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Phantom experiments on a PSAPD-based compact gamma camera with submillimeter spatial resolution for small animal SPECT

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Abstract

We demonstrate a position sensitive avalanche photodiode (PSAPD) based compact gamma camera for the application of small animal single photon emission computed tomography (SPECT). The silicon PSAPD with a two-dimensional resistive layer and four readout channels is implemented as a gamma ray detector to record the energy and position of radiation events from a radionuclide source. A 2 mm thick monolithic CsI:TI scintillator is optically coupled to a PSAPD with a 8mm×8mm active area, providing submillimeter intrinsic spatial resolution, high energy resolution (16% full-width half maximum at 140 keV) and high gain. A mouse heart phantom filled with an aqueous solution of 370 MBq ^{99m}Tc-pertechnetate (140 keV) was imaged using the PSAPD detector module and a tungsten knife-edge pinhole collimator with a 0.5 mm diameter aperture. The PSAPD detector module was cooled with cold nitrogen gas to suppress dark current shot noise. For each projection image of the mouse heart phantom, a rotated diagonal readout algorithm was used to calculate the position of radiation events and correct for pincushion distortion. The reconstructed image of the mouse heart phantom demonstrated reproducible image quality with submillimeter spatial resolution (0.7 mm), showing the feasibility of using the compact PSAPD-based gamma camera for a small animal SPECT system.

Index Terms

Avalanche photodiodes; Biomedical nuclear imaging; Single photon emission computed tomography; Scintillation detectors

I. INTRODUCTION

Radionuclide imaging techniques such as single photon emission computed tomography (SPECT) and positron emission tomography (PET) provide important functional and physiological information for the management of diseases including cancers and cardiovascular diseases. In addition to their clinical uses, smaller versions of SPECT and PET, namely microSPECT and microPET, are gaining popularity among biological researchers because of the ever-expanding availability of small animal models for human diseases. Rodent models of human genetics are particularly interesting because of their genetic similarity, and they provide cost-effective experimental platforms in biological research. The noninvasive nature of radionuclide imaging techniques allows longitudinal investigations of physiologic changes over time in the same animal model.

Several investigators have developed innovative nuclear imaging techniques specific to dedicated small animal *in vivo* imaging systems [1]–[8]. These radionuclide imaging systems (microSPECT and microPET) generally offer high spatial resolution (submillimeter) suitable for small animal imaging and often have high photon detection efficiency that allow small animal studies to be completed in a reasonable time period with relatively low radiation exposure to imaged animals.

In most microSPECT and microPET systems, photomultiplier tubes (PMTs) coupled to a scintillator are used as radionuclide photodetectors. PMTs offer high signal gain (10^5 – 10^7) and low electronic noise at a relatively low cost. However, there are limitations in the use of vacuum-tube-based detection for radionuclide imaging, such as the fragility, bulkiness and limited intrinsic spatial resolution.

As an alternative to PMTs, solid-state detectors have been developed for radionuclide imaging systems. For example, cadmium zinc telluride (CZT) is already replacing PMT-based detectors in some commercial radionuclide scanners. At room temperature, CZT detectors outperform PMTs in energy resolution, providing better energy-based means to reject scatter radiation and a higher signal-to-noise ratio. In addition, finely pixelated CZT detectors can increase the intrinsic spatial resolution, achieving up to 380 μm experimentally [9]. However, there are disadvantages of using CZT detectors, such as high manufacturing cost, limited supply and complexities in implementation that typically require custom-designed application-specific integrated circuits (ASICs). In this perspective, position-sensitive avalanche photodiodes (PSAPDs) are another interesting solid-state detector with intrinsic position sensing capability, offering high gain at a potentially lower cost than direct-conversion solid-state detectors like CZT. Although a large-area PSAPD suffers from increased noise due to intrinsic capacitance, the PSAPD has a simplified position-readout structure that significantly reduces the required number of readout channels and provides a compact form factor in building high performance radionuclide imaging systems especially for small volume imaging applications such as animal imagers or targeted volume of human subjects (e.g., heart and brain).

Most commercial SPECT systems use PMT-based gamma cameras coupled to continuous NaI:Tl scintillators. Although continuous crystals may suffer from slower count rates since each radiation event paralyzes the larger detector area [10], they have several advantages over segmented scintillators including a simple fabrication process, higher sensitivity (due to no non-scintillating regions or gaps) and lower cost. In addition, the non-scintillating regions in segmented scintillators can cause multiple reflections inside the crystal segments, which lead to loss of optical photons within the scintillator, reducing the energy resolution. Our group previously investigated the imaging properties of a continuous CsI:Tl scintillator

coupled to PSAPD and demonstrated its feasibility as a small-animal imaging gamma camera [11], but we did not demonstrate any SPECT imaging capabilities.

We describe our development and evaluation of a compact and high resolution gamma camera composed of a continuous CsI:Tl scintillator coupled to a PSAPD with a focus on demonstrating the SPECT imaging capability of this prototype system. We imaged a realistic mouse heart phantom with a defect, acquiring multiple angular projections using a PSAPD and a single pinhole collimator and then reconstructed the data. The single pinhole (500 μm diameter) collimator offers a high spatial resolution and thus is suitable for imaging the mouse heart phantom.

II. OVERVIEW OF PSAPD

An avalanche photodiode (APD) is a silicon-based semiconductor device with a p-n junction. Once optical photons, generated by interactions between a scintillator and gamma rays, impinge on the APD, it produces charges that drift at high velocities when a high reverse-bias voltage is applied. The moving electrons collide with atoms of doped crystal, creating additional charges through impact ionization, which results in an increased electric current through the photodiode. The energy of incident gamma ray radiation is proportional to the generated electric current, providing spectral information of the radiation source. However, the APD does not have any intrinsic position-sensing capability for imaging applications. A closely-packed APD array structure has been investigated as a way to implement a position-sensing capability, but this requires a large number of preamplifiers and also generates large dead spaces between the small APD modules [12], [13], [14].

In order to reduce the number of readout channels while addressing the position of a radiation event on a large contiguous detection area, a resistive layer is placed at the back face of the PSAPD as shown in Fig. 1(a). The resistive layer enables accurate determination of the event location using charge-sharing effects among the four corner electrodes at the back-face [15]. Electrons, generated by radiation events within the coupled scintillator, travel through the resistive layer to four anodes. Position-dependent signals from these four corner anodes of the PSAPD can be used to determine the location of a radiation event. The voltage at each anode is proportional to the generated current and resistance of the path of the current to the anode. Anger logic can be used to calculate the location of the event with the readout voltage from the four anodes [15]. However, it inherently generates an image with highly nonlinear pincushion distortion [16],[17]. We corrected the pincushion distortion by calculating each position (X_{rot} , Y_{rot}) using only the corresponding diagonal pairs of the anode signals:

$$\begin{aligned} X_{rot} &= \frac{S1-S3}{S1+S3} \\ Y_{rot} &= \frac{S2-S4}{S2+S4}, \end{aligned} \quad (1)$$

where $S1$, $S2$, $S3$, $S4$ are the voltage signal from the four anodes of the PSAPD. The final position can be determined after rotating the coordinate frame of the image by 45 degrees

$$\begin{aligned} X &= X_{rot} \cos(45^\circ) + Y_{rot} \sin(45^\circ) \\ Y &= Y_{rot} \cos(45^\circ) - X_{rot} \sin(45^\circ), \end{aligned} \quad (2)$$

where X and Y are the corrected coordinates of each event [18].

The energy and timing information for energy spectrum analysis and triggering is determined by the signal from top cathode contact, which is equal to the sum of all four

anode voltages. Fig. 1(b) shows a photograph of the fabricated PSAPD with an 8mm×8mm active area from Radiation Monitoring Devices Inc. (Watertown, MA), which was used for all experimental measurements presented in this paper. The PSAPD has a gain of ~1000 with ~98 electrons-rms noise at room temperature and about 60% quantum efficiency.

III. CONTINUOUS CsI:TL SCINTILLATOR

A photograph of the continuous CsI:TL scintillator used for the experiment is shown in Fig. 2. The scintillator has an active area of 8mm×8mm and a 2 mm thickness, which was polished and encapsulated in white epoxy resin (approximately 54% stopping power for 140 keV photons). We chose CsI:TL as the scintillator material due to its high light output (approximately 65,000 photons/MeV), ease of availability, high durability and higher stopping power compared to conventional NaI:TL scintillators. A high stopping power allows a thinner crystal size to be used, which reduces spatial blurring of a radiation event within the scintillator.

IV. POINT SPREAD FUNCTION OF PSAPD

The point spread function (PSF) can define the inherent resolution of an imaging system. We measured the PSF of our gamma camera system by placing a small ^{99m}Tc -pertechnetate source having a 370 MBq activity in a syringe (a cylindrical volume with a 10 mm diameter and 5 mm height) 1 m away from the 0.5 mm diameter tungsten knife-edge pinhole. The PSAPD was located 33 mm below the pinhole. The far-field source can thus be regarded as a point source at the image plane. The resulting PSF, which is processed using the pincushion correction algorithm (rotated diagonal readout algorithm) described in section II [18], is circularly symmetric as shown in Fig. 3(a). Reflected photons from the sidewall of the CsI:TL scintillator and uniform bias build-up over the entire surface area were also filtered out. The uniform bias build-up is caused by noise problem with sample-and-hold board, temperature drift and small gain variations over the PSAPD surface, which increases with total count time. A Gaussian fit was applied, and the measured full-width at half maximum (FWHM) of the PSF was 0.7 mm, as illustrated in Fig. 3(b).

V. MEASURED ENERGY SPECTRUM OF PSAPD

Each projection image has scattered events outside the 140 keV photopeak of ^{99m}Tc -pertechnetate. Fig. 4 shows the measured energy spectrum produced by a ^{99m}Tc -pertechnetate flood source. The measured spectrum shows a photopeak at 140 keV and 16% FWHM, which is within the range of commercially available gamma camera's energy resolution. Projection data can be spectrally filtered around the photopeak, removing most of the scatter radiation events to form the image.

VI. SPECT SYSTEM CONFIGURATION AND MOUSE HEART PHANTOM MEASUREMENT

The imaging setup is shown in Fig. 5. A photograph of the PSAPD with an evaluation circuit board is shown in Fig. 6. The custom-made mouse heart phantom simulates the left ventricular wall of a mouse heart, with a 10.7 mm height, 4.9 mm diameter, and 0.85 mm wall thickness as illustrated in the inset of Fig. 5. The mouse heart phantom was filled with a 370 MBq aqueous solution of ^{99m}Tc -pertechnetate (140 keV) and imaged through a 500 μm diameter pinhole. A cold defect (2mm×6mm in size, 0.7mm thick) is present in the side wall of the mouse heart phantom and contains a lower concentration of ^{99m}Tc -pertechnetate solution. The CsI:TL scintillator was optically coupled to the PSAPD, which was mounted on an evaluation board inside an aluminum box. A tungsten circular knife-edge pinhole with a

0.5 mm diameter and 60 degree acceptance angle was placed on top of the shielded aluminum box. A translation stage and micrometer were used to precisely control the pinhole's position. The mouse heart phantom was fixed onto a rotation stage that can be precisely translated in Cartesian coordinates (xyz directions) above the pinhole.

The distance from center of the pinhole to PSAPD was 33 mm, and the distance from the pinhole to the center of mouse heart phantom was 55 mm, producing a 60% minified image of the phantom on the PSAPD. The field-of-view is 8mm×8mm (13.8° angle), which is determined by the geometry. For each projection, the translation direction was adjusted to place the projection image at the center of PSAPD, so that the projection image shift is minimized at each angular rotation. To minimize dark current shot noise, the PSAPD was cooled to -41°C with $\pm 0.5^{\circ}\text{C}$ fluctuation, which was achieved by continuously flowing cooled nitrogen gas inside the aluminum box. The operating temperature was determined by observing the flood image of a detector comprised of a 16×16 array of discrete CsI:Tl crystals. At -41°C , the visibility of segmentation was optimal. A -1580 V DC bias voltage was applied across the PSAPD, for a gain of approximately 1000. Each anode signal was connected to a Cremat CR-110 charge sensitive preamplifier (Cremat, Inc. Watertown, MA) with 1.4 gain (volts/pC) for the impedance matching. As shown in Fig. 6, there are four preamplifiers used to obtain position signals and one preamplifier for the energy signal. The signals from the preamplifiers are fed into Canberra 2020 pulse-shaping amplifiers (Canberra Industries, Meriden, CT) with 250 ns pulse shaping times and 35 dB gains. The energy signal triggers a sample-and-hold board to send the shaped signals from the pulse-shaping amplifiers to a data acquisition board located inside a personal computer that records the events in list mode. The event data were then transferred to a different computer for position calculations using Anger logic, and the pincushion distortion was corrected by the rotated diagonal algorithm. All collected events were binned into a 128×128 matrix as projection data before reconstruction.

VII. SPECT IMAGE RECONSTRUCTION

We took 34 projections over a 204 degree rotation (6 degree increment) of the mouse heart phantom with defect. For each angular projection, more than 170,000 counts were accumulated, and each projection took approximately 400 seconds resulting in a 425 counts/sec count rate and 1.15×10^{-6} sensitivity on average. Raw projection data were post-processed by spectral filtering (15 percent around 140 keV). The uniformity was corrected using a previously recorded flood image (200,000 counts) that is shown in Fig. 7(a). The pincushion distortion corrected image with the correction method explained in section II is illustrated in Fig. 7(b). The reflection from the edge of the scintillator further reduces the effective field-of-view of the detector to 6mm×6mm (10.4 degree angle). The image of the mouse heart phantom was reconstructed using a cone-beam iterative maximum likelihood expectation maximization (MLEM) algorithm with 10 iterations without attenuation correction [19]. The size of the two-dimensional reconstructed image space is 6mm×6mm with a 0.047 mm isotropic voxel size. Fig. 8(a) shows a long-axis view of the mouse heart phantom, where we can clearly distinguish the heart wall of the phantom. The other long-axis view of the mouse heart phantom is shown in Fig. 8(b), where the upper-right corner shows less activity due to the defect within the phantom. A short-axis image of the phantom is shown in Fig. 8(c), where the defect is represented as a region with lower activity at the bottom of the image. The noise in the reconstructed images is likely from both the projection images and statistical noise from the MLEM reconstruction. In addition, we did not apply any post-filtering to our reconstruction images. A circumferential profile of the short-axis image showing activity distribution of designated area away from the center of the annulus as a function the angle is illustrated in Fig. 8(d). The circumferential profile of short-axis image shows a non-uniform activity distribution due to the cold defect inside the phantom.

The location of defect can be found where the activity distribution is reduced in the circumferential profile (at 280°).

VIII. DISCUSSION

The experimental demonstration of the mouse heart phantom study with our PSAPD-based compact gamma camera configuration suggests that a PSAPD coupled to a continuous CsI:Tl scintillator can be used for high resolution small animal SPECT imaging applications with submillimeter spatial resolution. A single 8mm×8mm PSAPD might be too small for the whole body imaging of small animals. However, the reconstructed image of the mouse heart phantom from our demonstration suggests that this compact gamma camera might eventually be used for myocardial perfusion imaging or small, targeted volume imaging of small animals.

Gas nitrogen cooling method was implemented to keep the temperature at – 41 degree (Celsius) in order to suppress the dark current shot noise in the PSAPD. While the gas nitrogen cooling provides a cost efficient cooling method, it is bulky and difficult to automate. A thermo electric cooler (TEC) has been suggested as an alternate cooling method [10], but it would require the PSAPD and preamplifier circuit to be placed inside a vacuum chamber in order to avoid condensation, which would probably not reduce system complexity and size. Thus, a more sophisticated compact temperature control technology without condensation might be required to build a commercial PSAPD-based gamma camera.

The continuous CsI:Tl crystal optically coupled to PSAPD showed a good energy resolution (16%) around the photopeak energy (140 keV) of the ^{99m}Tc-pertechnetate. The 2 mm thick CsI:Tl scintillator has a stopping power of ~54% at 140 keV, a relatively low value that decreases the count rate for a given photon flux and increases the dose level for small animal imaging. However, a thicker continuous crystal would inevitably generate larger parallax in the cone-beam geometry of pinhole imaging system, which could significantly degrade the spatial resolution of the gamma camera at the edges of the crystal. This trade-off should be carefully investigated to choose the ideal thickness of the crystal specific to potential applications.

We used a simple rotated diagonal readout algorithm to correct for the pincushion distortion of each projection image. A better distortion correction method can be applied using a complex statistical method, although it requires training and calibration before the software implementation [20].

In addition, multiple PSAPDs can be coupled to form a single large area scintillator for whole body small animal imaging [10]. Also, the PSAPD-based gamma camera is a potential candidate for a SPECT/MRI combined modality imaging because of its insensitivity to high magnetic fields.

IX. CONCLUSION

We have presented the characterization and experimental demonstration of a novel PSAPD-based compact gamma camera, which has a resistive layer for position sensing, high intrinsic spatial resolution (submillimeter), reasonably good energy resolution and a compact size for application in small animal imaging. The 8mm×8mm PSAPD was coupled to a 2 mm thick continuous CsI:Tl scintillator that has 54 % stopping power at 140 keV and high light output (≈ 65,000 photons/MeV). The reconstructed SPECT image of a mouse heart phantom clearly shows the radioactivity distribution within the phantom. The location of a

defect with submillimeter dimensions in a mouse heart phantom was observed in the reconstructed SPECT images, indicating a submillimeter system spatial resolution.

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Fig. 1.
 (a) Schematic drawing of a PSAPD that consists of a large area APD and resistive layer. (b)
 Photograph of the fabricated PSAPD with an 8mm×8mm active area.

Fig. 2.
Photograph of the CsI:TI scintillator and a dime coin.

Fig. 3.

(a) A PSF image for a small animal imaging SPECT setup obtained with single pinhole, CsI:Tl crystal and PSAPD. A ^{99m}Tc -pertechnetate source with 370 MBq activity in a syringe is imaged from far-field (1 m away from the pinhole) onto the detector. (b) A line profile of the PSF after Gaussian fit shows submillimeter (0.7 mm) FWHM resolution.

Fig. 4. Measured energy spectrum of $^{99\text{m}}\text{Tc}$ using the PSAPD optically coupled to a continuous CsI:Tl scintillator. A 16% FWHM energy resolution at the 140 keV photopeak of $^{99\text{m}}\text{Tc}$ source was measured.

Fig. 5.

Schematic drawing of our CsI:Tl/PSAPD SPECT system setup with a single tungsten knife-edge pinhole used for the mouse heart phantom study. A mouse heart phantom filled with an aqueous solution of $^{99\text{m}}\text{Tc}$ -pertechnetate is projected through the pinhole with a 0.5 mm diameter aperture onto the CsI:Tl/PSAPD. The inset shows the dimensions of the mouse heart phantom with a defect lesion used for our experimental measurement.

Fig. 6. Photograph of the SPECT small imaging system using an 8mm×8 mm PSAPD/CsI:Tl on an evaluation circuit board with five preamplifiers.

Fig. 7.

(a) A flood image measured with PSAPD and CsI:Tl scintillator using ^{99m}Tc -pertechnetate source. (b) The flood image after pincushion distortion correction.

Fig. 8.

Reconstructed images of mouse heart phantom with defect. (a) A long-axis view of the mouse heart phantom. The center rod of the phantom is visible as a cold area within the U-shaped activity distribution. (b) The other long-axis view of the phantom showing the cold defect area. At the upper-right side of image, the defect is visible as less concentrated activity. (c) Summed short-axis image of the phantom with defect. The location is indicated in Fig. 8(b). The defect is observable at the bottom part, where it shows less concentrated activity compared with the rest of activity distribution. (d) Circumferential profile of the mouse heart phantom slices shown in Fig. 8(c).