Published in final edited form as:

Phys Med Biol. 2013 May 21; 58(10): 3397–3412. doi:10.1088/0031-9155/58/10/3397.

Design and performance of a small-animal imaging system using synthetic collimation

R J Havelin¹, B W Miller², H H Barrett², L R Furenlid², J M Murphy³, and M J Foley¹

¹School of Physics, National University of Ireland Galway, Ireland. ²Center for Gamma-Ray Imaging, The University of Arizona, Tucson, AZ, USA. ³Regenerative Medicine Institute, National University of Ireland Galway, Ireland.

Abstract

This work outlines the design and construction of a single-photon emission computed tomography (SPECT) imaging system based on the concept of synthetic collimation. A focused multi-pinhole collimator is constructed using rapid-prototyping and casting techniques. The collimator projects the centre of the field of view (FOV) through forty-six pinholes when the detector is adjacent to the collimator, with the number reducing towards the edge of the FOV. The detector is then moved further from the collimator to increase the magnification of the system. The object distance remains constant, and each new detector distance is a new system configuration. The level of overlap of the pinhole projections increases as the system magnification increases, but the number of projections subtended by the detector is reduced. There is no rotation in the system; a single tomographic angle is used in each system configuration. Image reconstruction is performed using maximum-likelihood expectation-maximization (MLEM), and an experimentally measured system matrix. The system matrix is measured for each configuration on a coarse grid, using a point source. The pinholes are individually identified and tracked, and a Gaussian fit is made to each projection. The coefficients of these fits are used to interpolate the system matrix. The system is validated experimentally with a hot-rod phantom. The Fourier crosstalk matrix is also measured to provide an estimate of the average spatial resolution along each axis over the entire FOV. The 3D synthetic-collimator image is formed by estimating the activity distribution within the FOV, and summing the activities in the voxels along the axis perpendicular to the collimator face.

1. Introduction

Small-animal molecular imaging is an important tool in the study of disease. Single-photon emission computed tomography (SPECT) enables the visualization of biological processes *in vivo* in small animals (Meikle et al 2005, Cherry 2004). SPECT has been used to investigate the targeting of radioisotope-labelled mesenchymal stem cells to specific locations, while also investigating engraftment capabilities (Dwyer et al 2011). Most SPECT systems use a collimator for image formation. Common examples include parallel-hole collimators and pinhole collimators, the merits of which have been well studied (Barrett and

Swindell 1981, Jaszczak et al 1994). The collimator increases the spatial information of the photons by reducing the possible emission locations of each detected photon. Single-pinhole imaging is often plagued by relatively poor geometric efficiency, and one method for increasing the sensitivity is to use multi-pinhole collimators (Barrett and Swindell 1981).

A multi-pinhole collimator has an array of pinholes that allow the object to be imaged by different detectors or different elements of the same detector. Multi-pinhole systems are usually designed to have little or no projection overlap on the detector. This constraint reduces the number of pinholes that can be included in a collimator. Overlap of these pinhole projections (multiplexing) can lead to a loss of spatial information because a photon detected in this region could have passed through one of several pinholes. Statistical iterative algorithms can be used to demultiplex these data and minimize the loss of spatial resolution, while increasing the active detector area (Peterson et al 2009). The system described in this work uses the technique known as synthetic collimation which combines multiplexed and non-multiplexed data to produce high-resolution, artefact-free reconstructions (Wilson et al 2000). By combining images of an object at different magnification factors it has been shown in simulations (Wilson et al 2000, Shokouhi et al 2010, Mahmood et al 2010), and experimentally with a slit-slat collimator (Mahmood et al 2011), that the effect of multiplexing can be removed. The data contain information on how the projections overlap which enables us to reconstruct the object using maximum-likelihood estimation (Wilson et al 2000).

This paper outlines the design and construction of a focused multi-pinhole collimator, the calibration of the system by experimental measurement of the system matrix, the interpolation of this system matrix, and the validation of the algorithm through reconstruction of a hot-rod phantom. To the authors' knowledge this is the first multi-pinhole system to experimentally implement the synthetic collimator using a single tomographic angle. In this work z is defined as direction perpendicular to the collimator face, and a series of voxels along this axis is known as a tube (Clarkson et al 1998). Wilson et al (2000) defined the 3D synthetic-collimator image as the image that is formed by discretizing the field of view (FOV) into a set of voxels and summing the estimated activities in the voxels in each of the tubes. A 2D synthetic-collimator image is defined as an image that is formed by directly estimating the activity in the perpendicular tubes.

2. Methods

The SyntheticSPECT system consists of a BazookaSPECT gamma-ray detector (Miller et al 2006) coupled to a fibre-optic taper (Miller et al 2012a). The BazookaSPECT detector consists of a Lanex[®] scintillator, image intensifier, optical lens, and fast-frame-rate CCD camera. Data are transferred to the processing computer via a firewire interface, and the use of graphics processing units (GPUs) enables image processing in real time. The BazookaSPECT detector uses a CCD sensor to achieve high resolution and a large space-bandwidth product. This sensor is operated at a high frame rate, or short exposure time, so that the optical photons associated with each gamma-ray interaction do not overlap. Each photon interaction appears as a signal spread over a region of a few adjacent pixels, which is

called a cluster. These pixel data are used to estimate the gamma-ray interaction location (section 2.2).

BazookaSPECT detectors use a micro-channel plate (MCP) image intensifier to provide up-front optical gain. This amplification minimizes the effect of light loss from imaging the intensifier output screen onto the CCD sensor. Incident photoelectrons from the photocathode strike channel walls of the MCP to produce secondary electrons, eventually leading to an electron cascade. The amplified charge is converted to optical photons using a phosphor screen deposited on the output window of the image intensifier. A fibre-optic taper, with a 10 cm diameter entrance face and 2.5 cm diameter exit face, is inserted between the scintillator and intensifier to increase the active area of the detector (Miller et al 2012a). The output window of the dual-MCP is demagnified eight times, and is imaged by the CCD camera. The intrinsic resolution of the large-area BazookaSPECT detector has been measured as $\sim 200 \mu\text{m}$ (Miller et al 2012a).

Image multiplexing is the overlapping on the detector of different pinhole projections. This overlap allows for more efficient use of the detector surface so that more pinholes can be included in the collimator, thus increasing the sensitivity. Regions of overlapping projections cannot be related to one particular aperture, and this ambiguity leads to reduced spatial resolution, and artefacts, in the tomographic reconstruction (Wagner et al 1981). It has been proposed that combining data with multiple magnification factors could remove this effect as these data would contain information on how the projections are multiplexed (Wilson et al 2000). This concept is implemented to achieve high-resolution reconstructions while maximizing the detector coverage. The system is designed so that when the collimator is placed adjacent to the detector surface there is no multiplexing at the centre of the field of view, and a small amount at the edge. The object-to-pinhole distance (d_{OP}) remains constant, and projection data are acquired when the detector is at six distances behind the collimator. The amount of multiplexing varies with the magnification of the system.

2.1. Multi-pinhole collimator

The multi-pinhole collimator, made of a tungsten epoxy with a density of 12 g/cm^3 , was constructed using rapid-prototyping and casting methods (Miller et al 2011). The double-knife-edge (DKE) pinholes were positioned in a pseudo-random pattern at the centre of the collimator, with inter-pinhole distances of 9 mm. Multi-pinhole apertures should not be arranged in a symmetrical pattern due to artefacts in the resulting reconstructions (Vunckx et al 2008). The pinholes were 1.0 mm in diameter, and they were focused towards a common FOV. The FOV was chosen to be 25.4 mm at a distance (d_{OP}) of 23 mm from the central pinhole. This distance was chosen to maximize sensitivity, and ensure complete separation of pinhole apertures. The focused pinholes at the edge of the collimator would impinge on the geometry of the other pinholes if the centre of the FOV was placed closer to the collimator. This configuration results in minimal pinhole projection overlap when the pinhole-to-detector distance (d_{PD}) is at a minimum, which is set by mechanical constraints. The opening angles of the pinhole apertures were calculated by projecting a collapsing cone from a central slice that is orthogonal to a line joining the centre of the FOV and the pinhole location (figure 1).

One needs to find the location of the apex of the cone that results in a pinhole of the required diameter at the centre of the collimator. From figure 1 it is easy to see that

$$\tan\left(\frac{\alpha}{2}\right) = \frac{r_1 - r_p}{d_1} = \frac{r_1}{d_1 + x}, \quad (1)$$

where r_1 is the radius of the slice through the FOV, r_p is the radius of the pinhole, d_1 is the distance between the centre of the FOV and the pinhole, and x is the distance the apex of the cone lies behind the pinhole. Rearranging (1):

$$x = \frac{d_1 r_p}{r_1 - r_p}. \quad (2)$$

Using this value for x , and the corresponding value for α , the conical geometry may be input to SolidWorks (3D computer-aided design software) to create one edge of the DKE pinhole. The other edge of the pinhole is constructed in a similar manner, but the base of the cone is a distance d_1 behind the pinhole along the line connecting the centre of the FOV and the pinhole coordinate. These calculations were repeated for every pinhole location. The collimator has 110 pinhole apertures (figure 2), but the number of pinhole projections that are detected is reduced to 46 when used with a 10 cm fibre-optic taper.

2.2. System calibration

A discrete-to-discrete model of a SPECT system can be described by

$$\mathbf{g} = \mathbf{H} \mathbf{f}, \quad (3)$$

where the system matrix $\mathbf{H}$, maps an object, $\mathbf{f} = [f_1, \dots, f_N]^t$, into measured data $\mathbf{g} = [g_1, \dots, g_M]^t$. The object is decomposed as a set of N voxels, and the projected image as M data bins, therefore $\mathbf{H}$ is a $M \times N$ matrix. The CCD data are binned to a 320×240 array of pixels, but not all of these pixels image the intensifier. The $\mathbf{H}$ matrix is measured experimentally using a radioactive point source. The voxel function, f_n , is mimicked by stepping the point source through a 3D grid of measurement points in object space. For each photon interaction in the scintillator there is a certain amount of light spread, and the light is detected as a cluster of pixels. A frame-parsing algorithm (Miller et al 2009) extracts and processes each cluster. A centroid calculation is performed on the cluster to estimate the 2D interaction location. A projection image is stored for each voxel measurement, thus creating a system matrix that incorporates the imperfections, such as misalignments or non-uniformities, in the imaging system. This projection image is referred to as the point spread function (PSF). The mean system response is measured by recording many counts for each voxel position, and the object space is finely sampled with many voxel positions. This must be done for each system configuration ($d_{OP} : d_{PD}$ combination). The response was measured on a $13 \times 13 \times 13$ cubic grid of points, with spacings of 2.5 mm, and interpolated to a grid of $97 \times 97 \times 97$ points, corresponding to cubic voxels with side-length of 0.3125 mm. This grid is greater than the common FOV, but it was measured to enable more accurate interpolation at the edges. Storing a projection image for each voxel of the interpolated grid would require > 250 gigabytes of space for each system configuration. Although possible, it would be

inefficient to store and read these data for every reconstruction. Instead, it is assumed that a point source projection through a pinhole has a 2D Gaussian distribution on the detector (Chen et al 2005, Miller et al 2012b). A 2D Gaussian distribution is fitted to each PSF projection (section 2.3), and the coefficients of the fits are stored. Storing these coefficients requires < 0.5 gigabytes for each system configuration.

2.3. Gaussian fitting and interpolation

The estimated interaction positions are binned to the nearest pixel, and the counts at each pixel are integrated. The integrated pinhole response function is approximated by a Gaussian distribution and is represented as

$$f(x, y) = \frac{A}{2\pi\sigma_x\sigma_y\sqrt{1-\rho^2}} \times \exp \left\{ -\frac{1}{2(1-\rho^2)} \left(\frac{(x-\bar{x})^2}{\sigma_x^2} + \frac{(y-\bar{y})^2}{\sigma_y^2} - \frac{2\rho(x-\bar{x})(y-\bar{y})}{\sigma_x\sigma_y} \right) \right\}. \quad (4)$$

The 2D Gaussians are fitted using a constrained non-linear optimization function in MATLAB™ (fmincon), and six coefficients that characterize the Gaussian function are measured. The coefficients are the amplitude (A), the centroid location ($\bar{x}, \bar{y}$), the x and y spread of the projection image (σ_x, σ_y), and the correlation coefficient (ρ).

The number of pinhole projections detected at each voxel location ranges from zero to forty-six. These pinholes must be identified, and associated with each other before interpolation can be performed. The locations of the pinhole apertures are fixed, but the parameters of the detected projections change as the point source is translated through the 3D voxel grid in object space. It is necessary to match a pinhole aperture with its corresponding projection for each voxel position before interpolation can be performed. This labelling is done on a voxel-by-voxel basis starting with the “base voxel”, the voxel from which the most pinhole projections are detected. The projections from the base voxel are individually labelled, and the voxel is noted as processed. This labelling of the projections from the base voxel is analogous to labelling of the actual apertures. As each new voxel is processed, one must determine which apertures are associated with each of the projections from that voxel. This is a trivial task when the centroid positions of the projections through each aperture vary slowly between voxels. When a few voxels have been processed it is possible to extrapolate the parameters of the pinhole projections from adjacent, unprocessed voxels. A threshold is used to compare extrapolated parameters with measured parameters in an unprocessed voxel. If the threshold is met, then the pinhole projection can be accurately labelled. If it is not met, it is possible that this cluster was transmitted through a previously unlabelled aperture. This algorithm is suitable for data in which the inter-voxel locations of the pinhole projections vary slightly. It was not possible to find a suitable threshold level that identified each pinhole accurately in data with much pinhole projection overlap. To overcome this problem, two low-magnification data sets were taken. The pinholes were identified, and associated between each voxel and between each data set. These data were then linearly extrapolated to predict the locations of the pinhole projections in the high-magnification data. Due to the pinhole geometry, any pinhole projection visible in high-magnification data should be present in low-magnification data. Figure 4 shows the centroid positions of the

Gaussian fits for all experimentally measured PSF locations. When the projections from every voxel position were processed and labelled, it was possible to interpolate the coefficients to a finer grid using cubic interpolation.

2.4. Reconstruction

Image reconstruction was performed using maximum-likelihood expectation-maximization (MLEM). The elements of the system matrix were generated on-the-fly, using a GPU, from the interpolated Gaussian coefficients of the pinhole projections (Miller et al 2012b). The MLEM algorithm can be written as

$$\hat{f}_n^{(k+1)} = \frac{\hat{f}_n^{(k)}}{\sum_{m'=1}^M h_{m'n}} \sum_{m=1}^M \frac{g_m}{\sum_{n'=1}^N h_{mn'} \hat{f}_{n'}^{(k)}} h_{mn}, \quad (5)$$

where $\hat{f}_n^{(k)}$ is the estimated activity in voxel n after the k^{th} iteration, and h_{mn} is an element of $\mathbf{H}$ that represents the probability that a photon emitted from voxel n is detected in detector element m . The activity in each of the voxels is estimated, and summing these activities along the axis perpendicular to the collimator face produces the 3D synthetic-collimator image (Wilson et al 2000).

2.5. Fourier crosstalk matrix

The Fourier crosstalk matrix fully describes all deterministic properties of the imaging system and provides a summary measure of resolution of the hardware alone, averaged over the FOV. A short description is provided in this work, and a more thorough discussion can be found in Barrett et al (1995). From (3), the m_{th} detector measurement is given by

$$g_m = \int_S h_m(r) f(r) dr, \quad (6)$$

where S is the region defined by the support function $S(r)$, whose value is 1 if $r \in S$, and 0 otherwise, and the detector sensitivity function, $h_m(r)$, describes the response of the m_{th} detector to a point source at r . The object f can be represented by a Fourier series

$$f(r) = \sum_{k=-\infty}^{\infty} F_k \Phi_k(r), \quad (7)$$

where

$$\Phi_k(r) = e^{2\pi i \rho_k \cdot r} S(r), \quad (8)$$

is the k_{th} Fourier basis function. This vector index k spans an infinite set of integers (k_x, k_y, k_z), and the wavevector ρ_k has the values

$$\rho_k = \frac{k}{L}, \quad (9)$$

where L is the width of the cubic region enclosing the space. This gives

$$g_m = \sum_{k=-\infty}^{\infty} F_k \Psi_{mk}, \quad (10)$$

where

$$\Psi_{mk} = \int_S h_m(r) e^{2\pi i \rho_k \cdot r} dr. \quad (11)$$

An element of the Fourier crosstalk matrix is defined by

$$\beta_{kk'} = \sum_{m=1}^M \Psi_{mk}^* \Psi_{mk'}, \quad (12)$$

where M is the total number of detector elements. The diagonal element, β_{kk} , is the squared norm of the data when the object is a single Fourier-series component, and it quantifies how strongly a 3D spatial frequency contributes to the data. For tomographic systems it has been observed that β_{kk} falls off approximately as the reciprocal of the spatial frequency (Kim et al 2006). A factor of $|\rho_k|$ is included to get a summary measure of the spatial resolution of the hardware, and the equivalent MTF^2 is given by

$$MTF_{eq}^2 = |\rho_k| \beta_{kk} \quad (13)$$

It is found that the width of the MTF_{eq}^2 defined by its full-width half-maximum (FWHM), is a direct measure of the response of the system hardware to the Fourier components that fill the FOV. The resulting width is in units of spatial-frequency and is approximately Gaussian, so its Fourier transform is also approximately Gaussian. The FWHM of the resulting space-domain function along the three axes gives a measure of the 3D spatial resolution of the system, and may be used to compare tomographic systems because it is independent of the reconstruction algorithm. A Gaussian-distributed MTF_{eq} along the j axis can be written as

$$MTF_{eq}(j) = A_0 \exp\left(-\frac{j^2}{2\sigma^2}\right), \quad (14)$$

and its Fourier transform as

$$F\{MTF_{eq}(j)\} = A_0 \sqrt{2\pi\sigma^2} \exp\left(-2\pi^2\sigma^2\epsilon^2\right). \quad (15)$$

The FWHM of $MTF_{eq}(j)$ is $\sigma \sqrt{8 \ln(2)}$, and that of $F\{MTF_{eq}(j)\}$ is $\sqrt{2 \ln(2)} / \pi^2 / \sigma$.

The spatial resolution of the system along the j axis is

$$\text{Spatial Resolution} = \frac{4 \ln(2)}{\pi} \frac{1}{FWHM[MTF_{eq}(j)]}. \quad (16)$$

2.6. Phantom Imaging

As another measure of system performance, a hot-rod phantom with six sections containing capillaries with diameters 1.0, 1.2, 1.4, 1.6, 1.8, and 2.0 mm, was imaged (figure 5). The distance between the rods in each section equals the diameter of the rods in that section. There is also a $16 \times 16 \times 2 \text{ mm}^3$ reservoir at the base of the phantom, directly below the rods.

The phantom was filled with 160 MBq ^{99m}Tc . The centre of the phantom was placed approximately at the centre of the FOV, with the rods oriented perpendicular to the detector, and the reservoir situated between the rods and the detector. Six images (figure 6) were taken at detector distances corresponding to magnifications of approximately 0.4, 0.8, 1.1, 1.5, 1.6, and 2.0. The images were formed using the same frame-parsing technique as outlined earlier. The acquisition time for the first image was twenty minutes, and the acquisition time for each subsequent image was adjusted to account for isotope decay. The combined counts in the six images was $\sim 10^7$.

3. Results

3.1. Fourier crosstalk

The Fourier crosstalk matrix was used to estimate the average spatial resolution of the system. The plots of the MTF_{eq} , when all six system configurations were used, are shown in figure 7. The average spatial resolution, as each new system configuration was included in the calculation, is shown in figure 7d. The average spatial resolutions along the x and y axes ($\sim 2 \text{ mm}$) are very similar, as expected, and result in values close to that predicted for the lateral resolution by traditional pinhole theory (Accorsi and Metzler 2005). As this is a limited-angle tomography system, it was expected that the spatial resolution in the z axis would be lower than in the x and y axes. It was found that the average spatial resolution along the z axis is approximately 8 mm. As noted earlier, these values represent the average resolution over the FOV without considering the reconstruction algorithm. By using a statistical iterative reconstruction algorithm, such as MLEM, it is possible to get better resolution at certain slices through the object than is estimated by the Fourier crosstalk matrix. Results of a hot-rod phantom imaging study are presented in the next section to confirm this.

3.2. Phantom experiment

The object, a hot-rod phantom with a small uniform reservoir, was reconstructed using 400 iterations of the MLEM algorithm, and post-smoothed with a Gaussian filter. The edge of the FOV has been removed due to excess build-up of estimated activity, as is common with MLEM. Every second slice of the reconstructed object within the FOV is shown in figure 8. Each image is a slice of the object at different distances from the collimator. The first slices (top left) are furthest from the collimator, and the last slices (lower right) are closer to the collimator. The rods were not entirely filled, although some activity is visible in the smaller rods in the slices furthest from the detector. This is due to these rods being used as injection sites for the ^{99m}Tc , and some activity may have attached to the walls of the rods. The 1.4 mm rods are resolved in several of the slices, although they are not clearly resolved in the

3D synthetic-collimator image (figure 9). The 1.6 mm rods are the smallest diameter rods that are resolved in the 3D synthetic-collimator image. It appears that one of the rods in the 1.6 mm set did not completely fill with activity, and it is visible in only a small number of slices close to the collimator. This is the reason why it does not show a strong signal in the 3D synthetic-collimator image. The 1.8 mm and 2.0 mm rods are clearly resolved in most of the slices throughout the FOV. The reservoir of activity at the base of the phantom is clearly seen, although uniform activity was not estimated accurately. This was expected as it is known that large uniform objects are difficult to reconstruct in limited-angle tomography.

4. Conclusion and discussion

An algorithm was developed to identify and track multiple pinhole projections throughout the FOV. This algorithm was used to accurately track forty-six pinhole projections on the detector over the entire FOV. The number of pinhole projections detected varied between the voxels, and extrapolation was performed to ensure accurate pinhole identification. Incorrect pinhole identification would lead to errors in the image reconstruction. 2D Gaussian distributions were fitted to the integrated pinhole projections for each voxel position. The coefficients of these fits were used to interpolate the system matrix. This interpolation was validated by successfully reconstructing a hotrod phantom. The MLEM algorithm maximizes the probability of observing the detector data, at each system configuration, over all object densities. The large number of pinhole projections, the irregular pinhole pattern, and the varying magnifications, provide much information on an object distribution. Through the use of MLEM reconstruction the effect of multiplexing can be mitigated. It is common to discuss peak performance of an imaging system, rather than the average, however the Fourier crosstalk matrix provides a figure of merit for the average spatial resolution of the system over the entire FOV. The crosstalk matrix may be used to optimize the system parameters when designing a system as it is calculated using the sensitivity function, and it is independent of the reconstruction algorithm. This study presented the design and construction of a SPECT imaging system that uses synthetic collimation to estimate the activity distribution within the FOV. Although it is a limited-angle tomography system, it is shown that some depth information can be estimated, likely due to the large number of pinhole projections acquired at low magnification. The 3D synthetic-collimator image was formed by summing the reconstructed voxels along the axis perpendicular to the collimator face. The number of pinhole projections detected decreases with increased magnification, as the solid angle subtended by the detector is reduced. A detector with a larger area will detect more pinhole projections at high magnification, and will allow the coefficients of the tube functions to be better estimated (Wilson et al 2000). According to the findings of Clarkson et al (1998), the more data that are acquired, the better the estimates will be. In this work, all the data from six system configurations were used in the reconstruction. The pinholes were designed to have 1 mm diameters, although this may be larger in reality due to any problems filling the mold with the tungsten epoxy. Rods of 1.4 mm diameter can be distinguished in certain slices within the FOV, and 1.6 mm diameter rods are resolvable in the 3D synthetic-collimator image. The spatial resolution may be improved upon by reducing the diameter of the pinholes, increasing detector area, and by including data from higher-magnification system configurations.

Acknowledgements

This work is supported by the United States National Institutes of Health under grant number P41 EB002035, and is based upon works supported by Science Foundation Ireland under grant number 09/SRC/B1794.

References

- Accorsi R, Metzler SD. Resolution-effective diameters for asymmetric-knife-edge pinhole collimators. *IEEE Trans. Med. Imaging*. 2005; 12:1637–1646. [PubMed: 16353374]
- Barrett HH, Denny J, Wagner RF, Myers KJ. Objective assessment of image quality II: Fisher information, Fourier crosstalk and figures of merit for task performance. *J. Opt. Soc. Am. A*. 1995; 12:834–852.
- Barrett, HH.; Swindell, W. *Radiological Imaging: The theory of image formation, detection, and processing*. Academic Press; 1981.
- Chen YC, Furenlid LR, Wilson DW, Barrett HH. Springer chapter Calibration of Scintillation Cameras and Pinhole SPECT Imaging Systems. 2005:195–201.
- Cherry S. In vivo molecular and genomic imaging: new challenges for imaging physics. *Phys. Med. Biol.* 2004; 49:R13–R48. [PubMed: 15012005]
- Clarkson E, Barrett HH, Wilson DW. Synthesizing a parallel-projection image from pinhole data. *SPIE*. 1998; 3336:251–259.
- Dwyer RM, Ryan J, Havelin RJ, Morris JC, Miller BW, Liu Z, Flavin R, O'Flatharta C, Foley MJ, Barrett HH, Murphy JM, Barry FP, O'Brien T, Kerin MJ. Mesenchymal stem cell-mediated delivery of the sodium iodide symporter supports radionuclide imaging and treatment of breast cancer. *STEM CELLS*. 2011; 29:1149–1157. [PubMed: 21608083]
- Jaszczak RJ, Li J, Wang H, Zalutsky MR, Coleman RE. Pinhole collimation for ultra-high-resolution small-field-of-view. *SPECT Phys. Med. Biol.* 1994; 39:425–437. [PubMed: 15551591]
- Kim H, Furenlid LR, Crawford MJ, Wilson DW, Barber HB, Peterson T, Hunter WCJ, Liu Z, Woolfenden JM, Barrett HH. SemiSPECT: A small-animal single-photon emission computed tomography (SPECT) imager based on eight cadmium zinc telluride (CZT) detector arrays. *Med. Phys.* 2006; 33:465–474. [PubMed: 16532954]
- Mahmood ST, Erlandsson K, Cullum I, Hutton BF. The potential for mixed multiplexed and non-multiplexed data to improve the reconstruction quality of a multi-slit-slat collimator. *SPECT system Phys. Med. Biol.* 2010; 55:2247–2268.
- Mahmood ST, Erlandsson K, Cullum I, Hutton BF. Experimental results from a prototype slit-slat collimator with mixed multiplexed and non-multiplexed data. *Phys. Med. Biol.* 2011; 56:4311–4331. [PubMed: 21709344]
- Meikle SR, Kench P, Kassiou M, Banati RB. Small animal SPECT and its place in the matrix of molecular imaging technologies. *Phys. Med. Biol.* 2005; 50:R45–R61. [PubMed: 16264248]
- Miller BW, Barber HB, Barrett HH, Liu Z, Nagarkar VV, Furenlid LR. Progress in BazookaSPECT: high-resolution dynamic scintigraphy with large-area imagers. *SPIE Optical Engineering + Applications*. 2012a; 8508:85080F.
- Miller BW, Barber HB, Barrett HH, Wilson DW, Chen L. A low-cost approach to high-resolution, single-photon imaging using columnar scintillators and image intensifiers. *IEEE Nuclear Science Symposium Conference Record*. 2006; 6:3540–3545.
- Miller BW, Barber HB, Furenlid LR, Moore SK, Barrett HH. Progress in BazookaSPECT. *Proc. SPIE*. 2009; 7450:74500C.
- Miller BW, Moore JW, Barrett HH, Frye T, Adler S, Sery J, Furenlid LR. 3D printing in x-ray and gamma-ray imaging: A novel method for fabricating high-density imaging apertures. *Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*. 2011; 659:262–268.
- Miller BW, Van Holen R, Barrett HH, Furenlid LR. A system calibration and fast iterative reconstruction method for next-generation. *SPECT imagers IEEE Trans. Nucl. Sci.* 2012b; 59:1990–1996.

- Peterson TE, Shokouhi S, Furenlid LR, Wilson DW. Multi-pinhole SPECT imaging with silicon strip detectors. *IEEE Trans. Nucl. Sci.* 2009; 56:646–652. [PubMed: 20953300]
- Shokouhi S, Wilson DW, Metzler SD, Peterson TE. Evaluation of image reconstruction for mouse brain imaging with synthetic collimation from highly multiplexed SiliSPECT projections. *Phys. Med. Biol.* 2010; 55:5151–5168. [PubMed: 20714046]
- Vunckx K, Beque D, Defrise M, Nuyts J. Single and multipinhole collimator design evaluation method for small animal. SPECT *IEEE Trans. Med. Imaging.* 2008; 27:36–46. [PubMed: 18270060]
- Wagner RF, Brown DG, Metz CE. On the multiplex advantage of coded source aperture photon imaging. *Proc. SPIE.* 1981; 314:72–76.
- Wilson DW, Barrett HH, Clarkson EW. Reconstruction of two- and three-dimensional images from synthetic-collimator data. *IEEE Trans. Med. Imaging.* 2000; 19:412–422. [PubMed: 11021685]

Figure 1.

The double-knife-edge pinhole geometry of an off-centre pinhole. The centre of the pinhole aperture is on the central plane of the collimator. The central slice of the FOV, which is used to project the collapsing cone to create the pinhole, is on a plane that is orthogonal to a line between the centre of the FOV and the pinhole aperture. An identical slice is formed a distance d_1 on the detector side of the collimator to create the double-knife-edge. The opening angle, α , is unique to each pinhole aperture and is calculated using (1).

Figure 2.

The (a) front view, (b) back view, (c) side view, and (d) isotropic view of the collimator with the approximately spherical FOV visible. This was designed using SolidWorks, and constructed using rapid-prototyping. It was then cast using a tungsten epoxy. The spherical object consists of the central slices of the FOV from which cones are projected to create the focused pinholes (figure 1). The sphere is incomplete due to the limited angular sampling of the system, and this is noticeable in (a) and (d) as a bright spot along the z axis of the object.

Figure 3.

(a) A raw projection image, acquired when a point source was placed at the centre of the FOV, is processed and a Gaussian fit is made to each cluster. (b) These Gaussian fits are re-projected. A single cluster is highlighted in each image with a small white box. (c) The magnified image of the cluster in (a), and several mesh views of the cluster. (d) The magnified image of the cluster in (b), and several mesh views of the cluster.

Figure 4.

Centroid positions of the Gaussian coefficients fitted to the experimental pinhole projections for magnifications: (a) 0.4, (b) 0.8, (c) 1.1, (d) 1.5, (e) 1.6, (f) 2.0. The pinholes have been identified, and their detector positions are plotted. A range of colours is used to distinguish between the different pinhole projections. The PSF voxel grid can clearly be seen in the projections. The amount of projection overlap is proportional to the magnification. A small circular insensitive area of the intensifier can clearly be seen in the same location in all images.

Figure 5. Image of the phantom used in this study. The diameters of the rods are 1.0, 1.2, 1.4, 1.6, 1.8, 2.0 mm, and the separation between the centres of the rods in each section is equal to twice the diameter of those rods. There is also a $16 \times 16 \times 2 \text{ mm}^3$ reservoir at the base of the rods.

Figure 6.

A hot-rod phantom was imaged at six geometric configurations corresponding to magnifications of: (a) 0.4, (b) 0.8, (c) 1.1, (d) 1.5, (e) 1.6 and (f) 2.0.

Figure 7.

The normalized MTF_{eq} along the: (a) x axis, (b) y axis, (c) z axis. A Gaussian function (solid line) has been fitted to the MTF_{eq} data (dots). The centre of each plot deviates from an approximate Gaussian due to $|\rho_k|$, and is ignored in the fitting procedure. The average spatial resolution of the system is shown in (d), where the x axis denotes the number of system configurations used in the calculation. The average lateral resolution of the system improves as data from high-magnification configurations are included in the calculation but the resolution along the z axis does not change.

Figure 8.

Every second slice (thickness = 0.3125 mm) through the z-axis of the object, after excluding the edges of the FOV. The first slice is furthest from the collimator, and the last slice is nearest to the collimator. The rods are partially filled, and so they are not visible in each slice. The injection sites, where some activity may have adhered to the walls of the rods, can be seen in the first few slices. The larger rods are becoming resolved at slice 13, and are resolvable until slice 26 where the activity from the small reservoir becomes dominant.

Figure 9.

3D synthetic-collimator image of the rod phantom. It is formed by summing the reconstructed voxels along the z axis, with z defined as the direction perpendicular to the collimator face. The line profiles for some of the rods are shown next to a green line highlighting the profile. The profiles were selected by joining the centroid of activity within each rod with the centroid of a neighbouring rod.