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Performance Evaluation of Small Animal PET Scanners With Different System Designs

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Abstract

This study evaluated the image quality metrics of small animal PET scanners based upon measured single detector module positioning performance. A semi-analytical approach was developed to study PET scanner performance in the scenario of multiple realizations. Positron range blurring, scanner system response function (SRF) and statistical noise were included in the modeling procedure. The scanner sensitivity map was included in the system matrix during maximum likelihood expectation maximization (MLEM) reconstruction. Several image quality metrics were evaluated for octagonal ring PET scanners consisting of continuous miniature crystal element (cMiCE) detector modules with varying designs. These designs included 8 mm and 15 mm thick crystal detectors using conventional readout with the photosensors on the exit surface of the crystal and a 15 mm thick crystal detector using our proposed sensor-on-the-entrance (SES) design. For the conventional readout design, the results showed that there was a tradeoff between bias and variance with crystal thickness. The 15 mm crystal detector had better detection task performance, while quantitation task performance was degraded. On the other hand, our SES detector had similar detection efficiency as the conventional design using a 15 mm thick crystal and had similar intrinsic spatial resolution as the conventional design using an 8 mm thick crystal. The end result was that by using the SES design, one could improve scanner quantitation task performance without sacrificing detection task performance.

Keywords

Image quality metrics; maximum likelihood expectation maximization (MLEM) reconstruction; monolithic crystal detector; system response function

I. Introduction

SMALL animal PET imaging offers researchers a non-invasive technique to evaluate the bio-distribution of new PET tracers and to perform longitudinal imaging studies [1]. The small dimensions of the structures to be studied require a small animal PET system to have high image resolution and high detection sensitivity. Our group has previously reported on

high intrinsic spatial resolution, continuous miniature crystal element (cMiCE) small animal PET detector modules [2]–[5]. Compared to discrete crystal PET detectors, cMiCE detectors have a number of advantages including low fabrication cost, high packing fraction, continuous sampling, and intrinsic depth-of-interaction (DOI) decoding capability. The intrinsic resolution performance of cMiCE detector modules with varying geometries has been tested and the results reported [4]–[7]. However, predicting the performance of a whole PET scanner for different imaging tasks is a challenge, especially when there is a tradeoff between image resolution and sensitivity.

Monte Carlo simulations have been widely used when studying PET scanner performance [8], [9]; however, these are computationally intensive and complex to implement [10]. In this work, we used a semi-analytical approach to investigate PET scanner performance with varying system designs in the scenario of multiple realizations.

II. Methods

A. cMiCE PET Scanner Design

We evaluated the performance of octagonal PET scanners consisting of cMiCE detector modules with different designs, as shown in Fig. 1. The field of view (FOV) of the scanners was 120 mm. An energy window of [410, 710] keV was applied to the test events. The cMiCE detector modules studied were: (1) 8-mm conventional design cMiCE detector: a $50 \times 50 \times 8\text{-mm}^3$ LYSO crystal coupled to a Hamamatsu H8500 PMT on the exit surface [5]; (2) 15-mm conventional design cMiCE detector: a $50 \times 50 \times 15\text{-mm}^3$ LYSO crystal coupled to a Hamamatsu H8500 PMT on the exit surface [4]; and (3) 15-mm sensor-on-entrance-surface (SES) design cMiCE detector: a $50 \times 50 \times 15\text{-mm}^3$ LYSO crystal coupled to a 144-channel SiPM array on the entrance surface [6], [7].

The SES design was motivated by the hypothesis that having the photosensors on the entrance surface, closer to the location of most gamma ray interactions, will improve the intrinsic spatial resolution performance compared to the conventional exit surface design. Prior simulation results predicted greater than 20% improvement in detector intrinsic spatial resolution with SES designs [6], [7]. Preliminary experimental results showed 14% improvement in X/Y detector intrinsic spatial resolution [15] when using three-dimensional X/Y/Z positioning.

B. Modeling Procedure

Fig. 2 shows the block diagram of the modeling procedure [14]. The 2D test phantoms were forward projected to form perfect sinograms with 240 distance bins and 240 angular bins. Each distance bin was 0.25 mm. After adding ^{18}F positron range blurring, the sinograms were further blurred with the spatially variant scanner system response function (SRF) to simulate the detector measurement uncertainties and the non-uniform sensitivity of the scanner. Poisson noise with varying count levels was added to the blurred sinograms. The maximum likelihood expectation maximization (MLEM) algorithm was used for image reconstruction. Several figures of merit were calculated to study the scanner performance.

1) Phantoms—Three 2D phantoms were created to test scanner performance. The pixel size of the phantoms was $0.25 \times 0.25\text{ mm}^2$. The point source phantom [Fig. 3(a)] had point sources, consisting of a single pixel, at 5 mm, 10 mm, 15 mm, 20 mm and 25 mm away from the scanner center in a warm background. It was used to characterize the image resolution. The background of the phantom had a diameter of 60 mm. The ratio of activity in the point source to background was 200:1.

One hot spot phantom [Fig. 3(b)] had 1-mm, 2-mm, 3-mm, 4-mm and 5-mm diameter hot spots at a radius of 7 mm away from the scanner center in a cold background. It was used to calculate the recovery coefficient.

The second hot spot phantom [Fig. 3(c)] was similar to the first except it had a signal-to-background ratio of 2. The background cylinder had a diameter of 30 mm. The second hot spot phantom was used to characterize the noise properties and the SNR properties of images.

The phantoms were forward projected to form sinograms. Positron range blurring and the scanner system response function were included in the forward projection process. After the sinograms were formed, Poisson noise was added to simulate different system detection efficiencies.

2) Positron Range Blurring—The empirical exponential functions estimated by Derenzo were used for implementing the blurring effects due to positron range [16].

$$q(x) = Ae^{-x/B} + (1 - A)e^{-x/C}. \quad (1)$$

The parameters corresponding to ^{18}F , $A = 0.851$, $B = 0.054$, $C = 0.254$, were used in this paper.

3) Scanner System Response Function (SRF)—The positioning performances of the conventional design cMiCE detector modules were measured experimentally. The positioning performance of the 15-mm SES design cMiCE detector was assumed to be 20% better than the 15-mm conventional design cMiCE detector based upon simulation studies [6], [7] and related experimental measurements [15]. A parametric model [17], which is a more general form of a Gaussian model and a Cauchy model, was used to better represent the positioning error profiles. The parametric function is defined as

$$f(x; a, b, c, d) = a \cdot \left(1 + \frac{(x - b)^2}{c^2 \cdot d} \right)^{-d} \quad (2)$$

where x is the spatial position, and a, b, c, d are parameters to describe the function. If $d = 1$, the parametric model is a Cauchy distribution. If $d \rightarrow \infty$, the parametric function will converge to the Gaussian model.

Fig. 4 shows the X/DOI(Z) positioning error profiles for three cMiCE detectors.

For the 8-mm conventional design cMiCE detector, the X intrinsic resolution was 1.21 mm FWHM for the center area ($36 \times 36 \text{ mm}^2$) and 1.56 mm FWHM for the edges ($36\text{--}48 \text{ mm}$). The DOI (Z) intrinsic resolution was 2.79 mm FWHM for the whole effective area ($48 \times 48 \text{ mm}^2$).

For the 15-mm conventional design cMiCE detector, the X intrinsic resolution was 1.45 mm FWHM for the center area ($34 \times 34 \text{ mm}^2$) and 1.82 mm FWHM for the edges ($34\text{--}46 \text{ mm}$). The DOI(Z) intrinsic resolution was 3.80 mm FWHM for the whole effective area ($46 \times 46 \text{ mm}^2$). The effective area for the 15-mm conventional design cMiCE detector was smaller than the 8-mm conventional design cMiCE detector, because event decoding becomes more difficult when crystal thickness increases, especially at the edge of the crystal. Therefore in practice, the edge of the crystal will be masked.

For the 15-mm SES design detector, we assumed the effective area was the same as the 15-mm conventional design cMiCE detector. The X intrinsic resolution was 1.16 mm FWHM for the center area ($34 \times 34 \text{ mm}^2$) and 1.46 mm FWHM for the edges ($34\text{--}46 \text{ mm}$). The DOI(Z) intrinsic resolution was 3.04 mm FWHM for the whole effective area ($46 \times 46 \text{ mm}^2$).

The 4D scanner system response function $\text{SRF}(s, \theta, s_e, \theta_e)$, where s and θ refer to distance and angle in sinogram space and s_e and θ_e refer to error in s and θ , was generated as follows: (1) 50,000 events were simulated to generate $\text{SRF}(s_0, \theta_0, s_e, \theta_e)$ for each line of response $\text{LOR}(s_0, \theta_0)$; (2) For each $\text{LOR}(s_0, \theta_0)$, the true incident positions (X, Z) on the corresponding detector pair were calculated based upon the scanner geometry and the exponential decrease in photon beam intensity of the photon beam in the crystal, and the sensitivity for each LOR was calculated based upon path lengths in the corresponding detector pair; (3) X/DOI(Z) positioning errors based on the parametric fitted intrinsic resolution profiles in Fig. 4 were added to generate the estimated positions (X', Z'); (4) The errors in sinogram space (s_e, θ_e) were calculated from (X, Z) and (X', Z') based upon the scanner geometry; (5) 2D histograms were computed to generate $\text{SRF}(s_0, \theta_0, s_e, \theta_e)$.

4) Poisson Noise—Poisson noise was added to the blurred sinograms. For hot spot phantoms, the total number of counts per image was 3.6M for the 15-mm cMiCE scanners and 2M for the 8-mm cMiCE scanner. For the point source phantom, the total number of counts was 10M and 18M for the 15-mm and 8-mm cMiCE scanners respectively. The ratio of the total counts was chosen based upon the thickness difference and the effective area difference of the cMiCE detector modules [4], [5]. The gamma ray interaction probability (singles event) in the 15-mm thick LYSO crystal is 1.46 times that of the 8-mm LYSO crystal. Therefore, the sensitivity for singles events increases by a factor of 1.46 and the sensitivity for coincidence events increases by a factor of 2.14. The effective area of the 15-mm LYSO crystal is 91% of the 8-mm LYSO crystal. Therefore, the sensitivity for singles events degrades by 0.91 and the sensitivity for coincidence events decreases by a factor of 0.84. Therefore, the overall sensitivity ratio for coincidence events of the 15-mm thick crystal scanner and the 8-mm scanner is 1.8.

5) Reconstruction—The MLEM algorithm was used for image reconstruction and included a realistic model of the system [18]. One hundred twenty eight iterations were used. To generate the sensitivity map, a uniform cylindrical phantom with 60-mm diameter was forward projected and convolved with the scanner SRF. The sensitivity for each LOR was taken as the ratio of the blurred sinogram versus the un-blurred sinogram. When the sensitivity map measured using a uniform phantom was included in the system matrix, the non-uniform sensitivity of the scanner was compensated.

C. Image Quality Metrics

Several figures of merit were calculated to study the image resolution properties, the noise properties and the signal-to-noise ratio (SNR) properties of the reconstructed images [12]–[14]. The image resolution was characterized by the full width half maximum (FWHM). The recovery coefficient (RC) was defined as the ratio of reconstructed activity to true activity. Image roughness (IR) and ensemble noise (EN) were used to study the noise properties of the images. The region-of-interest SNR (SNR_{ROI}) and the non-prewhitening SNR (SNR_{NPW}) were used to study the quantification task performance and the detection task performance of the scanner, respectively.

The reconstructed signal in the hot spots was modeled as

$$f_{ir} = f_0 + n_{ir} \quad (3)$$

where f_{ir} is the reconstructed value at pixel i for realization r , f_0 is the true activity in the hot spots and n_{ir} is the noise term.

For realization r , the mean of the pixels in the k th region of interest (ROI) is

$$m_{r,k} = \frac{1}{I} \sum_{i \in ROI_k} f_{ir} \quad (4)$$

where I is the number of pixels in ROI_k . Circular ROIs with the same diameter as the hot spots are used.

The mean of pixels across different realizations for ROI_k is

$$\bar{m}_k = \frac{1}{R} \sum_{r=1}^R m_{r,k} \quad (5)$$

where R is the number of realizations.

1) Image Spatial Resolution—The image resolution was characterized using the point source phantom with a signal-to-background ratio of 200:1 [Fig. 3(a)] based upon one image realization. The spatial resolution of the system was characterized by the FWHM in the radial and tangential directions. Following the NEMA NU 4 standard [19], FWHM were measured directly from one-dimensional response functions through the peak of the image, which were formed by summing all one-dimensional profiles within 4 mm of the peak in both orthogonal directions. MLEM was used for image reconstruction, because standard filtered back projection (FBP) image reconstruction does not work well for detector systems with relatively large sensitivity gaps in the system response. The cMiCE scanner geometry has large gaps because events positioned near the edge of our detector are not kept due to positioning inaccuracies in those regions. Methods have been developed to use FBP image reconstruction for detector systems with gaps [20]; however, the technique reduces image resolution and our intent is to use MLEM image reconstruction for any cMiCE system implementations.

2) Recovery Coefficient—The mean recovery coefficient was characterized using the hot spot phantom with cold background [Fig. 3(b)] based upon one image realization. The mean of the RC for ROI_k is defined as

$$RC_{mean_k} = \frac{\text{mean}(f_{i,k})}{f_{0,k}} = \frac{\frac{1}{I} \sum_{i \in ROI_k} f_{i,k}}{f_{0,k}} \quad (6)$$

where $f_{i,k}$ is the reconstructed value at pixel i in ROI_k . This is determined by the ratio of the size of the hot spots to the image resolution [21] and represents the quantitation task performance of the scanner.

3) Image Roughness (IR)—The image roughness was characterized using the hot spot phantom with a signal-to-background ratio of 2 [Fig. 3(c)] and 50 image realizations. IR measures the pixel-to-pixel variability in the image. It is the image noise perceived when viewing an individual image [13]. For ROI_k and realization r , image roughness is defined as

$$IR_{r,k} = \frac{\sqrt{\frac{1}{I-1} \sum_{i \in ROI_k} (f_{i,r} - m_{r,k})^2}}{m_{r,k}}. \quad (7)$$

This metric can be calculated for a single realization. The overall image roughness can also be calculated as the average over all realizations. The image roughness affects the detection task performance of the scanner.

4) Ensemble Noise (EN)—The ensemble noise was characterized using the hot spot phantom with a signal-to-background ratio of 2 [Fig. 3(c)] and 50 image realizations. EN is a measure of noise across independent realizations. Due to statistical variations in the data, if the same object is imaged multiple times, the reconstructed images will not be the same. For each ROI_k , it is defined as

$$EN_k = \frac{\sqrt{\frac{1}{R-1} \sum_{r=1}^R (m_{r,k} - \bar{m}_k)^2}}{\bar{m}_k}. \quad (8)$$

This metric can only be computed when multiple realizations are available. The ensemble noise has a big impact on the detection task performance of the scanner.

5) SNR_{ROI} —The SNR_{ROI} was characterized using the hot spot phantom with a signal-to-background ratio of 2 [Fig. 3(c)] and 50 image realizations. SNR_{ROI} is a measure of ROI accuracy and precision. It has been proposed as a practical metric for representing quantification performance [12]. It is defined for ROI_k as

$$SNR_{ROI,k} = \frac{f_{0,k}}{\sqrt{\frac{1}{R} \sum_{r=1}^R (m_{r,k} - f_{0,k})^2}}. \quad (9)$$

This metric is determined by the recovery coefficients for multiple realizations.

6) SNR_{NPW} —The SNR_{NPW} was characterized using the hot spot phantom with a signal-to-background ratio of 2 [Fig. 3(c)] and 50 image realizations. SNR_{NPW} has been used as a measurement of detection task performance in binary classification problems [12]. It is defined as

$$SNR_{NPW,k} = \frac{\bar{m}_k^{feature} - \bar{m}_k^{background}}{\sqrt{\frac{s_1^2 + s_0^2}{2}}}, \quad (10)$$

$$s_{1,0} = \sqrt{\frac{1}{R-1} \sum_{r=1}^R (m_{r,k} - \bar{m}_k)^2}$$

where $\bar{m}_k^{feature}$ is the average of ROI_k over all realizations when a target is present for phantoms with hot spheres, $\bar{m}_k^{background}$ is the same average when the target is absent for

replicates without hot spheres, and s_1 and s_0 are the corresponding sample standard deviations through all realizations when the target is present and absent, respectively. This metric is determined by the recovery coefficient and the ensemble noise.

III. Results

Fig. 5 shows the image resolution averaged over radial and tangential directions for point sources at different distances from the scanner center. The image resolution of the 15-mm SES design design cMiCE scanner was 0.29-mm (19%) better than the 15-mm conventional design cMiCE scanner and 0.06-mm (4%) better than the 8-mm conventional design cMiCE scanner on average.

Fig. 6 shows the mean recovery coefficient for ROIs with the same size as the hot spots. We can see that the recovery coefficient results were consistent with the image resolution although smaller differences in recovery coefficients between scanner configurations were observed. The recovery coefficient of the 15-mm SES design design cMiCE scanner was 0.055 (13%) better than the 15-mm conventional design cMiCE scanner and 0.014 (4%) better than the 8-mm conventional design cMiCE scanner on average.

Fig. 7 shows reconstructed images with and without image smoothing. For image smoothing a 0.75-mm FWHM post Gaussian filter was applied.

Fig. 8(a) displays the image roughness of the images. The 15-mm SES design cMiCE scanner had similar image roughness as the 15-mm conventional design cMiCE scanner, which was 0.099 (39%) better without smoothing and 0.023 (34%) better with smoothing than the 8-mm conventional design cMiCE scanner on average.

Fig. 8(b) displays the ensemble noise of the images. The 15-mm SES design cMiCE scanner had similar ensemble noise as the 15-mm conventional design cMiCE scanner, which was 0.015 (55%) better without smoothing and 0.008 (40%) better with smoothing than the 8-mm conventional design cMiCE scanner on average.

Fig. 9(a) shows the SNR_{ROI} that represents the quantitative task performance of the scanners. The SNR_{ROI} of the 15-mm SES design cMiCE scanner was 0.58 (10%) better without smoothing and 0.45 (8%) better with smoothing than the 15-mm conventional design cMiCE scanner, while it was 0.19 (4%) better without smoothing and 0.14 (3%) better with smoothing than the 8-mm conventional design cMiCE scanner on average.

Fig. 9(b) shows the SNR_{NPW} that represents the detection task performance of the scanners. The 15-mm SES design had similar SNR_{NPW} as the 15-mm conventional design cMiCE scanner, which was 10.55 (32%) better without smoothing and 10.30 (27%) better with smoothing than the 8-mm conventional design cMiCE scanner on average.

Fig. 10 shows the bias-variance tradeoff for 2-mm and 4-mm diameter hot spots in a warm background for the three different scanners. The bias is represented by 1 minus the recovery coefficient (1-RC). The variance is represented by the ensemble noise (EN). The six data points on each line correspond to 0–1.875 mm FWHM Gaussian filter smoothing applied to the reconstructed images. As seen, the 15-mm SES design cMiCE scanner provided the lowest ensemble noise for the same bias level among the three scanners. For example, at 0.68 recovery coefficient (0.32 bias), the ensemble noise for the 15-mm SES design cMiCE scanner was 39% lower than the 15-mm conventional design cMiCE scanner and 56% lower than the 8-mm conventional design cMiCE scanner for a 2-mm diameter feature.

IV. Discussion

The image quality metrics for three different cMiCE scanners were compared for the same reconstruction settings. The comparison results without smoothing are summarized in Table I. The newly proposed SES design and 15-mm cMiCE detector modules provided superior performance compared to conventional exit surface 8 mm and 15 mm designs for all evaluated metrics. Of particular value is that the SES design provided lower ensemble noise at matched recovery coefficient. For conventional cMiCE detectors, the metrics evaluated here followed expected trends. For example, when increasing the crystal thickness from 8 mm to 15 mm the noise was reduced, the image resolution was degraded, and the detection task performance, characterized by SNR_{NPW} was improved. However, the quantitation task performance, characterized by the recovery coefficient and SNR_{ROI} was degraded.

There are limitations with this study. First, we did not model the sensitivity difference between the SES design cMiCE detector and the conventional design cMiCE detector. The photo-sensors on the entrance surface of the SES design cMiCE detector could cause sensitivity loss compared to the conventional design cMiCE detector. The amount of sensitivity loss will depend upon the final implementation of the SiPM design. The attenuation to 511-keV gamma photons due to 2 mm of silicon is about 4%. With this threshold in mind, it is anticipated that the SiPM will not cause a substantial reduction in sensitivity. The SES design cMiCE detector has the potential to have greater effective area compared to the conventional design cMiCE detector, which could improve the sensitivity of the SES design cMiCE detector. Experimental studies will be conducted to accurately compare the sensitivities of the cMiCE detectors with conventional design and SES design. Second, the simulations here were performed for two-dimensional imaging only. The study will be scaled to three-dimensions in the future. Third, the attenuation and scatter effects, which are not severe for small animal studies, were not included in this study. It should be incorporated if scaled to human whole body imaging.

V. Conclusion

In this paper, the performance of octagonal ring cMiCE scanners were studied based upon single cMiCE detector module positioning performance using a semi-analytical approach. Task based imaging performance with different detector designs was investigated. There is a tradeoff between bias and variance when increasing the thickness of the cMiCE detector modules. However, using the SES design for cMiCE detector modules could improve the scanner quantitation task performance without sacrificing detection task performance.

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Fig. 1. Octagonal PET scanners with (a) 8-mm conventional design cMiCE detectors; (b) 15-mm conventional design cMiCE detectors; (c) 15-mm SES design cMiCE detectors.

Fig. 2.
Modeling procedure for whole PET scanners.

Fig. 3. 2D phantoms. The gray circle with 60-mm diameter is for illustration. (a) Point source phantom used to characterize the image resolution; (b) Hot spot phantom with cold background used to calculate the recovery coefficient; (c) Hot spot phantom with signal-to-background ratio of 2 used to test noise properties and SNR properties.

Fig. 4. X/DOI(Z) positioning error profiles with parametric fit. (a) 8-mm conventional design cMiCE detector; (b) 15-mm conventional design cMiCE detector; (c) 15-mm SES design cMiCE detector.

Fig. 5.

Image resolution FWHM averaged over radial and tangential directions with varying cMiCE scanner designs. The point source phantom had a signal-to-background ratio of 200:1. Reconstruction was done using 128 iterations of the MLEM algorithm. No smoothing was applied.

Fig. 6. Mean recovery coefficient with varying cMiCE scanner designs. Reconstruction was done using MLEM at 128 iterations. No smoothing was applied.

Fig. 7.

Reconstructed images with varying cMiCE scanner designs. Reconstruction was done using MLEM with 128 iterations. (a) 15-mm conventional design, no smoothing; (b) 15-mm SES design, no smoothing; (c) 8-mm conventional design, no smoothing; (d) 15-mm conventional design, with smoothing; (e) 15-mm SES design, with smoothing; (f) 8-mm conventional design, with smoothing.

Fig. 8. Noise with varying cMiCE scanner designs. Reconstruction was done using MLEM with 128 iterations. (a) Image roughness; (b) Ensemble noise.

Fig. 9. SNR with varying cMiCE scanner designs. Reconstruction was done using MLEM with 128 iterations. (a) SNR_{ROI}; (b) SNR_{NPW}.

Fig. 10.

Bias (1-RC) versus variance (ensemble noise) with varying cMiCE scanner designs. Reconstruction was done using MLEM with 128 iterations. The 6 data points on each line represent 0–1.875 mm FWHM Gaussian filter smoothing. (a) 2-mm diameter hot spot with a signal-to-background ratio of 2; (b) 4-mm diameter hot spot with a signal-to-background ratio of 2.

TABLE I

Improvement of a 15-mm SES Design cMiCE Scanner Compared With Conventional Design cMiCE Scanners

Metrics	Improvement	
	15-mm, conventional	8-mm, conventional
Image resolution	0.29 mm (19%)	0.06 mm (4%)
Recovery coefficient	0.055 (13%)	0.014 (4%)
Image roughness	0.003 (1%)	0.099 (39%)
Ensemble noise	0.00001 (6%)	0.015 (55%)
SNR_{ROI}	0.58 (10%)	0.19 (4%)
SNR_{NPW}	3.39 (9%)	10.55 (32%)