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High-resolution, anamorphic, adaptive small-animal SPECT imaging with silicon double-sided strip detectors

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Abstract

We are developing a prototype gamma-ray imaging system that consists of two sets of movable, keel-edged copper-tungsten blades configured as crossed slits. These apertures can be positioned independently between the object and detector, producing an anamorphic image in which the axial and transaxial magnifications are not constrained to be equal. The detector is a 60 mm × 60 mm, millimeter thick, one-megapixel silicon double-sided strip detector. The flexible nature of this system allows the application of adaptive imaging techniques. We will discuss system details, calibration and acquisition methods, and our progress towards biological imaging applications.

Keywords

SPECT; small-animal; anamorphic; adaptive; double-sided strip detector; silicon; crossed slits; ¹²⁵I; calibration; parameter estimation; contracting grid

1. INTRODUCTION

Small-animal SPECT imaging is a useful tool for studying disease biology and for monitoring response to treatment in rodent models. As interest has increased in imaging small lipid plaques such as those in Alzheimer's, Parkinsons, and atherosclerotic disease, so has the need for high-resolution imaging systems.¹ Some current pre-clinical systems allow high-magnification imaging, but with a fixed field of view (FOV).²⁻⁴ We will discuss the design and construction of a prototype SPECT system which offers flexible magnification in addition to high-resolution imaging and report on calibration challenges and current system status.

2. SYSTEM DESIGN

Small-animal SPECT imagers rely on imaging radioactive subjects through pinhole apertures onto typically square camera or rectangular faces. While these apertures can be made with high precision, a drawback is often the radial symmetry of the magnification; the subject being imaged rarely matches the aspect ratio of the camera, and much of the active

area of the detector is lost in imaging the empty space around the object. Some systems compensate for this loss by imaging over the FOV with a complicated scan; as an alternative, we would like to magnify the object such that the majority of the detector is filled by the entire region of interest.

2.1 Crossed slit apertures

This type of anamorphic magnification can be accomplished by replacing the pinhole with a pair of crossed slits, which essentially decouples the radially symmetric magnification of the pinhole into separate and independent axial and transaxial magnifications.⁵ When the vertical slit is positioned closer to the object than the horizontal slit, this configuration produces images with increased transaxial resolution as well as reconstructions with fewer axial artifacts.^{6, 7} Separating the vertical and horizontal slits results in an anamorphic projection of the object onto the detector face, and the magnifications in the x and y directions are set by adjusting the relative distances between the object, slits, and detector. A simplified schematic of this imaging configuration is illustrated in Figure 1(a).

The high-precision slits developed for this system consist of two pairs of 10-mm-thick machinable copper/tungsten blades with a 30-degree half-keel edge and 250- μm bevel. These blades are mounted to aluminum plates; one blade is fixed and the other is permitted to slide on captured brass ball bearings. Spring pressure between the blade plates maintains the parallel slit width as determined by linear actuators mounted on the side of the slit frame. A close-up view of the inner slit construction is provided in Figure 1(b).

2.2 High-resolution detector

Double-sided strip detectors (DSSDs) can be used to an advantage in SPECT imaging because they offer N^2 pixels but require only $2N$ sets of readout electronics. A DSSD consists of a bulk slab of semiconductor material with orthogonal sets of parallel conducting strips located on either side of the bulk, as shown in Figure 2(a). Each side of the detector triggers on detected events independently of the other; the true location of detected events can only be determined by matching time stamps between events on each side.⁸ Silicon, a material with relatively low atomic number, is nevertheless appropriate for detecting low-energy gamma rays such as those emitted by ^{125}I -labeled radiopharmaceuticals. Our detector is a 60 mm $\times$ 60 mm, millimeter-thick, megapixel silicon double-sided strip detector from Sintef and furnished with electronics by Gamma-Medica/Ideas, shown in Figure 2(b). This DSSD features 1024 conducting strips on each side, offering megapixel resolution with a 59- μm strip pitch.

2.3 Design specifications

In order to create a flexible imaging system, we allow computer-controlled adjustment of both slit and object locations. Each slit is mounted on an aluminum extrusion frame, and the detector is mounted in an opaque custom housing. Two linear stages, one rotation stage, and a motorized z -table control the object position. The slits are mounted to a dual-lead-screw stage which determines the relative distance between the slits; this stage is mounted to a second linear stage which positions both slits between the source and detector. The linear stages can be positioned in steps as low as 2.5- μm ; two additional linear actuators control

the slit widths with $0.05\ \mu\text{m}$ stepping resolution. A photograph of the assembled system is provided in Figure 3. The pictured configuration provides a FOV suitable for imaging rodent brains, and is adjustable to a maximum of $5\times$ magnification.

3. SYSTEM CALIBRATION

We anticipate that with precision-machined apertures and a high-resolution detector, this system will produce high-quality 3D reconstructions from a set of projection images, provided we can produce an accurate and reliable system calibration. The following section discusses the requirements and challenges associated with calibrating such an adaptable system.

3.1 System matrix acquisition strategies and challenges

Reconstructions based on projection data relies on determining an estimate of the imaged object which is consistent with the measured data, according to the imaging equation

$$\mathbf{g} = \mathbf{H}\mathbf{f} + \mathbf{n}, \quad (1)$$

where $\mathbf{f}$ is a $1 \times m$ vector of voxels in the object, $\mathbf{g}$ is a $1 \times n$ vector consisting of a concatenation of all pixels acquired of $\mathbf{f}$, and $\mathbf{n}$ represents noise acquired in the measurement process. The system matrix $\mathbf{H}$ is an $m \times n$ matrix which maps a region of interest in object space into the projected data of image space, and is a series of measurements of the point spread function (PSF) across the field of view of the imaging system. Each element $h_{i,j}$ represents the probability of an event emitted by a point source in position i being detected in pixel j . It is important to note that the dimensions of $\mathbf{H}$ increase linearly with increased resolution in both object space *and* image space. Our system uses high-resolution projections to produce a high-resolution reconstruction, which, for a voxel space of $101 \times 101 \times 101$, a megapixel detector, and 60 projection views, requires that the entire system matrix $\mathbf{H}$ consists of over 64 trillion elements.

If we were to attempt to measure one projection view of the system matrix by placing a point source at each voxel position with a one-minute acquisition, it would take 1.96 years. Certainly, some circumspection is advisable before attempting to directly measure and store such a matrix. It is of course possible to acquire sparse measurements of $\mathbf{H}$ and interpolate between the points to regenerate the full system matrix,^{9, 10} but the requirements to store such a matrix are daunting: a matrix representing 101^3 voxels viewed over 60 projections requires 235 TB of storage space. We can reduce the needed storage space by storing the sparse data, where only the non-zero portion of the point source projection is stored, decreasing the size of the matrix to 221 GB. We could simplify the sparse data even further, representing the nominally rectangular projection image as a set of six coefficients which describe the center location, height, width, amplitude, and rotation angle, reducing the storage to 1.38 GB. However, if we characterize the system as a whole by estimating the 11 geometric parameters which define the relative positions of the object, slits, and detector, we need only 0.04 kB of storage space; this also requires that we must calculate $\mathbf{H}$ matrix

elements on the fly as needed. Table 1 presents these conventional approaches to $\mathbf{H}$ matrix storage, as well as the storage space required for each.

3.2 Geometric model

Since the time and storage requirements for acquiring PSF measurements for all possible system configurations are impractical, it is more appropriate to use a subset of point source measurements to extract the geometric parameters which describe the system.

Bequé et. al. describe the geometric parameters necessary to characterize a single-pinhole SPECT camera;¹¹ several additional parameters are required to describe our system's multiple apertures. For a non-rotated detector with sides parallel to the horizontal and vertical slits, the center of the PSF projection on the 2D detector face (u, v) for a point source located at (x, y, z) can be expressed as:

$$u = -f_x \frac{x - m_x}{d_x - z} - (e_x - m_x) \quad (2a)$$

$$v = -f_y \frac{y - m_y}{d_y - z} - (e_y - m_y), \quad (2b)$$

where the parameters correspond to the descriptions listed in Table 2, and are also illustrated in Figure 4. In the more general case where the detector is not located in a plane parallel to the slits, we calculate the intersection of the central ray with a tilted detector plane (x', y', z') and rotate the resulting point back to the normal position to determine the absolute pixel position (u, v):

$$\begin{bmatrix} u \\ v \\ s_d \end{bmatrix} = R_{-\psi} R_{-\phi} R_{-\theta} \begin{bmatrix} x' \\ y' \\ z' \end{bmatrix}, \quad (3)$$

where s_d is the distance in the z -direction between the center of rotation of the object and the center of the detector, and $R_{\psi} R_{\phi} R_{\theta}$ are the three-dimensional rotation matrices given by:

$$R_{\psi} R_{\phi} R_{\theta} = \begin{bmatrix} \cos\psi & 0 & -\sin\psi \\ 0 & 1 & 0 \\ \sin\psi & 0 & \cos\psi \end{bmatrix} \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\phi & \sin\phi \\ 0 & -\sin\phi & \cos\phi \end{bmatrix} \begin{bmatrix} \cos\theta & \sin\theta & 0 \\ -\sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{bmatrix}. \quad (4)$$

This model assumes that the slits are oriented orthogonally with respect to each other, and that the object's axis of rotation is parallel to the vertical slit. It should also be noted that the point (u, v) as defined above is specified in units of distance and requires a further arithmetic transformation to obtain the actual pixel number.

3.3 Geometric data acquisition

We have developed a geometric calibration method which replaces the ideal ^{125}I point sources with therapeutic brachytherapy rods, which are 4.7 mm long with an 800- μm outer diameter, and can be treated as sealed sources to minimize the risk of radioactive

contamination. These rods are inserted into bores in a rapid-prototype-printed geometric calibration phantom, which allows us to reproducibly position the rods in height and radial spacing to mimic a desired FOV. A rendering of the phantom with inserted rods, shown in red, is provided in Figure 5(a); the printed phantom is also visible in Figure 3. The current phantom allows us to define a cylindrical FOV up to 35 mm in height with an 8-mm maximum radius.

To acquire the data necessary for estimating the geometric parameters, we position the geometric source such that the lowest brachytherapy rod is nearest to the vertical slit. Any initial offset in rotation is later estimated as to remove systematic error in angle. We acquire 181 projection images corresponding to a two-degree rotation step size, re-sampling at the starting position to verify complete rotation. Acquisition times are determined at the beginning of the calibration procedure such that each rod's projection contains at least 4500 events.

After measuring projections of the phantom through 360 degrees, we move both slits by a distance z (typically on the order of 10–50 mm) to reduce the magnification factor and acquire an additional 181 projection images of the calibration phantom. Measuring at multiple magnifications with the same source-to-detector distance s_d provides information necessary to estimate s_d when analyzing the acquired data.

Since the brachytherapy rods can by no means be considered a point source, we process each projection image, masking the region corresponding to each rod and calculating its center position. A sample projection image of the three brachytherapy rods illustrated in Figure 5(a) is shown in Figure 5(b), superimposed over the calculated center points for all projection images. Nonuniformity in the rods' internal activity distribution, visible in Figure 5(b), currently prevents the use of simple centroid calculations to determine the center of each rod along the axial direction of the FOV.

4. GEOMETRIC PARAMETER ESTIMATION

The calibration-data acquisition methods described in Section 3.3 are applicable to many SPECT imaging configurations. The following section describes the estimation techniques we apply to our system's calibration measurements to extract the necessary geometric parameters.

4.1 Contracting grid search

Several methods exist for extracting the geometric parameters from the calibration phantom data, but not all are immediately applicable to our adaptive system. Piatt and Zeng describe a backprojection-based estimation technique specifically for these crossed-slit apertures,¹² but performing these measurements with nonuniform brachytherapy rods complicates this technique. The most direct method for estimating the parameters uses a contracting grid method,¹³ in which we forward project an ideal phantom through sets of virtual system configurations using geometric parameters sampled from across the twelve-dimensional parameter space. The predicted data is compared to the measured data with a cost function that sums squared distances between predicted and observed locations for each data point.

The smallest squared-distance sum acquired from the samples indicates the starting parameter values for the next iteration of the contracting grid, which samples new parameters from a smaller region of the subspace surrounding the best result from the previous iteration.¹⁴

Iterating over a progressively refined parameter space allows us to converge on the best estimates for the system parameters, which satisfies

$$\{\hat{\Delta}, \hat{d}_x, \hat{d}_y, \hat{f}_x, \hat{f}_y, \hat{m}_x, \hat{m}_y, \hat{e}_x, \hat{e}_y, \hat{\theta}, \hat{\phi}, \hat{\psi}\} = \underset{\{\Delta, d_x, d_y, f_x, f_y, m_x, m_y, e_x, e_y, \theta, \phi, \psi\}}{\operatorname{argmin}} \sum_{i=1}^N ((u_{m,i} - u_{p,i})^2 + (v_{m,i} - v_{p,i})^2) \quad (5)$$

where (u_m, v_m) is the data measured by the system, (u_p, v_p) is the predicted data from the current set of estimated parameters for N data points (i.e., the product of the number of projections, sources, and slit positions).

4.2 Simulation study and measured data

The contracting-grid estimation procedure has been tested for both simulated and measured data. Data is simulated by forward-projecting an ideal point source representing the center of the brachytherapy rod through slits specified by user-generated system parameters and at multiple slit positions as described in Section 3.3. A uniformly-distributed random offset is added to each point (u, v) such that the new point (u', v') is located within an $n \times n$ pixel grid surrounding the original location.

Starting with user-supplied estimates of the geometric parameters, the contracting grid iterates through subsets of parameters to converge on the best estimate of all twelve unknown parameters. In simulations, we found that iterating over subsets of $\{(\Delta, d_x, d_y, f_x, f_y), (m_x, m_y, e_x, e_y), (\theta, \phi, \psi)\}$ provides the fastest convergence to the expected geometric parameters. The addition of an initial estimation step to determine an accurate estimate for reduces the number of total iterations required for the rest of the parameters to converge. Figure 6(a) plots simulated data with up to ± 5 pixels of random offset compared with the predicted values generated from the estimated geometric parameters.

Figure 6(b) shows the results using contracting grid estimation with the experimentally measured data shown in Figure 5(b). While there is reasonably good agreement between the measured and predicted data, it is likely that some of the small discrepancies are due to inaccuracies in determining the centers of the nonuniform brachytherapy rods. We will continue to investigate these calibration techniques by re-measuring with more uniform brachytherapy rods and/or smaller ^{125}I sources.

5. CONCLUSIONS

We have developed a high-resolution, adaptive SPECT platform which uses two adjustable slit apertures to fill the detector with anamorphic projections of a desired region of interest. Calibration of the system over the entire magnification range using direct point source measurements are impractical due to long acquisition times and large data storage requirements, so we have implemented a geometry-based calibration method which uses a

contracting-grid estimation technique to extract the necessary geometric parameters which describe the system to enable on-the-fly system matrix regeneration. We are ready to acquire phantom data and begin the final evaluation of the system's tomographic-imaging performance.

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Figure 1.

A simplified diagram of a crossed-slit aperture configuration (a). The separated slits allow separate axial and transaxial magnifications, producing an anamorphic projection of the object onto the detector. Close-up of the internal construction of the adjustable slit design (b). Ten-mm thick copper-tungsten blades are mounted in an aluminum frame. One blade is fixed and the other is spring-tensioned and able to slide along brass ball bearings to change the blade separation.

Figure 2.

Schematic of DSSD configuration (a). Parallel strips on one side of the detector are arranged orthogonal to those on the opposite side and operate independently to detect absorption events. The 60 mm $\times$ 60 mm silicon DSSD (b) has 1024 $\times$ 1024 pixels with 59- μ m strip pitch and a 1-mm-thick bulk.

Figure 3.

A photograph of the anamorphic SPECT system with mounted geometric calibration phantom. Two orthogonal slits are independently adjusted to permit maximum magnification of the object onto the high-resolution DSSD.

Figure 4.

Diagram of geometric parameters described in Table 2. Geometric parameters determined by the vertical slit (a) and horizontal slit (b) with respect to the defined center of the FOV and center point of the detector. Detector rotation parameters (c), shown as seen from the object position, are defined with respect to the center point of the detector.

Figure 5.

A SolidworksTM rendering of the geometric phantom used in these data acquisitions. The phantom allows brachytherapy rods to be inserted into holes predetermined heights and radial distances from the center of the phantom to mimic the desired field of view (a). Calibration data obtained with three brachytherapy rods located vertically separated by 7.5 mm, and at a radial distance of 5 mm from the center of rotation is superimposed over a single projection image of the three rods (b).

Figure 6.

Simulated calibration data at two slit positions (a). Up to ten pixels of uniform random noise have been added to each position. Measured calibration data at two slit positions (b). Nonuniform tracer distributions in the brachytherapy rods currently limits our ability to reliably estimate the geometric parameters. In both (a) and (b), red and blue points represent the original data, and the yellow and green points represent the data generated by the geometric parameters estimated using the contracting grid method and Equation 5.

Table 1

Storage requirements for system matrix using single precision floating point numbers.

Storage type	Description	Storage size
single full PSF	1024×1024 pixels	32 MB
full measured system matrix	60 projections, 101×101×101 voxels	235 TB
sparse matrix storage	assumes 31×31 pixels/PSF	221.31 GB
coefficient storage	6 parameters/PSF	1.38 GB
geometric system parameters	11 parameters total	0.04 kB

Table 2

Geometric parameters estimated using contracting grid methods.

Parameter	Description
	Rotational offset between calibration phantom and ideal position
d_x	Distance between center of rotation and vertical slit
d_y	Distance between center of rotation and horizontal slit
f_x	Distance between vertical slit and detector plane
f_y	Distance between horizontal slit and detector plane
m_x	Mechanical offset of vertical slit in the x direction
m_y	Mechanical offset of horizontal slit in the y direction
e_x	Mechanical offset of detector in the x direction
e_y	Mechanical offset of detector in the y direction
θ	Rotation about detector center in the $x - y$ plane
ψ	Rotation parallel to the y axis through the detector center
ϕ	Rotation parallel to the x axis through the detector center