Published in final edited form as:

Phys Med Biol. 2011 February 7; 56(3): 685–702. doi:10.1088/0031-9155/56/3/010.

MR-based keyhole SPECT for small animal imaging

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Abstract

The rationale for multi-modality imaging is to integrate the strengths of different imaging technologies while reducing the shortcomings of an individual modality. The work presented here proposes a limited-field-of-view (LFOV) SPECT reconstruction technique that can be implemented on a multi-modality MR/SPECT system that can be used to obtain simultaneous MRI and SPECT images for small animal imaging. The reason for using a combined MR/SPECT system in this work is to eliminate any possible misregistration between the two sets of images when MR images are used as *a priori* information for SPECT. In nuclear imaging the target area is usually smaller than the entire object; thus, focusing the detector on the LFOV results in various advantages including the use of a smaller nuclear detector (less cost), smaller reconstruction region (faster reconstruction) and higher spatial resolution when used in conjunction with pinhole collimators with magnification. The MR/SPECT system can be used to choose a region of interest (ROI) for SPECT. *A priori* information obtained by the full field-of-view (FOV) MRI combined with the preliminary SPECT image can be used to reduce the dimensions of the SPECT reconstruction by limiting the computation to the smaller FOV while reducing artifacts resulting from the truncated data. Since the technique is based on SPECT imaging within the LFOV it will be called the keyhole SPECT (K-SPECT) method. At first MRI images of the entire object using a larger FOV are obtained to determine the location of the ROI covering the target organ. Once the ROI is determined, the animal is moved inside the radiofrequency (rf) coil to bring the target area inside the LFOV and then simultaneous MRI and SPECT are performed. The spatial resolution of the SPECT image is improved by employing a pinhole collimator with magnification >1 by having carefully calculated acceptance angles for each pinhole to avoid multiplexing. In our design all the pinholes are focused to the center of the LFOV. K-SPECT reconstruction is accomplished by generating an adaptive weighting matrix using *a priori* information obtained by simultaneously acquired MR images and the radioactivity distribution obtained from the ROI region of the SPECT image that is reconstructed without any *a priori* input. Preliminary results using simulations with numerical phantoms show that the image resolution of the SPECT image within the LFOV is improved while minimizing artifacts arising from parts of the object outside the LFOV due to the chosen magnification and the new reconstruction technique. The root-mean-square-error (RMSE) in the out-of-field artifacts was reduced by 60% for spherical phantoms using the K-SPECT reconstruction technique and by 48.5–52.6% for the heart in the case with the

MOBY phantom. The KSPECT reconstruction technique significantly improved the spatial resolution and quantification while reducing artifacts from the contributions outside the LFOV as well as reducing the dimension of the reconstruction matrix.

1. Introduction

Multi-modality imaging combines functional and the corresponding anatomical images obtained by two either side-by-side or integrated imaging systems. This paper presents a reconstruction technique developed for limited-field-of-view (LFOV) SPECT imaging, hereafter called the keyhole SPECT (K-SPECT) method, by using a multi-modality MR/SPECT system designed for simultaneous imaging. We show that the new reconstruction technique results in improved image quality and accuracy in the SPECT images by using *a priori* information from the full field-of-view (FOV) MRI and original SPECT image without any *a priori* information. In this type of combined system MR provides precise positioning data and anatomical reference images, helps reduce the dimensions of the system sensitivity matrix for iterative reconstruction in SPECT by removing information coming from outside the LFOV, and could also be used to perform correction for attenuation.

Nuclear imaging techniques such as SPECT or PET have proven to be useful molecular imaging techniques due to their higher detection sensitivity compared to CT or MRI. However, one of the major limitations of nuclear imaging techniques such as SPECT is the poor spatial resolution that is in the order of several millimeters with parallel-hole collimators. The limitation could be improved by pinhole collimation and image magnification. Unfortunately this is only possible at the expense of a loss in detection sensitivity and increased imaging time to retain a good signal-to-noise ratio (SNR) in the images. One obvious way to increase the detection sensitivity while obtaining high spatial resolution is to use multi-pinhole collimators (Jung *et al* 2004). A further disadvantage of increasing the image magnification is related to the necessity of using larger detectors resulting in increased system costs. Luckily one of the important aspects of systems using labeled radiotracers such as in SPECT is the fact that the imaging agent is mainly accumulated at the target organ while the other surrounding tissues represent a low frequency background with a lower uptake signal if the isotope is appropriately labeled (Wirwar *et al* 2001, Beekman and Vastenhouw 2002). In such situations it may be sufficient only to image the target region known as the region of interest (ROI) with high resolution without paying much attention to the region outside as originally proposed by Nalcioğlu *et al* (1979) for CT.

In this work we modeled an existing multi-modality system that combines SPECT with MR as previously reported by us (Hamamura *et al* 2010a, 2010b). The purpose of the current study was to develop a new reconstruction technique that would provide artifact-free high spatial resolution SPECT images from a LFOV covering only the target area using *a priori* information provided by MRI and the original SPECT image. In this study the term keyhole SPECT (K-SPECT) is used to describe reconstruction from a LFOV in the presence of signals from outside the LFOV while using *a priori* information from both modalities as will be discussed in detail later. Mathematical simulation results using numerical phantoms are presented.

1.1. Simultaneous imaging

Simultaneous imaging can reduce the effect of inevitable motion between sets of image acquisitions for two or more different imaging which proves to be extremely useful if the information from the two modalities is to be co-registered or information from one is to be used as *a priori* information for the other. It also eliminates the necessity for post-image

processing due to the misalignment of a set of images with another set obtained by a second device. A combined MR/SPECT system that could be used for simultaneous image acquisition was reported by our group previously (Hamamura *et al* 2010a, 2010b). However, unlike the current study there the FOVs for both MRI and SPECT were chosen to be identical.

1.2. Multi-pinhole SPECT and use of image magnification

A SPECT imaging system is characterized by a lower detection sensitivity compared to positron emission tomography (PET) due to its use of mechanical collimators. This becomes even more serious when single pinhole collimators are used for improving the spatial resolution by image magnification. In order to improve the sensitivity of a SPECT imaging system, a multiple pinhole collimator can be used instead of the single pinhole without losing spatial resolution if the detector size is not the limiting factor (Vunckx *et al* 2008). In quantum-limited imaging systems such as SPECT, the number of acquired photons, hence the image SNR, is related to the amount of radioisotope injected as well as the detection sensitivity of the collimator/detector system. Maximum allowable radiation dose also puts certain limitations on the amount of radioactive material that can be injected into the subject (Jung *et al* 2004). By using a multiple pinhole collimator, the sensitivity can be increased considerably with a sufficiently large detector area and the radiation dose level can be reduced compared to single pinhole collimators (Jung *et al* 2004). Unfortunately, according to previous studies, a pinhole collimator with more than nine pinholes designed to increase detection sensitivity would also increase the possibility of multiplexing in a SPECT system if the detector size is limited (image overlap on the detector) resulting in loss of resolution and SNR (Cao *et al* 2005, Meikle *et al* 2002, Ryder *et al* 2008). Since detector size is directly related to the overall cost of a SPECT system one cannot indefinitely increase its size to eliminate image multiplexing. In the present study we assumed the size of the detector to be limited to the overall size of the object. Therefore, the sensitivity improvement was pursued by using a nine-pinhole collimator while the resolution was recovered by avoiding multiplexing with carefully calculated acceptance angles and by maximizing magnification to 1.6 for the given configuration.

As shown in figure 1, in the case of MR-based K-SPECT, the circular ROI can be determined from the MR image (figure 1, left). Once it is determined, the animal is moved inside the radiofrequency (rf) coil (figure 1, right) in order to bring the ROI inside the circular LFOV and to perform simultaneous MRI and SPECT scanning. It should also be pointed out that the collimators are embedded into the rf coil as shown in the figure. Additionally by manipulating the acceptance angle and inclination of the pinhole with respect to the rotation axis of the system, the area to be scanned can be chosen appropriately (Beekman and Vastenhouw 2004).

2. Methods

This study investigates the performance of the K-SPECT reconstruction technique by simulation using numerical phantoms. Different types of numerical phantoms were used. The use of numerical phantoms makes it possible to study the effects of various parameters and quantify the levels of error in different situations since both the input and the output are known. The overall system parameters studied here by simulation were for an MR-compatible SPECT system with a 50.8 mm × 50.8 mm (2" × 2") detector to cover a full FOV of 50 mm in diameter. This is an expansion of the 1" × 1" pixellated CZT detectors used by Hamamura *et al* (2010a, 2010b) by placing four such modules to form a 2" × 2" detector with an array of 32 × 32 pixels in each pixel with a pitch size of 1.6 mm. The dimensions of the system simulated here are shown in figures 1 and 2.

2.1. System parameters

We used a 20 mm × 20 mm non-magnetic radio-opaque material for the pinhole collimator that can be embedded into the rf coil as we have previously shown (Hamamura *et al* 2010a, 2010b). The collimator had nine pinholes and the effective pinhole diameter of each tapered pinhole was 1 mm. The pinholes were placed on a Cartesian raster with 6.5 mm center-to-center spacing. Figure 2 shows the orientation of pinholes and the schematic configuration of each pinhole projection. The layout of the pinholes was chosen to provide maximal sampling in the transverse direction. While this choice results in reduced azimuthal sampling this could be remedied by moving the animal bed inside the system in a stepwise manner along the longitudinal direction to acquire more data similar to spiral CT. The system was designed to have a 10 mm diameter LFOV in the center and a magnification factor of 1.6. This configuration resulted in nine non-overlapping projection images of the LFOV on the square detector.

The acceptance angles of the pinholes were chosen to collect the emitted gamma rays from an area of a 10 mm diameter sphere object located at the center of the imaging space. They were also calculated based on the distance of the pinholes from the rotation axis of the object space and the size of the LFOV. Figure 2 on the right shows the LFOV of 10 mm and the projections of the object onto the detector through pinholes. The projections passing through each pinhole are detected at the corresponding area of a 16 mm diameter circle on the 2" × 2" detector plane. Therefore, the average magnification factor was 1.6 since the distance between the collimator and detector was 1.6 times the distance between the object center and the pinhole collimator. The geometrical sensitivity matrix for a pinhole collimator was generated by the expression in equation (1) for all nine pinholes for 90 angular samplings (Peterson *et al* 2005). In the simulation studies we assumed the detector/collimator assembly to be rotated with equally spaced angular sampling around the longitudinal axis to collect different views for the reconstruction process.

Detection sensitivity for a pinhole is given by

$$g_c = \frac{D^2 \cos^3 \theta}{16h^2}, \quad (1)$$

where D is the diameter of the pinhole, h is the distance between object and the pinhole and θ is the angle between the central ray passing through the pinhole and the normal to the surface of the detector plane.

2.2. Numerical phantoms

The numerical phantoms used in this simulation study are shown in figure 3. The images at the top row in figure 3 show spherical phantoms with a 10 mm diameter (in the simulations we also used spheres with 5.4 and 8.0 mm diameters) that are uniformly filled with radioactivity at the center (top-left) and off-center (top-middle) of object space, and two spheres, one at the center of the LFOV and another outside the LFOV (top-right). The spherical target objects were embedded into a prism with dimensions 29 mm × 29 mm × 58 mm. Various background activities were included in different studies to obtain different target-to-background (T/B) ratios. Additionally, the digital mouse whole-body (MOBY) phantom, where the intensities of each organ represent the uptake of the radiotracer in the organ, was used as an '*ex vivo*' mouse model (Chen *et al* 2007) for cardiac imaging. Note that two different sets of mouse phantoms were used to simulate uniform activity within the heart chamber (bottom left in figure 3) and myocardium (middle at the bottom in figure 3). The image at the bottom right of figure 3 is a resolution phantom comprising cylinders of

1.8 mm diameter spaced at 3.6 mm center to center. The cylinders are to mimic the hot regions of radioactivity and the background is set to zero in this model. The diameter of each cylinder was chosen to take into account the collimator and detector resolution. The resolution phantom also included cylinders outside the LFOV to study the effect of activity coming from outside the LFOV.

2.3. Image reconstruction for the LFOV using a priori information

At first the system matrix was generated for the nine-pinhole SPECT system using $64 \times 64 \times 128$ pixels and 90 equally spaced axial angular views around 360° . We used the maximum likelihood-expectation maximization (ML-EM) technique for image reconstruction. The ML-EM algorithm is given in equation (2). The images were represented as a matrix of $64 \times 64 \times 128$ pixels with the dimensions of $0.45 \text{ mm} \times 0.45 \text{ mm} \times 0.45 \text{ mm}$ per voxel. The attenuation and the scatter were not modeled in this study:

$$\lambda_j^{n+1} = \frac{\lambda_j^n}{\sum_m S_{m,j}} \sum_i S_{i,j} \frac{Q_i}{\sum_k S_{i,k} \lambda_k^n} \quad (2)$$

where Q_i is the measured value for the projection bin i , λ_j^n is the reconstructed value in voxel j at the n th iteration and $S_{i,j}$ is the sensitivity matrix for the contribution of voxel j to the projection bin i .

In tomographic imaging, projection data are the integration of intensities of contributing voxels that are along a trajectory contributing to the projection. The projection step in equation (2) is further described in equation (3) to explain the projection data acquisition procedure through the pinhole apertures from a scanner. Each projection in equation (3) was calculated with the previously calculated sensitivity matrix, $S_{\theta,p}(x, y, z)$ for an object with activity of $A(x, y, z)$, with $M_p(x, y, z \rightarrow u, v, \theta)$, the mapping function of x, y and z from image space into the u, v and θ in the projection space (Beque 2005):

$$Q_p(u, v, \theta) = \iiint A(x, y, z) S_{\theta,p}(x, y, z) M_p(x, y, z \rightarrow u, v, \theta) dx dy dz \quad (3)$$

where Q_p is for the projections of each aperture p , n is the number of voxels and M_p is the mapping function from object voxel at (x, y, z) to the detector pixel at (u, v) for projection angle θ .

In equation (3) integration is done along a ray that passes through all the object voxels that contribute to a detector pixel at (u, v, θ) . Therefore, the intensity of a voxel in the image space includes contributions from the surrounding voxels including random and structured noise. According to Manglos *et al* the probability that a photon emitted from an object voxel j will be detected at detector pixel i can be the combination of geometric efficiency and the weight that is proportional to the volume of voxel j contributing to projection i pixel (Manglos *et al* 1989) when one uses discrete sampling. Then the discrete version of the sensitivity matrix can be written as

$$S_{i,j}(x, y, z) = g_c W_{i,j} \quad (4)$$

where g_c is the geometrical efficiency in equation (1) and $W_{i,j}$ is the contribution of the j th voxel to i th projection bin.

The geometric efficiency, g_c , remains the same as long as the configuration of the system remains unchanged. The weighting factors, $W_{i,j}$, are calculated based on the volume of the cone that the gamma ray passes through the voxel for a given point on the projection. As a result, the weighting factors are proportional only to the volume. In this work we propose to use anatomical *a priori* information from MRI and the first-order estimate of the radioactivity distribution from SPECT without any *a priori* to improve the quantitative accuracy of K-SPECT within the LFOV while reducing the dimensions of the reconstruction matrix. In figure 4, the K-SPECT image reconstruction procedures are summarized in a flowchart, and explained in detail in the following subsections. It should be emphasized that the procedures outlined in figure 4 take place after the initial MR imaging to determine the ROI. The procedures shown here start with the simultaneous acquisition of the MRI and SPECT data. Although the distribution of the radioactivity may be heterogeneous within the target visualized from MRI, our results show that the K-SPECT reconstruction using the anatomical *a priori* information from MRI improves the quantification.

2.3.1. Identification of the ROI in K-SPECT from the high-resolution MR image

—At first the ROI that covers the target organ needs to be determined from the MR images. This is done by performing a whole-body MRI and then selecting a 3D spherical volume of interest (VOI) from these images to cover the target region. Once the VOI is determined from the MRI images, the animal bed can be moved to position the VOI at the center of the LFOV of the detector system. In the remainder of this work we will only be discussing the central trans-axial slice through the VOI, which will be indicated as the ROI. After this re-alignment process the object remains at the same position so that the center of rotation within the object remains the same during the entire simultaneous MRI/SPECT image acquisition. The circular ROI covers both the target organ as well as the surrounding background within the LFOV.

Since the images from MRI and SPECT are very different in content, image co-registration by software leads to image distortions, which is a typical problem for the post-image-processing methods even when markers are used (Cherry 2006). However, with the combined MRI/SPECT imaging system, the image co-registration by software is not necessary because the two scanners are mechanically fully co-registered and remain so while all the images are acquired simultaneously.

2.3.2. Determination of the adaptive weighting matrix using *a priori* information from the initial SPECT image

—Although the signal intensity distribution in MRI is different from that in the SPECT image due to the different physical and biological origins for each signal MRI can still provide a high-resolution anatomical image of the target region. Once the ROI is determined from the MR image, it can be used to form a template to separate the target and non-target regions in the SPECT image reconstruction. The average counts in the target and background regions are calculated from the initial SPECT image. Then each pixel of the template covering the target organ generated by the MR image is assigned the same average T/B value while the pixels outside the target organ but within the LFOV are assigned a value of 1. Finally, the pixels outside the LFOV are given a value of 0. This weighting factor map is then used to modify the system matrix to take into account the average emission probability from each pixel using the MR and initial SPECT images. If one wishes to make the situation more complicated, a different weighting map that takes into account pixel by pixel variations of the emission probability can also be generated. However, the current work proves that a simple weighting factor map seems to be adequate as will be seen from the results. In our simulation studies we did not take the effects of attenuation into account. As is well known, MRI information could also be used to perform the necessary attenuation correction.

2.3.3. Generation of an adaptive system matrix by using two priors—In order to reject the contributions from outside the LFOV and take into account the emission probabilities within the LFOV, it is necessary to generate a weighting map so that only voxels inside the LFOV contribute during the reconstruction process. Equations (5a) and (5b) show how the *a priori* information from the reconstructed image using SPECT without *a priori* information and the anatomical information from MRI are used to generate the adaptive system matrix:

$$S'_{i,j} = \sum_k S_{i,k} \xi_{k,j} \quad (5a)$$

where

$$\xi_{k,j} = \begin{cases} T/B & \text{if } (k, j) \in \text{target} \\ 1 & \text{if } (k, j) \in \text{LFOV} \cap \text{target}^c \\ 0 & \text{if } (k, j) \in \text{LFOV}^c \end{cases} \quad (5b)$$

The elements of the weighting matrix, $\xi_{k,j}$, within the LFOV given in equation (5b) are calculated as described in the previous subsection. All the *a priori* information obtained from the MRI and the initial SPECT image is included in this weighting matrix that is nothing but an ‘un-normalized’ probability distribution matrix. It should be emphasized that a new weighting matrix needs to be generated only once during the image reconstruction procedure for a given object. ‘LFOV^c’ in equation (5b) indicates that the voxels do not belong to the LFOV, and ‘target^c’ in equation (5b) indicates that the voxels do not belong to the ROI (target).

2.3.4. LFOV only image reconstruction—With the modified system matrix for the LFOV, the image reconstruction is performed using the ML-EM algorithm shown in equation (7) with equations (5a) and (5b). In this paper, this method using the adaptive sensitivity matrix (equation (7)) will be called the K-SPECT method to distinguish it from standard reconstruction using the ML-EM algorithm with the detection probability matrix given in equation (6) where no *a priori* information is used, namely

$$S'_{i,j} = S_{i,j}. \quad (6)$$

The simulation results presented in the following section show that incorporation of *a priori* information results in the improvement of the SPECT images by reducing the artifacts arising from radioactivity outside the LFOV when compared to SPECT images that do not use any *a priori* information during reconstruction:

$$\lambda_j^{n+1} = \frac{\lambda_j^n}{\sum_m S'_{m,j}} \sum_i S'_{i,j} \frac{Q_i}{\sum_k S'_{i,k} \lambda_k^n}. \quad (7)$$

2.4. Importance of positioning the ROI at the center of the imaging space

It is important to align the centers of the ROI and LFOV with the rotation axis accurately. The LFOV used here was 10 mm in diameter. The alignment of the ROI at the center of the imaging space reduces the chance of a part of the object of interest to be left outside the LFOV or inclusion of an object of no interest within the LFOV. To show the effect of the

misalignment of the ROI from the center, a spherical numerical phantom with an off-centered ROI was generated and the result is shown in section 3.4.

2.5. Error evaluation method

In order to compare the reconstructed image (I_r) with the actual image (I_a —data from the phantom), the errors were evaluated using the root-mean-square-error (RMSE) criterion given by

$$\varepsilon^2 = \frac{\sum_{n=1}^N [I_a - I_r]^2}{\sum_{n=1}^N [I_a]^2} \quad (N, \text{ the number of voxels}). \quad (8)$$

where I_a and I_r are defined above.

3. Results

The results shown in this section were obtained using the 3D phantoms described above and 3D reconstruction in all cases. However, in what follows we will only be presenting a central axial reconstructed slice of the 3D data set since the off-centered slices will also display artifacts due to truncation of projections in the longitudinal direction in addition to the insufficient sampling of cone beam projections. As is well known, these artifacts could be reduced by moving either the animal bed or the gantry in incremental steps in the longitudinal direction to acquire additional data. This will be the subject of a future study.

3.1. Effects of out-of-field objects on the resolution phantom

The resolution phantom shown in figure 3 was reconstructed by using both techniques with a LFOV of 10 mm diameter. The LFOV is overlaid on the phantom and reconstructed images in figure 5 in red indicate its position. The results are shown in figure 5. In this case we assumed no background signal.

In the case of figure 5(c) the reconstruction was performed over the entire reconstruction area in contrast to figure 5(b) where it was only performed within the LFOV. The intensity profiles shown in figure 5(d) indicate that the K-SPECT profile is very close to the actual profile obtained from the phantom whereas the profile obtained using reconstruction without the *a priori* underestimates the signal intensities considerably within the LFOV (between two black solid lines).

3.2. Reduction of artifacts from outside the LFOV

The image reconstruction of an ROI positioned inside of the LFOV was performed using the adaptive system matrix (equation (5a)), which was generated by reducing the dimensions of the original system matrix using the *a priori* information. The RMSE criterion (equation (8)) was used to evaluate the artifacts within the ROI using the K-SPECT reconstruction and compare it with the ML-EM method (equation (5a)) that did not use any *a priori* information (to be called the ‘standard method’ henceforward).

Figure 6 shows the reduction of artifacts from outside the LFOV. The object was a sphere 8 mm diameter embedded within a prism of dimensions 29 mm × 29 mm × 58 mm using a uniform background with a T/B activity ratio of 5:1, figure 6. In this case the LFOV diameter was 10 mm whereas the ROI diameter was 8 mm. The reconstructed image with the ML-EM with no *a priori* is shown in figure 6(d). Due to the background noise the

artifact inside the ROI is high (RMSE = 0.32). The reconstructed image using the K-SPECT method is shown in figure 6(c) and the error (RMSE = 0.08) is improved by 74.5% within the ROI. The global RMSE for the area of the LFOV is 0.24 for (c) and 0.41 for (d), which is improved by 40.4% by using the K-SPECT method. The image shown in figure 6(d) shows larger artifacts along the diagonal directions. This is due to the prism shape of the entire object resulting in larger background signals along the diagonal directions compared to the vertical and horizontal directions. It is seen that the K-SPECT method eliminates these artifacts considerably.

An additional example of the image artifacts recovered by using the adaptive system matrix is shown in figure 7. The image in figure 7(a) is the input phantom of two 10 mm diameter spheres, one is at the center of the LFOV that would be taken as the ROI and the other one is outside of the LFOV representing a high intensity object outside the field of interest. The area of the LFOV is the same as the sphere at the center of figure 7(a). Therefore, the sphere at the center of figure 7(a) covers the whole area of the LFOV. Figure 7(b) shows the reconstructed image of the ROI with the K-SPECT method. Figure 7(c) shows the reconstructed image of the ROI using the 'standard' ML-EM method that does not take into account any *a priori* information. The RMSE of the area for the LFOV for figure 7(b) (RMSE = 0.17) is improved by 60.1% compared to figure 7(c) (RMSE = 0.43). Figures 7(d) and (e) show horizontal and diagonal profiles through figures 7(a)–(c). It is seen that in all cases the intensity profiles obtained by the K-SPECT method are much closer to the actual ones when compared to the ML-EM reconstruction without *a priori* data. Thus both the overall artifact reduction as quantified by the RMSE and plotted image profiles demonstrate significant improvements due to the use of *a priori* data during the reconstruction process.

3.3. Simulation with the MOBY phantom

The image reconstructions were performed with the digital mouse phantom (MOBY) provided by Dr Segars' group at Duke University (Chen *et al* 2007). The phantoms were generated either with high activity in the heart chamber (blood pool imaging) or in the myocardium (myocardial uptake imaging) separately to show different uptake patterns. The evaluation of the reconstructed images with respect to the input digital phantom was done using the RMSE criteria as described earlier using equation (8).

3.3.1. Heart chamber imaging—The image in figure 8(a) is the input phantom of digital mouse with activity inside the heart chamber. The image in figure 8(b) was reconstructed by using the system matrix generated with the K-SPECT method, and that the image in (c) was reconstructed by using the 'standard' ML-EM method. Images shown are the axial center slice of a 3D image data set. By using the adaptive system matrix (K-SPECT technique), the output image of the ROI is improved. The RMSE of the area for the LFOV (K-SPECT) for (b) (RMSE = 0.19) is improved by 48.5% compared to (c) (RMSE = 0.38). The improved image due to inclusion of *a priori* data can be observed in figures 8(b) and (d).

3.3.2. Myocardium imaging—The digital mouse phantom was generated with a high uptake in the myocardium muscle wall as shown in figure 9(a). The images in figures 9(b) and (c) were reconstructed by using the new adaptive system matrix (K-SPECT method) and the 'standard' ML-EM method without any *a priori* information, respectively. The same axial slices reconstructed by both methods are shown in figures 9(b) and (c). It is seen that the image reconstructed by using the adaptive system matrix is improved over the other. The RMSE for the LFOV reconstruction with K-SPECT for figure 9(b) (RMSE = 0.25) is improved by 52.6% compared to that for figure 9(c) (RMSE = 0.53) without *a priori* information during reconstruction. We note that in figures 9(c) and (d) one cannot even

distinguish the walls of the two heart chambers without *a priori* information provided by MRI.

3.4. Importance of alignment of the ROI within the LFOV

For the K-SPECT reconstruction, it is important to position the ROI within the area of the LFOV. When they are misaligned, which represents partial correlation between MRI and SPECT, the high radioactive area can be left outside the LFOV; therefore, the activity from the area is treated as noise in the K-SPECT. As an example, the image in figure 10(b) shows the reconstructed image of the spherical phantom, figure 10(a), when the LFOV fully covers the ROI. If the LFOV and the ROI are misaligned as shown in figure 10(c), the resultant reconstructed image is shown in figure 10(d). We see that in addition to truncation of the target area the signal intensity in the image is non-uniform.

3.5. Effect of the T/B ratio on K-SPECT reconstruction

To study the effect of the T/B ratio on the K-SPECT image reconstruction method three phantoms with different T/B ratios were generated as shown in figures 11(a), (b) and (c). The phantom was a 29 mm × 29 mm × 58 mm prism with a 5.4 mm sphere positioned at the center. Thus the ROI covering the tar object (the sphere) was 5.4 mm in diameter and the LFOV was 10 mm in diameter as previously. We assumed three different T/B ratios, namely 2:1, 5:1 and 10:1 (see figures 12 (a), (b) and (c)).

The simulation result showed that the normalized RMSE by the intensity within the ROI was 0.34%, 0.25% and 0.15% for the T/B ratios of 2:1, 5:1 and 10:1, respectively. Therefore, as expected the K-SPECT image reconstruction method reduces the error better for the objects with higher T/B ratios.

4. Discussion

The overall purpose of this study was to develop and test a new SPECT reconstruction algorithm that could be used to image a target region (organ) in a small animal while placing a constraint on the size of the detector to be used. The advantages of such an approach include the lower cost of the system due to smaller detector size and less demanding computation due to reduced size of the reconstruction space. In order to achieve these we designed a system using multi-pinhole collimators that could be used to acquire non-overlapping and magnified images of the target on the nuclear detector. While pinhole collimators with accurately designed acceptance angles could reduce contribution from outside the field of interest, they cannot remove contributions from overlapping tissues within the field of interest. In order to minimize the contributions from such objects we used anatomical *a priori* information from MRI and radioactive uptake *a priori* information from the first-order SPECT reconstruction without any *a priori* information.

In this study we did not model attenuation and scatter. However, the former can be corrected using an attenuation map that can be obtained from the segmented MR image. Scatter on the other hand could be corrected by using the well-known three-energy-window technique commonly used in clinical SPECT (Ogawa *et al* 1991). In the present approach the object can be sampled adequately within the axial direction by rotating the detectors around the longitudinal axis, but the data in the azimuthal direction are not fully sampled for cone beam geometry. However, the azimuthal sampling can be improved by moving the patient bed in steps similar to spiral scanning in CT. This will be the subject of a future study. For the proposed study, it is very important to position the whole area of the ROI inside the LFOV due to the differences of imaging mechanisms between MRI and SPECT. The ROI determination could affect the SPECT image accuracy because if a lesion were left outside

of the LFOV the activity from the region would not be sampled adequately resulting in reduced accuracy and artifacts.

5. Conclusions

The present simulation study investigated the performance of an iterative reconstruction technique (ML-EM) to reconstruct SPECT images within a LFOV that covers the target area using *a priori* information provided by MRI and SPECT (reconstructed without *a priori*). The performance of the K-SPECT algorithm was compared with the ML-EM reconstruction without any *a priori* information. Our results show that by using *a priori* anatomical information from the MRI and activity distribution information from the SPECT image, artifacts caused by radioactivity outside the LFOV can be reduced and spatial resolution improved. While simultaneous data acquisition by both systems is not essential, the availability of such a capability can be used for absolute co-registration both spatially and temporally. The new technique also has some computational advantages. The size of the 3-D system matrix was $64 \times 64 \times 128$ pixels, whereas it was $25 \times 25 \times 25$ pixels for the K-SPECT method due to the rejection of the contributions from voxels outside the LFOV. Thus, the number of computations was reduced by 97%. Finally, unlike the previous studies that used *a priori* information from multi-modality imaging mostly for attenuation correction or for post-processing, the current study used the information to remove the artifacts arising from objects outside the LFOV at the image reconstruction stage to improve the image accuracy and the quantification for the SPECT images.

Acknowledgments

The authors express special thanks to Dr Paul Segars at Duke University for providing the software for the MOBY phantom. This project was supported in part by CIRM grants TG2-01152 (KSL), RT1-01120-1 (ON), NIH grant R01EB007219 (GTG) and by the Director, Office of Science and Office of Biological and Environmental Research, Medical Sciences Division of the US Department of Energy under contract DE-AC02-05CH11231 (GTG). It was also supported in part by the World Class University program through the National Research Foundation of Korea funded by the Ministry of Education, Science and Technology, South Korea (grant no R31-20004-(ON)).

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Figure 1.

Left: an animal body (the ellipse) is set at the center of the RF coil, but the ROI is outside of the LFOV seen by the nuclear detector. Right: the animal is moved to the left in order for the ROI's center to coincide with the center of the LFOV. The dimensions shown in the figure are the actual values used in the simulation studies.

Figure 2.
Left: layout of the nine-pinhole collimator. Right: an axial view of the imaging system.

Figure 3.

Top row: axial view of uniformly filled numerical phantoms: from the left, 10 mm diameter sphere at the center of image, 10 mm diameter sphere off-centered and two 10 mm diameter spheres, one at the center of the LFOV and another off-centered. Bottom row: from the left, axial view of the MOBY phantom with uniform radioactivity in the heart chamber, axial view of the heart wall with uniform uptake and the resolution phantom with cylinders of 1.8 mm diameter with 3.6 mm center-to-center spacing. The dotted circle indicates the area of the LFOV.

Figure 4.
Flowchart of the K-SPECT image reconstruction method. The details for the procedures are explained in sections 2.3.1 through 2.3.4.

Figure 5.

(a) Resolution phantom; (b) reconstructed image using the K-SPECT technique; (c) reconstructed image using the standard ML-EM method that does not use any *a priori* information; and (d) horizontal intensity profiles through all three images.

Figure 6.

(a) Spherical phantom (8 mm in diameter) with 5:1 contrast; (b) illustrative description of (a) the ROI (8 mm in diameter) within the LFOV (10 mm in diameter); (c) reconstructed image of (a) with the K-SPECT method, and (d) reconstructed image of (a) with the standard ML-EM method with no *a priori*.

Figure 7.

(a) Two spherical digital phantoms with 10 mm diameter: one at the center of image space and another off-centered; (b) reconstructed image of the phantom within the LFOV with the K-SPECT method; (c) reconstructed image of the same phantom with the ML-EM reconstruction without *a priori* data; (d) horizontal profiles through (a)–(c); and (e) diagonal profiles through (a)–(c).

Figure 8.

(a) MOBY phantom-cardiac chamber, (b) reconstructed image with the K-SPECT method, (c) reconstructed image with the ML-EM reconstruction without *a priori* and (d) corresponding intensity profiles along the lines shown in (a)–(c).

Figure 9.

(a) MOBY phantom-myocardium, (b) reconstructed image with the K-SPECT method, (c) reconstructed image with the ML-EM reconstruction without *a priori* and (d) corresponding intensity profiles along the lines shown in (a)–(c).

Figure 10.

(a) Spherical phantom (10 mm diameter); (b) reconstructed image of (a) when the ROI is aligned with the center of the LFOV using the K-SPECT reconstruction method, (c) example of misaligned ROI with the LFOV (1.5 mm off in both x - and y -axis directions from the center of the LFOV) and (d) reconstructed image of (a) with the figurative scheme shown in (c).

Figure 11.
The input phantoms with T/B ratios of (a) 2:1, (b) 5:1 and (c) 10:1 used in the simulation.

Figure 12.

The effect of T/B on the K-SPECT method. In all cases the first column is the phantom, the second column is a reconstructed image without any *a priori*, the third column is a reconstructed image with the K-SPECT method and the fourth column is a horizontal intensity profile through the corresponding three images for each case. Results for different T/B ratios are given in (a)–(c).