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Development and characterization of a high-resolution microSPECT system for small-animal imaging

Abstract

We developed a high-resolution microSPECT system and investigated its performance characteristics for small animal imaging. The microSPECT system consists of a stationary compact gamma camera with interchangeable pinhole and parallel-hole collimators and vertical object rotation mechanism. The modular camera is based on a pixellated NaI(Tl) crystal array with 1.2 mm pixel size and 1.4 mm pixel pitch coupled to a 5" diameter Hamamatsu R3292 PSPMT. The pinhole collimator has a 10cm focal length fitted with keel-edge pinhole apertures with diameters of 1.0, 1.5 and 2.0 mm. The system performance was characterized by the measurements of the point source response function (PSRF) using ~300 μ m point sources of ^{99m}Tc. The system performance in SPECT imaging was evaluated using micro SPECT phantom and ^{99m}Tc-MDP bone scan of a mouse. The asymmetric PSRF and detection efficiency falloff were observed for the pinhole apertures with keel-edge design when the point source was scanned from the central axis to the edge of the field-of-view of pinhole collimator. This system can achieve 1.1 mm spatial resolution using 1 mm pinhole aperture at 2.5 cm distance to the pinhole. High-resolution and high-quality SPECT images were demonstrated from imaging micro SPECT phantoms and ^{99m}Tc-MDP bone scan of a mouse.

Keywords

high, characterization, resolution, development, microspect, imaging, system, small, animal

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Chapter 21

DEVELOPMENT AND CHARACTERIZATION OF A HIGH-RESOLUTION MICROSPECT SYSTEM FOR SMALL ANIMAL IMAGING

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Abstract: We developed a high-resolution microSPECT system and investigated its performance characteristics for small animal imaging. The microSPECT system consists of a stationary compact gamma camera with interchangeable pinhole and parallel-hole collimators and vertical object rotation mechanism. The modular camera is based on a pixellated NaI(Tl) crystal array with 1.2 mm pixel size and 1.4 mm pixel pitch coupled to a 5" diameter Hamamatsu R3292 PSPMT. The pinhole collimator has a 10cm focal length fitted with keel-edge pinhole apertures with diameters of 1.0, 1.5 and 2.0 mm. The system performance was characterized by the measurements of the point source response function (PSRF) using ~300µm point sources of ^{99m}Tc. The system performance in SPECT imaging was evaluated using micro SPECT phantom and ^{99m}Tc-MDP bone scan of a mouse. The asymmetric PSRF and detection-efficiency falloff were observed for the pinhole apertures with keel-edge design when the point source was scanned from the central axis to the edge of the field-of-view of pinhole collimator. This system can achieve 1.1 mm spatial resolution using 1 mm pinhole aperture at 2.5 cm distance to the pinhole. High-resolution and high-quality SPECT images were demonstrated from imaging micro SPECT phantoms and ^{99m}Tc-MDP bone scan of a mouse.

Key words: microSPECT system, small animal imaging.

1. INTRODUCTION

The rapid growth in molecular genetics and the development of mouse models of human diseases have led to significant interest in *in vivo* small animal imaging. Several instrumentation approaches [1-4] have been utilized

to develop high-resolution animal SPECT for functional small animal imaging. Compact modular cameras based on pixellated crystal and position sensitive photomultiplier tube (PSPMT) are a low cost alternative to conventional gamma cameras for use in pinhole SPECT systems with high detection efficiency and resolution [5]. We have developed a compact, high-resolution microSPECT system in our lab for small animal imaging. Our approach was to use a dedicated mini camera with pinhole collimator. The modular camera was based on a pixellated NaI(Tl) crystal array and a single 5" Hamamatsu PSPMT. The system performance was characterized using small point source. The system spatial resolution and sensitivity were measured. High-resolution phantom and *in vivo* mouse imaging were performed to demonstrate the system capability.

2. IMAGING SYSTEM AND METHOD

Figure 23-1 shows the microSPECT system developed in our lab. The system was designed to have a simple motion control scheme where the camera was placed in horizontal stationary position while imaging object was rotated vertically in front of the collimator. The rotary stage was mounted on (x, y, z) linear translation stage from the Velmex Inc. for accurately three-dimensional positioning of the object.

2.1 Compact Gamma Camera

The compact gamma camera is based on a pixellated NaI(Tl) scintillation crystal array from Saint Gobain Crystals and Detectors Inc. attached to a 5" diameter Hamamatsu R3292 position sensitive PMT (PSPMT). The 11.2 cm x 11.2 cm pixellated crystal array consists of $1.2 \times 1.2 \times 6 \text{ mm}^3$ pixel elements separated by 0.2 mm gaps that are filled with optically opaque and reflective materials. The light output from the scintillator is detected by the optically coupled PSPMT using a subtractive resistive readout [6] to lead out four signal outputs

Figure 23-1. A photograph of the microSPECT system based on a compact gamma camera using a pixellated NaI(Tl) crystal array and a 5" Hamamatsu R3292 PSPMT. The camera was placed in stationary position and the object was rotated vertically in front of the collimator.

(X^+ , X^- , Y^+ and Y^-). The signals were digitized by 12-bit PCI-6110E ADC card from the National Instruments. The data acquisition system was based on a Macintosh G3 workstation using the Kmax software package from the Sparrow Inc. A truncated centroid algorithm [7] was used to calculate the position and energy of the detected gamma photons. The effective field-of-view of the camera was ~ 10.2 cm in diameter within a useful pixel array of 73×73 . The camera was optimized for ^{99m}Tc imaging. The measured energy resolution was $\sim 16\%$ FWHM for 140-KeV photons. The energy window was set at 130-155 KeV for ^{99m}Tc imaging.

The camera can be fitted with interchangeable pinhole and parallel-hole collimators. The parallel-hole collimator designed for imaging the whole body of small animals and the pinhole collimator was used in imaging regional activity uptakes in the animals. The pinhole collimator has a focal length of ~ 10 cm and an acceptance angle of 62° . The pinhole apertures were interchangeable and were made of tungsten alloy with diameters of 1.0, 1.5 and 2.0 mm. The pinhole apertures had keel edge design to minimize the photon penetration. Two general-purpose parallel-hole collimators were designed for the camera, one for high-resolution and the other for high-sensitivity imaging. The design parameters of the two parallel-hole collimators are listed in Table 23-1. The design of all the collimators was optimized for 140-KeV photons.

The system was carefully calibrated for the system misalignments using a novel calibration method developed in our group [8]. The measured distance from the pinhole aperture to the image plane of the detector was 10.8 cm.

Table 23-1. Design parameters of the two parallel-hole collimators

Type	Material	Technique	Hole length (mm)	Hole size (mm)	Septa (mm)
HRES	Lead	Cast	40	1.4	0.16
HSEN	Lead	Foil	23	1.5	0.20

2.2 Experimental Method

The performance of the microSPECT system was carefully characterized by its point source response function (PSRF) at different source positions. The full-width-at-half-maximum (FWHM) of the PSRF was used to determine the system spatial resolution while the volume under the PSRF was used to determine the system sensitivity.

The point sources used in the PSRF measurements were made with ~ 300 μm resin beads that absorbed high ^{99m}Tc concentrations up to 0.1- 0.2 mCi. We scanned the point source along the central axis and transaxially across the field-of-view (FOV) of the pinhole collimator. For each source position, a 10 minute planar image of the point source was acquired. From the

measured PSRF, the system spatial resolution and sensitivity were determined as a function of source-to-collimator distance, source position offset from the central axis and the pinhole diameter.

The system performance in pinhole SPECT imaging was evaluated using a micro SPECT phantom from the Data Spectrum Inc. This cylindrical phantom has two types of inserts of 4.5 cm in diameter. The first insert is made with six sets of small plastic rods while the second insert has the same sets of hole channels. The rod and hole diameters are 1.2, 1.6, 2.4, 3.2, 4.0 and 4.8 mm, respectively. The phantoms with either cold-rods or hot-channels were imaged using the 1.0 mm pinhole aperture. The micro SPECT phantoms were filled with ~5mCi of ^{99m}Tc -pertechnetate in water solution. To avoid truncation in the projection data, the phantoms was placed at a distance of ~5 cm from the pinhole aperture resulting in a magnification factor of ~2.

The projection data were acquired using 120 angular views equally spaced over 360° and the acquisition time was 40 seconds per view. The radius-of-rotation (ROR) was ~5 cm, resulting in a magnification of ~2. The projection data were reconstructed using a 3D pinhole OS-EM algorithm with 10 iterations and 10 subsets. Reconstruction matrix size was $80 \times 80 \times 80$ with a voxel size of 0.35 mm. A 3D Butterworth filter with cutoff frequency of 0.25 cycles/voxel was used for the post-reconstruction.

A mouse bone scan with ^{99m}Tc -MDP injection was also performed using 1.0 mm pinhole aperture to evaluate the pinhole micorSPECT image quality. The mouse was IV injected with 10 mCi ^{99m}Tc -MDP through the tail vein. The mouse was sacrificed and scanned after 2.5 hours postinjection. A total of 120 projections with angular views equally spaced over 360° were acquired from the animal. The scan interval was 40 seconds per view. The ROR was ~2.6 cm, resulting in a magnification of ~4. The projection data were reconstructed using a 3D pinhole OS-EM algorithm with 6 iterations and 10 subsets and with correction of system geometric misalignments. Reconstruction matrix size was $80 \times 80 \times 80$ with a voxel size of 0.35 mm. A 3D Butterworth filter with cutoff frequency of 0.3cycle/voxel was used for the post-reconstruction.

3. RESULTS

The measured point source response functions for the keel-edge pinhole aperture using ^{99m}Tc point source are shown in Figure 23-2. In the central axis direction, the image of the point source grows larger as the point source moves closer to the pinhole due to the magnification nature of the pinhole collimation. However, in the transaxial direction across the FOV of the

Figure 23-2. Sample of point source response function results obtained using a $300\mu\text{m}$ diameter resin bead soaked with $0.15\text{ mCi } ^{99\text{m}}\text{Tc}$ and 2.0 mm pinhole aperture with keel-edge design: (a) along the axis direction and (b) along the transaxial direction at the source-to-pinhole distance of 2.5 cm .

pinhole collimator, the PSRF becomes increasingly asymmetric as the point source moves further off the central axis of the pinhole collimator. The shape of the PSRF is narrower in the radial than in the tangential direction.

Figure 23-3 shows the axial spatial resolution and sensitivity as a function of source-to-collimator distance for the three pinhole apertures and two parallel-hole collimators. All three pinhole apertures provide much improved spatial resolution as compared to the parallel-hole collimators. In contrast with the parallel-hole collimators, the pinhole collimation exhibits a rapid increase in detection efficiency as the source-to-collimator distance

Figure 23-3. Measured axial (a) spatial resolution and (b) sensitivity of the microSPECT system as a function of source-to-collimator distance.

decreases. However, the useful field-of-view is reduced as the distance is decreased. When imaging a mouse with a diameter of 2.5 cm, we can place the center of the mouse as close as ~ 2.6 cm from the pinhole aperture. Our system can achieve a spatial resolution and sensitivity of ~ 1.2 mm and ~ 2 cps/ μ Ci using the 1 mm pinhole aperture.

The transaxial spatial resolution and sensitivity for the three pinhole apertures are shown in Figure 23-4. The measurements were made at a source-to-pinhole distance of 2.5 cm using a 300 μ m diameter point source with 0.15 mCi ^{99m}Tc . The detection efficiencies for the three pinhole apertures show a significant falloff from the central axis to the edge of the FOV of the pinhole collimator. The PSRF shows increased asymmetry as the point source moves off the central axis to the edge of FOV of pinhole collimator with the a smaller FWHM values in the radial than in the tangential direction.

Figure 23-4: Measured (a) spatial resolution and (b) sensitivity of the microSPECT system in the transaxial direction for three pinhole apertures at source-to-pinhole distance of 2.5 cm. In (a), the solid symbols denote the FWHM values in the radial direction while the open symbols represent the FWHM values in the tangential direction in the image plane.

Figure 23-5 shows the reconstructed transaxial images of the microSPECT phantoms with cold-rods and hot-channels. With the ~ 5 cm ROR and ~ 2 magnification, the microSPECT system with 1 mm pinhole aperture can clearly resolve both cold-rods and hot-channels from 4.8 mm down to 1.6 mm but not the 1.2 mm rods and hot-channels.

Figure 23-6 shows the reconstructed coronal images through the chest of a normal mouse. Individual ribs of the mouse are clearly resolved in the high-resolution reconstructed images. The results demonstrate that our

microSPECT system based on compact camera is capable of high quality small animal imaging.

Figure 23-5. Reconstructed transaxial images of the micro SPECT phantoms with (a) cold-rods and (b) hot-channels obtained from the microSPECT system using the 1.0 mm pinhole aperture. The radius-of-rotation was ~ 5 cm in both cases. The phantom was filled with ~ 5 mCi ^{99m}Tc -pertechnetate in water solution. The rod and hole diameters in the six sectors are 1.2, 1.6, 2.4, 3.2, 4.0 and 4.8 mm.

Figure 23-6. Pinhole SPECT bone scan of a normal mouse: coronal image slices through the chest of the mouse.

4. DISCUSSION

We have characterized the performance of a high-resolution microSPECT system based on a compact gamma camera with a pixellated

crystal array and a 5" Hamamatsu PSPMT. As shown in the micro SPECT phantom images using ^{99m}Tc , our microSPECT system with pinhole collimator can clearly resolve the 1.6 mm cold-rods and hot-channels with a ROR of ~ 5 cm. When imaging a smaller object such as a mouse using a smaller ROR and larger magnification factor, improved resolution in order of 1-1.5 mm can be achieved. The measured point source sensitivities at 2.5 cm from the pinhole are approximately 2, 3 and 5.2 counts/sec/ μCi for the 1.0, 1.5 and 2.0 mm pinhole apertures, respectively.

The PSRF of a pinhole collimator with keel-edge pinhole apertures becomes increasingly asymmetric towards the edge of the field-of-view of the collimator with concurrent decrease in sensitivity. The variations in PSRF and sensitivity are dependent on the aperture design parameters, including hole diameter and keel thickness, and position of the activity source relative to the pinhole aperture. These factors are important considerations in the specifications and design of a pinhole collimator for high-resolution SPECT imaging.

5. CONCLUSION

The modular camera based on a pixellated crystal array and a single 5" Hamamatsu PSPMT is an effective approach to high-resolution microSPECT system for small animal imaging. However, to achieve high-resolution SPECT images, careful collimator design, system calibration and iterative image reconstruction methods with accurate correction of system geometric misalignments are required.

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