Title: A CdZnTe detector for MRI-compatible SPECT Systems

Topic area: Radionuclide Imaging Instrumentation

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1. Executive Summary

The key objective of this project is to develop the enabling technology for future MRI-compatible nuclear (e.g. SPECT) imaging system, and to demonstrate the feasibility of performing simultaneous MR and SPECT imaging studies of the same object. During the past three years, we have developed (a) a MRI-compatible ultrahigh resolution gamma ray detector and associated readout electronics, (b) a theoretical approach for modeling the effect of strong magnetic field on SPECT image quality, (c) a maximum-likelihood (ML) based reconstruction routine with correction for the MR-induced distortion. With this support, we have also constructed a four-head MR-compatible SPECT system and tested the system inside a 3-T clinical MR-scanner located on UI campus. The experimental results obtained with this system have clearly demonstrated that sub-500um spatial resolution can be achieved with a SPECT system operated inside a 3-T MRI scanner. During the past three years, we have accomplished most of the major objectives outlined in the original proposal. These research efforts have laid out a solid foundation the development of future MR-compatible SPECT systems for both pre-clinical and clinical imaging applications.

2. Research Progress

Specific Aim 1 (Year 1): Optimize the design of the CZT detector. *Fully accomplished.*

Specific Aim 2 (Year 1): Develop a novel readout system that combines both the ERPC ASIC and the NCI ASIC. *Fully accomplished.*

Specific Aim 3 (Year 1): Characterize the response of the CZT detectors under a strong magnetic field. *Fully accomplished.*

Specific Aim 4 (Year 2): Fabricate two modular MRI-compatible ERPC CZT detectors. *Fully accomplished.*

Specific Aim 5 (Year 2): Develop and evaluate a prototype MRI-compatible SPECT system. *Fully accomplished.*

2.1 The Development of the ERPC Detector Technology

During the course of this project, we have developed and refined a small-pixel CZT/CdTe detector platform, called energy-resolved photon-counting (ERPC) detector. The ERPC detector consists of multiple CZT detectors that are flip-chip bonded onto a newly developed readout ASIC. The ASIC is realized through a mixed signal, 4 metal 2 poly CMOS process based on commercial 350 nm technology. The overall dimensions of the ASIC are approximately 22 mm × 11 mm, accommodating a total of 2048 readout channels arranged in an array of 32×64 pixels. The pixel pitch size is 0.35 mm × 0.35 mm, which matches the pixel configuration of the CdZnTe or CdTe detectors in use. Each CMOS pixel has a bump-bonding pad of 25 μm in diameter. The pixel readout circuitry includes an AC-coupled charge-sensitive amplifier, a peak-hold (P/H) circuit, a comparator and a multi-function counter used for both photon counting and A-to-D conversion. The pixel circuitry also contains various logic units for controlling, address decoding, and selection between readout modes. The amplifier has a shaping time of ~1 μs. The comparator in each pixel has a typical differential topology that uses an external analog control voltage to adjust the threshold level. All the wire-bonding pads, including the control signals, power feeds, and output signals, are located on one side of the ASIC (as shown in Fig. 3.b in [8]). In order to compensate for the pixel-to-pixel variations in the channel offset and gain, each channel is also equipped with two 8-bit digital-to-analog converters (DACs). These allow accurate alignment of the readout channels on the detector.

One of the key features of the ERPC ASIC is the capability to perform on-pixel A-to-D conversion with variable precision. Following an interaction in the detector, the

Fig. 1: Pixel circuitry implemented in the EPRC ASIC.

trigger signal from an anode pixel is used to initiate a time-to-digital converter (TDC) located on the same pixel. At the same time, the triggering signal is also used to start a ramp generator. The ramp generator is implemented using an 8-bit digital-to-analog converter (DAC) that is driven by a clock signal operating at 10 MHz. The ramp generator outputs a steadily increasing ramp signal that is compared with the signal amplitude held by the on-pixel P/H circuitry. When these two amplitudes are sufficiently close to each other, a trigger signal is generated to stop the TDC. Therefore, the output of the TDC is proportional to the signal amplitude induced on the corresponding anode pixel. Depending on the desired count rate capability, the analog signal can in principle be digitized with different precision by changing the step size of the ramp generator. For each event, it takes a maximum of $<10\ \mu\text{s}$ to perform a 6-bit A-to-D conversion and around $25.6\ \mu\text{s}$ for an 8-bit conversion. After the A-to-D conversion, the pixel address and the digital amplitude are sent out, and the ASIC is reset to receive future incoming events. A schematic of the pixel circuitry is shown in Fig. 1. Using this readout mode, each ASIC is in principle capable of handling 0.1 M counts per second (cps) with 6-bit ADC precision and 25 kcps with 8-bit precision. If necessary, the eight ASICs on each ERPC detector can be designed to operate independently. Therefore, the entire ERPC detector is capable of a count rate of 0.2 Mcps with 6 bit ADC precision. For high resolution SPECT imaging, the event rate exposed to gamma ray detectors is generally limited by the use of high-resolution collimation apertures [9, 10]. Therefore, the count rate of the ERPC detector should be more than adequate for most high-resolution SPECT applications.

In the current ERPC detector, the CdTe/ASIC hybrids are wire-bonded to digital readout printed circuit boards (PCBs), as shown in Fig. 2. These PCBs provide the power feed, logic and timing signals, and data pathway for the ASICs. Each readout board also has a 32 MB data buffer for temporary storage of pixel addresses and digital signal amplitudes. The readout operation of the camera is controlled by FPGAs mounted on the digital boards, which act as a bridge between the ERPC ASICs and the control software. For the ERPC detector, a universal threshold is used for all readout channels. The threshold level is controlled by an 8-bit DAC located

Fig. 2: **Left:** A prototype ERPC detector with eight detector hybrids, offering a detection area of $4.4\ \text{cm} \times 4.4\ \text{cm}$. Note that in this prototype setup, the readout PCBs are located on two ends of the detection-area. **Right:** A compact ERPC CdTe detector with the readout circuitry behind the detection area. This detector will be the basis for the proposed MRI compatible CZT detector.

Fig. 3: CdTe and CZT detectors evaluated with the ERPC readout system.

Fig. 4: Measured Co-57 energy spectra. The energy information was obtained by adding signals from 9 adjacent pixels together. Position 1-8 indicates 8 equally spaced depth-of-interaction positions below a given anode pixel. The experimental data was obtained by scanning a fine pencil-beam of Co-57 gamma rays with an angle of incidence of 35 degrees.

on the readout board. The selectable threshold level has a resolution corresponding to 0.46 keV. The eight ASICs are mounted onto a copper back-plate that is attached to a Peltier cooling unit for heat dissipation. The digital PCBs are connected to the host PC through either a USB 2.0 or a CameraLink interface.

The spatial and energy resolutions of the ERPC detector have previously been reported in [8]. With the first generation prototype as shown in Fig. 2, most readout channels have an energy resolution between 2 and 3.5 keV. Fig. 4 shows a Co-57 energy spectrum measured on a selected channel. Typical energy spectrum with all events detected on the entire camera, after careful alignment of all readout channels on the camera, has a FWHM of ~4 keV around the 122-keV photopeak. This is slightly worse than the energy resolution achievable on individual channels. This degradation is due to the remaining misalignment between the readout channels. An energy resolution of 4 keV should allow a nice separation between gamma ray lines associated with most radioisotopes commonly used for SPECT imaging applications.

2.2 Development of a Sub-500 μm Resolution MRI-Compatible SPECT System

The long-term goal of this project is to develop a sub-500 μm resolution MRI-compatible SPECT system as shown in Fig. 5. This system will consist of multiple ERPC detector modules, each having a detection-area of 4.4 cm x 4.4 cm. The ERPC detector architecture offers several attractive features for this application. It utilizes pixelated CdTe detectors and a custom-designed CMOS readout system to provide an excellent intrinsic resolution in 3-D – around 350 μm in X and Y directions, and sub-500 μm along the depth of the detector, which is well suited for use in a compact and ultrahigh resolution SPECT system. The ERPC detector has an excellent MRI-compatibility, as demonstrated in a series of preliminary studies. In order to demonstrate the feasibility of using the ERPC detectors for the proposed SPECT system, we have constructed a four-head MRI-compatible SPECT system and carried out a series of experimental studies. These effects will be detailed in the following sections.

2.3 Development of a Prototype MRI-Compatible SPECT System

As one of the major achievement through this project, we have developed a prototype MRI-compatible SPECT system and conducted a series of SPECT imaging studies using this system installed inside a 3T clinical brain

Fig. 5: **Left:** Schematic of the proposed SPECT/MRI system. It consists of the following components: 1) A non-magnetic gantry, (2) MRI bore with ~20 cm in diameter with the gradient coil in place, (3) the existing patient-bed and a dedicated animal holder fixed atop, (4) non-magnetic detector holder made of plexiglass and with an O. D. of ~18 cm, (5) eight ERPC CZT detectors with front-end readout PCBs, (6) collimation apertures, (7) RF coil built around a plastic tube of ~4 cm diameter. **Right:** Cross-section of the proposed MRI-compatible SPECT system.

MR scanner. The prototype MRI-compatible SPECT system consists of four ERPC modular detectors installed on a non-magnetic system gantry as shown in Fig. 6 (in the figure, there is only one detector attached). It consists of a plexiglass structure mounted on a copped plate, which is in turn installed on aluminum beam that allows the who setup to be rotated inside the MR scanner. The photo of the system also shows the pipes carrying compressed air for detector cooling purpose. In our future effort, we will produce an upgraded system gantry that has a more compact profile fitted to the shape of the detector ring and uses carbon-fiber material to replace plexglass to provide a better mechanical strength and a lighter weight. The ERPC detectors are encapsulated in a compact copper housing that has ventilation channels running through the detectors for heat-dissipation. The connection between the detectors and remote control PCs is provide by cables of 10 m length. The system can be rotated inside the MR scanner to obtain a sufficient angular sampling.

As reported in our previous publications [11, 12], we have experimentally evaluated several materials, including copper beryllium, tungsten carbide, lead, pure tungsten, tungsten powder composite, for making MRI-compatible gamma ray apertures. In this study, we have used a simple MRI phantom consisting of three sections with different features. For a short T_1 relaxation time, the phantom was filled with a 3 mM Cu_2SO_4 solution ($T_1 = 150$ ms). The phantom was placed inside a horizontal imaging scanner (Oxford Instruments, Abington, UK) equipped with a Unity/Inova console (Varian, Palo Alto, CA) operating at 4.7 T with a bore of 22 cm internal diameter. A custom-made high-pass “birdcage” transmitter/receiver RF coil, with an internal diameter of 3.0 cm, was used. A spin-echo multislice pulse sequence was employed. To test the MR compatibility of the aperture materials, we attached the detector and test apertures against the outer surface of a custom-built RF-coil. Several MR images of the phantom, acquired without and with the presence of the detector and collimators are shown in Fig. 7 [11, 12]. Among the

Fig. 7: MR images of a phantom with the presence of certain SPECT components. The images were acquired with the spin echo sequence that is routinely used for mouse brain studies.

Fig. 6: Upper: A prototype MRI-compatible SPECT system installed on a Siemens 3T MR scanner. Lower left: The non-magnetic gantry with a single ERPC detector; Lower right: A collimation aperture made of multiple layers of a 0.5 mm thick pure tungsten sheet.

collimator materials compared, the multi-layer pure tungsten aperture offers the best option. It has an adequate stopping power for ultrahigh-resolution SPECT imaging, while maintaining a reasonable MR image quality [11-13].

We have used the electric-discharge machining (EDM) technique to produce pinholes of 75 μm to 500 μm diameter on pure tungsten sheet of 0.5-6 mm in thickness. Example of the SPECT apertures produced using this technique can be found in [8, 14, 15]. For SPECT imaging at 140keV, the apertures consist of multiple layers of pure tungsten sheets of 500 μm thickness (lower-right panel in Fig. 6). Pinholes of 300-500 μm will be fabricated with the angle-of-acceptance ranging between 60 degrees.

2.4 Development of an Image Reconstruction Routine for SPECT Imaging in MRI

For CdTe and CZT detectors working inside a MR scanner, the magnetic field exerts the Lorentz force on moving charge carriers, which alters their drifting trajectories inside the detector. This causes the so-called *field-induced distortion* as shown in Figs. 8 and 9. Over the past few years, we have developed a theoretical approach for modeling this effect precisely. This model has been incorporated into a dedicated reconstruction process, which serves as the key for achieving ultrahigh resolution SPECT images inside MR scanner.

Theoretical modeling of charge transport. The charge transport under electric field and magnetic field can be modeled by the Boltzmann transport equation [16]. Its solution shows that the response of electrons to the magnetic force differs slightly from the response of electrons to the electric force. Instead of the mobility of electrons μ , which is referred to the applied electric field, one should use a new Hall mobility μ_H . The difference between these two mobility's in our physical picture of electrons suffering scattering during their transport, is a different kind of "average" time relevant for electric and magnetic force. The drifting velocity, being proportional to the applied force, can be obtained as [17]

$$\begin{bmatrix} v_x \\ v_y \\ v_z \end{bmatrix} = -\frac{\mu}{1 + \mu_H^2 B^2} \times \begin{bmatrix} 1 + \mu_H^2 B_x^2 & \mu_H^2 B_x B_y - \mu_H B_z & \mu_H^2 B_x B_z + \mu_H B_y \\ \mu_H^2 B_x B_y + \mu_H B_z & 1 + \mu_H^2 B_y^2 & \mu_H^2 B_y B_z - \mu_H B_x \\ \mu_H^2 B_x B_z - \mu_H B_y & \mu_H^2 B_y B_z + \mu_H B_x & 1 + \mu_H^2 B_z^2 \end{bmatrix} \times \begin{bmatrix} E_x \\ E_y \\ E_z \end{bmatrix}, \quad (1)$$

where μ is the charge carrier mobility and μ_H is the Hall mobility. B_x, y and z and E_x, y and z are the components of magnetic field and electric fields in three directions. In the simplest form, where $\mathbf{E} = E_x$ and $\mathbf{B} = B_y$, one has

$$\begin{bmatrix} v_x \\ v_y \\ v_z \end{bmatrix} = -\frac{\mu}{1 + \mu_H^2 B^2} \times \begin{bmatrix} E_x \\ 0 \\ -\mu_H B_y E_x \end{bmatrix}. \quad (2)$$

In this model, the Lorentz angle, θ , for electrons drifting inside the ERPC detector could be derived using the following equation [17],

$$\tan(\theta) = \mu_H B. \quad (3)$$

Under the 9.4 T magnetic field, the Lorentz angle θ is roughly 45 degrees for a CdTe detector of 2 mm thickness and with 300 V bias.

Comprehensive modeling of detector response. The effect of Lorentz force on charge transport is incorporated into a comprehensive Monte Carlo simulation that accounts for (a) the transport of gamma rays and secondary particles, (b) the charge-collection process (charge carrier drifting, repulsion and diffusion) in a CdTe crystal, (c) the induced charge on electrodes that is derived based on the weighting potential from a commercial package Maxwell, (d) the effect of the magnetic field on carrier drift trajectory and (e) the response of CR-RC shapers and the discrimination process of the proposed readout system. A diagram of this simulation package is shown in Fig. 10. This effort will allow us to derive the mean response of the ERPC detector for single-site interactions occurred at any given locations inside the detector, which will be used in the reconstruction routine to recover high resolution SPECT images.

Fig. 8: Geometry of the beam-scanning measurement. The cross section of the beam is 100 μm x 100 μm . The incident angle of the beam is 45 degree.

Fig. 9: Compare modeled and measured 2-D event distributions on four adjacent pixels with and without the 3T M-field.

Fig. 10: Schematic of the simulation package for modeling the response of the ERPC detectors inside strong magnetic field.

of a 2 mm thickness CdTe detector operated inside a 3T magnet. The results demonstrated an excellent agreement between modeled and measured detector response. Further studies have been reported in the recent IEEE NSS/MIC meeting in Knoxville.

The importance of a precise detector response function for SPECT imaging inside MR scanners has been demonstrated by a preliminary experimental study. Two ERPC CdTe detectors of 2 mm thickness was installed on the experimental setup shown in Fig. 6. Each detector was coupled to an aperture with 9 pinholes of 300 μm diameter. Both detector-aperture and aperture-axis distances were around 3.5 cm. The detector was rotated around a resolution phantom filled with 2.5 mCi Tc-99m solution. We have repeated the measurement inside and outside the 3 T MR scanner for comparison. The experimentally acquired phantom images are shown in Fig. 13. Clearly, the proposed performance target of 500 μm SPECT resolution can be achieved for with the prototype system operated inside a clinical MR scanner. The precise modeling of detector response in strong magnetic field has greatly helped to resolve the 0.5 mm diameter hot rods in the phantom.

Fig. 11: Left panel: A non-magnetic x-y and tilting stage and pencil-beam collimator designed for evaluating the performance of imaging detectors inside a 3 T MRI scanner. Right panel: Experimental setup for testing detectors inside a 3 T Siemens MRI scanner.

Experimental validation. To validate and optimize the detector modeling effort, we have compared the modeled detector responses with experimental data acquired with actual ERPC detectors operated inside the 3T magnet. For this measurement, a single ERPC CdTe detectors was scanned with gamma ray beams in two geometries. The first one uses a “parallel” gamma ray beam of 100 μm width to irradiate the detector from various incident angles (Fig. 11). The second one have several pinholes of 200 μm diameter placed in front of the detector, and a Co-57 point source moving around known locations. This measurement geometry allowed us to create more realistic incident beams typically seen in SPECT imaging. The experimentally derived projection data was compared with theoretical modeled results for determining the accuracy of the modeling.

Fig. 12 shows a comparison between measured and simulated detector response function (distribution of detected events across a number of adjacent pixels)

Fig. 12: Compare the modeled and measured event distributions on four adjacent pixels with and without the 3T M-field. Note that these results show an excellent agreement between measured and modeled response functions for the 2 mm thickness CdTe detector.

Fig. 13: Experimentally acquired phantom image obtained with the setup shown in Fig. 6. A single ERPC detector (1 mm thickness, CdTe) were rotated with 30 angular steps. The phantom contains 2.5m Ci of Tc-99m solution. Images were reconstructed with OSEM algorithm with 200 iterations.

In this project, we have clearly achieved the specific aims outlined in the original proposal. In particular, we have made significant progress in the development of several key components towards future MRI-compatible SPECT instrumentations, which include (a) a MRI-compatible ultrahigh resolution gamma ray detector and associated readout electronics, (b) a theoretical approach for modeling the effect of strong magnetic field on SPECT image quality, (c) a maximum-likelihood (ML) based reconstruction routine with correction for the MR-induced distortion.

Within this support, we have assembled a four-head MR-compatible SPECT system and tested the system inside a 3-T clinical MR-scanner located on UI campus. The experimental results obtained with this system have clearly demonstrated that sub-500um spatial resolution can be achieved with a SPECT system operated inside a 3-T MRI scanner. Based on these progresses, we have recently secured a R01 grant from NIBIB to continue the development of a full-scale SPECT system for use in a high-field (9T) MR scanner located at the University of Chicago. This effort will hopefully lead to a novel SPECT system with unprecedented imaging capability, offered in conjunction with the excellent soft-tissue contrast from a state-of-art MR scanner.

3. Publications

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