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Multi-pinhole SPECT Imaging with Silicon Strip Detectors

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Abstract

Silicon double-sided strip detectors offer outstanding intrinsic spatial resolution with reasonable detection efficiency for iodine-125 emissions. This spatial resolution allows for multiple-pinhole imaging at low magnification, minimizing the problem of multiplexing. We have conducted imaging studies using a prototype system that utilizes a detector of 300-micrometer thickness and 50-micrometer strip pitch together with a 23-pinhole collimator. These studies include an investigation of the synthetic-collimator imaging approach, which combines multiple-pinhole projections acquired at multiple magnifications to obtain tomographic reconstructions from limited-angle data using the ML-EM algorithm. Sub-millimeter spatial resolution was obtained, demonstrating the basic validity of this approach.

I. INTRODUCTION

THE ability to achieve the spatial resolution required for small-animal imaging applications using pinhole SPECT has been amply demonstrated over the past fifteen years [1], [2], [3], [4]. Practical applications in small-animal imaging also place demands on the sensitivity of the imaging system, and more recently several groups have sought to increase the sensitivity through the use of multiple-pinhole apertures in combination with either conventional gamma cameras [5], [6] or custom-built scintillator cameras [4], [7]. In these approaches, magnification of the projected image onto a detector of modest intrinsic spatial resolution (~ 1 -3 mm) is used to obtain high spatial resolution in the reconstructed images (< 1.5 mm).

Our approach to multiple-pinhole imaging is to utilize a radiation detector with intrinsic spatial resolution more than an order of magnitude better than these scintillator-based approaches. The chief advantage of such an approach is that equivalent image resolutions can be achieved with much lower magnification. As an example, Fig. 1 shows the planar image resolutions as a function of magnification for an object 2.5 cm from a 300 μm -diameter pinhole for detectors with two different spatial resolutions, where the calculations were performed using the standard formula for pinhole planar image resolution [8]. For any given multiple-pinhole configuration, the reduction in the required magnification results in reduced multiplexing of the pinhole projections and a smaller required total detector area.

Previous work has also shown the potential power of combining high-spatial-resolution detectors ($<0.5\text{mm}$ FWHM) with multiple-pinhole apertures in a synthetic-collimator imaging configuration [9]. Wilson and colleagues showed that by collecting projection data at multiple magnifications via variation of the aperture-detector spacing, high-resolution tomographic images can be obtained using iterative reconstruction even in the presence of multiplexing. These simulations further showed that high-quality reconstructions of radiotracer distributions might be possible even when the object is imaged from only a single collimator position, i.e. no rotation of either subject or imaging system.

We have chosen to use a silicon double-sided strip detector (DSSD) to explore experimentally the potential of this approach. Silicon detectors are a suitable choice for the high-spatial resolution detector needed for a synthetic-collimator imaging system because the technology is well developed from extensive use in high-energy physics experiments. The use of photolithography to pattern the readout electrodes allows manufacture of detectors with strip pitches down to $20\text{ }\mu\text{m}$. The reason that they have not found widespread use to date in nuclear imaging is because they have very low efficiency at the gamma-ray energies typically of interest (i.e. 140 keV). The detection efficiency is useable, however, for the distribution of photon energies emitted in the decay of ^{125}I ($27.2\text{--}35.5\text{ keV}$) — about 10% total detection efficiency in a standard, $300\text{-}\mu\text{m}$ thick piece of silicon. Silicon detectors of greater thickness can be fabricated, increasing the detection efficiency for ^{125}I emissions. The modest detection efficiency, however, might be useful in the synthetic-collimator approach, as a stack of detectors could be employed to collect projection data at multiple magnifications simultaneously, since much of the incident radiation passes through an individual detector without interacting. The double-sided strip detector geometry facilitates such a stacked configuration because no inactive material need intervene between detectors.

Because ^{125}I is widely used in molecular biology, owing to the wide array of molecules that can be easily iodinated and to the fact that its half-life (59.4 days) is convenient for radiolabeling, such a system tailored for the imaging of ^{125}I -labeled tracers is potentially of practical use as well. Several recent reports of systems tailored for small-animal imaging of ^{125}I using novel detector systems indicate both demand for such imaging capability and interest in ^{125}I imaging as a testbed for new imaging concepts [10], [11], [12].

The objective of the work presented here was to demonstrate the potential of silicon DSSDs for pinhole SPECT, in particular the ability to image at low magnification. As part of this study we conducted an initial, qualitative investigation of the impact of using data from multiple pinhole magnifications and limited viewing angles in the SPECT reconstructions.

II. System Description

We have developed a prototype system to demonstrate the potential for high-resolution imaging using silicon detectors together with multiple-pinhole collimation and to explore issues relevant to the design of a fully customized system. The compact nature of the detector and the relative ease of collimating photons in the 30 keV energy range allow easy exploration of different imaging configurations.

A. Silicon Detector and Readout Electronics

The silicon detector used for the prototype imaging system is a $300\text{ }\mu\text{m}$ -thick DSSD. It has 560 strips on the p-side and 1260 on the n-side, at a strip pitch of $50\text{ }\mu\text{m}$ on both sides. The detector possesses over 700,000 resolvable spatial elements spread over an active area of $28\text{ mm} \times 63\text{ mm}$.

The electronics utilize the VaTaGP2.2 application-specific integrated circuit (ASIC), manufactured by IDEAS ASA, Norway (now Gamma Medica-Ideas). Each strip on the detector is wirebonded to a separate channel of a 128-channel ASIC, which provides a preamplifier, shaper amp, comparator, and sample-and-hold circuitry. An external trigger threshold is set for each detector side independently. The ASICs also have internal 3-bit trim DACs that can be used to vary the trigger level for each channel individually about the global threshold to attain better triggering uniformity. Individual noisy strips can be disabled, eliminating a possible source of spurious events from the data stream. The entire system is event-driven with a sparse readout that presents the address of the strip that triggered the readout, the pulse height of that channel, and the pulse heights of its nearest neighbors.

The data acquisition is controlled by three field-programmable gate arrays (FPGAs), one for each detector side plus a master FPGA. Event readout is initiated when the master FPGA receives trigger signals from both detector sides within its coincidence window. The FPGAs for each detector side then generate the necessary clocking sequence to extract data from the ASICs and transfer the data to the master FPGA. List-mode data then are passed from the master FPGA to the host PC through a National Instruments data-acquisition PCI card. While the time to read out a single event is approximately 15 microseconds, suggesting a reasonably high count-rate capability, we found the system performance to be most reliable at count rates below about 1 kHz. During the sparse readout of the individual detector sides, only the first channel in the sequence from first to last strip that has its trigger token set is read out, and this token is set for any strip that passed threshold, whether or not it was involved in the coincidence. Because of this, it is possible to read as the hit channel one that did not create the signal generating the coincidence, resulting in incorrectly assigning the location of the event. Many of these events can be removed from the data stream via a pulse-height cut, but the real events are lost. Setting thresholds low to maximize the trigger efficiency also creates a situation in which some strips generate noise triggers at a rate dependent on the true event rate (i.e., no noise triggers if the source is removed), presumably due to feedback from the digital readout process. These effects were difficult to fully characterize but exhibited a clear dependence on event rates. They are not fundamental to double-sided detectors, but rather are particular to this system architecture.

B. Multiple-Pinhole Apertures

We have chosen to use molybdenum for our collimator material because its K-edge at 20 keV results in a high attenuation factor over the energy range of interest despite its low atomic number and density ($Z=42$, $\rho = 10.22 \text{ g/cm}^3$) as compared to gold ($Z=79$, $\rho = 19.32 \text{ g/cm}^3$) and tungsten ($Z=74$, $\rho = 19.3 \text{ g/cm}^3$). The linear attenuation coefficient of molybdenum is plotted alongside several other common collimator materials in Fig. 2, showing the suitability of molybdenum as a collimator material for imaging emissions from ^{125}I decay. In fact, a 500 μm -thick piece of molybdenum is sufficient for use as an aperture. This material has the added advantages of being less expensive than gold and easier to machine than lead or tungsten. While we previously utilized apertures with high-precision pinholes fashioned using electron-discharge machining [14], we have developed a technique for making apertures using micro-drill bits that enables rapid, inexpensive production of imaging apertures. Drilling a hole with a 300- μm drill bit and then drilling partway through with a 500- μm drill bit results in a pinhole that provides a reasonable approximation of a single knife-edge with a full opening angle of 76° (38° cone angle). Fig. 3 shows the layout for a 23-pinhole aperture produced using this technique, while Fig. 4 is an electron micrograph image of one of these pinholes.

C. Simulation studies with MCNP

To maximize the detection efficiency of the silicon DSSDs for low-energy photon detection, we would like to set a sufficiently low trigger threshold to detect all photons that interact in

the silicon bulk and produce charges collected either by a single strip on each side or by multiple strips due to charge sharing effects. If one assumes that the collected charges will be distributed across no more than two strips on a detector side, then attaining the maximum detection efficiency requires setting a trigger threshold level that is less than half that of the lowest photon energy to be detected. However, noise limits how low the threshold can be set while avoiding excessive noise triggers, and some amount of channel-to-channel threshold variation is likely to be present even after adjusting the trim DACs in the ASICs.

We have used simulation studies to determine the maximum detection efficiency in an ideal silicon detector and compare it with experimental efficiencies of the current silicon DSSD at different threshold levels to estimate the lowest boundaries that could be set on trigger thresholds on both p- and n-strips with minimum number of noise-triggers. This approach was used because the limited count-rate capability of the system (described in II.A) complicated the direct assessment of efficiency from flood illumination. For the simulation study, we modeled a 300- μm silicon detector together with a pinhole collimator made of molybdenum using MCNP5 simulations, a general purpose Monte Carlo code [15]. For the collimator parameters in the simulation we used a knife-edge pinhole with 38° cone angle, 300 μm neck diameter and 500- μm collimator thickness. A point source was placed in front of the collimator at several different distances. The comparison of simulated to measured data indicated that when thresholds were set to minimize noise triggers the count rate fell nearly a factor of three below the expected. While it is difficult to account for this discrepancy in detail, there are contributions from dead or disabled channels, events lost due to charge being shared between strips, and residual channel-to-channel threshold variations. We expect these problems to be greatly reduced in the next-generation system described in Section IV.

In conjunction with these same simulation studies, the photon flux on the detector surface could be considered as a useful tool to investigate the fraction of photons that entered the silicon detector after either scattering in molybdenum or directly penetrating through the collimator material, particularly in the area around the pinhole edge. Anger included the penetration effects on the pinhole sensitivity by including an “effective diameter” into the analytical calculation [8]. Metzler derived a more detailed mathematical formulation of pinhole sensitivity for pinhole diameters between 1 and 4 mm [16], to make an accurate estimation of the penetrative sensitivity, particularly for point sources where the penetration vector is not perpendicular to the detector surface. The penetration effect becomes even more pronounced in collimator systems with micro-pinholes. One benefit of SPECT imaging with low-energy photons is the reduced probability of penetration and scatter in collimators. Van der Have and Beekman [17] investigated the photon penetration and scatter fractions in micro-pinholes made of several materials with Monte Carlo simulations performed for ^{125}I (27-35 keV) and $^{99\text{m}}\text{Tc}$ (140 keV) and pinhole diameters ranging between 50 and 500 μm , indicating a very low fraction of scattered photons and a fairly low fraction of penetration photons for ^{125}I in all of those materials. Our simulation study investigates a micro-pinhole molybdenum collimator. Both analytical calculations [16] and MCNP5 simulations were used in our study to determine the fraction of penetration photons for a point source positioned 20 mm away from the pinhole center. Collimator parameters used for this simulation were 300 μm for the pinhole diameter and 500 μm for the thickness of the molybdenum. The two methods showed good agreement, as can be seen in Table I. The MCNP5 simulations also allowed identification of photons that Compton scattered in the molybdenum pinhole before reaching the detector. The fraction of Compton-scattered photons was estimated to be 1.8%.

III. Imaging Studies

A. Intrinsic Spatial Resolution

The spatial resolution of the DSSD is expected to be close to its strip pitch, which is 50 μm on both sides, if no sub-strip position estimation method is used. For the experimental measurement of the intrinsic resolution, then, the size of the source projection on the detector should be sufficiently small with respect to the strip pitch to approximate an impulse to the detector. However, the detector housing of the prototype restricted our ability to produce such a source distribution due to a gap of approximately 7 mm between the entrance window and the detector surface. The spatial resolution was tested by placing a tungsten slit of 10 μm width on the detector entrance window and a small vial of ^{125}I 25 cm from the slit. The slit was placed at an angle with respect to the orthogonal detector strips, and the width of the distribution of radiation at the detector surface was estimated to be 90 μm . The FWHM of the detector response convolved with projection profile was determined by fitting a Gaussian to the profile along one strip direction (the vertical direction in Fig. 5(a)) at several different points. The mean FWHM value taken from these multiple measurements was 167 μm . An example of one such measurement is shown in Fig. 5(b). While precise measurement of the spatial resolution was difficult due to the poorly constrained geometry as well as the complications in deconvolving the detector discretization and a finite, square-profile source, the results are consistent with a FWHM spatial resolution that is less than three times the strip pitch.

B. Energy Resolution

Because the maximum energy loss when a 27 keV photon undergoes a Compton scattering is 2.6 keV, the use of energy windowing to suppress scatter contribution to an image is of little use, particularly considering that there are several closely spaced emissions from ^{125}I between 27 and 35 keV. The key factor is for the signal to noise to be sufficient that trigger thresholds can be set low enough to capture events even when charge is shared across strips when photons interact in the region between two strips.

Using software provided by the manufacturer, a gain calibration was performed for all 640 p-strips using an ^{241}Am source. The resulting gain and offset values for each strip are applied to the ADC values after subtraction of the stored pedestal value for that strip. With the nearest neighbor readout implemented, the energy measurements of one or both neighbors can be added to that of the strip that triggered the readout if desired, although there is a corresponding increase in the noise when this is done. In practice one would generally only add the signals from the neighbors if they exceeded some threshold indicative of significant charge sharing for that event. Fig. 6 shows energy spectra for both ^{125}I and $^{99\text{m}}\text{Tc}$ that are composed of the pulse-height measurements from the hit strip only (ie. no nearest neighbor readout) summed across all 128 channels of a single ASIC. The silicon detector has negligible photopeak efficiency for the 140 keV gamma ray (and is thus not shown in Fig. 6), but the spectrum does clearly show both the Compton edge near 50 keV and the 18 keV X-ray line from $^{99\text{m}}\text{Tc}$ decay, indicating that the trigger efficiency should be high for ^{125}I emissions even in the presence of charge sharing.

C. SPECT Imaging

We have performed imaging studies utilizing the 23-pinhole aperture shown in Fig. 3 to image a phantom consisting of several glass capillary tubes (1.1 mm I.D.) filled with a solution of Na^{125}I and inserted into holes drilled in a 25.4 mm-diameter polycarbonate cylinder. The total activity in the phantom was approximately 1 mCi. The purpose of the cylinder was to simulate an attenuating medium similar in size and density to a mouse.

Projection data were collected for one hour each at eight angular positions, each separated by 45 degrees, and at two magnifications for each view. An average of 310,000 counts was recorded in each projection image. For this study the phantom was rotated in front of the aperture-detector assembly. The aperture-to-detector distances were 6.7 mm and 13.7 mm, and the radius of rotation was 25.8 mm. Note that this acquisition configuration resulted in a substantial de-magnification of the imaged field of view onto the detector surface. Fig. 7 provides a schematic view of the acquisition geometry.

Prior to image reconstruction, the projection data were downsampled to 200 μm -isotropic effective detector pixel size to reduce the impact of nonfunctioning detector strips and efficiency variations. An image of one set of projection data acquired at the smaller magnification is shown in Fig. 8 after this downsampling. A single transverse slice of the reconstructed image after 10 iterations of maximum-likelihood expectation-maximization reconstruction is shown in Fig. 9, alongside a schematic view of the phantom. The reconstructed slice shown in Fig. 9 utilized only the projection data collected at the lower magnification. Fig. 10 shows the same slice from a reconstruction done using only data from the larger magnification on the left, as well as a reconstruction done using all of the projection data. While the capillaries are quite well resolved in all cases, it is apparent that the best combination of spatial resolution and contrast is achieved in the reconstruction utilizing the full projection data set.

The spatial resolution of the reconstructed image using the full dataset was estimated by fitting a Gaussian convolved with the 1.1 mm diameter of the capillaries to line profiles through the image slices. Furthermore, variations of the spatial resolution across the imaging plane and along the axial direction were assessed from the variations in the width of the fitted Gaussian in the transverse images of three capillaries from the upper “V” shape. The average deconvolved FWHM from all three capillaries was 0.7 mm (Fig. 11) with less than 0.1 mm variation along the axial direction (Fig. 12). The center-to-center spacing of the capillaries in the upper “V” was 2.5 mm.

D.Synthetic Collimator Studies

We also investigated the ability to perform tomographic reconstructions utilizing only a subset of the angular views. The left of Fig. 13 shows a transverse slice of the reconstruction using only data acquired at two projection angles separated by 90 degrees, but including both magnifications. While the image quality is somewhat degraded relative to reconstructions done using data from all projection angles, it is largely free of serious distortions or artifacts. In contrast, the reconstruction shown on the right in Fig. 13 that used data from both magnifications but only a single projection angle shows poor resolution in the direction moving away from the aperture-detector assembly, as is typical of such limited-angle-tomography schemes.

One of the original motivations for the synthetic-collimator imaging approach was to synthesize ideal planar projections free of the depth-dependent resolution degradation from which parallel-hole collimation suffers. To investigate the capabilities of the prototype system in this regard, the tomographic reconstruction shown on the left in Fig. 13 was reprojected in a plane parallel to the aperture. This synthesized planar image is shown on the left in Fig. 14. For comparison, a reprojection of the reconstruction carried out using the full data set (Fig. 10, right) is shown on the right in Fig. 14. The planar image created from the single viewing angle shows greater intensity variations in the vertical direction due to uncorrected variations in detector efficiency, but otherwise is of high quality.

IV. Conclusions

We have demonstrated the ability to perform tomographic reconstructions of multi-pinhole data acquired at multiple magnifications using a silicon double-sided strip detector of high spatial resolution. We have also explored the ability to reconstruct images using data from a small number of views using our prototype imaging system. We believe this approach is well suited for imaging applications requiring high spatial resolution over a small field of view, such as mouse brain imaging.

The next step is to develop a fully customized system that will significantly improve system sensitivity through the use of silicon detectors that are both larger in active area ($6\text{ cm} \times 6\text{ cm}$) and thicker (1 mm). In addition, new ASICs have been designed to improve the noise performance and the threshold uniformity, which should also lead to improved sensitivity. The detectors will be mounted in a transmission configuration so that projections at multiple magnifications can be acquired simultaneously by stacking two or more detectors behind an imaging aperture. The use of multiple detectors and multiple imaging heads should also improve the quality of the reconstructed images. In particular, the larger number of pinholes made possible with increased detector area will improve the angular sampling, which we expect will lead to improvements in the synthetic-collimator imaging capabilities.

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VI. References

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Fig. 1.

Resolution as a function of magnification for an object 2.5 cm in front of a 300 μm -diameter pinhole. The upper curve is the result if a detector with 1.5 mm spatial resolution is used, while the lower is with a detector of 0.05 mm spatial resolution.

Fig. 2. Attenuation curves of common collimator materials compared with molybdenum in the energy range between 10 and 50 keV [13].

Fig. 3. Drawing of the pinhole pattern for the 23-pinhole aperture. The dimensions are in millimeters.

Fig. 4. Electron micrograph of a pinhole of 300-micrometer diameter shown from the side in which a 500-micrometer recess has been drilled.

Fig. 5.

(a) Profile of the slit collimator on the silicon DSSD. Gaps in the distribution are due to dead or disabled detector strips. (b) One example of a profile along the vertical direction in (a) with a Gaussian fitted to the data.

Fig. 6.
Single-strip pulse-height spectra from all channels of one ASIC.

Fig. 7. Schematic view of the acquisition geometry for the SPECT imaging studies for the larger of the two magnifications. The arrows indicate that the phantom was rotated in front of the aperture (axis of rotation parallel to the short dimension of the detector), while the DSSD was translated to change the magnification. Figure is drawn to scale.

Fig. 8.

An example of the projection data acquired at the lower magnification with the dimensions of the silicon detector indicated.

Fig. 9.

A cross-sectional schematic of the phantom with length scale (left), and a transverse slice of the image reconstructed using only data acquired at the lower magnification (right).

Fig. 10. Transverse slices from reconstructions performed using only data from the larger magnification (left) and from all projection data (right).

Fig. 11.

Line profile from the transverse slice shown on the right in Fig. 10. The profile was taken across the top of the outer “V” of the phantom, intersecting the middle two capillaries of the inner “V”.

Fig. 12.

The FWHM of the fitted profiles from multiple transverse image slices of the capillary located at the bottom of the outer “V”. These profiles were taken from the image reconstructed using all of the projection data.

Fig. 13.

Transverse slice from reconstructions performed using data from both magnifications but only two viewing angles separated by 90° (left) and only a single viewing angle (right).

Fig. 14.

Reprojected planar views created from tomographic reconstructions using only data acquired from a single angle (left) and data from all angles (right).

TABLE I

FRACTION OF PENETRATIVE AND GEOMETRIC COLLIMATOR SENSITIVITY

	Geometric	Penetrative
Analytical calculations	89%	11%
Monte Carlo simulation	86%	14%