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Detectability Comparison of Simulated Tumors in Digital Breast Tomosynthesis using High-Energy X-ray Inline Phase Sensitive and Commercial Imaging Systems

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Abstract

This study compared the detectability of simulated tumors using a high-energy x-ray inline phase sensitive digital breast tomosynthesis (DBT) prototype and a commercial attenuation-based DBT system. Each system imaged a 5-cm thick modular breast phantom with 50-50 adipose-glandular percentage density containing contrast-detail (CD) test objects to simulate different tumor sizes. A

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commercial DBT system acquired 15 projection views over 15 degrees (15d-15p) was used to acquire the attenuation-based projection views and to reconstruct the conventional DBT slices. Attenuation-based projection views were acquired at 32kV, 46mAs with a mean glandular dose (D_g) of 1.6mGy. For acquiring phase sensitive projection views, the prototype utilized two acquisition geometries: 11 projection views were acquired over 15 degrees (15d-11p), and 17 projection views were acquired over 16 degrees (16d-17p) at 120kV, 5.27mAs with 1.51mGy under the magnification (M) of 2. A phase retrieval algorithm based on the phase-attenuation duality (PAD) was applied to each projection view, and a modified Feldkamp-Davis-Kress (FDK) algorithm was used to reconstruct the phase sensitive DBT slices. Simulated tumor margins were rated as more conspicuous and better visualized for both phase sensitive acquisition geometries versus conventional DBT imaging. The CD curves confirmed the improvement in both contrast and spatial resolutions with the phase sensitive DBT imaging. The superiority of the phase sensitive DBT imaging was further endorsed by higher contrast to noise ratio (CNR) and figure-of-merit (FOM) values. The CNR improvements provided by the phase sensitive DBT prototype were sufficient to offset the noise reduction provided by the attenuation-based DBT imaging.

Keywords

Digital breast tomosynthesis; phase contrast imaging; high energy x-rays; phase retrieval; radiation dose

1. Introduction

Digital breast tomosynthesis (DBT) is an emerging quasi-three-dimensional (3D) x-ray imaging modality with demonstrated value in breast cancer detection [1–3]. In DBT, a set of low dose projection views is acquired over a limited angular range. A set of tomographic slices is reconstructed from the limited angle projection views to provide better visibility and discrimination of breast masses by reducing the structured noise caused by the overlapping breast tissues [4–6]. As with 2D digital mammography, DBT projection views are sensitive to the attenuation coefficients of breast tissues. For the diagnostic x-ray energy range of 10–100 keV, the contrast difference between a tumor and fibro-glandular tissue is less than 10% because their respective attenuation coefficients are similar. It has been reported that for breast elements such as soft tissue, phase shift coefficients are at least 2–3 orders of magnitude larger than their attenuation coefficients for the diagnostic energy range [7].

Implementation of the in-line phase sensitive imaging approach is simple, provided that the imaging system is spatially coherent [8,9], as it does not involve the introduction of any optical element between the sample and detector. With synchrotron sources, in-line phase sensitive imaging technique has demonstrated its value as compared to the attenuation-based imaging [10–13]. For the implementation of the inline phase sensitive technique with polychromatic sources in a clinical environment, two key challenges need to be addressed. The first challenge is to achieve adequate x-ray transverse coherence while providing sufficient photon flux to provide short exposure times. Micro-focus x-ray sources operating with large source-to-object distances can offer sufficient lateral coherent lengths [9, 14]; however, a very long exposure time is required for imaging due to their limited output

current values. To address this challenge, a high-energy beam of approximately 100–120 kV has been proposed and utilized to acquire phase sensitive images of soft tissue-equivalent phantoms with shorter exposure time [15–19]. The second challenge is that the interfaces and contours of different tissues are greatly accentuated in a phase contrast image due to the differential nature of the phase shifts. Thus, the bulk of the phase contrast in a given tissue area may be lost if the phase shifts vary slowly. One needs to disentangle tissue phase shifts from the combined attenuation/phase contrast in a phase sensitive projection to fully exhibit phase contrast. To address this challenge, we have proposed and implemented a single distance phase retrieval method [20–22]. Responding to these challenges, we have developed and characterized a high-energy x-ray inline phase sensitive prototype that fulfils the spatial coherence requirements as discussed in ref [9]. The prototype has shown advantages over attenuation-based imaging systems [15–18].

In this study, the detectability of simulated tumors of different sizes and contrast was compared using a low-energy commercial DBT system and a high-energy in-line phase sensitive DBT system. The overall exposure time utilized to acquire the inline phase sensitive projection views falls within the range of exposure times used by different commercial systems. To the best of our knowledge, a comparison of relative detectability between a clinical DBT system and high-energy phase sensitive DBT imaging has not been presented previously.

2. Methods and Materials

2.1 Breast Phantom

We employed a modular phantom (CIRS Inc., Norfolk, VA, USA) comprised of multiple slabs that were made of epoxy resin ($C_{21}H_{25}ClO_5$) mimicking a 50% adipose-50% glandular breast tissue. The adipose and glandular equivalent materials were homogeneously blended for uniform background slabs, while heterogeneous blending was used for non-uniform background slabs. Three slabs were sandwiched together to create a 5-cm thick phantom with the middle slab having a thickness of 1 cm and the outer slabs each having a thickness of 2 cm. The front slab facing the x-ray tube had non-uniform background while the middle and the back slabs had uniform backgrounds. To simulate different tumor sizes and densities, the middle slab was machined to include a contrast detail (CD) test pattern. This pattern consisted of a 6×6 matrix of circular discs having diameters of 0.25, 0.5, 1, 2, 3 and 4.25 mm with drilled depths of 0.1, 0.2, 0.4, 0.6, 0.8 and 1 mm.

2.2 Phase Sensitive Tomosynthesis Prototype

A benchtop inline phase sensitive tomosynthesis prototype was used for the acquisition of the phase sensitive projection views of the phantom. The prototype has been characterized and utilized in various biomedical imaging studies [15–18]. As shown in Figure 1(a), the prototype incorporates a micro-focus x-ray source (Model L8121-03, Hamamatsu Photonics, Japan) that consists of a tungsten (W) target with a focal spot size ranging from 7–50 μm as its output power varies from 10–75 W. The prototype also incorporates a CMOS flat panel detector (C7942SK-25, Hamamatsu Photonics, Japan) with an active pixel sensor (APS) architecture. The detector has a pixel pitch of 50 μm and an active photodiode area of 120

mm $\times$ 120 mm on which a scintillator made of cesium iodide doped with thallium (CsI:TI) is mounted to convert incident x-ray photons to light photons. The source to object (SOD) distance was 68 cm while the source to detector distance (SDD) was 136 cm which corresponded to a magnification (M) of 2. A motorized rotational stage (SGSP-160YAW, OptoSigma, USA) was utilized to provide the tomosynthesis mechanism. During imaging, the phantom was placed at the rotational center of the stage, equivalent to the traditional isocentric motion mode, in which both the x-ray source and detector rotate around a fixed pivot point synchronously. The two acquisition geometries utilized in this study are summarized in Table. 1.

For both angular geometries used to acquire DBT images with the prototype system, the acquisition of angular projection at 0 degrees was possible. All phase sensitive projection views were acquired using 120 kV, 500 μ A and with a total exposure time of 10.54 sec (5.27 mAs) under the 50 μ m focal spot size. A 2.5 mm aluminum (Al) filter was utilized to harden the beam and exclude low-energy photons. The half value layer (HVL) corresponding to these acquisition settings was measured to be 4.3 mm thickness of Al. These specific acquisition parameters are considered optimal when utilizing high-energy x-rays for phase sensitive imaging of soft tissues [23]. All projection views were acquired in a step-and-shoot manner, whereby the rotational stage was stationary during the acquisition of each projection view.

2.3 Attenuation-based Tomosynthesis System

A commercial system (Selenia Dimensions 3D, Hologic, Marlborough, USA) was used to acquire the attenuation-based projection images and to reconstruct the conventional tomographic slices. The system utilized a tungsten (W) target with a nominal focal spot size of 300 μ m. The projection views were recorded with an amorphous-selenium (a-Se) flat-panel detector that directly converts the incident x-ray photons into electric charge. The detector size was 29 cm $\times$ 24 cm with a matrix array of 4096 $\times$ 3328 pixels and a pixel size of 70 μ m. The source to image-detector distance (SDD) was 70 cm. As shown in Figure 1 (b), the system operates with continuous x-ray tube motion, taking 15 projection views over a 15-degree angular span (15d-15p). The distance between detector and center of rotation was 0 mm. All projection views were acquired using the system's automatic exposure control (AEC) mode. In AEC mode, the system automatically selects a suitable tube voltage (kV), anode/filter combination, and mAs value (the product of tube current and exposure time) depending on the compressed thickness of the breast and its attenuation to a pre-pulse x-ray exposure [23]. Projection views were acquired at 32 kV, 46 mAs, and 0.7 mm Al filter. The conventional slices reconstructed by the system using a proprietary filtered back projection method, resulting in an in-plane pixel size of approximately 0.1 mm with slice separation of about 1 mm. The phase sensitive acquisition geometry of 15d-11p is similar in angular range, while the 16d-17p geometry is similar in the number of projection views to the commercial system's acquisition geometry (15d-15p).

Finally, the simulated x-ray spectra were generated for the two x-ray tubes utilizing the tungsten (W) target as shown in figure 8.3. The spectra were generated according to the method specified in the literature [25]. In the simulations, the input filter was 0.7 mm

aluminum (Al) for the 32-kV beam spectrum while it was 2.5 mm Al for 120 kV beam spectrum. It is evident from the 120-kV spectrum that low energy photons have less contribution in imaging the phantoms as most of them are readily blocked by the Al filtration.

2.4 Phase Retrieval and Image Reconstruction

When utilizing high-energy x-rays, attenuation-based contrast tends to diminish, and images bear little resemblance to conventional ones. With the inline phase sensitive imaging technique, phase contrast effects arise only at the boundaries between different tissue types and thus the area contrast is nominal. To fully exhibit the phase contrast of the simulated tumor disks in the phantom, its phase map must be retrieved from its phase sensitive projection views. A single distance phase retrieval algorithm based on the phase-attenuation duality (PAD) method was applied as a preprocessing step to each projection view for retrieving the phase map. This method states that when materials or tissues composed of low-Z elements ($Z < 10$) are imaged with high-energy x-rays (60–500 keV), both the attenuation and phase shifts of that tissue are uniquely related to the projected electron density (ρ_e) [20–22]. Under such conditions, the phase map can be retrieved from just a single-phase contrast image. This method has been applied recently for biomedical applications [15–17, 26–29]. Epoxy resin is composed of chemical elements with $Z < 10$, thus, the requirement of phase-attenuation duality is readily met. In utilizing the PAD method with a polychromatic x-ray beam, it was necessary to approximate the average value of the wavelength (λ) corresponding to a 60 keV monochromatic x-ray beam which was approximated to be the average x-ray output energy from the tungsten (W) target tube operating at 120 kV.

The series of phase retrieved projection views were preprocessed by employing a ramp filter and then modified FDK back projection algorithm was applied to the filtered projections as [30–31]

$$f(x, y_0, z) = \int_{\min\theta}^{\max\theta} \frac{c(x, y_0, z) \cdot D^2}{(D - s)^2} \int_{-\infty}^{\infty} \frac{D}{\sqrt{D^2 + u^2 + v^2}} \times P(u, v, \theta) \cdot H\left(\frac{D \cdot t}{D - s} - u\right) du d\theta \quad (1)$$

where $s = -x\sin\theta + y\cos\theta$, $t = -x\cos\theta + y\sin\theta$, $f(x, y_0, z)$ represents the reconstructed image of a given slice y_0 , D is the source-to-object distance (SOD, R_1), $H(\cdot)$ represents the one-dimensional ramp filter along the tube-swept orientation on the detection plane aiming to invert the blurring caused by the sampling and the back projection, $P(u, v, \theta)$ is the projection value of the projection coordinate (u, v) from a projection view θ , and $C(x, y_0, z)$ is the compensation weighted factor which is experimentally determined as [32]

$$C(x, y_0, z) = 1/\cos[1.3z/(D - \sqrt{x^2 + y_0^2 + z^2})] \quad (2)$$

The reconstruction algorithm results in an in-plane pixel size of approximately 0.025 mm.

2.5 Analyses and Comparison of the Images

The reconstructed in-plane slices containing the CD pattern were cropped to include only rectangular regions of identical size containing the simulated tumors/discs. All images were displayed on a 5 Megapixel LCD monitor (EIZO SMD 21500D, 2048×2560 , 800:1 contrast ratio, 1024 gray levels, 750 cd m^{-2} maximum luminance) in a dark room. The monitor was calibrated using the DICOM grayscale standard display function. During the observer study, images were randomly presented to 9 independent observers, each with greater than 5 years of experience in evaluating and grading medical images. The readers were instructed to grade each perceptible disc on 4-point (0 to 3) scale: 3 = disc is completely perceived, including its margins; 2 = disc is perceptible, but without conspicuous margins/circular shape; 1 = greater than half, but not the full disc is perceptible; and, 0 = disc is either not perceptible or less than half is seen. Reading and scoring times were not limited. Threshold contrast and contrast-detail (C–D) curves were generated for each acquisition technique from pooled readers' scores. C–D analysis relates the threshold contrast necessary to perceive an object as a function of object diameter and is widely accepted as a simple and effective method for comparing medical imaging systems and techniques [15, 33–35]. A system with higher performance yields a C–D curve located closer to the x-y axis. A student t confidence interval was constructed around each data point for determining the variance among the observers for that point. This study utilized a 95% confidence interval with $n - 1$ degrees of freedom, where n represents the number of observers.

Contrast-to-noise ratios (CNRs) of the disk targets in each phantom image were calculated to quantitatively compare the imaging systems. The CNR of a disk target is defined according to the Rose model as follows [15, 36,37]

$$CNR = \frac{s_T - s_B}{\sqrt{(\sigma_T^2 + \sigma_B^2)/2}} \times \sqrt{a_D/a_p} \quad (3)$$

where S_T and S_B denote the mean pixel values of the target and backgrounds calculated over a region of interest (ROI), σ_T^2 and σ_B^2 are the corresponding pixel value variances, and a_D and a_p are the areas of a disk target and a pixel, respectively. Four ROIs of sizes equal to the ROI of the disks were positioned in heterogeneous background regions adjacent to each disk. The ROI size for the target disks varied with the diameter of the disc. Because the CNR for any given disk is influenced by the radiation dose and since the two imaging systems utilized different radiation dose levels, we defined a figure of merit (FOM) to characterize the imaging performance of the conventional DBT and phase contrast modalities as

$$FOM = CNR^2 / \text{Dose} \quad (4)$$

The FOM conveniently eliminates the parameter of exposure level from the comparative analyses and therefore, reflects the influence of photon energy in terms of dose efficiency [38]. We measured the CNR and the FOM values for four target discs of 3, 2, 1 and 0.5 mm in diameter with a drilled depth of 1 mm. The mean glandular dose (D_g) values for the DBT systems were calculated as $D_g = D_g N_{Tomo} \cdot k$, where $D_g N_{Tomo}$ (mGy/mGy) represents the normalized average glandular dose for a complete DBT acquisition and k (mGy) is the incident air kerma at the entrance surface of the breast. For a DBT system with a fixed number of projections at fixed angular locations, $D_g N_{Tomo} = D_g N_{Mammo} \cdot \overline{RGD}$, where $D_g N_{Mammo}$ represents the normalized average glandular dose for mammography acquisition and $\overline{RGD}$ is the mean relative glandular dose value for the complete scan [39]. RGD describes the change in the mean glandular dose between a zero-degree projection acquisition and a non-zero degree angle. $D_g N_{Mammo}$ values are determined by experimental and computer simulation methods based on the following factors: radiation beam quality (x-ray energy or HVL), x-ray tube target material, filter material, breast thickness and breast tissue composition [40,41]. The $D_g N_{Mammo}$ value for the attenuation based system was determined from the dose tables, which derived from the Monte Carlo simulations [42–43] and its corresponding $\overline{RGD}$ value was 0.996 as found in the tables reported in [39]. The dose tables only provide $D_g N_{Mammo}$ values for x-ray energies up to 35 keV. To facilitate the calculation of $D_g N_{Mammo}$ values for higher energies, we extended the Monte Carlo simulation to 150 keV. Our breast dosimetry simulation is based on the same Monte Carlo N-Particle Transport Code (MCNP) software package as described in our previous works [42,43]. For the 120 kV beam utilized for the acquisition of phase sensitive images, the $D_g N_{Mammo}$ value was computed from the x-ray spectral average of the Monte Carlo simulation-derived values for various photon energies. The x-ray spectrum was measured with an x-ray spectrometer (Amptek Incorporated, MA, USA) having a $3 \times 3 \times 1 \text{ mm}^3$ CdTe detector. The HVL derived from the measured spectrum was verified to match the directly measured HVL. The incident air kerma (k) values were measured with a calibrated ionization chamber (Model 9095, Radcal Corporation, CA, USA).

3. Results

The total incident air kerma (k) values, estimated $D_g N_{Tomo}$ values and the resultant D_g values corresponding to the acquisition of phase sensitive and attenuation based projection views for the DBT are given in Table 2.

The low dose projection views of the phantom acquired at 0° angle using the two imaging systems are given in figure 3. The high energy phase sensitive projection views, 3(b) and 3(c), yield an improved perception of the simulated tumors as compared to the attenuation-based projection view, 3(a). As compared to the phase contrast projection view, 3(b), the phase retrieved projection view, 3(c), has an enhanced bulk contrast for the simulated tumors. Thus, the phase retrieved projection views were used for the DBT slice reconstruction.

Figure 4 illustrates a reconstructed DBT in-plane slice depicting the simulated tumor pattern embedded in the modular 50-50 adipose-glandular density phantom acquired with the conventional DBT system using the AEC mode. Of 60 reconstructed tomographic slices, this

slice represented the best imaging quality regarding the disc clarity and conspicuity and was cropped to include only the rectangular regions of identical size surrounding the simulated tumors/discs. Apart from window/leveling, no image processing method was applied to this slice used for the observer study.

Figure 5 provides the in-plane phase sensitive tomographic slices of the simulated tumors reconstructed from two different angular geometries. Figure 5 (a) is the in-plane slice reconstructed from 15d-11p geometry and 5 (b) is the in-plane slice reconstructed from 16d-17p geometry. Due to the limited size of the CMOS detector and the magnification factor utilized, only the CD pattern of the phantom was captured on the image. On these phantom images, the most difficult disks to perceive (smaller with lower contrast) are in the upper right and the easiest disks to perceive (larger with higher contrast) are in the lower left.

Figure 6 compares the threshold contrast detection performances of the phase sensitive and attenuation-based DBT systems. At similar dose levels, the reconstructed phase sensitive DBT images exhibit superior target perception compared to the attenuation-based DBT image. The C–D curve indicates that observers perceived more simulated 4.25, 2, 0.5 and 0.25 mm diameter tumors on the phase sensitive tomographic slices. Thus, the threshold contrast required for tumor perception for the phase sensitive slices is lower than that of the attenuation-based slice for those diameters. For the two modalities, observers reported similar detection scores for simulated tumors of 3 and 1 mm diameter and thus, the threshold contrasts were identical.

Figure 7 compares observer scores of four different tumor discs extracted from the phase sensitive (15d-11p) and attenuation-based DBT slices. Our results demonstrated better conspicuity of simulated tumors on phase contrast tomographic slices. For example, for the 2mm, 0.6mm depth tumor disk (Figure 5b), 2 observers reported a score of 3 (fully perceptible round shape with conspicuous margins), 5 observers reported a score of 2 (fully perceptible but not in a circular shape/less conspicuous margins) and 2 observers reported a score of 1 (greater than 50%, but not fully perceptible) with the attenuation-based DBT image; while 6 observers gave a score of 3 and 3 observers gave a score of 2 for the same tumor disk with phase sensitive DBT image.

The superior performance of the phase sensitive imaging system in our observer study is further supported by the calculated CNR and FOM values. Figure 8 provides a graphical comparison of CNR ratios calculated for simulated tumors in the phase sensitive and attenuation-based tomographic slices for several diameters with 1 mm drilled depth. The phase sensitive slice (16d-17p configuration) has 1.53–3.06 times the CNR as that of the attenuation-based slice. Similarly, for the phase sensitive slice with 15d-11p configuration, the improvement in CNR is 0.71–2.34 times the CNR of the attenuation-based slice.

The improvement of CNR with the phase sensitive imaging system directly impacts the FOM ratios with the commercial system. From Table 3, one can see that the FOM values of the phase sensitive slice (16d-17p) range from a factor of 2.5–9.97 greater than the FOM values of the attenuation-based slice. Similarly, FOM values for the phase sensitive slice

(15d-11p) are 0.54–5.84 greater than the FOM of the attenuation-based slice. Of all the simulated tumor disks, the attenuation-based DBT system had better CNR and FOM values for only the 4.25 mm diameter tumor disk when compared with the phase sensitive system (15d-11p configuration).

4. Discussion and Conclusion

This study demonstrates the potential benefits of utilizing a high-energy x-ray phase sensitive system for breast imaging applications. The detector quantum efficiency (DQE) decreases with an increase in the x-ray energy, as do the attenuation and phase coefficients of tissue. Therefore, the use of a high energy x-ray beam is inherently disadvantageous for phase imaging in a comparison study with low energy attenuation-based clinical images. However, due to the limited output power of the micro focus x-ray tubes, a high energy x-ray beam is required for phase imaging to reduce the exposure times to clinically acceptable values. The commercial attenuation-based imaging system operates at low tube voltage (kV) with different filter thickness and SID; hence we cannot apply the same tube current (mA) and exposure time (s) settings as of our phase sensitive prototype. For a fair comparison, we allowed the commercial system to apply its optimized techniques, as determined by its AEC settings. The AEC mode settings resulted in a mean glandular dose value which was slightly higher than the phase sensitive prototype.

From the projection views of the phantom acquired at 0°, it was evident that the high energy phase retrieved images provided better discrimination of the simulated tumors as compared to the low energy attenuation-based projection image. It is widely known that for soft tissue ($Z < 10$) and its equivalent materials, attenuation-based imaging at 120 kV would be of inferior contrast due to their weak attenuation properties. Phase sensitive imaging allows the opportunity to utilize high energy x-rays for imaging soft tissue equivalent materials at low dose levels.

With phantom imaging analyses, the phase sensitive DBT imaging prototype demonstrated improved observer ratings, contrast-to-noise ratio (CNR) and figure of merit (FOM) compared to the commercial system. The SNR improvement provided by the phase sensitive slices was sufficient to detect the smallest discs that were undetectable with the attenuation-based slices, and the C–D curves indicated that the phase sensitive images provided better contrast resolution and spatial resolution. For example, with 4.25 mm tumor disk diameter, the reported threshold contrast was 0.31 versus 0.38 for the phase sensitive (16d-17p) and attenuation-based tomographic slices, indicating improved contrast resolution. Similarly, for smaller disk diameter of 0.25 mm, the reported threshold contrasts of 0.63 and 1.13 for phase sensitive and attenuation-based tomographic slices, respectively, clearly show an improvement in the spatial resolution.

With the employment of geometric magnification in clinical radiology, it is well-known that the boundaries of tissues are obscured due to the blurring caused by the finite focal spot size of the x-ray tubes. As a part of its requirement, in-line phase sensitive imaging effectively utilizes the geometric magnification with no blurring. The observer rating study indicated better conspicuity of simulated lesion shape and margins with phase-sensitive tomographic

slices. For instance, for the tumor disk with 0.25 mm diameter and 0.6 mm drilled depth, 1 observer reported a score of 3, 3 observers reported a score of 2 and 4 observers reported a score of 1 with the attenuation-based slice; while 2 observers reported a score of 3, 5 observers reported a score of 2 and 2 observers reported a score of 1 for the same tumor disk with the phase sensitive slice. It is our general observation that by employing a wider tomosynthesis angle (32d-17p) with phase sensitive imaging, the conspicuity and perception of the shape of the disks improve while the spatial resolution (smaller discs and micro-calcifications) decreases. The details of those observations are beyond the scope of this study and will be presented in the near future.

While the phase sensitive tomographic slices produced CNR values that were significantly greater than the CNR values as of attenuation-based slices, it was interesting to note that the CNR values decreased as the disk diameter increased. There are several reasons for this result including (a) with the heterogeneous background of the phantom, the variation of pixel values within an ROI increases as the size of an ROI increased, resulting in a large standard deviation value that results in a lower CNR value; (b) the ramp filter accentuates the high-frequency noise, and in the case of limited view tomography, also excessively suppresses the low frequency content, whose impact is clearly distinguishable for large area objects. For detectors with small components of additive noise, where most of the noise results from x-ray quantum fluctuations, the ratio of squared CNR to exposure is essentially independent of the exposure level; thus, the FOM would be expected to be a measure of performance that would not change with the incident exposure. The FOM values calculated for the phase sensitive slices, (16d-17p) and (15d-11p), are 2.5–9.97 and 0.54–5.84 times the FOM of the attenuation-based slice.

The two-phase sensitive DBT geometries that we evaluated utilized about the same tomosynthesis angle but with different numbers of equally spaced projections. Our observers preferred the slices reconstructed with a larger number of projections, 16d-17p. For a fixed tomosynthesis angle, one may utilize a greater number of projections for refined angular sampling, but there are few limiting factors: (a) for a fixed mean glandular dose, each additional low dose projection introduces additional electronic noise from the detector, which increases the overall noise of the reconstructed volume and (b) the total scan time generally increases with the number of projections, particularly in a step-and-shoot configuration, which may increase motion artifacts.

The algorithm used for the reconstruction of phase sensitive tomographic slices was not fully optimized and suffers from streaking artifacts as seen at the boundaries of the simulated tumors which may obscure anatomical features. By employing optimization filters, such as spectrum apodization and slice thickness filters, these artifacts could be minimized and the sensitivity of phase sensitive DBT imaging technique will further increase. The epoxy resin ($C_{21}H_{25}ClO_5$) phantom utilized in this study to mimic a 50% adipose-50% glandular breast tissue does not produce the exact same photon-breast tissue interactions. For a breast tissue under 60 keV beam, the ratio of $\delta/\beta = 1915$, while for the epoxy resin phantom, this ratio of $\delta/\beta = 1728$ [44,45], where δ represents the refractive index decrement that is responsible for x-ray phase shift, while β represents the imaginary part of the refractive index that is responsible for x-ray attenuation. As compared to the epoxy resin phantom, these ratios

suggest that the x-ray phase shifts of a breast tissue are more sensitive than its attenuation coefficients. Therefore, it is expected that for a breast tissue, the phase shift induced contrast would be higher than the epoxy resin phantom using the high energy inline phase sensitive imaging system. Furthermore, due to technical difficulty and a high cost of inserting dense CD objects in the breast phantom slabs, the CD array of discs was used. As opposed to real tumors in a breast, the discs in our phantom are less attenuating than the background. Nevertheless, CD array of discs embedded in complex heterogeneous backgrounds provide useful differential contrast for reader preference studies and CNR analyses that are necessary for systems comparisons. We plan to use complex breast imaging phantoms with various testing objects in different planes of the phantom to further highlight the benefits of utilizing inline phase sensitive DBT imaging in providing improved depth resolution. In future study, the phase sensitive system could be further optimized for phase contrast visibility by using the procedure proposed in one of our previous work [14,46]. In addition, some tomography optimization techniques could be useful as well [47]. To our best knowledge, 10.5 sec is the shortest reported exposure time for successful inline phase sensitive DBT imaging outperforming a commercial DBT system regarding target detection and CNRs. Furthermore, this exposure time falls within the range of exposure times used by commercial systems. In collaboration with our industrial partners, a clinical phase sensitive imaging system is under development for future Phase 1 clinical trials.

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1. A high-energy x-ray phase sensitive and a commercial DBT systems were compared.
2. A modular breast imaging phantom was used for the comparison purposes.
3. Simulated tumor margins were better visualized for phase sensitive DBT imaging.
4. Phase sensitive DBT showed an improvement in contrast and spatial resolutions.
5. Superiority of phase sensitive DBT was endorsed by higher CNR and FOM values.

Figure 1. (a) Schematic of the inline phase sensitive x-ray imaging prototype used to acquire high-energy phase sensitive projection images; (b) Schematic of the commercial DBT system used for the acquisition of low-energy attenuation-based projection images.

Figure 2.

Simulated x-ray spectra for the two x-ray tubes with tungsten target (a) 32 kV, 0.7 mm Al filter as used by the clinical DBT system (b) 120 kV, 2.5 mm Al filter as used by the phase sensitive prototype.

Figure 3.

(a) Attenuation-based projection view acquired at 0° with the commercial DBT system at 32 kV, 3.06 mAs and 0.106 mGy (b) Phase contrast projection view acquired at 0° with the phase sensitive prototype at 120 kV, 0.31 mAs and 0.09 mGy (c) Phase retrieved image processed with PAD algorithm.

Figure 4. In-plane slice containing the simulated tumors reconstructed from attenuation-based projection images of the phantom acquired with the commercial DBT system at 32 kV, 46 mAs, 1.6 mGy over 15° angular span with 15 projections.

Figure 5.

In-plane slices reconstructed from phase sensitive projections of the phantom containing the simulated tumors acquired with the phase sensitive prototype at (a) 120 kV, 500 μ A, 5.27 mAs, 1.51 mGy over 15° angular span with 11 projections; (b) 120 kV, 500 μ A, 5.27 mAs, 1.51 mGy over 16° angular span with 17 projections.

Figure 6.
Contrast-detail curves for the phase sensitive and attenuation-based tomographic slices for the 50% glandular-50% adipose phantom.

Figure 7.

Comparison of the observer scores for the simulated tumors extracted from the attenuation-based and the phase sensitive tomographic slices having (a) 2mm diameter, 1mm drilled depth; (b) 2mm diameter, 0.6mm drilled depth; (c) 1mm diameter, 0.8mm drilled depth; and, (d) 0.5mm diameter, 0.6mm drilled depth.

Figure 8. Graphical comparison of CNR values for the simulated tumors calculated with phase sensitive and attenuation-based tomographic slices.

Table 1

Two combinations of DBT protocols used for the acquisition of the phase sensitive projection views.

Protocol	Scan Angle (Degrees)	First and Last Angle (Degrees)	Number of Projection Views	Angular Increments (Degree)	Exposure Time per Projection (sec)
15d-11p	15	-7.5, +7.5	11	1.5	0.95
16d-17p	16	-8, +8	17	1	0.62

Table 2

The mean glandular dose (D_g) values corresponding to the acquisition settings of the two imaging systems.

	k (mGy)	$D_g N_{Tomo}$ (mGy/mGy)	D_g (mGy)
Phase sensitive scan: 120 kV, 5.27 mAs	2.798	0.540	1.51
Attenuation based scan: 32 kV, 46 mAs,	5.791	0.276	1.60

Table 3

Comparison of the FOM ratios calculated for various disk diameters with 1 mm drilled depth with the phase sensitive and attenuation-based tomographic slices.

	1 mm	2 mm	3 mm	4.25 mm
$FOM_{Phase} (16d-17p)/FOM_{Attn} (15d-15p)$	9.18	9.97	3.05	2.50
$FOM_{Phase} (15d-11p)/FOM_{Attn} (15d-15p)$	3.71	5.84	2.33	0.54