HHS Public Access

Author manuscript

IEEE Nucl Sci Symp Conf Rec (1997). Author manuscript; available in PMC 2015 November 13.

Published in final edited form as:

IEEE Nucl Sci Symp Conf Rec (1997). 2001 November ; 3: 1826–1829. doi:10.1109/NSSMIC.

2001.1008697

A new design for a SPECT small-animal imager

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Abstract

We demonstrate, using computer models, the feasibility of a new SPECT system for imaging small animals such as mice. This system consists of four modular scintillation cameras, four multiple-pinhole apertures, electronics, and tomographic reconstruction software. All of these constituents have been designed in our laboratory. The cameras are 120mm×120mm with a resolution of approximately 2mm, the apertures can have either single or multiple pinholes, and reconstruction is performed using the OS-EM algorithm. One major advantage of this system is the design flexibility it offers, as the cameras are easy to move and the apertures are simple to modify. We explored a number of possible configurations. One promising configuration had the four camera faces forming four sides of a cube with multiple-pinhole apertures employed to focus the incoming high-energy photons. This system is rotated three times, so that data are collected from a total of sixteen camera angles. It is shown that this hybrid system has some superior properties to single-aperture-type systems. We conclude that this proposed system offers advantages over current imaging systems in terms of flexibility, simplicity, and performance.

I. Introduction

Small-animal imaging has emerged as an important area of nuclear-medicine research [1]. Animals such as mice serve as models for studies ranging from neural function to the course and treatment of coronary disease and cancer [2,3]. Autoradiography, where the animal is injected with a tracer, sacrificed, sectioned, and imaged using radiographic film, is still a widely employed method for “imaging” animal models. However, this method offers poor statistical power, as one animal serves for only one time point, and inter-animal differences increase the number of animals that must be sacrificed at each such point. Far greater statistical power and reduced animal usage is possible with *in-vivo* imaging methods. One animal, followed throughout the course of the experiment, provides data for a number of time points, and inter-animal differences are easier to monitor as they are registered through the entire experiment rather than at a single data point.

Typically a SPECT system for *in-vivo* animal imaging has consisted of a clinical Anger camera with a single- or multiple-pinhole collimator [2,4]. While these systems have produced good high-resolution images, they tend to be cumbersome and difficult to modify, and they require access to the expensive clinical camera. Recently, other systems have been proposed which use compact special-purpose cameras rather than clinical Anger cameras [5]. These compact cameras use segmented scintillation crystals, a position-sensitive photomultiplier tube, and a single-pinhole aperture. However, while their spatial resolution, determined by the ~ 2 mm pitch of the segmentation, is excellent, the combination of segmented crystals and PSPMTs makes them relatively expensive.

We propose a SPECT system that offers some advantages over these current small-animal imagers. This system consists of four modular cameras, each using a single unsegmented scintillation crystal, with a multiple-pinhole collimators focusing the photons onto each camera face, as shown in Fig. 1. The cameras include $12\text{cm} \times 12\text{cm} \times 0.5\text{cm}$ NaI(Tl) scintillator, a 1.5cm light guide, and nine non-position-sensitive photomultiplier tubes. The photomultiplier signals from the photon interactions in the scintillator are digitized and stored in a list [6]. A maximum-likelihood approach is then used to estimate the position and energy of the interaction. The expected resolution of the camera is on the order of 2mm. A similar, though less sophisticated, modular-camera design is currently being used in our FASTSPECT I small- or large-animal imaging system, but FASTSPECT is as bulky and expensive as a clinical system. Thus, in this present study, we explore a simpler method to utilize our new modular cameras specifically for small-animal imaging. While it is possible to use a single-pinhole aperture with this system, in this paper we demonstrate, using computer simulations, advantages for multiple-pinhole apertures when collecting data for a modular-camera system.

II. Methods

All experiments were carried out with analytic computer simulations using code developed in our laboratory. The system geometry is shown in Fig. 1. The camera was assumed to have a resolution of 2mm. Attenuation and scatter were not included in the computer model. Depth of interaction was also not included in the initial simulations, though we show some of its effects later in this paper. Several slices from the digital mouse-brain phantom used in this study are presented in Fig. 2. This phantom, available at www.mbl.org (unassociated with our group), was generated by fixing the animal's brain, sectioning it into $30\mu\text{m}$ slices, staining it with cresyl violet, and optically imaging it [7,8]. While this does not represent a radiotracer distribution, it presents the simulated imaging system with a complex phantom that should provide reconstruction difficulties. A cylindrical background source, with activity/unit volume of 10% of the average activity in the brain, traversed the entire field of view. For this study we assumed a total activity in the phantom of 2mCi and varied the collection time. Seventy percent of the 140KeV photons were assumed captured by the scintillation crystal. The total phantom size was $24.6\text{mm} \times 24.6\text{mm} \times 24.6\text{mm}$, and the size of the voxels used to generate the projections was 0.2mm. The data were reconstructed onto a 0.6mm grid, thus approximating the true continuous-to-discrete projection process *vs.* discrete-to-discrete reconstruction that is inherent in all tomographic imaging. Reconstruction was performed using the ordered-subsets expectation-maximization (OS-

EM) algorithm. Opposite projections served as two-projection subsets. Since different numbers of projection angles and different noise levels were used, we looked at various iteration stopping points. Though the effect of iteration number will be explored, in most cases the iteration stopping point was selected qualitatively.

III. Results

The first experiment involved studying the effects of pinhole size on the properties of reconstructed images. Identical single-pinhole apertures collimated the high-energy photons striking each of the four cameras. The pinhole-to-center-of-rotation (COR) distance was 16mm, giving a 3.75 magnification of the COR onto the camera, and data were collected over 64 projection angles. We used 1.0mm and 2.0mm pinhole sizes and looked at 960 and 96 second acquisition times. Figure 4 gives the reconstructions after 4, 7, 10, 15, 20, 30, 50, 70 and 100 iterations for (a) 1.0mm-pinhole data and 960 second acquisition time, (b) 2.0mm-pinhole data at the same acquisition time, and (c) and (d) 1.0mm- and 2.0mm-pinhole data collected for 96 seconds acquisition time.

A number of qualitative observations can be made from Fig. 4. First, we see that larger pinholes reduce resolution in the noise-free case, but that data taken with the smaller pinholes degrade more quickly with reduced imaging time. We also see that what appears to be a good iteration stopping point changes with both pinhole size and imaging time. Neither is a surprising result, but the later fact underscores the need for using a quantitative measure of image quality (something we shall do in future work). One fortunate effect seen in Fig. 4 is that image properties appear to be fairly constant over a broad range of iterations in the region of the qualitatively “best” stopping point. Thus, after studying all stopping points, we can hope that presenting only one image will give an idea of the reconstructed-image properties for a given data set. For the rest of this study we shall make comparisons using only one such stopping point.

We next explored the possibility of identical multiple-pinhole apertures on each of the four cameras. In this study we compared two different multiple-pinhole apertures – an aperture with 25 1.5mm pinholes (25mm pinhole-COR distance) and an aperture with 64 1.0mm pinholes (20mm pinhole-COR distance) – with the single 1.0mm-pinhole aperture studied in Fig. 4. For the multiple-pinhole apertures data were taken from only 16 camera angles. We retained the 64 projection angles for the single-pinhole system. Results are given in Fig. 5a for noise-free images and for imaging times between 960 seconds and 9.6 seconds. The iteration stopping points are given in Fig. 5b. We see that that, once again, the larger (25 1.5mm) pinholes lead to reduced resolution in high-count regimes. However, the 64 1.0mm pinholes appear to give both good resolution at long imaging times and to break up more slowly than the single-pinhole images at shorter imaging times. While this study cannot be called conclusive, it implies that multiple pinholes give the possibility of both high resolution and good sensitivity over a range of photon count levels.

It is not necessary that each of the four cameras has the same aperture type, and we next studied the effects of using different apertures on each of the cameras. We compared systems with four collimators having 1) 36 0.75mm pinholes and a 20mm pinhole-to-COR

distance and 2) 36 1.5mm pinholes and a 25mm pinhole-to-COR distance with a system that alternated collimator 1) with collimator 2). The results are given in Fig. 6, and appear inconclusive, with no real advantage seen in combining the two systems. Eventually we expect to use a system with combined resolutions and sensitivities, but since our proposed imaging system presents such a large number of options in the full design parameter space, we leave optimization to future studies.

Finally we studied the issue of depth of interaction. This is an important effect for pinhole imaging, as a photon traveling in a line not perpendicular to the face of the detector crystal can interact in any of two or more detector pixels, thus reducing the resolution of the imaging system. If depth of interaction is not properly modeled in the reconstruction algorithm, an incorrect point response function (PRF) will be incorporated into the reconstruction process. However, in our laboratory we do not use analytic estimates of the PRF but rather measure it with a point-like source moved to every reconstruction voxel. This position-dependent measured PRF is then incorporated into the reconstruction algorithm.

In order to see how depth of interaction would affect us, we compared a simulation where depth of interaction was modeled in neither the projection process or the reconstruction and a simulation where depth of interaction was included in both. The results are given in Fig. 7 after 10 OS-EM iterations for a system with four apertures, each with 36 0.75mm pinholes. While there may be some loss of resolution when depth of interaction is included in the simulations, qualitatively these images appear very similar, though we shall continue to explore this potential problem.

IV. Conclusions and Future Studies

We have studied design parameters for a simple animal imaging system consisting of four modular scintillation cameras. We have shown that this design offers both high sensitivity and good spatial resolution. We have demonstrated advantages for some aperture types, particularly one with a large number of relatively small pinholes. We have studied a multiple-resolution aperture set, but have seen no obvious advantage to this configuration. However, we will continue to explore the possibility of multiple resolutions and multiple sensitivities for the four collimators, as we expect that ultimately this type of system will prove superior to single-resolution apertures.

In order to finalize an optimal system configuration, we must explore much more thoroughly the large number of parameters available in the collimator design, including magnification, pinhole size, pinhole number, and pinhole position. This will be facilitated by, first, a means of quantifying image quality and, second, a means of using this quality measure to explore an exceptionally large parameter space. There are a number of different means of quantifying image quality for a given imaging task [9]. Some of these methods are germane to small-animal imaging, as they quantify image quality in terms of relevant tasks such as the determination of lesion size or uptake [10–12]. We shall select one of these methods that best matches future proposed uses of our imaging system and use this for optimizing the final system design design.

Acknowledgments

This work was supported by NIH NCRR P41 grant RR14304.

V. References

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Figure 1.
The basic system design

Figure 2.
Slices from the phantom used in this study

Figure 3.
The slice used for comparison at the reconstruction-grid resolution.

Figure 4.

A study of the effect of pinhole size for 1.0mm and 2.0mm pinholes with 960 and 96 second acquisition times.

(a)

100	100	70	10
100	100	50	10
100	70	50	10

(b)

Figure 5.

(a) Comparison of (first row) 25 1.5mm pinholes, (second row) 64 1.0mm pinholes, and (third row) (1 1.0mm pinhole) for (first column) noise-free data and data after (second column) 960 seconds, (third column) 96 seconds, and (fourth column) 0.6 seconds imaging time with (b) the iteration stopping points.

(a)

100	100	70	10
100	100	50	10
100	70	50	10

(b)

Figure 6.

(a) Comparison of (first row) 36 0.75mm pinholes, (second row) 36 1.5mm pinholes, and (third row) the first two types of collimators alternated across the four cameras. The columns represent noise-free, and 960, 96, and 9.6 imaging seconds and (b) is the iteration stopping points.

Figure 7. Reconstructions from a system that included depth of interaction in neither the projection nor reconstruction (top row) and in both the projection and reconstruction (bottom row) after 10 OS-EM iterations for noise-free, 960-second, 96-second and 9.6.-second data.