DOI-based reconstruction algorithms for a compact breast PET scanner

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Purpose: The authors discuss the design and evaluate the performance of combined event estimation and image reconstruction algorithms designed for a proposed high-resolution rectangular breast PET scanner (PETX). The PETX scanner will be capable of measuring the depth of interaction by utilizing detector modules composed of depth-of-interaction microcrystal element (dMiCE) crystal pairs. This design allows a unique combination of event estimation and fast projection methods.

Methods: The authors implemented a Monte Carlo simulator to model the PETX system using only true coincident events. The performance of the dMiCE crystal pairs was determined experimentally over a range of depths of interaction. This distribution was used to simulate the noisy dMiCE detector signals and to estimate the line of response for each decay. Three different statistical methods were implemented to determine photon event positioning. Images were reconstructed from these line of response estimators with the exact planogram frequency distance rebinning algorithm, which is an exact analytical reconstruction algorithm for planar systems. Reconstructed images were analyzed with contrast, noise, and spatial resolution metrics.

Results: The authors' simulations demonstrate the ability for the PETX system to produce quantitatively accurate images from true coincident events with a contrast recovery coefficient of greater than 0.8 for 5 mm spheres at the axial center of the scanner and a spatial resolution (FWHM) of 3 mm throughout most of the imaging field of view.

Conclusions: The authors' proposed positioning and reconstruction algorithms for the PETX system show the potential for creating high-quality, high-resolution, and quantitatively accurate images within a clinically feasible reconstruction time. © 2011 American Association of Physicists in Medicine. [DOI: [10.1118/1.3547712](https://doi.org/10.1118/1.3547712)]

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I. INTRODUCTION

There is considerable interest in using positron emission tomography (PET) for oncology diagnosis¹ and measuring response to cancer therapy.^{2,3} The interest in whole-body PET has also lead to the development of specialized breast-specific positron emission mammography (PEM) and PET scanners.^{4–6} Several investigators have built breast-specific PET scanners^{6–8} and a few also include analysis of the depth of interaction (DOI).^{9–11}

In this paper, we evaluate the performance of combined event estimation and image reconstruction algorithms designed for a proposed high-resolution rectangular breast PET scanner with DOI estimation (PETX). The PETX system (Fig. 1) is tomographic (due to 360° sampling¹²) and thus has the potential to create quantitatively accurate images. In contrast, the incomplete angular sampling of PEM (i.e., focal plane tomography) systems leads to anisotropic reconstruction and limits quantitative accuracy.^{4,5}

The PETX system surrounds the breast closely, which increases sensitivity significantly, but also leads to increased parallax error (Fig. 2) compared to other breast-specific PET scanners.^{8,11} To compensate for the increased parallax error,

DOI estimation will be provided by using the depth-of-interaction microcrystal element (dMiCE) detectors^{13,14} (Fig. 1).

A sketch of the scintillation crystal blocks of the system is shown in Fig. 1. Each of the modules is in coincidence with the others. The amount of separation between the superior and inferior detector modules is variable to accommodate variable breast size and amount of breast compression. The detector modules each have a crystal block of lutetium fine silicate (Zecotek Photonics, Inc., Vancouver, BC)¹⁵ that is partitioned into $4 \times 2 \times 20$ mm³ dMiCE light-sharing crystal pairs.^{13,14} Each crystal element is coupled to its own 2×2 mm² micropixel avalanche photodiode developed by Zecotek Photonics, Inc. (Vancouver, BC).¹⁶ Each dMiCE crystal pair is optically separated from the others. A light reflector placed between the two crystal elements in the dMiCE pair determines the light shared between the pair. The differential distribution of the scintillation light shared can be used to determine the depth of a photon interaction.

The PETX system is motivated by the potential to evaluate, guide, and monitor breast cancer therapies beginning in the neoadjuvant setting and following progress during

FIG. 1. (Left) Sketch of detector modules of rectangular breast PET scanner. The superior-inferior detector panels have variable separation. Here we have shown the maximum separation of 80 mm. (Right) dMiCE crystal pair showing the light-sharing interface. Each crystal pair is optically separated from the others.

therapy. Efforts at optimizing oncology treatments using PET in this way demonstrate great promise,^{2,3} including studies involving the locally advanced breast cancer stage.¹⁷ The goal of the present device is to apply these techniques to early stage disease (e.g., lesions less than 2 cm), for which whole-body PET spatial resolution is inadequate. This task will likely require accurate quantitative measurements of lesion tracer uptake. For this reason, emphasis is placed on accurate and uniform quantification within the imaging volume. Qi *et al.*⁷ have shown that both tomographic sampling and DOI capability are needed for the best quantitative accuracy. Performance goals for quantification are to achieve quantitative recovery that is consistent throughout the field of view to within 10% standard error and reproducible to within 10% accuracy. Primary lesion detection is not an intended primary task for the PETX system.

Quantitative PET imaging requires accurate data correction algorithms. The major effects that need to be corrected are random coincidences, scattered coincidences, attenuation, geometrical sensitivity, dead time, and detector sensitivity. Correction methods have been successively implemented for similar breast PET systems,¹⁸ but are beyond the scope of this study. Also not included in this study is an evaluation of the potential count rate performance of the PETX scanner (other than the true coincidence sensitivity

due to simple geometrical factors). Instead, the focus of this study is the development and evaluation of algorithms that estimate line of response (LOR) positions and reconstruct images from the LORs with high accuracy in a clinically feasible time. This includes the development of algorithms for correction of variations in geometric sensitivity and some aspects of detector sensitivity.

In Sec. II, we discuss the implementation of a Monte Carlo simulator of the proposed scanner, the experimental determination of the distribution of the dMiCE crystal pair detector signals over depth, description of three different statistical LOR estimation algorithms, and describe the exact planogram frequency distance rebinning¹⁹ (PFDRX) image reconstruction algorithm and data correction algorithms that are implemented for this scanner. The physical effects modeled by our simulator are summarized in Table I. Section III outlines the results of reconstructing images from our LOR estimation algorithms along with contrast, noise, and spatial resolution measurements. We conclude with some remarks about the system performance.

In the following, random variables will be denoted with capital letters and their realizations with the corresponding lowercase letter. Bold characters denote vectors or sets.

II. METHODS

The system is currently under development, beginning with simulation tests, which are used here to evaluate three algorithms for estimating LORs. The simulation process was partitioned into a few steps. First, the distribution of the annihilations was simulated and photons were tracked as they interact in the scintillation crystals. Then signals were generated by these interactions by generating realizations of random variables for each dMiCE light-sharing pair. The probability distribution of the dMiCE signal pairs were experimentally determined for a variety of depths of interaction. Next, this coincidence information was saved in list-mode format and processed by three different statistical algorithms for estimating LORs. We refer to these LOR estimation algorithms as Anger, maximum likelihood (ML), and Bayesian.^{20,21} These will be described in detail later in

FIG. 2. A transaxial slice of the detector blocks of the proposed system showing the region containing all LORs corresponding to signals from a pair of detector elements with an unknown DOI.

TABLE I. A list of the physical effects simulated along with a partial list of the effects not simulated.

Simulated	Major effects not simulated
Positron decay statistics	Positron range
Effects simulated in detector modules:	Noncollinear annihilation photons
Beer–Lambert photon path length	Attenuation and scatter in breast
Photoelectric absorption	Coincidence timing
Compton scatter	Random coincidences
Klein–Nishina distribution	Pulse pileup
dMiCE light distribution	Backscatter

this section. Finally, images were reconstructed with the PFDRX algorithm¹⁹ and are evaluated by contrast, noise, and spatial resolution metrics.

All software for the simulation, LOR estimation, and image reconstruction algorithms was written in C++ and ran on a 3.06 GHz Intel Core 2 Duo processor.

II.A. Simulation of annihilation photons

A Monte Carlo photon-tracking PET simulator, referred to as PETTRACKER, was developed to simulate the system. The user specifies the PET system by the size, location, and type of scintillation material of the detector modules. The energy-dependent photoelectric absorption and Compton scatter attenuation coefficients of the scintillation material were contained in lookup tables. We used the attenuation coefficients of lutetium based scintillators in our simulation.

Digital phantoms were composed of a superposition of geometrical objects. For each object that makes up the phantom, we generated a random number of positron annihilations that were uniformly distributed (spatially) over the object. The number of positron annihilations was taken from a Poisson distribution with a mean equal to the volume of the object multiplied by the specified mean radioactivity. Positron range was not simulated. The trajectory of the annihilation photons was isotropically distributed and each annihilation pair was perfectly antiparallel. Attenuation and scatter of the photons through the phantoms was not simulated. Thus, every photon either struck the inner face of a detector module or missed the system entirely. Photon interactions within

the scintillator were simulated. Using the energy-dependent attenuation coefficients for photoelectric absorption and Compton scatter, the path length between interactions, type of interaction, and (if applicable) scattering angle based on the Klein–Nishina formula²² were simulated with Monte Carlo methods. Simulation of the Klein–Nishina distribution was implemented by a procedure described in Ref. 23. Photons were tracked until they were completely absorbed in the PET detector or scattered out of the system. Scatter from one module to another was included. For each annihilation photon pair where both photons interact in the PET system, the three-dimensional interaction locations and amounts of energy deposited by each interaction were recorded. Random coincidences were not recorded.

We considered four different phantoms for our experiments. For each of the phantoms, we simulated a 3 min scan, but since attenuation, detector dead time, etc., were not considered in our simulation, longer scan times will be necessary to collect similar count statistics with measured data.

The first phantom developed was a point source at the center of the field of view of the scanner. This phantom was developed to assess the geometrical sensitivity of the scanner.

The second phantom developed was the large breast-shaped phantom shown in Fig. 3. This phantom had a background activity of 5 kBq/ml and spherical hot spots (lesions) with diameters of 2, 3, 4, and 5 mm. The ratio of the activity of the hot spots to background was either 2, 4, or 8. The separation between the superior and inferior detector modules was set to 80 mm.

The third phantom was a smaller breast phantom, similar to the breast phantom described above. It is simulated with the separation distance of the superior and inferior detector modules set to 53 mm. Smaller separation distances between coincidence detector modules result in higher detection sensitivity, but increased parallax error. This phantom is shown in Fig. 4.

The fourth phantom was a point source grid phantom which was simulated to measure system spatial resolution with the superior-inferior detector panels 80 mm from each other. The phantom is sketched in Fig. 5.

FIG. 3. Transaxial, sagittal, and coronal views of the large breast phantom. The pixelized dMiCE modules are included to provide scale. The separation distance of the superior-inferior detector modules was 80 mm. The dashed line shows the location of the profiles in Fig. 9.

FIG. 4. Transaxial, sagittal, and coronal views of the small breast phantom. The pixelized dMiCE modules are included to provide scale. The separation distance of the superior-inferior detector modules was 53 mm.

II.B. Characterization of dMiCE Signals

The distribution of the light measured by the current version of the dMiCE crystal pairs was experimentally determined as discussed in Ref. 14. We provide a summary to motivate the development of a probabilistic model of the dMiCE light response.

A single dMiCE crystal pair was placed in a dark box. Data were collected by stepping an electronically collimated (with a coincidence detector) 511 keV gamma point source down the long axis of the dMiCE crystal pair. Data were collected at depths of $d \in \{2, 6, 10, 14, 18\}$ mm, where $d = 0$ mm is the end of the crystal furthest from the photosensor.

In the following, we let the expectation and variance of a random variable be given by $E(\cdot)$ and $\text{Var}(\cdot)$, respectively.

Let $\mathbf{M} = (M_1, M_2)$ be a random variable for the signals measured by a dMiCE crystal pair that are produced by a single photon interaction. For our model, we assumed that the distribution of (M_1, M_2) is a bivariate Gaussian, where the parameters of mean $\boldsymbol{\mu}$ and covariance matrix $\mathbf{K}$ only depended on the location and the amount of energy deposited by the photon interaction. Let $\mathbf{C} = \mathbf{C}_1 \cup \mathbf{C}_2 \subseteq \mathbb{R}^3$ be the set that describes the region in space that the dMiCE crystal pair occupies. Note that $\mathbf{C}_1$ and $\mathbf{C}_2$ denote the two crystals in a particular dMiCE crystal pair. Also, let $\mathbf{x}$ be the interaction position of a photon, d be the depth of the interaction, and λ

be the amount of energy deposited by an annihilation photon. We define the random variable composed of the primary and secondary dMiCE signal pairs M_p and M_s by

$$(M_p, M_s) \equiv \begin{cases} (M_1, M_2), & \mathbf{x} \in \mathbf{C}_1, \\ (M_2, M_1), & \mathbf{x} \in \mathbf{C}_2. \end{cases}$$

In other words, the primary signal is the signal measured by the photosensor coupled to the crystal in which the interaction occurred. Thus, the distribution of (M_p, M_s) is also bivariate Gaussian and we additionally assumed, for a fixed system design, that the mean $\boldsymbol{\mu}$ and covariance matrix $\mathbf{K}$ of (M_p, M_s) depend only on d and λ .

Our experiment measured samples of the random variable (M_p, M_s) . Due to the small cross-sectional area of the crystal elements and the experiment measured gammas traveling perpendicular to the long axis of the dMiCE crystal pair, we assumed that photons interacted only once in the dMiCE pair. In the rare case when a photon interacted more than once in the same crystal, it was likely that the interactions were close to each other and the signals recorded should have been similar to the case where the photon interacted only once and deposited the amount of energy equal to the sum of the energies deposited by the multiple interactions. Although the point source was not perfectly collimated, we assumed that the depth of interaction was exactly at the depth that the collimated point source was aimed. We also

FIG. 5. Transaxial, sagittal, and coronal views of the point source phantom. The pixelized dMiCE modules are included to provide scale. The separation distance of the superior-inferior detector modules was 80 mm.

only considered those interactions where all of the energy was deposited into the crystal pair. Thus, we filtered out any signal pairs where their sum did not fall into the photo peak. This allowed us to characterize the mean and covariance matrix of (M_p, M_s) for $\lambda=511$ keV and $d=2, 6, 10, 14, 18$ mm. Now let

$$\boldsymbol{\mu}(d, \lambda) \equiv \begin{bmatrix} E(M_p|d, \lambda) \\ E(M_s|d, \lambda) \end{bmatrix},$$

$$\mathbf{K}(d, \lambda) = \begin{bmatrix} \text{Var}(M_p|d, \lambda) & \text{Cov}(M_p, M_s|d, \lambda) \\ \text{Cov}(M_p, M_s|d, \lambda) & \text{Var}(M_s|d, \lambda) \end{bmatrix}.$$

Through our experiments, we found estimates of $\boldsymbol{\mu}(d, \lambda=511 \text{ keV})$ and $\mathbf{K}(d, \lambda=511 \text{ keV})$ for $d \in \{2, 6, 10, 14, 18 \text{ mm}\}$. The parameters for other values of d were estimated through interpolation. The model parameters for variable λ are given by

$$\boldsymbol{\mu}(d, \lambda) = \frac{\lambda}{511} \boldsymbol{\mu}(d, 511 \text{ keV}),$$

$$\mathbf{K}(d, \lambda) = \frac{\lambda}{511} \mathbf{K}(d, 511 \text{ keV}).$$

With this assumption, the energy resolution is given by

$$\begin{aligned} \nu(d, \lambda) &\equiv \frac{\text{FWHM}(M_p + M_s|d, \lambda)}{E(M_p + M_s|d, \lambda)} \\ &= \frac{\sqrt{\lambda/511 \text{ keV}} \text{FWHM}(M_p + M_s|d, 511 \text{ keV})}{\lambda/511 \text{ keV} E(M_p + M_s|d, 511 \text{ keV})} \\ &= \sqrt{\frac{511 \text{ keV}}{\lambda}} \nu(d, 511 \text{ keV}), \end{aligned}$$

where we have denoted the full width at half maximum by FWHM. Thus, the energy resolution goes with the inverse of the square root of the energy deposited which agrees with the theory of gamma-ray detection with scintillators.²⁴

These experimentally determined distributions were used to simulate detector signals from the output of PETTRACKER. Thus, each interaction simulated with PETTRACKER was read and, based on its position, the depth of interaction was calculated. Then, with the depth of interaction (d) and amount of energy deposited (λ) by the interaction, we generated a realization of a bivariate Gaussian with mean $\boldsymbol{\mu}(d, \lambda)$ and covariance matrix $\mathbf{K}(d, \lambda)$. The module number, detector coordinates, and dMiCE signal pairs were recorded.

II.C. LOR estimation algorithms

The LOR for each coincidence was estimated by three statistical estimation algorithms from the simulated detector signals. These LOR estimation algorithms are described below.

- (1) Anger estimation is the standard interaction positioning algorithm for PET scanners.^{25,26} Anger estimation entails identifying the crystal element of interaction by calculating the two-dimensional centroid of the signals mea-

sured. The depth of interaction is assumed constant at the mean penetration depth based on the Beer–Lambert law. The end points of the LOR are the locations at the mean penetration depth of the estimation of the crystal element of interaction. From this centroid of the signals measured and constant depth of interaction, we calculated each end point of the LOR.

- (2) Based on the experimentally determined dMiCE response, we built lookup tables for the ML estimates of the depth of interaction and energy deposited shown in Fig. 7. The ML line of response positioning algorithm used these tables to estimate the three-dimensional annihilation photon interaction positions in the detector modules. For each signal pair, we estimated the interaction position that produced this signal pair as the point on the long central axis of the crystal of interaction at the ML estimate of the depth of the interaction. Then, for each set of signal pairs produced from an annihilation photon, a three-dimensional energy-weighted (with energy also estimated by ML) centroid was used to estimate the interaction position. The LOR was determined by the interaction estimates performed for each of the coincident photons.
- (3) The Bayesian LOR estimation algorithm^{20,21} jointly estimated the interaction positions of a coincidence pair simultaneously. The algorithm was described in Refs. 20 and 21, which we summarize here. The LORs were estimated by numerical calculation of an expectation of the first points of interaction of the pair of annihilation photons conditioned on all the dMiCE signal pairs. In the case that multiple dMiCE signal pairs were measured in a detector module, the order of the interactions of the coincidence annihilation photon pair was estimated by maximum likelihood.

The order of interaction (ML estimate) and position of first interaction (Bayesian estimate) were calculated by models of the pdf's of the detection process (i.e., the pdf of $\mathbf{M}$) and the process of photon interactions in matter. The photon process model takes into account the energy-dependent attenuation coefficients of photoelectric absorption and Compton scatter, the path length distribution of a photon interaction (Beer–Lambert law), and the Klein–Nishina formula which describes the probability that an incident photon with a certain amount of energy will scatter at a given angle (in the case of a Compton scattering event). The photon process is a joint pdf of both annihilation photons and assumes that both annihilation photons originated from a perfectly antiparallel annihilation. In Sec. II B, we provided a pdf to model the detection process, but the algorithm can support any pdf. A similar LOR estimation algorithm has been developed by Prax and Levin.²⁷

As a gold standard, the known interaction positions from the output of PETTRACKER were used to determine the LORs. We refer to this set of LORs as Perfect. These LOR data were used only to illustrate the upper bound to the quality of an LOR estimation algorithm, which could not be attained in practice.

FIG. 6. Distribution of the outcome of the annihilations from a point source centered in the field of view and the superior-inferior detector panels set 80 mm apart.

Before coincidences were processed by any of the above LOR estimation algorithms, they were filtered by the amount of energy deposited and the number of dMiCE signal pairs they generated. Any coincidence where one annihilation photon generated more than three dMiCE signal pairs was thrown out. Although rare, these events usually resulted in a poor estimation of the first point of interaction and thus were discarded. We also filtered out coincidences where the estimated energy deposited by a single interaction was less than 50 keV or if the total estimated energy deposited was less than 300 keV. Interactions that deposited less than 50 keV were too noisy to process. The amount of energy deposited was estimated by a lookup table of the ML estimate of energy deposited.

II.D. Data correction and image reconstruction algorithms

The estimated LOR data was binned into two planogram coordinate²⁸ sets; one data set included those LORs whose azimuthal angle lies in $[-45^\circ, 45^\circ]$ and the other for $[45^\circ, 135^\circ]$. Planogram coordinates are a native sampling geometry for PET scanners with parallel planar detectors. The maximum copolar acceptance angle was set to 45° . Image reconstruction was performed with the PFDRX

algorithm.¹⁹ The PFDRX algorithm is an exact analytic image reconstruction algorithm, similar to FORE,²⁹ based on the planogram frequency-distance rebinning algorithm. Reprojection³⁰ is required to complete the truncated projections and was calculated by the planogram Fourier reprojection algorithm.¹⁹

Scaling factors based on detector sensitivity and data sampling issues were calculated to provide quantitatively accurate images from the simulated data. These scaling factors were saved into a lookup table and applied to the binned coincidence data. We compensated for the loss of detector sensitivity due to energy discrimination (events that deposit too little energy) and crystal thickness. We also corrected for the variable solid angle of the bins of the planogram histogram data.¹⁹

To compensate for those coincidences lost through energy discrimination, we simulated a uniform phantom that filled up the field of view and measured the fraction of events that were lost due to energy discrimination. The correction factor for the variable geometric detector sensitivity due to the detector crystal penetration distance of a coincidence pair was calculated analytically, as was the correction for the variable solid angle of the bins of the planogram histogram data.

FIG. 7. Statistics of the experimentally determined distribution of the dMiCE signal pairs. The axes are unitless (ADC channel). The figure on the left shows plots of the mean of the ratio of a signal to the sum of the signals. Error bars indicate the sample standard deviation. The two figures on the right are maps of dMiCE ML parameters. Dot marks mean values of primary and secondary signals for 511 keV of the energy deposited and the variable depth of interaction, $d \in \{2, 6, 10, 14, 18 \text{ mm}\}$. The half maximum contour lines of the pdf of $(M_p, M_s) [p(m_p, m_s, |d, \lambda = 511 \text{ keV})]$ are also plotted for variable d .

TABLE II. Performance statistics for the estimation of the first point of interaction of an annihilation photon with the Anger, ML, and Bayesian LOR estimation algorithms.

	Number of signal pairs	1, 2, or 3	1	2	3
	Samples	801 905 844	493 968 086	268 058 972	39 878 786
Anger	Depth bias	−0.20 mm	−0.27 mm	0.33 mm	−0.16 mm
	Depth std dev	4.94 mm	4.95 mm	4.82 mm	4.67 mm
	Position error mean	4.83 mm	4.23 mm	5.56 mm	7.42 mm
	Position error std dev	3.24 mm	2.68 mm	3.60 mm	4.57 mm
ML	Depth bias	−0.06 mm	−0.11 mm	0.32 mm	−0.72 mm
	Depth std dev	3.37 mm	3.39 mm	3.13 mm	3.41 mm
	Position error mean	3.64 mm	2.76 mm	4.77 mm	7.22 mm
	Position error std dev	3.19 mm	2.12 mm	3.76 mm	4.92 mm
Bayesian	Depth bias	−0.10 mm	−0.05 mm	−0.26 mm	0.08 mm
	Depth std dev	2.77 mm	2.72 mm	2.82 mm	3.21 mm
	Misorder rate	32.36%	N/A	32.38%	32.27%
	Position error mean	2.68 mm	2.29 mm	3.23 mm	3.84 mm
	Position error std dev	2.13 mm	1.71 mm	2.44 mm	3.22 mm

III. RESULTS

The distribution of the outcome of the simulated annihilations for a point source centered in the field of view is shown in Fig. 6. Overall geometric system sensitivity was measured at 39.0%.

For comparison, the same experiment was performed by simulating the dedicated breast PET scanner described in Ref. 31 based on the geometry (two 120×120 mm² parallel planar detectors spaced 206 mm apart) and scintillator material (LSO) properties. The overall geometric system sensitivity of this system was measured at 6.8%.

Statistics of the measured results of the dMiCE detector response experiment are shown in Fig. 7. The mean of the primary dMiCE signal over the summed dMiCE signals as

they vary with the depth of interaction is shown in Fig. 7. The quality of the depth information can be observed from this plot. The ability to distinguish interactions at different depths is related to the slope of the plot of the ratio of the primary signal over the sum of the two signals. The resolution (FWHM) of the measured depth of interaction was 7 mm. The average energy resolution for a deposition of 511 keV was 19.45%. The covariance between the light-sharing signal pair was found to be negligible.

Plots of the ML estimates of depth and energy deposited, given by $d_{\text{ML}}(\mathbf{M})$ and $\lambda_{\text{ML}}(\mathbf{M})$, respectively, are shown in Fig. 7.

We assessed the quality of the accuracy of estimating the position of the first point of interaction of an annihilation

FIG. 8. Images of large breast phantom reconstructed from projections generated by the three statistical LOR estimation algorithms and with the set of true LORs.

photon in the PET system with the Anger, ML, and Bayesian LOR estimation algorithms by computing some statistics of the estimation accuracy. These performance statistics are shown in Table II. The depth bias and depth standard deviation were calculated by the sample mean and sample standard deviation, respectively, of the difference between the true and estimated depths of interaction. The mean position error is the sample mean of the Euclidean distance between the true and estimated first points of interaction. The misorder rate is the percentage of the events that the estimation algorithm incorrectly estimated which interaction was first. Note that the Anger and ML positioning algorithms do not estimate the order of interactions, so the misorder rate is not given here. The performance statistics are also shown for the specific cases where an annihilation photon generated one, two, or three signal pairs.

The number of valid coincidences processed per second for the Anger and ML statistical LOR estimation algorithms was 198 300 and 190 240, respectively. Much of this processing time was spent reading and writing data to the hard disk. In comparison, the Bayesian LOR estimation algorithm processed approximately 4720 valid coincidences per second. However, when we only processed those coincidences where each annihilation photon created at most two dMiCE signal pairs, the Bayesian LOR estimation algorithm processed approximately 8760 valid coincidences per second. Imposing this restriction on the data only lowered the sensitivity by about 5%. Also, note that the performance of the Bayesian LOR estimation algorithm was the worst for events where three dMiCE signal pairs were produced.

Images reconstructed from data generated by the three statistical LOR estimation algorithms along with the set of true LORs are shown in Fig. 8 for the large breast phantom and Fig. 12 for the point source phantom. The reconstructed images for the small breast phantom are similar to the reconstructed images of the large breast phantom.

A representative cross-sectional plot of the large breast phantom is shown in Fig. 9. The cross-section for the exact phantom is included for comparison.

Plots of the contrast recovery coefficients for the 2, 3, 4, and 5 mm diameter spheres centered at slices $z = -15, 0, 15$ in the large breast phantom are shown in Fig. 10. The CRC for a hot spot of interest was measured by

CRC

$$= \frac{\text{mean hot spot activity/mean background activity}}{\text{true hot spot activity/true background activity}}.$$

Noise was measured by calculating the standard deviation of the mean activity of multiple spherical background regions (each with a diameter of 5 mm) in the reconstructed images. A plot of how the signal to noise ratio varies axially (z) for images reconstructed from the data generated by the three statistical LOR estimation algorithms and the set of true LORs is shown in Fig. 11.

The discrete analog of the normalized L^2 error of the breast phantom images is shown in Table III. The normalized L^2 error is defined by $\|\tilde{f} - f\|_2 / \|f\|_2$, where f is the true image,

FIG. 9. Cross-sectional plots of large breast phantom.

$\tilde{f}$ is the reconstructed image, and $\|\cdot\|_2$ is the L^2 norm. This metric provides a sense of the global accuracy of the reconstructed image.

Figure 13 shows plots of the spatial resolution, i.e., the FWHM of the point sources in the point source phantom. The first data point in each plot is the FWHM measurement of the center point source in a particular direction (e.g., x, y, z) and the subsequent data points show the FWHM of the next point source lying along the particular direction. For example, the left plot in Fig. 13 shows the x -FWHM of the point sources located at $(0,0,0)$, $(18.75,0,0)$, $(37.5,0,0)$, $(56.25,0,0)$, and $(75.00,0,0)$. The orientation of the Cartesian coordinate axes is shown in Fig. 1.

IV. DISCUSSION

We have developed data processing algorithms for a proposed rectangular breast PET scanner with detector modules capable of measuring the depth of interaction. Numerical experiments based on simulated data have been performed to provide an initial characterization of the performance of our scanner and the LOR estimation, data correction, and image reconstruction algorithms used to form the images. These experiments show that this system has the potential to produce quantitatively accurate images with high contrast, good spatial resolution, and low noise statistics.

Our simulations demonstrate the ability for the PETX system to produce quantitatively accurate images from true coincident events with a contrast recovery coefficient of greater than 0.8 for 5 mm spheres at the axial center of the scanner and a spatial resolution (FWHM) of 3 mm throughout most of the imaging field of view.

The low noise property was due to the high geometrical sensitivity of the scanner which was 39.0% for a separation of 80 mm between the superior-inferior detector panels. The superior-inferior detector panels are movable to accommodate variable levels of breast compression and images were reconstructed for the maximum separation distance of 80 mm to a separation distance of 53 mm. These separation

FIG. 10. Contrast recovery coefficients vs diameter of the spherical lesions in the large breast phantom.

distances were chosen because the mean separation of the detector panels of PEM scans performed at the Swedish Cancer Institute in Seattle was about 70 mm.

Table II provides statistics of the performance of the three statistical LOR estimation algorithms based on their ability to correctly identify the depth of interaction and the crystal where the first interaction of an annihilation photon occurred. We have also shown the impact of the three statistical LOR estimation algorithms on image quality. All these studies are indirect metrics of the quality of the estimation of an LOR. In a previous publication,²¹ the authors analyzed the Bayesian LOR estimation algorithm with focal plane tomography, which is a direct LOR performance metric.

We implemented an analytic image reconstruction algorithm to allow a fair measurement of the spatial resolution of the system. The OSEM algorithm is not commonly used to determine spatial resolution because iterative methods can achieve arbitrarily good resolution for point sources in air.

Images reconstructed from LORs determined by Anger estimation were of the lowest quality of the three statistical LOR estimation techniques based on contrast, noise, and spatial resolution. Images reconstructed with Anger LOR estimation also contained visible artifacts caused by parallax and the pixelated crystals with a one-to-one (one photosensor for every crystal element) readout scheme. This caused significant digitization effects for the LOR estimates.²¹

Line of response estimation with our ML algorithm provided a substantial improvement over Anger estimation while requiring little extra computation. The Bayesian LOR

estimation algorithm provided the highest accuracy as illustrated in Table II. The increased accuracy of LOR estimation produced images with better contrast which can be seen in the images in Figs. 8 and 12. The increased contrast was verified quantitatively in the cross-section plots in Fig. 9 and the contrast recovery coefficients plotted in Fig. 10. Images reconstructed from the Bayesian LOR estimates also showed an improvement over those images reconstructed from the ML LOR estimates in measurements of signal to noise as shown in Fig. 11. Slight improvements in spatial resolution were also achieved with the Bayesian algorithm as shown in Fig. 13.

The disadvantage of the Bayesian LOR estimation algorithm was the computation time required. However, we have not attempted to increase the efficiency of this algorithm. The Bayesian LOR estimation algorithm created joint estimates of the position of the first interaction of an annihilation pair by numerically computing a conditional expectation. The integral was computed over all possible points of interaction as determined by which dMiCE signal pairs receive a signal. Many of the values of the integrand were small and thus have little influence on the overall quantity of the integral. Thus, one approach to speeding up the algorithm was focused on quickly determining the largest values of the integrand and only considering these in the computation. This was done by using the lookup tables for the ML estimates of the depth of interaction and integrating over a window of values around this initial depth estimate. For our experiments, we chose a window size of 12 mm. Without this win-

FIG. 11. Signal to noise ratio in background for the large and small breast phantoms.

FIG. 12. Images of point source phantom reconstructed from various LOR estimation algorithms. Note the change of scale for the intensity maps.

FIG. 13. Resolution of point source phantom. The top row shows the FWHM and the bottom row shows the full width at quarter maximum (FWQM). The plot of the FWQM for the images reconstructed from Anger LOR estimates have been omitted because they are invalid due to aliasing.

TABLE III. Normalized L^2 error.

	Large breast phantom	Small breast phantom
Anger	0.576	0.502
ML	0.436	0.400
Bayes	0.413	0.378
Perfect	0.377	0.336

dow, the algorithm would integrate over the whole dMiCE crystal pair (20+20=40 mm) for each dMiCE signal pair received. Smaller windows would lead to further increases in computation speed, but may degrade the overall quality of the LOR estimate. Future work would be necessary to assess this tradeoff. The Bayesian LOR estimation code has many subroutines that could be computed in parallel and could benefit from a pipeline style computing architecture. Thus, the Bayesian algorithm is a candidate for specialized processing units such as field-programmable gate arrays or graphics processing units.

Other detector designs to measure the depth of interaction have been developed, including the use of segmented crystals^{32–34} or by the use of additional detectors on the entrance face of the detector modules.^{35,36} The Bayesian LOR estimation code can be extended to work with these DOI schemes. For the algorithm to be tractable, one must have a one-to-one readout scheme of pixelated detector crystal elements and photosensors.

V. CONCLUSION

Our proposed breast PET system with paired depth-of-interaction sensors shows the potential for creating high-quality, high-resolution, and quantitatively accurate images with a clinically feasible reconstruction time.

Line of response estimation with our ML algorithm provided a substantial improvement over Anger estimation while requiring very little extra computation. The Bayesian LOR estimation algorithm provided the most accurate LOR estimates at the cost of an increase in computation time.

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