Implementation and evaluation of an expectation maximization reconstruction algorithm for gamma emission breast tomosynthesis

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Purpose: We are developing a dual modality tomosynthesis breast scanner in which x-ray transmission tomosynthesis and gamma emission tomosynthesis are performed sequentially with the breast in a common configuration. In both modalities projection data are obtained over an angular range of less than 180° from one side of the mildly compressed breast resulting in incomplete and asymmetrical sampling. The objective of this work is to implement and evaluate a maximum likelihood expectation maximization (MLEM) reconstruction algorithm for gamma emission breast tomosynthesis (GEBT).

Methods: A combination of Monte Carlo simulations and phantom experiments was used to test the MLEM algorithm for GEBT. The algorithm utilizes prior information obtained from the x-ray breast tomosynthesis scan to partially compensate for the incomplete angular sampling and to perform attenuation correction (AC) and resolution recovery (RR). System spatial resolution, image artifacts, lesion contrast, and signal to noise ratio (SNR) were measured as image quality figures of merit. To test the robustness of the reconstruction algorithm and to assess the relative impacts of correction techniques with changing angular range, simulations and experiments were both performed using acquisition angular ranges of 45° , 90° and 135° . For comparison, a single projection containing the same total number of counts as the full GEBT scan was also obtained to simulate planar breast scintigraphy.

Results: The in-plane spatial resolution of the reconstructed GEBT images is independent of source position within the reconstructed volume and independent of acquisition angular range. For 45° acquisitions, spatial resolution in the depth dimension (the direction of breast compression) is degraded with increasing source depth (increasing distance from the collimator surface). Increasing the acquisition angular range from 45° to 135° both greatly reduces this depth dependence and improves the average depth dimension resolution from 10.8 to 4.8 mm. The 135° acquisition results in a near-isotropic, spatially uniform 3D resolution of approximately 4.3 mm full width at half maximum. Background nonuniformity (cupping) artifacts arise primarily from angular incompleteness for small angular range acquisition but primarily from gamma ray attenuation at larger angular range. However, background artifacts can be largely eliminated if both prior information regularization and AC are applied. An artificial decrease in lesion voxel value with increasing lesion depth can also be substantially reduced through a combination of AC and RR. In experiments using compressible gelatin breast phantoms, lesion contrast and SNR are about 2.6–8.8 times and 2.3–5.6 times higher, respectively, in GEBT than in planar breast scintigraphy depending on the acquisition angle, the gamma camera trajectory, and the lesion location. In addition, the strong reduction in lesion contrast and SNR with increasing lesion depth that is observed in planar breast scintigraphy can be largely overcome in GEBT.

Conclusions: The authors have demonstrated a promising EM-based reconstruction scheme for use in GEBT. Compared to planar breast scintigraphy GEBT provides superior and less position-dependent lesion contrast, lesion SNR, and spatial resolution as well as more accurate quantification of lesion-to-background activity concentration ratio. © 2012 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4764480>]

Key words: attenuation correction, limited angle reconstruction, molecular breast imaging, tomosynthesis

I. INTRODUCTION

X-ray mammography is the gold standard for screening and early detection of breast cancer, yet it has several limitations. First, its ability to detect small lesions in radiodense breast tissue is limited. Mammographic sensitivity is reported to be 80%–98% for fatty breasts versus 29%–63% for radiodense breasts.^{1–4} Second, the false-positive rate in mammography is high, ranging from 21% to 38%.^{5–7} Averaged over the 44 participating sites in a recent multicenter study, the positive predictive value (PPV) of mammography plus ultrasound was 4.1%.⁸ Furthermore, just 38.8% of patients with BI-RADS 4 or 5 mammograms resulting in a recommendation for biopsy, surgical consultation, or fine-needle aspiration were associated with a breast cancer diagnosis during follow-up.⁸ These numbers motivate the development of technologies that would enable better depiction of early lesions in the breast, or as adjunct modalities that provide additional information beyond that provided by x-ray mammography. Breast scintigraphy, known as scintimammography, breast-specific gamma imaging, or molecular breast imaging, uses radiotracers such as ^{99m}Tc-sestamibi whose higher energy gamma emission radiation is not affected by variations in radiodensity within the breast.⁹ In recent years, several groups have developed small field of view gamma cameras dedicated to breast scintigraphy and commercial systems incorporating one or two such cameras are now available. Their narrow inactive borders permit camera placement adjacent to the chest wall and in contact with the breast, thereby permitting the entire breast to be imaged and resulting in reliable detection of tumors less than 1 cm in size.^{10–13} However, mammography and breast scintigraphy are two-dimensional (planar) imaging techniques, providing no resolution in the third dimension. The inevitable superposition in the image of breast structures or tracer distribution unfavorably reduces image contrast and generates correlated background “structural” noise that can possibly mask small cancers. In addition, breast scintigraphy suffers from gamma ray attenuation and depth-dependent spatial resolution, which are difficult or impossible to correct in the absence of lesion depth information. In the interest of obtaining three-dimensional information, systems for dedicated breast CT and breast SPECT utilizing compact detectors are under development.^{14,15,22} X-ray breast tomosynthesis (XBT), in which multiple views of the breast are obtained over a limited angular range, is also currently a topic of vigorous research and commercial XBT systems have recently become available for clinical screening and diagnostic breast imaging.^{16–19}

With the goal of obtaining spatially aligned structural and functional breast images in a tomosynthesis format, a dual modality tomosynthesis (DMT) scanner prototype is currently being developed at the University of Virginia.^{20,21} The DMT scanner is a hybrid structural/functional device that uses an upright mammography-style gantry on which x-ray transmission tomosynthesis (XBT) and gamma emission tomosynthesis (GEBT) are performed in quick succession with the breast in a single configuration. In a pilot study of DMT ($n = 21$), the addition of GEBT to XBT improved specificity from 57%

to 100%, positive predictive value from 50% to 100%, and accuracy from 67% to 95%.²¹ The work reported here describes the implementation and evaluation of a maximum likelihood expectation maximization (MLEM) reconstruction algorithm that was developed specifically for the GEBT component of the DMT scanner.

Compared to prone breast SPECT, in which the breast is pendant and uncompressed, GEBT has several advantages. First, the acquisition time is potentially shorter because only a limited number of views are required. The pilot study of DMT used five views of 2 min each for a total of 10 min per breast (a single MLO compression was used for each breast). Ultimately, however, the total acquisition time will depend on the amount of injected radiotracer, system gamma ray detection sensitivity, and the tolerable image noise level. Second, with the breast under light compression and the camera viewing the breast over a relatively limited angular range centered on the compression direction, the effects of attenuation and scatter are reduced because of the reduced breast thickness. Third, since there is no patient table between the patient and gamma camera in upright GEBT, with the patient standing or seated, as there is in prone breast SPECT, the gamma camera can be placed closer to the chest wall allowing for a more complete visualization of posteriorly located breast tissue.^{15,21,22} However, GEBT poses several challenges. As is true for XBT, the limited angular range and/or few projection views obtained in GEBT results in a mathematically incomplete dataset for reconstruction, potentially producing artifacts in the undersampled direction. Moreover, due to the asymmetrical acquisition geometry, the effects of attenuation and detector blurring can make the image quality of reconstructed objects more sensitive to their locations relative to the gamma camera trajectory than they are in 360° SPECT.

We therefore seek reconstruction approaches that are successful when using incomplete data sets that have a small number of views sparsely distributed over an angular range of less than 180°. The expectation maximization (EM) algorithm is a prime candidate for this situation for three reasons.^{23,24} First, analytical reconstructions such as filtered-back-projection (FBP), though normally much faster than iterative reconstruction, can produce severe artifacts when performed using real, undersampled projection data because they assume a noise-free complete data set. Alternatively, the maximum likelihood expectation maximization algorithm seeks the statistically most probable solution; therefore the reconstruction is smoother, more robust, and less prone to artifacts when compared to FBP. Second, it is important to include *a priori* information or regularization in the reconstruction process when using incomplete data, which can be done easily with statistical reconstruction algorithms. Finally, detector blur and attenuation of gamma rays by breast tissue can be incorporated into the detection probability of an emission event.

Several groups have approached limited angle SPECT problems using iterative algorithms including MLEM.^{25–27} Most of the prior work involves simulation of 2D or 3D projection data with or without additive noise. The effects of detector blurring, limited photon statistics, attenuation, and

scatter were not included simultaneously. Other closely related work in the context of breast imaging^{20,28} used experimental data in which each of those factors were naturally included in the projection images. However, systematic evaluation of the reconstruction approach was not the focus of those studies.

The aim of this study is to evaluate a MLEM reconstruction algorithm for limited angle SPECT in the context of breast imaging. Both simulations and phantom experiments were performed to evaluate the reconstruction algorithm under realistic physical conditions including detector blurring, limited photon statistics, attenuation, and scatter. Evaluation was done over several image acquisition angles spanning the range of acquisition angles likely to be used in GEBT. Results are compared to those obtained using planar breast scintigraphy under conditions of equal total number of detected events.

II. EXPECTATION MAXIMIZATION-BASED IMAGE RECONSTRUCTION

II.A. Regularization via masking

In 360° SPECT, sufficient angular sampling assures that activity is not incorrectly attributed to voxels lying outside the breast. However, in GEBT, the incomplete angular sampling does not provide sufficient information to prevent activity from being erroneously attributed to regions outside the breast in the undersampled direction. The acquisition geometry for GEBT is illustrated in Fig. 1. Undersampling in the z dimension (defined here as the direction of breast compression) can result in activity being attributed to the triangular regions (shadow regions in Fig. 1) above and below the breast. However, regularization using prior information from the previous XBT scan can be used to prevent this.

FIG. 1. Schematics illustrating the acquisition geometry in GEBT. Two extreme angular views are shown. The AOR coincides with the y axis. The mask indicates the region in which voxels are initialized with values of unity during reconstruction. Voxels outside the region are initialized with values of zero.

The general update equation executed at the $(n + 1)$ th iteration in our implementation is expressed as^{23,24,31}

$$f_j^0 = \begin{cases} 0 & \text{for } j \in \Omega \\ 1 & \text{for } j \notin \Omega \end{cases}, \quad (1)$$

$$f_j^{n+1} = \frac{f_j^n}{\sum_i a_{ij} b_{ij}} \sum_i a_{ij} b_{ij} \frac{p_i}{\sum_k a_{ik} b_{ik} f_k^n}, \quad (2)$$

where f_j is the radioactivity to be reconstructed for voxel j , p_i is the number of detected counts at the detector bin i , a_{ij} is the depth-dependent camera blurring, b_{ij} is the attenuation factor, and Ω denotes the breast region between the support and compression paddle as determined from XBT. We initialize the matrix f by setting the value of voxels outside the breast region Ω to be zero. The form of Eq. (2) assures that in subsequent iterations voxels not lying in Ω retain zero value.

II.B. Resolution recovery

We express the distance-dependent camera blurring a_{ij} as a normalized Gaussian whose shape is principally determined by the parameters of the parallel-hole collimator, the intrinsic resolution of the detector and the voxel j 's location relative to the detector bin i :²⁹

$$a_{ij} = \frac{1}{2\pi\sigma_{ij}^2} \exp \left\{ -\frac{(r_j - q_i)^2}{2\sigma_{ij}^2} \right\}, \quad (3)$$

$$2\sqrt{2 \ln 2} \sigma_{ij} = R_s = \sqrt{R_c^2 + R_i^2} = \sqrt{\left(D \frac{Z}{L} \right)^2 + R_i^2}, \quad (4)$$

where r_j and q_i denote the transverse locations of the voxel and the detector bin, respectively, measured in the detector plane, and Z denotes the perpendicular distance of the j th voxel above the detector surface. D and L are the diameter and the length of the collimator holes, respectively (see Fig. 2). R_c is the collimator resolution and R_i is the intrinsic resolution of the detector. R_s is the camera resolution defined as the full width at half maximum (FWHM) of the Gaussian blurring function.

If blurring by the gamma detector is negligible compared to that by the collimator (the contribution of the intrinsic resolution is relatively small in Eq. (4)), the dimensions of an inverse cone projector-backprojector can be usefully determined by considering only the voxels whose transverse offsets relative to the location of the detector bin of interest are sufficiently small to permit them to contribute counts as determined by the physical parameters of the parallel hole collimator. The collimator's geometric response function can be evaluated as the autocorrelation of the collimator's front aperture,^{30,31} or equivalently, as the overlap of two aperture functions, offset by a distance r_T [Fig. 2(b)], which is the distance between the source voxel and the axis of the collimator hole, referenced to the collimator hole entrance:³¹

$$r_T = \frac{L}{Z}(r_j - q_i). \quad (5)$$

Points lying on the surface of the cone of acceptance of the collimator satisfy $r_T = D$ (i.e., the two aperture functions are

FIG. 2. Schematic showing the parallel-hole collimation geometry. (a) Definition of the inverse cone (dashed cone). (b) Evaluation of geometric camera response as the overlap of two aperture functions (inset at lower right).

tangent to each other), which corresponds to a cone angle of

$$\alpha = \arctan\left(\frac{D}{L}\right). \quad (6)$$

The projector-backprojector cone is illustrated as the dashed line in Fig. 2(a). Though in our implementation we use a Gaussian function to define the a_{ij} instead of the auto-correlation function, note that using this cone angle the cone diameter is exactly twice the FWHM of the Gaussian if the intrinsic resolution term is neglected in Eq. (4).

II.C. Attenuation correction

A major advantage of hybrid imaging systems (e.g., SPECT-CT, PET-CT, or DMT) is the availability of anatomical transmission data to provide attenuation maps that can be used during iterative reconstruction of emission data to correct for attenuation by the breast of emitted gamma rays. Bilinear extrapolation is typically used to calculate voxel-specific linear attenuation coefficients at the gamma ray energy from measured linear attenuation coefficients at the energy distribution present in the transmission scan.^{32,33}

As shown in Eq. (2), during each iteration in our EM reconstruction, all voxels within the inverse cone are weighted by

a_{ij} and b_{ij} before being summed to the corresponding detector bin. Since a 3D conical ray projector-backprojector was used for implementing the summing operation in Eq. (2), explicitly calculating the summation for the attenuation factor along lines passing through the center of each voxel within the cone would be time consuming and unnecessarily complicated. As long as the attenuation coefficient does not vary dramatically over distances comparable to the cone diameter, attenuation factors for the individual voxels lying within the cone can be estimated from the single attenuation factor calculated along the cone axis at the cost of some reduction in the spatial specificity of the attenuation correction. Implementation of this concept is illustrated in Fig. 3 and Eq. (7).

The attenuation factor b_{ij} for voxel j is expressed as

$$b_{ij} = \exp \left\{ -\frac{1}{\cos \theta_{ij}} \sum_{k=0}^{j'} \mu_k \Delta l \right\}, \quad (7)$$

where θ_{ij} is the angular distance of voxel j away from the axis of the cone centered at detector bin i . Δl is the length of a line segment along the cone axis which for simplicity is set to be equal to the voxel side length. μ_k is the linear attenuation coefficient at the midpoint of each line segment, calculated using trilinear interpolation from the nearest eight voxels. j' is the index of the segment midpoint closest to the

FIG. 3. Schematic showing the calculation of the attenuation factor, b_{ij} . The line integral for the attenuation along the ray axis is back-projected to the off-axis voxels lying within the cone according to Eq. (7).

projection point j'' of the center of voxel j onto the cone axis. The summation in Eq. (7) is performed from the detector bin to segment j' .

III. METHODS

III.A. Benchtop GEBT system

The benchtop GEBT gamma camera, built at the Jefferson Lab (Newport News, VA) includes 12 Hamamatsu H8500 position sensitive photomultiplier tubes (PSPMTs) tiled in a 3×4 array. The PSPMTs are optically coupled to a $15.4 \text{ cm} \times 21.0 \text{ cm}$ NaI(Tl) crystal array with a crystal pitch of 1.4 mm. Each crystal is $1.2 \text{ mm} \times 1.2 \text{ mm} \times 6 \text{ mm}$ thick with 0.2 mm intercrystal gaps. Although this camera has a smaller crystal pitch (1.4 mm) than the camera used in the DMT pilot study (2.2 mm), 2×2 pixel rebinning was used to result in an effective pixel size of 2.8 mm. The camera has 13% FWHM energy resolution at 140 keV. It is equipped with a low energy parallel hole lead collimator with a hole length of 2.0 cm, hexagonal hole size of 1.2 mm, and septal thickness of 0.33 mm, which results in a measured camera sensitivity of 1.10×10^{-4} when an energy acceptance window of $+16\%$, -13% is used. The camera was supported in front of a computer controlled rotation stage mounted on a linear translation stage (Fig. 4). The combined rotational and translational motion permitted both viewing angle and the axis of rotation (AOR)-to-camera distance (measured from the collimator surface) to be varied. Simulation of this system and data acquisition was performed using the SIMIND Monte Carlo program.³⁴ In the simulations, the camera's spatial resolution, sensitivity, energy resolution, and energy window were selected to match those of the real gamma camera. The performance of the EM reconstruction algorithm in terms of resolution recovery (RR), artifact reduction, and attenuation correction (AC), was then evaluated in both the simulated and real benchtop GEBT systems. Imaging properties of interest were the FWHM of the position-dependent system point spread function, background uniformity, the depth de-

pendence of the lesion voxel values, and the lesion contrast and SNR.

III.B. Simulations

In the first simulation, a 5-row $\times$ 5-column array of 25 spherical point sources with 0.02 mm diameters were placed in air so that they were spaced 3 cm from each other in both the x and y directions. The five sources in a given row shared the same z coordinate. The z coordinates tested were -4 , -2 , 0 , $+2$, and $+4$ cm with respect to the AOR. The simulated camera trajectory was a circular orbit with a radius of 9.85 cm measured from the collimator surface to the AOR. Nine projection views were acquired over angular spans of 45° , 90° , and 135° . A single projection was also obtained to simulate planar breast scintigraphy, in which the collimator surface was placed 4.1 cm away from the AOR, or almost touching the first row of sources.

In the second simulation, the phantom was modeled as a rectangular parallelepiped 15 cm long $\times$ 15 cm wide $\times$ 8 cm (to match the gelatin phantom dimensions). The thickness of the phantoms was chosen to be approximately equal to the average compressed breast thickness observed in the pilot DMT study (7.7 cm).²¹ In that study, the compression force was based on the technologist's assessment of the minimum force necessary to maintain proper positioning and immobility along with interaction with the subject regarding whether they would be comfortable for a 10 min scan. A retrospective analysis showed that on average the compressed thickness was $(17 \pm 11)\%$ greater during DMT than for the same breast during the preceding clinical mammogram. The phantom contained three simulated lesions with identical x coordinates, evenly spaced y coordinates, and z coordinates that positioned them 2, 4, and 6 cm, respectively, below the phantom's top surface. The lesions were spherical with 15 mm diameters. Recent previous phantom studies of breast scintigraphy by other groups have used lesions ranging in diameter from 4 to 20 mm with a mean value of 13 mm.^{13,35} In addition to being consistent with the prior literature, the 15 mm lesion size was viewed as being both clinically relevant and large enough to ensure that the contrast measurements were affected minimally by noise, the pixilated nature of the image, or partial volume averaging. The phantom and lesions were filled with a ^{99m}Tc -water solution with 10:1 target to background activity concentration ratio (T:B). The simulated camera trajectory was a circular orbit of a radius of 9.85 cm with the phantom centered at AOR. Nine projection views were acquired over angular spans of 45° , 90° , and 135° to test the robustness of the reconstruction algorithm and to assess the relative impacts of correction techniques with changing angular range. A rough optimization of the number of views was performed and nine projections were chosen as a reasonable compromise between angular sampling density and the amount of quantum noise in the projection views. With the goal of simulating conditions likely to be encountered in clinical breast scintigraphy, the acquisition time per frame was adjusted to result in a projection view count density of 130 cts/cm² when the collimator surface was parallel to

FIG. 4. Benchtop GEBT system used for the gelatin phantom studies described in this paper.

the 15 cm $\times$ 15 cm surface of the phantom. This projection view count density is about 30% of the average of that observed (420 cts/cm²) for the corresponding view in the DMT pilot study.²¹ In that study five 2-min projection views were obtained following injection of 925 MBq (25 mCi) of ^{99m}Tc-sestamibi using a parallel hole collimator with approximately 1.8 times the sensitivity of that used in this study. The choice of 130 cts/cm² thus takes into account this study's greater number of projection views (nine) and lower camera sensitivity, and simulates a 10-min scan with a total scan count density of approximately 1150 cts/cm². For comparison of GEBT with planar breast scintigraphy, a single projection resulting from the same number of detected photons as in GEBT was simulated with the collimator surface in contact with the top (15 cm $\times$ 15 cm) surface of the phantom.

III.C. Experiments

The spatial resolutions of the real and simulated cameras were determined by placing a 0.8 mm diameter ^{99m}Tc capillary source at a small angle with respect to the crystal array matrix and translating it in 1 cm steps over a distance ranging between 0 and 12 cm from the surface of the collimator. For each capillary-to-collimator separation, row-by-row profiles through the line source images were fitted to Gaussians and their average FWHMs were recorded.

Gelatin breast phantoms 840 ml (average breast size) in volume were made containing two thin-walled spherical lesions with 15 mm inside diameters. The volume of the gelatin phantom was calculated as the product of the average thickness observed in the DMT pilot study and an image-based assessment of the average projected breast area observed in that study. The lesion-to-background activity concentration ratio was 10:1. To simulate compression, the gelatin phantom was inserted into an acrylic box with internal dimensions of 15 cm $\times$ 15 cm $\times$ 7.7 cm. Following compression, the lesions were approximately 1.6 and 4.3 cm below the top surface of the phantom. To generate GEBT scans with a number of different angular ranges up to 135°, 25 equally spaced projection images were acquired over a 135° angular range and nine-view subsets were chosen and grouped to form three scans of the same acquisition time (10 min) but with different angular spans (45°, 90°, and 135°). The count density per view was the same as that in the simulation; 130 cts/cm². Both circular (10 cm radius) and spatial resolution-maximized (SRM) orbits in which the camera was positioned as close as possible to the phantom in each view were tested. For comparison of GEBT with planar breast scintigraphy, a single projection was obtained with the collimator surface in contact with the 2 mm thick top (15 cm $\times$ 15 cm surface area) of the acrylic box. The total number of detected events was adjusted to be equal to that of the full GEBT scans. For the purpose of attenuation correction during reconstruction, the linear attenuation coefficient of the gelatin was measured using a narrow beam transmission geometry and a collimated ^{99m}Tc flood source.

III.D. Reconstructions and image analysis

For all reconstructions, the geometrical collimator response and the projector-backprojector cone described above were used. AC of the simulated water phantom data was performed assuming a uniform linear attenuation coefficient of $\mu_k = 0.150 \text{ cm}^{-1}$, which is the linear attenuation coefficient of water at 140 keV. For reconstruction of gelatin phantom projection data the measured linear attenuation coefficient of 0.149 cm^{-1} was used. The reconstruction for the point source simulation was performed without the mask since it was unnecessary for the in-air point sources. The reconstructions for the box phantom simulation were performed (a) without AC and without the breast region mask, (b) without AC but with the mask, and (c) with both AC and the mask. For the gelatin phantom data, reconstructions were performed with either AC or no AC but always with masking. Before reconstruction, the simulated projection data were rebinned from 128×128 into 64×64 matrix size and the experimental projection data were rebinned from 150×110 into 75×55 matrix size. The reconstructed volume matrix was $80 \times 80 \times 80$ for the simulations and $94 \times 94 \times 69$ for the experimental data, with 2.24 mm isotropic voxel size in both cases. Nine iterations on three ordered subsets of a total of nine views were conducted. This number of iterations was chosen because the rate of improvement of lesion contrast in the reconstructed images with further iteration begins to decrease after the first few iterations. All reconstructions were performed on a Dell T7500 Precision work station and in a MATLAB environment. The current running time is less than 3 min.

For the simulated point source data, the centers of 25 point sources in the reconstructed volume were found and 1D profiles through them in the x , y , and z directions were drawn and fitted with Gaussians. The FWHMs of the Gaussians for the five sources located at the same z coordinate were then averaged and reported as the 3D resolutions at that z location. The spatial resolutions of the planar scintigraphy images of the same phantom in the x and y directions were also measured. For the simulated box phantom data, the background uniformity of the reconstructed volumes was assessed by first summing the four slices closest to the middle plane (the plane containing the x and y axes) then extracting profiles on either side of the 4 cm deep lesion as illustrated in Fig. 5(a) and finally averaging the profiles. Lesion intensity and background intensity were measured in single slices located at each of the lesion centers. The background intensity is defined as the average background pixel value in a 50×25 pixel region of interest (ROI) near the lesion and lesion intensity was defined as the average pixel value in a 4×4 pixel ROI centered on the lesion, as illustrated in Fig. 5(b). Lesion contrast and signal to noise ratio (SNR) were then calculated as follows:

$$\text{Contrast} = \frac{N_L - N_B}{N_B}, \quad (8)$$

$$\text{SNR} = \frac{N_L - N_B}{\sigma_B}, \quad (9)$$

where N_B and σ_B are the average pixel value and the standard deviation of the background ROI, respectively. N_L is the

FIG. 5. (a) The horizontal lines indicate the locations of profiles drawn on the summed slices. (b) A rectangular background ROI (50×25) for background and a square lesion ROI (4×4) for lesion.

average pixel value in the lesion ROI. In the gelatin phantom image analysis, lesion contrast was measured in a similar way as in the simulated data, but with the size of the background ROI adjusted to 20×30 pixels.

IV. RESULTS

IV.A. Simulated point source phantom

Figure 6 shows the experimental measurements and theoretical predictions of the depth-dependent camera blurring. The “experimental” and “simulated” data are the FWHMs of the imaged line source measured at a series of capillary-to-collimator distances. The “geometrical” and “analytical” curves are the collimator resolution R_c and the camera resolution R_s as defined in Eq. (4).

Figure 7 shows the measured spatial resolution for changing point source z position. Results are shown for both GEBT and planar breast scintigraphy. As predicted by Fig. 6, in planar imaging the x and y resolutions decrease rapidly with increasing source distance. In GEBT, the x and y dimension resolutions are essentially independent of source location and there is also little to no dependence on acquisition angular range. GEBT also provides resolution in the z dimension; however, the z resolution depends strongly

FIG. 6. Experimental measurements and theoretical predictions of the depth-dependent detector blurring.

FIG. 7. GEBT spatial resolutions for the 25 point source phantom simulation. The “ x ,” “ y ,” and “ z ” resolutions are the FWHM of the 1D profile through the image of the source in the slice containing the source center. “planar x ” and “planar y ” are the resolutions measured in the simulated planar view of the same phantom in the x and y directions. The error bars represent the standard deviations of the measurements over the five sources in a row.

on angular range, improving as the angular span increases. For 45° angular range, the z resolution exhibits a prominent degradation trend (increasing FWHM) as the source-to-collimator distance (at the 0° viewing angle) increases (i.e., when the source has a more negative z coordinate). The rate of change of the z resolution with changing source-to-collimator separation is reduced for 90° angular range and is almost zero for an angular range of 135° . The near-isotropic and spatially

FIG. 8. Comparison of GEBT and planar scans of the simulated point source phantom. GEBT scanning used nine evenly spaced views over a total angle of 135° . Sources are shown parallel to the x - y plane or x - z plane. The point sources in a given row share the same z coordinate and the sources in a column have z coordinates of +4, +2, 0, -2, and -4 cm, respectively, going from the top to the bottom of the images.

uniform resolutions resulting from 135° acquisition can be visually appreciated in Fig. 8, where the FWHM of the sources is 4.12 ± 0.31 mm in the x direction, 3.95 ± 0.15 mm in the y direction and 4.79 ± 0.39 mm in the z direction.

IV.B. Simulated box phantom

Figure 9 shows image slices parallel to the x - z plane taken from reconstructions of the simulated box phantom. Leakage of activity from the upper and lower phantom surfaces due to incomplete angular sampling is apparent if no correction was applied. The severity of the leakage decreases with increasing angular range. With regularization via masking, activity leakage has been eliminated, but nonuniform background intensity is apparent due to attenuation. When both masking and AC were done, the background intensity uniformity is greatly improved, although residual streak artifacts due to angular undersampling remain. Note, however, that these streak artifacts

FIG. 9. Coronal slices (parallel to the x - z plane) of the reconstructed simulated box phantom.

FIG. 10. Profiles through the background regions of the reconstructions of Fig. 9, but oriented parallel to the x - y plane.

do not appear in the x - y slices, which are the ones typically viewed in tomosynthesis.

Figure 10 shows profiles through the background regions of slices from the reconstructions of Fig. 9 but oriented parallel to the x - y plane. The reconstructions done with no masking and no AC suffer from severe cupping artifacts and resulting underestimation of the activity concentration in the breast region arising from the combination of activity leaking from the upper and lower phantom surfaces due to undersampling and the effects of uncorrected attenuation. Comparison of the 45° and 135° graphs shows that for the narrowest angular span the cupping artifact is almost entirely corrected by masking even without AC, whereas for the largest angular range masking alone actually increases the severity of the artifact. The reconstructions in which both masking and AC were used show that for larger angle (e.g., 135°) acquisition AC is the most effective means for restoring background intensity uniformity. For intermediate angular range (e.g., 90°), the relative importance of masking and AC for restoring background intensity uniformity is more comparable.

Figure 11 shows lesion intensity [defined as N_L in Eqs. (8) and (9)] plotted versus lesion depth in the simulated

FIG. 11. The normalized intensities of the lesions in the box phantom. The lesion size is 15 mm with target-to-background ratio (T:B) of 10:1.

box phantom reconstruction. All intensity values are normalized to that of the 2 cm deep lesion. The attenuation-corrected and uncorrected results are presented as well as those from the single view planar image. In all GEBT reconstructions the prior mask and RR were applied. When AC was not applied, there is a sharp decrease in lesion intensity with increasing lesion depth. AC effectively brings the intensity difference between the shallow and middle lesion from around 30% to below 6% and brings the difference between the shallow and deep lesion intensities from around 50% to below 12%. Comparison with planar imaging is also shown; however, the lesion intensity is calculated by subtracting the average pixel value in the background ROI from the average pixel value in the lesion ROI to account for the superimposition of background counts and lesion counts.

Figure 12 shows the images of the simulated box phantom reconstructed from the 135° angular span. The slices shown contain the centers of the shallow, middle and deep lesions. The same window/level setting was applied to all slices from a given reconstruction with the upper window level chosen to avoid saturating the brightest lesion. The images with no

FIG. 12. In-plane slices (parallel to the x - y plane) of the simulated box phantom reconstructed from the 135° angular span acquisition showing 15 mm lesions located at 2, 4, and 6 cm depth with T:B = 10:1.

FIG. 13. Lesion contrast of images reconstructed from the simulated box phantom data. Error bars indicate the standard deviation of four repetitions of the simulation.

AC provide visual evidence of the strong depth dependency of the lesion intensity in the absence of AC, while the bottom row slices show the effectiveness of AC in recovering the true uniform lesion intensity.

Figures 13 and 14 show the results of lesion contrast and SNR analysis for the simulated box phantom. The prior mask, RR, and AC were applied. For all angular ranges, GEBT reconstructions demonstrate substantial improvement in lesion contrast and SNR compared to the single view planar image. The wider the angular span, the higher the resulting contrast and SNR in the GEBT reconstructions. In the planar image, the lesion contrast and SNR were reduced by 53% and 54% as the lesion depth increases from 2 to 6 cm; whereas in GEBT, the lesion contrasts were reduced by only 12%, 19%, and 13% as lesion depth increased, for 45°, 90°, and 135° angular range, respectively. The variation of lesion SNR in GEBT for differently located lesion is less than 10% for all angular spans tested.

FIG. 14. Lesion SNR of images reconstructed from the simulated box phantom data. Error bars indicate the standard deviation of four repetitions of the simulation.

FIG. 15. In-plane slices (parallel to the x - y plane of the gelatin breast phantom) reconstructed from the 135° angular span acquisition, showing 15 mm lesions located at 1.6 and 4.3 cm depth with T:B = 10:1.

IV.C. Gelatin breast phantom

Figure 15 compares gelatin phantom GEBT slices from circular and SRM orbits, reconstructed from 135° angular span acquisitions. The prior mask, RR, and AC were applied during reconstruction. The same window/level was applied to both deep and shallow lesion slices for a given reconstruction. The deep and shallow lesions exhibit approximately equal intensity in the images from either orbit.

Figures 16 and 17 are plots of lesion intensity versus lesion depth. Results are shown for both GEBT orbits as well as for the planar scintigraphy projection. The lesion intensity was measured the same way that the simulated data were measured. With no AC applied, the deep lesion intensity is 34% and 31% less than that of the shallow lesion, for the circular and SRM orbits, respectively. With AC applied, the intensity differences are reduced to 14% and 12%. In the planar breast scintigraphy, this difference is 36%.

FIG. 16. The normalized intensities of the lesions in the gelatin phantom. The lesion size is 15 mm with target-to-background ratio of 10:1. Circular orbit was used in the acquisition.

FIG. 17. The normalized intensities of the lesions in the gelatin phantom. The lesion size is 15 mm with target-to-background ratio of 10:1. SRM orbit was used in the acquisition.

Figures 18 and 19 show the results of lesion contrast and SNR analysis, respectively. The prior mask, RR, and AC were applied. Similar conclusions as those found in the box phantom simulation can be drawn. Lesion contrast and SNR in the planar images are substantially lower than those in the GEBT slices using any orbit/angular range combination. In comparison to planar breast scintigraphy, the shallow lesion

FIG. 18. Lesion contrast of images reconstructed from the gelatin breast phantom data obtained using circular orbit and SRM orbit. Error bars indicate the standard deviation of three repetitions of the scan.

FIG. 19. Lesion SNR of images reconstructed from the gelatin breast phantom data obtained using circular orbit and SRM orbit. Error bars indicate the standard deviation of three repetitions of the scan.

contrast in GEBT is 2.6–6.2 times better using a circular orbit and 3.5–7.4 times better using a SRM orbit, depending on the angular range used. The lesion SNR in GEBT is also 2.3–3.8 times better than that in planar scintigraphy using a circular orbit and 3.0–4.6 times better using a SRM orbit. For the deep lesion, lesion contrast in GEBT is 3.6–7.4 times better than that in planar scintigraphy using a circular orbit and 4.9–8.8 times better using a SRM orbit. The lesion SNR in GEBT is also 3.3–5.0 times better than that in planar scintigraphy using a circular orbit and 4.3–5.6 times better using the SRM orbit. For all angular ranges contrast and SNR are higher for a given lesion using the SRM orbit compared to the circular orbit.

V. DISCUSSION

GEBT is a newly developed multiprojection modality for functional breast imaging. Through a combination of Monte Carlo simulations and phantom experiments, we have evaluated the performance of an EM reconstruction algorithm for GEBT using a limited angular range and few projection views. The results presented here suggest that, compared to planar breast scintigraphy, GEBT incorporating attenuation correction and resolution recovery can substantially mitigate the loss of lesion contrast and spatial resolution with increasing depth within the breast.

The in-plane spatial resolution in the reconstructed GEBT images is nearly independent of source position within the phantom, unlike that in the planar images, where resolution is rapidly degraded with increasing source depth. In fact, for all source positions the reconstructed in-plane resolution of GEBT is substantially superior to that of the gamma camera itself over a range of source-to-collimator separations, even in some cases where the camera was placed much closer to the sources for planar breast scintigraphy than for GEBT (10 cm collimator to AOR distance in GEBT versus 4 cm collimator to AOR distance in planar breast scintigraphy). This fact suggests the possibility of utilizing a higher sensitivity collimator, thus permitting either shorter acquisition times or a reduction in the amount of injected radiotracer without unacceptable lesion contrast reduction due to partial volume averaging. The spatial resolution of GEBT in the direction of breast compression (that is, the undersampled dimension along the z coordinate in Fig. 1) is dependent on the source depth. As the acquisition angular range increases, this depth dependence is reduced while the overall z resolution is greatly improved. At 135° angular range, a spatially uniform and near-isotropic resolution was proved achievable.

Two main image artifacts were observed in GEBT if no correction technique was applied. First, a background cupping artifact originates from both photon attenuation and data incompleteness. For narrow acquisition angle data undersampling along the z dimension dominates and regularization during reconstruction using a breast surface mask obtained from the prior x-ray tomosynthesis scan is needed. At larger angle the degree of undersampling is less and photon attenuation effects dominate. A combination of the attenuation correction and regularization implemented in this EM algorithm minimizes the cupping artifact over a range of acquisition angles. Second, lesion intensity artifacts due to both photon attenuation and detector blurring were observed for all angular ranges tested even after masking regularization was applied during reconstruction. This artifact also appears in the planar breast scintigraphy where the intensity of the lesion signal depends on the lesion's location relative to the gamma camera. The data presented here show that the incorporation of AC and RR into the EM algorithm can substantially improve quantitative assessment of lesion activity.

In simulations and experiments, lesion contrast and SNR in GEBT has proved to be substantially higher and less location dependent than those in planar breast scintigraphy under conditions of equal number of detected events. It is also observed that GEBT's performance improves as the angular acquisition range increases. However, only three distinctly different angular ranges with a fixed number of views were used to test the GEBT reconstruction algorithm performance over the entire range of acquisition angles likely to be utilized. Systematic optimization of the acquisition protocol in terms the number of projection views, interval spacing, and the total angular range is beyond the scope of the work presented here and will require further study.

In this study, no scatter from activity originating in the heart and liver has been included. While this is an acknowledged limitation of the phantom design, similar results in

terms of reconstruction algorithm performance are likely if these sources were present. Studies by our group and others have shown that in dedicated breast scintigraphy under mild compression using sestamibi the scatter contribution from outside of the breast to the image is relatively small except near the edge of chest wall. A previous study from our group using a gamma camera similar to the one used in this study showed that the scatter fraction is below 20% for a breast compressed at 6–8 cm thickness.³⁶ Similarly, using Monte Carlo simulation Hruska *et al.* found that for 6 cm compressed thickness, only 14% of events acquired in the standard 126–154 keV window have undergone scattering, and that only 18% of those originated in the torso (approximately 2.5% of all events in the window).³⁷ In this study the simulated and real cameras were operated using a 121–163 keV energy window and the phantoms had 7.7–8 cm thickness.

The total number of detected gamma rays used in this study, in both simulations and phantom experiments, was equal to that obtainable in a 10 min acquisition using a single gamma camera with an efficiency of 1.1×10^{-4} following injection of 925 MBq (25 mCi) of ^{99m}Tc-sestamibi. The current standard injected radiotracer activity of 740–1110 MBq (20–30 mCi), recommended for breast imaging by the radiopharmaceutical package insert, results in an effective whole body radiation dose of ~6–9 mSv. There is broad interest in exploring the impact on image quality of reduction in the injected activity in the interest of radiation dose reduction. Recent studies by Hruska *et al.*^{38,39} have shown that in planar breast scintigraphy using a double headed gamma camera with high efficiency collimators and wide energy windows (system efficiency of 5.1×10^{-4}), adequate image quality was attainable using an injected activity of 296 MBq (8 mCi) and 10 min imaging time. The results presented here compare GEBT and single-camera planar breast scintigraphy under the same hardware and imaging task conditions. Although neither the gamma camera nor the GEBT acquisition protocol has been systematically optimized, the results of this study suggest that with the implementation of regularization, attenuation, and resolution recovery GEBT may create further opportunity for radiation dose reduction.

Analogously to x-ray transmission tomosynthesis, GEBT could improve the detection of small lesions compared to the current planar standard via the removal of overlapping heterogeneous background tracer uptake within the breast. The excellent and nearly isotropic spatial resolution of GEBT could make it useful for procedures requiring good 3D localization such as gamma-guided biopsy.

VI. CONCLUSIONS

In this paper, an EM reconstruction algorithm developed specifically for the GEBT component of a dual modality breast tomosynthesis scanner was evaluated. In its current form the algorithm supports x-ray tomosynthesis derived masking regularization, resolution recovery, and attenuation correction. The effectiveness of these correction techniques in reducing the effects of angular undersampling and attenuation artifacts, as well as in improving the lesion contrast and SNR

were evaluated through a combination of simulations that were validated with phantom experiments. The study showed that an appropriate reconstruction scheme can greatly compensate for the limited angle acquisition geometry inherent in tomosynthesis and results in lesion contrast and SNR substantially higher than that obtained using planar scintigraphy under conditions of equal number of detected events.

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