]. By rotating the detector to multiple orientations and applying reconstruction algorithms, the three-dimensional (3D) distribution of radiopharmaceuticals within a patient can be obtained [7,8]. Current clinical SPECT systems predominantly utilize NaI scintillation crystals paired with lead or tungsten collimators [9,10]. However, the intrinsic inefficiency of NaI crystals results in poor resolution, significant artifacts, and challenges in simultaneously detecting multiple-energy gamma rays.

In recent years, advancements in crystal growth technology and readout systems have spurred considerable interest in SPECT systems based on cadmium zinc telluride (CZT, density 5.8 g/cm³) [11,12]. CZT is a room-temperature semiconductor material that offers excellent energy resolution and efficiently converts deposited gamma ray energy into electronic signals. Several CZT-based SPECT systems (e.g., D-SPECT) are currently used clinically, primarily for myocardial perfusion imaging [15-17].

Despite its potential to enhance clinical nuclear medicine, CZT-SPECT faces limitations. The thickness of CZT crystals affects the detectable energy range of gamma rays. For instance, the Veriton SPECT/CT system is limited to 200 keV due to its 6 mm thick CZT crystal [18], whereas the StarGuide™ SPECT/CT system can detect gamma rays above 200 keV using a 7.25 mm thick CZT crystal [19]. Furthermore, accurate detection of different radiopharmaceutical distributions often requires collimator swapping based on the radionuclide type, increasing costs and complicating clinical workflows. To overcome these challenges, we developed a CZT-SPECT system employing a 15 mm thick 3D-CZT crystal and evaluated its performance in detecting various radiopharmaceuticals through mouse phantom experiments.

Methods

System Configuration and Phantom Design

We utilized a pixelated 3D-CZT crystal fabricated by Kromek Group (Huddersfield, UK) as the detection component of our CZT-SPECT system. The crystal dimensions are $22 \times 22 \times 15 \text{ mm}^3$, segmented into 11×11 pixelated anodes with a single planar cathode [20]. Unlike scintillation detectors, the 3D-CZT enables recording of both cathode and anode signal trigger times for each event, allowing determination of the depth of interaction (DOI) through charge carrier drift velocity analysis [21]. Additionally, we employed a 3D-printed parallel-hole tungsten collimator with 1.2 mm diameter holes, 0.8 mm septal thickness, and 30 mm septal height, designed to match the 3D-CZT crystal such that each collimating hole aligns with a CZT anode pixel [22]. A 3D-printed mouse phantom composed of butanediol dimethacrylate ($\text{C}_{12}\text{H}_{18}\text{O}_4$, density 1.3 g/cm^3) was used to evaluate CZT-SPECT performance [23,20].

Given the metabolic characteristics of the radiopharmaceuticals employed, the kidneys were selected as the region of interest (ROI) [24].

Radiopharmaceuticals and Experimental Conditions

Various radiopharmaceuticals are used for disease diagnosis and therapy in clinical nuclear medicine. Commonly used agents include ^{99}Tc -DTPA (single photon decay, SPECT imaging) for whole-body bone scans and ^{18}F -FDG (positron decay, PET imaging) for whole-body glucose metabolism assessment [25,26]. Additionally, radionuclide therapy has gained prominence, exemplified by ^{177}Lu -PSMA-617 (β^- decay) for prostate cancer treatment [27,28]. Precise determination of radiopharmaceutical distribution is critical for accurate disease diagnosis and therapeutic efficacy evaluation [29]. This study analyzed the CZT-SPECT system's performance in monitoring ^{99}Tc -DTPA, ^{18}F -FDG, and ^{177}Lu -PSMA-617. Radiopharmaceutical details are provided in Table 1.

Four distribution conditions were investigated: (1) ^{99}Tc -DTPA in both kidneys; (2) ^{18}F -FDG in both kidneys; (3) ^{99}Tc -DTPA in one kidney and ^{18}F -FDG in the other; and (4) ^{177}Lu -PSMA-617 in both kidneys. All radiopharmaceuticals were encapsulated and embedded in the kidney regions of the mouse phantom [20]. Activity concentrations for all experiments are listed in Table 2. Measurements were performed using a rotating platform acquiring gamma ray data at 12 directions (30° intervals) with 1-minute acquisition per direction. The CZT-SPECT system and module arrangement are illustrated in Figure 1 [Figure 1: see original paper].

Image Reconstruction

QSPECT v3.0 software was used to reconstruct radiopharmaceutical distributions under various conditions [30]. The reconstruction employed a Maximum

Likelihood Expectation Maximization (MLEM) iterative algorithm with 10 iterations, and the resulting images were not subjected to additional filtering.

Based on the recorded energy spectra, the FWHM of each characteristic gamma ray peak detected by the CZT-SPECT system was determined through Gaussian fitting. Signals with deposited energies within $\pm\text{FWHM}/2$ of the characteristic gamma ray energy (e.g., $141 \pm \text{FWHM}/2$) were selected as effective signals for performance analysis and radiopharmaceutical distribution reconstruction.

Results

⁹⁹Tc Distribution Measurement

The recorded ⁹⁹Tc events are shown in Figure 2 [Figure 2: see original paper]. The excellent energy resolution of the CZT detector yields distinct ⁹⁹Tc characteristic peaks in the photoelectric event spectra, with an FWHM of approximately 3.35 keV at 141 keV ($R^2 = 96.93\%$). The DOI of recorded photoelectric events primarily ranges from 2–15 mm, with characteristic ⁹⁹Tc gamma ray DOI concentrated between 3–6 mm.

Using the selected effective signals, the MLEM algorithm reconstructed the ⁹⁹Tc spatial distribution, as shown in Figure 3 [Figure 3: see original paper]. The results demonstrate clear reconstruction of both kidney regions in the mouse phantom, indicating excellent performance of the CZT-SPECT system for detecting in-vivo distribution of ⁹⁹Tc-labeled radiopharmaceuticals.

¹⁸F Distribution Measurement

Conventional scintillator-based SPECT detectors cannot effectively image positron-emitting radiopharmaceuticals due to poor collimation of high-energy 511 keV gamma rays and inadequate energy resolution, which introduces substantial noise. Using our CZT-SPECT system, we analyzed its capability to monitor positron-emitting radiopharmaceutical distribution; the recorded signals are presented in Figure 4 [Figure 4: see original paper]. The superior energy resolution of the 3D-CZT crystal produces a clear 511 keV peak in the photoelectric event spectrum with an FWHM of approximately 7.52 keV at 511 keV ($R^2 = 92.24\%$). DOI analysis reveals that 511 keV gamma rays interact over a broader and deeper range within the 3D-CZT crystal (approximately 1–11 mm) compared to 141 keV gamma rays.

Based on selected effective ¹⁸F signals, the MLEM algorithm reconstructed the spatial distribution shown in Figure 5 [Figure 5: see original paper]. While the 3D distribution exhibits more background artifacts than ⁹⁹Tc, the Y-direction intensity profile clearly distinguishes both kidney regions, demonstrating that the CZT-SPECT system achieves excellent monitoring performance even for positron-emitting radiopharmaceuticals.

Simultaneous Multi-Radionuclide Distribution Measurement

Simultaneous imaging of multiple radiopharmaceuticals can improve diagnostic accuracy [31,32]. We analyzed the CZT-SPECT system's capability to detect multiple radiopharmaceuticals concurrently; the recorded photoelectric events are shown in Figure 6 [Figure 6: see original paper]. The total energy spectrum displays characteristic peaks for both nuclides, with DOI distributions consistent with single-nuclide measurements.

Effective signals for each radiopharmaceutical were selected based on energy resolution measured during single-nuclide experiments, and MLEM reconstruction was performed. The spatial distribution results are presented in Figure 7 [Figure 7: see original paper]. Both kidney regions were well reconstructed without cross-interference, although ^{18}F reconstruction noise exceeded that of ^{99}Tc . These results demonstrate that the CZT-SPECT system can simultaneously detect and reconstruct multi-radionuclide distributions.

^{177}Lu Distribution Measurement

Accurate monitoring of therapeutic radiopharmaceutical distribution is crucial for evaluating treatment efficacy. We analyzed the CZT-SPECT system's performance in imaging ^{177}Lu -labeled radiopharmaceuticals; the recorded photoelectric events are shown in Figure 8 [Figure 8: see original paper]. All characteristic ^{177}Lu energies are visible in the total gamma spectrum.

Analysis reveals FWHM values of 2.7881 keV ($R^2 = 95.63\%$) and 4.0320 keV ($R^2 = 93.31\%$) for 113 keV and 208 keV gamma rays, respectively. Due to their similar energies, the DOI distributions of these gamma rays are nearly identical, though the 113 keV distribution peaks at a slightly greater depth. Sinograms show clear curves for both energies, with more artifact counts at the edges for 113 keV gamma rays.

Using selected effective signals, spatial distributions were reconstructed for each gamma ray energy, as shown in Figure 9 [Figure 9: see original paper]. For 113 keV gamma rays, both kidneys are visible in the 3D reconstruction but with substantial edge artifacts, and the one-dimensional intensity distribution cannot distinguish the kidneys. In contrast, 208 keV gamma rays yield clear kidney visualization in both 3D reconstruction and Y-direction intensity profiles.

Based on one-dimensional intensity distributions from all four conditions, Gaussian fitting determined the center location and FWHM for each kidney region (Table 3). These results demonstrate that the CZT-SPECT system enables precise measurement of in-vivo radiopharmaceutical distributions for clinical nuclear medicine applications.

Discussion

Recent advances in targeted radionuclide-labeled drugs have provided critical support for early disease diagnosis and precision therapy, with increasing ra-

dionuclides expected to enter clinical practice. However, conventional SPECT systems face significant limitations in monitoring radiopharmaceuticals labeled with diverse radionuclides. This study established a CZT-SPECT system based on a 15 mm thick 3D-CZT crystal and evaluated its performance in monitoring various radiopharmaceutical distributions.

Characteristic energy peaks for each radionuclide were clearly resolved in the total photoelectric event spectra. The CZT-SPECT system achieved energy resolutions of 2.38%, 1.94%, and 1.47% for ^{99}Tc (141 keV), ^{177}Lu (208 keV), and ^{18}F (511 keV), respectively—substantially superior to traditional NaI-based SPECT systems (~10% at 141 keV) and commercial D-SPECT systems (CZT, 5.5% at 141 keV) [33]. Furthermore, the 3D-CZT crystal enabled DOI information acquisition. We experimentally investigated the interaction regions of different gamma rays within the 3D-CZT crystal, revealing energy-dependent DOI variations. For ^{99}Tc 's 141 keV gamma rays, the DOI range was 2.17–5.85 mm (peak at 4.01 mm, $R^2 = 92.59\%$) based on Gaussian fitting. The 208 keV gamma rays from ^{177}Lu and 511 keV gamma rays from ^{18}F primarily interacted within ~4 mm depth, but higher-energy gamma rays showed a larger proportion of deeper interactions with more uniform distribution as energy increased. These findings indicate that adequate CZT crystal thickness is essential for high-energy gamma ray detection, and a 15 mm thick crystal is sufficient for 511 keV gamma rays.

Qualitative and quantitative analyses of reconstructed spatial distributions demonstrate that the CZT-SPECT system can detect and reconstruct radiopharmaceutical distributions for both single and multiple radionuclides. For all three radionuclides, both 3D reconstruction and one-dimensional projection clearly distinguished the mouse phantom's two kidney regions. However, higher-energy gamma rays (>141 keV) produced more reconstruction artifacts, likely due to increased collimator penetration probability. Nevertheless, the system's excellent energy resolution effectively suppresses false counts, enabling accurate 3D distribution measurements for radionuclides such as ^{18}F . The center-to-center distance between kidney regions was approximately 14 mm, with reconstructed kidney FWHM values below 5 mm for all conditions, satisfying the Rayleigh criterion [34,35]. This indicates spatial resolution better than 14 mm for gamma rays up to 511 keV. Previous studies confirmed 4.5 mm spatial resolution for 141 keV gamma rays, surpassing both NaI-based SPECT and D-SPECT systems [33].

While these results demonstrate excellent radiation detection performance meeting diverse clinical nuclear medicine needs, the current study employed basic reconstruction algorithms without tissue attenuation correction. Future work should develop advanced reconstruction algorithms to enable quantitative SPECT imaging.

Conclusions

We established a CZT-SPECT system based on a 15 mm thick pixelated 3D-CZT crystal for wide-energy gamma ray detection. The system's excellent energy resolution and large crystal dimensions enable effective measurement of in-vivo distributions for various diagnostic and therapeutic radiopharmaceuticals labeled with different radionuclides, including ^{99}Tc , ^{18}F , and ^{177}Lu . These findings provide technical support for developing novel radiopharmaceuticals in the future.

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Statements & Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Disclosures and declarations

The authors have no relevant conflicts of interest to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Feng Tian and Wei Ding. The first draft of the manuscript was written by Dandan Zhang and Feng Tian, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval

This study does not involve relevant ethics approval.

Consent to participate

This study does not involve relevant participants.

Consent to publish

This study does not involve relevant human research participants.

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