Published in final edited form as:

J Xray Sci Technol. 2015 December 17; 23(6): 667–682. doi:10.3233/XST-150519.

Low Dose High Energy X-ray In-Line Phase Sensitive Imaging Prototype: Investigation of Optimal Geometric Conditions and Design Parameters

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Abstract

The objective of this study was to investigate the optimization of a high energy in-line phase sensitive x-ray imaging prototype under different geometric and operating conditions for mammography application. A phase retrieval algorithm based on phase attenuation duality (PAD) was applied to the phase contrast images acquired by the prototype. Imaging performance was investigated at four magnification values of 1.67, 2, 2.5 and 3 using an acrylic edge, an American College of Radiology (ACR) mammography phantom and contrast detail (CD) phantom with tube potentials of 100, 120 and 140 kVp. The ACR and CD images were acquired at the same mean glandular dose (MGD) of 1.29 mGy with a computed radiography (CR) detector of 43.75 μ m pixel pitch at a fixed source to image distance (SID) of 170 cm. The x-ray tube focal spot size was kept constant as 7 μ m while a 2.5 mm thick aluminum (Al) filter was used for beam hardening. The performance of phase contrast and phase retrieved images were compared with computer simulations based on the relative phase contrast factor (RPF) at high x-ray energies. The imaging results showed that the x-ray tube operated at 100 kVp under the magnification of 2.5 exhibits superior imaging performance which is in accordance to the computer simulations. As compared to the phase contrast images, the phase retrieved images of the ACR and CD phantoms demonstrated improved imaging contrast and target discrimination. We compared the CD phantom images acquired in conventional contact mode with and without the anti-scatter grid using the same prototype at 1.295 mGy and 2.59 mGy using 40 kVp, a 25 μ m rhodium (Rh) filter. At the same radiation dose, the phase sensitive images provided improved detection capabilities for both the large and small discs, while compared to the double dose image acquired in conventional mode, the observer study also indicated that the phase sensitive images provided improved detection capabilities for the large discs. This study therefore validates the potential of using high energy phase contrast x-ray imaging to improve lesion detection and reduce radiation dose for clinical applications such as mammography.

Keywords

phase sensitive; phase contrast; x-ray imaging; high energy; phase retrieval; mammography

1. Introduction

Mammography has been under the constant research focus mainly in providing adequate image quality for the diagnosis of breast cancer in early stages at a minimum dose to reduce the risks associated with the radiation exposure [1–4]. Phase sensitive x-ray imaging (PSXI) is an active research area with significant potential for clinical applications and studies have reported an improvement in the image quality [5–14]. The amount of the phase change is determined by the refractive index of the tissue which is equal to

$$n = 1 - \delta + i\beta \quad (1)$$

where δ , the refractive index decrement, is responsible for x-ray phase shift, and β the imaginary part of n , is responsible for the x-ray absorption. The requirement in conventional mammography that sufficient differences in β should exist between the tissues is fulfilled by operating at low tube energies and one gets a good soft tissue contrast [15, 16]. The compromise is made on the dose delivered to the tissue at the expense of superior image quality for the accurate diagnosis. PSXI also incorporates the effects of phase shifts in the form of additional contrast [7–9]. It has been estimated that the tissue's δ ($10^{-6} - 10^{-8}$) is at least 1000 times greater than β ($10^{-9} - 10^{-11}$) for x-rays in 10 keV–100 keV range [15]. It is this important fact that creates the opportunity of using high x-ray tube energies for low dose imaging in PSXI. Recently, mammography has been investigated with the synchrotron radiation [10, 12], also with high x-ray energies [13, 14]. In-line phase sensitive imaging is the simplest of the three PSXI techniques and it is different from the conventional attenuation mammography in that an air gap between the object and detector is introduced and an x-ray illumination with a sufficient degree of spatial coherence is employed [7–9, 11]. A good review article on the three types of the PSXI is ref [15]. In-line PSXI has been implemented with conventional polychromatic micro focus sources at high x-ray energy and the quality improvement in imaging has been reported [18–20]. In the past, optimization of the in-line PSXI has been investigated [4, 5, 8, 22], but to our best knowledge no experimental study has been performed in optimizing the high x-ray energies under different magnifications in the in-line PSXI for mammography application using the mammography phantoms. The phase contrast manifestation in the in-line PSXI has been investigated in the past [21–23] and the ratio of phase space shearing length to the lateral coherence length represents the coherence criteria for the phase sensitive imaging [23].

$$\frac{L_{shear}}{L_{\perp}} = \frac{R_2 s u}{M R_1} \quad (2)$$

where R_1 , R_2 and M are respectively the source-to-object distance, object-to-detector distance and the magnification. Moreover, L_{shear} given by $\lambda R_2 u / M$ represents the x-ray diffraction from object exit to the detector plane while $L_{\perp}$ given by $\lambda R_1 / s$ represents the partial coherence effects of the wave illuminated from a finite x-ray source of focal spot size s with the average x-ray wavelength λ . If $L_{shear} / L_{\perp} < 1$, the x-ray illumination is partially coherent, and the phase contrast associated with the structure component of spatial frequency u is visible.

When high x-ray energies are used in PSXI for the breast image acquisition, there will always be a weak attenuation contrast from the soft tissue but at the same time the relative strength of δ over β would enable the phase shifts to constitute an additional contrast to the image. If proper imaging parameters are used, we expect that the image acquired at low dose in the PSXI with high tube energy will have the same or better image contrast and target perception as compared to the conventional attenuation based imaging at low x-ray energies. We aim to experimentally investigate the optimal conditions for the in line PSXI at high x-ray tube energies over different magnifications at the same mean glandular dose (MGD) of 1.295 mGy using several phantoms. The MGD of 1.295 mGy is considered low when considering the thickness of the American College of Radiology (ACR) and contrast detail (CD) phantoms that we are using for imaging. The experimental results of the phase sensitive prototype are compared with the conventional contact mode images at similar and double doses. This study is a step closer towards the realization of the low dose PSXI imaging in the clinical mammography applications.

2. Materials and Methods

2.1. Phase Contrast X-ray Imaging System

The in-line phase contrast x-ray imaging system prototype utilized in this study consists of imaging and measurement components mounted on an optical rail. A micro focus x-ray source (Model L8121-03, Hamamatsu Photonics, Japan) with adjustable tube current and tube voltage ranging from 40 to 150 kilovolts is used in this study. The micro focus x-ray tube consists of a tungsten target and a beryllium (Be) output window with a thickness of 200 μm . The distance from the focal spot to the output window is 17 mm with the diameter of the focal spot ranging from small (7 μm), medium (20 μm) to large (50 μm) for tube operation at output powers of 10W, 30W and 75W respectively. As described in Table 1, phase sensitive images are acquired in four magnification (M) sets of 1.67, 2, 2.5 and 3 with a fixed source to image distance of 170 cm under a small focal spot size of 7 μm . A 2.5 mm thick aluminum (Al) filter is used in front of the x-ray tube for beam hardening and to block the low energy photons as mentioned in the previous study [28, 29]. The x-ray detection system for the imaging consists of a Konica Minolta Regius Computed Radiography (CR) system which is utilized in the clinical practice for the digital acquisition of x-ray images with a CR plate (31 cm $\times$ 24.6 cm) for mammography. The pixel pitch for the CR plate is 43.75 μm . ACR and CD are acquired at the same MGD of 1.295 mGy with 100 kVp, 120 kVp and 140 kVp while the acrylic edge images are acquired with the same mAs values corresponding to that MGD. The corresponding milli-ampere-second (mAs) values for MGD of 1.295 mGy in each of the phase contrast mode are given in Table 2.

2.2. Conventional X-ray Imaging System Configuration

For the conventional contact mode imaging, the same imaging setup with x-ray tube and detector mounted on the optical rail is utilized. Two protocols are used to acquire the conventional images with the tube voltage of 40 kVp and both protocol utilize a source to image detector (SID) distance of 68 cm and 7 μm x-ray tube focal spot size. The first protocol images are acquired with no anti-scatter grid while the second protocol utilizes an anti-scatter grid to reduce the scattering. A rhodium (Rh) filter of 25 μm thickness is used to

filter out the low x-ray energy photons. The mAs value corresponding to 40 kVp for MGD of 1.295 mGy in conventional imaging is 36.5 mAs while the double dose of 2.59 mGy corresponds to 72 mAs respectively.

2.3 Phase Retrieval and Dose Calculations

In order to fully exhibit the objects contrast within the phantoms, the phase map of the phantom must be extricated from the combined attenuation/phase contrast in a phase sensitive projection. In this study, the x-ray attenuation by the soft-tissue-like materials of low-Z ($Z < 12$) elements is dominated by the incoherent x-ray scattering due to the use of high energy x-rays, and the phase attenuation duality ensues. For the components of high-Z elements, the phase attenuation duality (PAD) does not hold. As a result, the retrieved phase values of high-Z components are with errors, but the retrieved phase values for the low-Z components are keeping accurate, since the PAD equation is a differential equation and its solution is unique in its locality. This physical situation enables us to use a recently developed innovative phase retrieval method known as the phase attenuation duality (PAD) method [24, 25]. As contrary to the general phase retrieval methods, PAD method can retrieve the phase map from only a single phase-sensitive low dose projection [26, 27]. The phase retrieval from a single phase-sensitive low dose projection $I(\mathbf{r}_D)$ is given as

$$\phi(\mathbf{r}) = \frac{\lambda r_e}{\sigma_{KN}} \cdot \ln \left\{ \left[1 - \left(\frac{\lambda R_2}{2\pi M} \cdot \frac{\lambda r_e}{\sigma_{KN}} \cdot \nabla^2 \right) \right]^{-1} \left(\frac{M^2}{I_{in}} I(\mathbf{r}_D) \right) \right\} \quad (3)$$

In the equation, $\phi(\mathbf{r})$ represents the phantom's phase map, λ is the average x-ray wavelength, σ_{KN} the Klein-Nishina total cross-section of Compton scattering, and $r_e = 2.818 \times 10^{-15}$ m is the classical electron radius. In addition, $I(\mathbf{r})$ is the acquired phantom's phase-sensitive intensity at the detector's transverse coordinate position $\mathbf{r}_D$ and I_{in} the entrance x-ray intensity. Derived from x-ray propagation equations, the operator ∇^2 denotes the two dimensional transverse Laplacian differential operator, and the operator $[1 - ((\lambda^2/\sigma_{KN})R_2r_e \nabla^2/2\pi M)]^{-1}$ is a pseudo-differential operator.

The MGD (D_g) is calculated as follows: $D_g = D_{gN} \cdot X_{ESE}$ [30–32], where D_{gN} is normalized MGD coefficient and X_{ESE} is the object entrance exposure. D_{gN} is determined by experimental and computer simulation methods based on the following factors: radiation beam quality (x-ray energy or half value layer (HVL)), x-ray tube target material, filter material, breast thickness and breast tissue composition [32]. For the phase contrast images, D_{gN} was estimated based on the previously-described Monte Carlo method [31, 33]. However, the previous studies only provide D_{gN} data for x-ray energies up to 35 keV. To facilitate D_{gN} calculation for higher energies, we extended the Monte Carlo simulation to 150 keV. For every x-ray energy beam utilized in this study, the D_{gN} values are computed from the x-ray spectral average of the Monte Carlo simulation-derived values for various photon energies. The x-ray spectrum is measured with an x-ray spectrometer having a $3 \times 3 \times 1$ mm³ CdTe detector (Amptek Incorporated, Bedford, Massachusetts), using a pair of tungsten collimators provided by the manufacturer.

2.4. Computer Simulation on Phase Contrast Manifestation

The goal of computer simulation is to compare the experimental results with it for an optimal phase-sensitive mammography system operated at high x-ray energy. In the simulations, the central parameter to calculate is the modulus of the relative phase contrast factor RPF ($\mathbf{u}$) which represents the qualitative measure of the coherence and the visibility of phase contrast at spatial frequency $\mathbf{u}$ [9, 23]. RPF ($\mathbf{u}$) is given as

$$RPF(\mathbf{u}) = c^2 h^2 OTF_{det} \left(\frac{\mathbf{u}}{M} \right) \times \left[\int \frac{\pi R_2 \mathbf{u}^2}{M E^2} \times S_{Exit}(E) dE \right] \quad (4)$$

where h is Planck's constant, c is the speed of light, and $S_{Exit}(E)$ is the normalized spectrum of the average exiting beam. $OTF_{det} \left(\frac{\mathbf{u}}{M} \right)$ is the detector's spatial frequency response at $\mathbf{u}$ with the finite focal spot size. The complete description and explanation of Eq. 4 can be found in ref [23].

2.5. Phantoms and Image Analysis

Three phantoms are utilized in this study in an effort to provide a comprehensive image quality evaluation and comparison of the systems. A laser cut edge of an acrylic plate of 1.42 mm thickness is used as a first phantom to verify that the phase contrast effect takes place at high energy. The laser fabricated acrylic edge phantom provides a visual indication of the edge enhancement provided by phase sensitive imaging at the boundary of edge. Also, the edge profiles determined from the acrylic edge images can serve as a graphical indication of the phase contrast effect in the form of overshooting that occurs at the boundary of acrylic and air. For the quantification of the edge, Edge Enhancement Index (EEI) is used which compares the degree of edge enhancement relative to the absolute change in the pixel intensity for digital systems across the edge [18, 19, 37]. The EEI is defined as

$$EEI = \frac{(P - T)/(P + T)}{(H - L)/(H + L)} \quad (5)$$

where P and T are the peak and trough intensities at the edge, and H and L represents the intensities that would result at these locations if there were no edge enhancement at the high and low intensity regions next to the edge.

An ACR phantom (Gammex, 156 D) of 4.4 cm thickness is used as a second phantom which is made of a 7 mm wax insert that contains 12 sets of test objects with a 3.4 cm acrylic base. This approximates a 4.2 cm thick compressed breast of 50% glandular and 50% adipose composition. The fibril structure object thickness ranges from 0.40 mm to 0.93 mm. The micro calcification object thickness is from 0.20 mm to 0.54 mm and the tumor like mass object thickness ranges from 0.25 mm to 1 mm respectively.

A CD phantom (Med Optics, Inc., Tucson, AZ) of 4.6 cm thickness is used to compare the comprehensive image quality evaluation and for the comparison the systems. The CD phantom typically consist of a matrix of discs with varying diameters along one axis to

represent object size and varying thicknesses along the other axis to produce contrast within the image. The CD phantom is a 7×7 matrix of discs with milled depth of 0.73 mm, 0.51 mm, 0.36 mm, 0.24 mm, 0.16 mm, 0.11 mm and 0.06 mm with ranging diameter of 4.82 mm, 3.50 mm, 2.32 mm, 1.60 mm, 0.70 mm, 0.30 mm and 0.18 mm, respectively. All the ACR and CD phantom images are presented on a computer monitor (S2240L, Dell Inc) to 4 well trained and experienced observers. Each observer completed the analysis independently, utilizing the same monitor and viewing conditions. The observers can adjust the window and level settings, as well as the magnification and rotation of the images, to suit their viewing preferences. Their results are averaged to determine individual scores for fibers, specks and masses, as well as an overall combination score for each of the comparison images. The analysis of the CD phantom involves an observer identifying the minimum perceptible thickness in the image for each diameter. Contrast detail (CD) curve analysis is widely accepted as an effective technique for comparison of medical imaging systems including mammography applications [3, 13, 38]. The CD curve relates the threshold contrast necessary to recognize an object as a function of the object's diameter. Curves for different systems or techniques can be easily compared, as a system exhibiting higher performance produces a CD curve located closer to the x-y axis. The CD curves are generated for each image according to the average observer score to compare the relative performance of the phase contrast, phase retrieval and conventional images. A Student t confidence interval of 95% is constructed around each data point for the purpose of determining the variance among the observers for that point. Quasi ideal signal to noise ratio (SNR_{qi}) is used to predict the disk detectability of the phase and phase retrieved images under the mentioned conditions. The SNR_{qi} is given as [34]

$$SNR_{qi} = C \sqrt{\eta \phi} \times \frac{a_0}{\sqrt{a_0 + a_a}} \quad (6)$$

where C is the subject contrast, η is the absorption efficiency of the CR plate, ϕ is the x-ray photon fluence, a_0 is the area of the disk, a_a ($\pi \sigma^2$) represents the sampling aperture area of the system. Based on the Rose model, at least 5 to 7 physical SNR is required to detect a low contrast mass in its background [34, 35]. We selected a threshold SNR of 6 for a mass to be detected by an observer. Once SNR_{qi} is calculated, the performance of phase contrast and phase retrieved images are compared. Finally, for quantitative comparison of the phase retrieved and phase contrast images, contrast-to-noise ratios (CNRs) of the disk targets in the phantom are calculated which is defined as [34, 36]

$$CNR = \frac{S_A - S_B}{\sqrt{(\sigma_A^2 + \sigma_B^2)/2}} \times \sqrt{a_D/a_p}, \quad (7)$$

where S_A denotes the mean pixel value of the disk target averaged over a region of interest (ROI), S_B is the mean pixel value of the background averaged over an ROI of the same size, σ_A^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.

3. Results and Discussion

3.1 Glandular Dose Calculation

The MGD corresponding to the phase sensitive and conventional techniques are calculated as detailed above. The tube current, entrance exposure readings, the estimated D_{gN} values and the resultant D_g for the investigated imaging modes are provided in Table 3. The MGD values facilitates the comparisons of phase sensitive imaging to the conventional contact mode imaging at similar doses but also at a reduced dose of half. The MGD of 1.295 mGy is considered as a low dose for image acquisition when considering the thickness of the phantoms that we are using in the study.

3.2 Acrylic Edge Phantom

The acrylic edge images acquired in conventional contact mode at 40 kVp with and without anti-scatter grid, and, in the phase contrast at 100 kVp in $M = 2$ and 2.5 are provided in Fig. 1 respectively. The edge is more clearly indicated by the white line highlighting the overshooting of the edge at $M = 2.5$ as compared to $M = 2$. It is noticeable that the edge is not highlighted in the conventional contact mode and there is barely an overshooting. This is further illustrated with the edge profiles determined for the images as shown in Fig. 2. As the edge line between air and acrylic is tilted, an average edge profile is generated for the comparison purposes. The phase contrast image at $M = 2.5$ exhibits large overshooting along the edge transition from air to acrylic which is a graphical indication of the larger edge enhancement for $M = 2.5$.

For the RPF (u), computer simulations are performed at 50, 60, 70 keV average photon energies to simulate the 100, 120 and 140 kVp tube voltages with a 5 cm thick breast of 50% adipose and 50% glandular tissue, with a target frequency of 15 lp/mm, x-ray tube focal spot size of 7 μm and with the 2.5 mm Al target filter. An optimal design of phase contrast system at high x-ray energy should achieve as large $|RPF(u)|$ as possible.

The results of our simulations are summarized in Table 4 and Fig. 3. The simulations reveal that $|RPF(u)|$ increases as increases with the object to detector distance R_2 and the magnification M only up to certain M . This is because, while an increase of R_2 could increase the x-ray diffraction effects, it would reduce the x-ray spatial coherence by a higher magnification factor. Based on the results in Table 4, the optimal $|RPF(u)|$ will be achieved with a magnification factor $M = 2.5$ for a 7 μm x-ray tube focal spot size. At 100 kVp, all of the resultant $|RPF(u)|$ are higher than 120 kVp and 140 kVp for the MGD of 1.295 mGy. The simulations show that Eq. 4 indeed provides the design guidelines for clinical low dose x-ray phase sensitive imaging systems.

The graphical interpretation of the measured EEI values with respect to the four magnification sets investigated is given in Fig. 4. The EEI for the conventional 40 kVp, 36.5 mAs acrylic edge image with/without the anti-scatter grid is 0.87 and 0.95, while for the 40 kVp, 71.5 mAs acrylic edge image with/without anti-scatter grid is 0.89 and 0.96. It is also evident that for all of the magnifications, the EEI values for 100 kVp and 120 kVp are very close to each other with the highest EEI of 1.5 at 100 kVp for $M = 2.5$. As the magnification increases from 1.67 to 2.5, the EEI increases substantially to its peak or saturation point.

When magnification increases from 2.5 to 3, the EEI slightly decreases maintaining approximately the same values as of $M = 2.5$. Although the computer simulations reveal that the $|RPF(u)|$ for $M = 2.5$ and 3 are almost the same, the EEI values suggest that there are enough differences in those magnifications to accomplish that the phase contrast effect is greater at $M = 2.5$. All the EEI values of the edge phantom images validate the computer simulations yielding the highest values for 100 kVp that are slightly greater than 120 kVp.

3.3. ACR Phantom

The ACR phantom phase contrast and phase retrieved images acquired at 100 kVp, 7.7 mAs at $M = 2.5$ are shown in Fig. 5. The qualitative comparison of the two figures indicates that phase retrieved image quality in terms of visibility of wax inserted objects is better as more masses, speck groups and fibers insert are perceptible as compared to that of the phase contrast image. Mathematically, the PAD phase retrieval process act as a low pass filter; hence it can reduce noise and enhance the SNR. That is the reason why that the third speck group of the phase retrieved image is easily perceptible as compared to that of the phase contrast image. The quantitative comparison based on the ACR average observer scores for the investigated geometry and x-ray energies are given in Fig. 6 and 7 respectively. The total observer score indicates that at $M = 2.5$, the ability of the observers to distinguish the smallest test objects is greater. Over the three sets of kVp's investigated at $M = 2.5$, the images acquired using 100 kVp yielded the highest average observer scores. It is also evident from the scores that the phase retrieval images yielded higher scores than the phase contrast images. Although the ideal score for this ACR phantom will be 12, a score of 9 that our phase retrieved image reported at $M = 2.5$ with 100 kVp is encouraging, which indicates the feasibility of acquiring acceptable quality images at a substantially low dose environment. The results of the average observer scores for both the phase contrast and phase retrieved image follow the computer simulations in reporting the optimal geometry and x-ray energy. Contrary to the computer simulations, there are enough differences between the average observer scores reported at $M = 2.5$ and 3, leading to conclusion that x-ray tube energy of 100 kVp at $M = 2.5$ is the optimal set of operation for mammography when considering high energy at the mentioned geometry using the in-line PSXI.

3.4. CD Phantom

The CD phantom phase contrast and phase retrieved images acquired at 100 kVp for $M = 2.5$ and $M = 3$ are shown in Fig. 8 and 9 respectively. The CD curves are generated in Fig. 10 and 11 for the acquired images where the x-axis represents the disc diameter ranging from 0.18 mm to 4.82 mm, while the y-axis represents the threshold contrast. At $M = 2.5$ and 3, the curves are closer to both the axes and more discs are detected by the observer as compared to the cases of $M = 1.67$ and 2. Comparing $M = 2.5$ and $M = 3$ images, the CD curves for $M = 2.5$ are better and more discs are perceived as compared to $M = 3$. Furthermore, the phase retrieval images yield more detection of the discs as compared to the phase contrast images. The 120 kVp phase contrast CD image at $M = 2.5$ yields slightly more score as compared to 100 kVp. The observer scores are in accordance with the computer simulations. The 100 kVp and 120 kVp images in $M = 2.5$ both have almost similar threshold contrast levels for the disc perception. This implies that due to the limited

micro focus tube current, the x-ray tube operated at 120 kVp could be well used for short exposure time.

For the measurement of quasi ideal signal to noise ratio (SNR_{qi}), the photon fluence in air (ϕ_0) and the linear attenuation coefficient (μ) values for the 4.6 cm thick CD phantom for three different X-ray energies are given in Table 5.

The calculated SNR_{qi} values for disc diameter of 1.60 mm at 100 kVp in $M = 2, 2.5$ and 3 is given in Table 6. This table indicates that for any disc whose SNR_{qi} is greater than the threshold SNR of 6, an observer can detect it in the scoring process. The images for $M = 2.5$ follow closely the predicted SNR_{qi} and more discs are detected as compared to $M = 2$ and 3 . At $M = 3$, the 0.16 mm milled depth disc is detected in phase retrieved image while the phase contrast image couldn't detect that disc.

The phase retrieved and phase contrast images acquired at 100 kVp in $M = 2.5$ are quantitatively compared. The ratio $CNR_{AKN/I}$ calculated for the three discs along with three different milled depths are given in Table 7. The table signifies that for the larger disks, the phase retrieved CNR is at least 3 times greater than the phase contrast only images. However, the detection of smaller disks requires much higher CNRs. For example, to detect the 0.30 mm disk, one needs a higher CNR by a factor of 16 ($=4.82/0.30$) than that for the detection of the 4.82 mm disk with equal milled depth. In this study, the three to four fold improvements in CNR for the large disks achieved with phase imaging are just not enough to detect the smaller disks and this is also reflected in the CD curves. Finally, the images acquired in the conventional contact mode with 1.295 mGy and 2.59 mGy are shown in Fig. 12.

For the same MGD, there is a large improvement in disc discrimination with the phase sensitive images as compared to the contact mode images for both the larger and smaller discs. It is clear from Fig. 13 that the double dose images acquired in the contact mode, the observer study indicates that the phase sensitive images provides improved detection capabilities for larger size discs. The image improvement in the phase sensitive image is contributed by the phase shifts induced contrast as well as due to the reduced scatters by the introduction of air gap between the object and the detector. The air gap also discard the employment of an anti-scatter grid and thus more primary x-rays can reach the detector. Increasing the x-ray tube voltage significantly reduces the required exposure time as well as the x-ray dose per projection, due to the fact that the x-ray tube radiation output increases with the least square of the tube voltage, and also because high x-rays are much more penetrating due to its shorter wavelengths. In the clinical world, the mammograms reveal the results according to the radiologist/physician perception to distinguish the objects from the background. The ACR phantom which has been accredited in simulating the human breast features reveal the end results according to the observer performances. We used the ACR and CD phantoms to access the improvement in detectability in terms of revealing features and the reported scores from the acquired images. It is known in the medical imaging community that for light element materials such as the acrylic used in the edge, ACR phantom, 100 kVp or 120 kVp attenuation imaging would be of extremely poor contrast. The acrylic edge images are provided to investigate the phase effects generated from a

tissue. The ACR and CD phantoms images help in the visualization of the contrast improvements as compared to the conventional contact mode imaging. The edge enhancement can also be appreciated to an extent within the phantom as shown in Fig. 14.

4. Discussion and Conclusion

This study demonstrates the potential benefits of using high energy x-rays for phase sensitive breast imaging. We investigated the optimal in-line phase sensitive geometry and high energy settings under the experimental conditions investigated herein and compared with the conventional contact mode images. The phase retrieval algorithm, PAD, utilizes the correlation between the x-ray phase shift and attenuation. For the lighter elements ($Z < 10$) and high energy x-rays ($E > 60$ keV), Compton scattering dominates the amount of attenuation experienced by the soft tissue. Hence, both the attenuation and x-ray phase shifts are determined by the tissue electron density over the ray path, and they have a full correlation [25]. In our RPF (u) simulations, we used 50, 60, 70 keVs average photon energies to simulate the 100, 120 and 140 kVp tube voltages. For the constant MGD of 1.295 mGy, the image quality and target discrimination is generally highest for $M = 2.5$ as compared to the other investigated magnifications. The computer simulation results show that the $|RPF(u)|$ for $M = 2.5$ has the highest values for the investigated kVp's, the experimental results validated those simulations and yielded a superior image quality in terms of image contrast and target discrimination for $M = 2.5$. The acrylic edge images indicated that the phase contrast effect also occurs at high x-ray energies in the form of overshooting at the boundary of air and acrylic while no overshooting of the edge is seen in the conventional contact mode images. The magnification of 2.5 had the highest EEI of 1.5 for 100 kVp and 1.46 for 120 kVp. The observer study for the ACR phantom images established that the highest scores were reported for 100 kVp in $M = 2.5$. The CD phantom images also demonstrated that the highest scores were reported at $M = 2.5$. Furthermore, the phase retrieved images have improved performance and detectability at the same MGD for the large discs of the CD phantom as compared to the phase contrast images. At $M = 2.5$, the phase contrast image at 120 kVp yielded slightly higher score than the 100 kVp, while the phase retrieved images for both the energies yielded the same observer scores. The images acquired at $M = 2.5$ follow closely towards the predicted SNR_{qi} as compared to the phase contrast images. All the experimental results validates the computer simulations. Although the computer simulations reveal that the $|RPF(u)|$ for $M = 2.5$ and 3 are almost the same, the experimental results conclude that there are enough differences in those magnifications to accomplish that the phase contrast effect is greater at $M = 2.5$. The micro focus x-ray tube operating at 100 kVp and 120 kVp results in very similar image performances in terms of the image contrast and observer scores. Due to the limited micro focus tube current, 120 kVp could be well used instead of 100 kVp for short exposure time. The results also signify that the CD phantom phase sensitive images have better image contrast and disc detection as compared to the conventional contact mode images. The improved image quality at low dose in phase contrast image is contributed by the phase-shifts resulted contrast, as well as the reduced scatters by the air gap. This study has been performed using the small tube focal spot size of $7 \mu\text{m}$ which has low photon flux and low output power and thus the exposure time is long for the image acquisition. The same optimal geometry and design parameters

can be used with the large focal spot size of 50 μm to reduce the exposure time. For example, if 120 kVp is used with a tube focal spot size of 50 μm under the same optimal geometry and design parameters for the MGD of 1.29 mGy, the calculated exposure time required for the image acquisition will be 9 sec as reported in [20]. The observer studies were not performed on a dedicated mammography LCD as there was not one available but in the future studies, we will use one in order to further validate the results. The reported scores might have been better if a dedicated mammography LCD was used but nevertheless our results are still applicable since they show a clear improvement in the phase contrast images. We aim to conduct more studies to investigate the impact of varying detector pitch sizes with the reported optimal geometry and design parameters. The use of high spatial resolution detectors may increase the edge enhancement and thus the phase retrieval will have more impact in improving the image visuality and target perception. We also expect that the future micro focus x-ray tubes will have more photon flux and power which will further benefit in implementation of the in-line PSXI in the clinical world applications.

Acknowledgments

This research was supported in part by the NIH under grant R01 CA193378, and supported in part by a grant from the University of Oklahoma Charles and Peggy Stephenson Cancer Center funded by the Oklahoma Tobacco Settlement Endowment Trust. We would like to acknowledge the support of Charles and Jean Smith Chair endowment fund as well. Xizeng Wu and Hong Liu are both considered corresponding authors.

Reference

1. Shapiro S, Strax P, Venet L. Periodic breast cancer screening in reducing mortality from breast cancer. *Journal of American Medical Association*. 1971; 215:1775–1785.
2. Brem RF, Michener KH, Zawistowski G. Approaches to improving breast cancer diagnosis using a high resolution, breast specific gamma camera. *Phys. Med.* 2006; 21:9–17.
3. Karellas A, Vedantham S. Breast cancer imaging, A perspective for the next decade. *Med. Phys.* 2008; 35:4878–4897. [PubMed: 19070222]
4. Kotre CJ, Birch IP. Phase contrast enhancement of x-ray mammography: a design study. *Phys. Med. Biol.* 1999; 44:2853–2866. [PubMed: 10588289]
5. Nesterests YI, Wilkins SW, Gureyev TE. On the optimization of the experimental parameters for x-ray in-line phase contrast imaging. *Rev of Sci Instrum.* 2005; 76:093706.
6. Shu-Ang, Zhou; Brahme, Anders. Development of phase-contrast X-ray imaging techniques and potential medical applications. *Phys. Med.* 2008; 24:129–148. [PubMed: 18602852]
7. Wu X, Liu H. Clinical implementation of x-ray phase-contrast imaging: theoretical foundations and design considerations. *Med. Phys.* 2003; 30:2169–2179. [PubMed: 12945983]
8. Pogany A, Gao D, Wilkins S. Contrast and resolution in imaging with a micro focus x-ray source. *Review of Scientific Instruments.* 1997; 68:2774–2782.
9. Wu X, Liu H. A general theoretical formalism for x-ray phase contrast imaging. *Journal of X-Ray Science and Technology.* 2003; 11:33–42. [PubMed: 22388096]
10. Quai E, Longo R, Zanconati F, Jaconelli G. First application of computed radiology to mammography with synchrotron radiation. *Radiol Med.* 2013; 118:89–100. [PubMed: 22744351]
11. Zhang D, Donovan M, Fajardo L, Archer A, Wu X, Liu H. Preliminary feasibility study of an in-line phase contrast x-ray imaging prototype. *IEEE Transactions on Biomedical Engineering.* 2008; 55:2249–2257. [PubMed: 18713694]
12. Edoardo, Castelli; Tonutti, Maura; Arfelli, Fulvia. Mammography with Synchrotron Radiation: First Clinical Experience with Phase-Detection Technique. *Radiology.* 2011; 259:684–694. [PubMed: 21436089]

13. Sztrokay A, Diemoz PC, Schlossbauer T. High-resolution breast tomography at high energy: a feasibility study of phase contrast imaging on a whole breast. *Phys. Med. Biol.* 2012; 57:2931–2942. [PubMed: 22516937]
14. Wong MD, Wu X, Liu H. Image quality and dose efficiency of high energy phase sensitive x-ray imaging: Phantom studies. *J X-ray Sci Technol.* 2014; 22:321–334.
15. Lewi RA. Medical phase contrast x-ray imaging: current status and future prospects. *Phys. Med. Biol.* 2004; 49:3573–3583. [PubMed: 15446788]
16. Hubbell, JH.; Seltzer, SM. Tables of X-Ray Mass Attenuation Coefficients and Mass Energy-Absorption Coefficients. 1996. <http://physics.nist.gov/PhysRefData/XrayMassCoef/cover.html>
17. Wu X, Dean A, Liu H. X-ray diagnostic techniques. *Biomedical Photonics Handbook*. 2003; Chap 26:26–34.
18. Donnelly E, Price R, Pickens D. Quantification of the effect of system and object parameters on edge enhancement in phase-contrast radiography. *Med Phys.* 2003; 30:2888–2896. [PubMed: 14655935]
19. Donnelly E, Lewis Kenneth G, Wolske Kristy M. Characterization of the phase-contrast radiography edge-enhancement effect in a cabinet x-ray system. *Phys. Med. Biol.* 2006; 51:21–30. [PubMed: 16357428]
20. Wong MD, Yan A, Ghani MU. Dose and detectability improvements with high energy phase sensitive x-ray imaging in comparison to low energy conventional imaging. *Phys. Med. Biol.* 2014; 59:N37–N49. [PubMed: 24732108]
21. Wu X, Liu H. A new theory of phase-contrast x-ray imaging based on Wigner distributions. *Med. Phys.* 2004; 31:2378–2384. [PubMed: 15487716]
22. Wu X, Liu H. A phase-space formulation for phase-contrast X-ray imaging. *Appl. Opt.* 2005; 44:5847–5854. [PubMed: 16231790]
23. Wu X, Liu H. Clarification of aspects in in-line phase-sensitive x-ray imaging. *Med. Phys.* 2007; 34:737–743. [PubMed: 17388191]
24. Wu X, Yan A. Phase retrieval from one single phase contrast x-ray image. *Optics Express.* 2009; 17:11187–11196. [PubMed: 19550519]
25. Yan A, Wu X, Liu H. Robustness of phase retrieval methods in x-ray phase contrast imaging: A comparison. *Med. Phys.* 2011; 38:5073–5080. [PubMed: 21978052]
26. Allen LJ, Oxley MP. Phase retrieval from series of images obtained by defocus variation. *Optics Communications.* 2001; 199:65–75.
27. Nugent KA, Gureyev TE, Cookson DJ, Paganin D, Barnea Z. Quantitative Phase Imaging Using Hard X Rays. *Physical Review Letters.* 1996; 77:2961–2964. [PubMed: 10062096]
28. Wong MD, Wu X, Liu H. Preliminary investigation on the effect of x-ray beam hardening on detective quantum efficiency and radiation dose. *IEEE SSIAI.* 2010:17–20.
29. Wong MD, Wu X, Liu H. The effects of x-ray beam hardening on detective quantum efficiency and radiation dose. *Journal of X-Ray Science and Technology.* 2011; 19:509–519. [PubMed: 25214383]
30. Boone J. Glandular breast dose for mono energetic and high-energy x-ray beams, Monte Carlo assessment. *Radiology.* 1999; 231:23–37. [PubMed: 10540637]
31. Wu X, Gingold E, Barnes G, Tucker D. Normalized Average Glandular Dose in Molybdenum Target-Rhodium Filter and Rhodium Target-Rhodium Filter Mammography. *Radiology.* 1994; 193:83–89. [PubMed: 8090926]
32. Bushberg, J.; Seibert, J.; Leidholdt, E., Jr; Boone, J. *The Essential Physics of Medical Imaging.* 3rd. Philadelphia, PA: Lippincott Williams & Wilkins;
33. Wu X, Barnes G, Tucker D. Spectral dependence of glandular tissue dose in screen-film mammography. *Radiology.* 1991; 179:143–148. [PubMed: 2006265]
34. Liu H, Karallas Andrew, Moore Stephen C. Lesion Detectability Considerations for an Optically-coupled CCD X-ray Imaging System. *IEEE Transaction on Nuclear Science.* 41:1183–1185. 1(1994).
35. Rose A. The sensitivity performance of the human eye on an absolute scale. *Journal of the Optical Society of America.* 1948; 38:196–208. [PubMed: 18901781]

36. Ghani, Muhammad. U.; Wu, Di; Li, Yuhua. Quantitative analysis of contrast to noise ratio using a phase contrast x-ray imaging prototype. *Proc. of SPIE*. 2013; 85820:85820, H1–H6.
37. Donnelly E, Price R. Quantification of the effect of kVp on edge-enhancement index in phase-contrast radiography. *Med. Phys.* 2002; 29:999–1002. [PubMed: 12094995]
38. Rong XJ, Shaw CC, Liu X, Lemacks MR. Comparison of an amorphous silicon/cesium iodide flat-panel digital chest radiography system with screen/film and computed radiography systems-a contrast-detail phantom study. *Med. Phys.* 2001; 28:2328–2335. [PubMed: 11764040]

Fig. 1. Comparison of the edge overshooting in conventional and phase contrast images of the Acrylic edge phantom (a) 40 kVp, 36.5 mAs (b) 40 kVp, 36.5 mAs with anti-scatter grid (c) 100 kVp, 12 mAs, $M = 2$ (d) 100 kVp, 7.5 mAs, $M = 2.5$. Average edge profiles are generated for the ROI shown on the images.

Fig. 2.

Average Edge profiles of the acrylic phantom acquired at (a) 40 kVp, 36.5 mAs with no anti-scatter grid (b) 100 kVp, 12 mAs, M = 2 (c) 100 kVp, 7.5 mAs, M = 2.5

Fig. 3.
The $|RPF(u)|$ for phase contrast mammography system with a focal spot size of 0.007 mm and detector pitch of 0.044 mm

Fig. 4.
Edge Enhancement Indicator (EEI) for the phase contrast acrylic edge phantom investigated for different x-ray energies under different magnification conditions

Fig. 5. Comparison of ACR Phantom Images for a $M = 2.5$ with an x-ray energy of 100 kVp, (a) Phase contrast Image (b) Phase Retrieved Image

Fig. 6.
ACR Phase Contrast images score comparison for the range of x-ray energy/magnification factor combination

Fig. 7.
ACR Phase Retrieval images score comparison for the range of x-ray energy/magnification factor combination

Fig. 8. Comparison of CD phantom at $M = 2.5$, (a) phase retrieval image 100 kVp, 7.7 mAs (b) phase contrast image at 100 kVp, 7.7 mAs

Fig. 9.
Comparison of CD phantom at $M = 3$, (a) phase retrieval image 100 kVp, 12 mAs, (b) phase contrast image at 100 kVp, 5.5 mAs

Fig. 10. CD curves plotted against the disc diameter (mm) and the threshold contrast for the phase retrieved images (Akn) and phase contrast images (I) for magnification factor 1.67 and 2.

Fig. 11. CD curves plotted against the disc diameter (mm) and the threshold contrast for the phase retrieved images (Akn) and phase contrast images (I) for magnification factor 2.5 and 3

Fig. 12. CD phantom images acquired in conventional contact mode (a) 40 kVp, 36.5 mAs, 1.295 mGy (b) 40 kVp, 71.5 mAs, 2.59 mGy (c) 40 kVp, 36.5 mAs, 1.295 mGy with an anti-scatter grid (d) 40 kVp, 71.5 mAs, 2.59 mGy with an anti-scatter grid

Fig. 13. CD curves plotted against the disc diameter and the threshold contrast for the conventional contact mode images of the contrast detail phantom.

Fig. 14.

Edge enhancement effect can be seen within the CD phantom of diameter 4.82 mm and drilled depth of 0.51 acquired at 120 kVp, 5.06 mAs, $M = 2.5$.

Table 1

The phase sensitive imaging parameters utilized with x-ray tube focal spot size of 7 μm

Magnification	M = 1.67	M = 2	M = 2.5	M = 3
Source to object R1 (cm)	102	85	68	57
Object to detector R2 (cm)	68	85	102	113.5
$L_{shear}/L_{\perp}$	0.032	0.04	0.048	0.053

Table 2

The milliamperere-second (mAs) values required for imaging at 100 kVp, 120 kVp and 140 kVp for the MGD of 1.295 mGy

X-ray Energy	M = 1.67	M = 2	M = 2.5	M = 3
100 kVp	18.5	12	7.7	5.5
120 kVp	12.12	7.88	5.06	3.65
140 kVp	8.52	5.60	3.60	2.55

Table 3

The MGD measurements for tube voltages of 40 kVp, 100 kVp, 120 kVp and 140 kVp

X-ray Energy	Current (μA)	X_{ESE} (mR)	$D_{\text{gN}}(\text{mGyR}^{-1})$	$D_{\text{g}}(\text{mGy})$
40 kVp	250	528	2.45	1.295
40 kVp	250	1056	2.45	2.59
100 kVp	100	258	5.02	1.295
120 kVp	83	240	5.40	1.295
140 kVp	71	225	5.75	1.295

Table 4

RPF (**u**) obtained from computer simulations performed for 5 cm, 50%-50% breast without considering a Bucky grid at a dose of 1.295 mGy at a target frequency of 15 lp/mm, 7 μ m x-ray focal spot size and 2.5 mm Al filter

X-ray Energy	M = 1.67	M = 2	M = 2.5	M = 3
100 kVp	1.013E-03	1.25E-03	1.37E-03	1.36E-03
120 kVp	7.06E-04	8.72E-04	9.57E-04	9.51E-04
140 kVp	5.20E-04	6.42E-04	7.05E-04	7E-04

Table 5

The Photon fluence (ϕ_o) in air and linear attenuation coefficient (μ) for the acrylic material of the CD phantom for each set of X-ray energy

X-ray Energy	ϕ_o (photons/mm ²)	μ (1/mm)
100 kVp	6.157×10^{-7}	0.0135
120 kVp	4.565×10^{-7}	0.0130
140 kVp	3.564×10^{-7}	0.0120

Table 6

The calculated SNR_{qj} at disk diameter 1.60 mm along seven milled depths for 100 kVp in M = 2, 2.5 and 3. I, Akn, the phase contrast and phase retrieved images, tells the observer study results for those disks respectively

Depth	M = 2	I	Akn	M = 2.5	I	Akn	M = 3	I	Akn
0.73 mm	57.65	Y	Y	71.88	Y	Y	86.67	Y	Y
0.51 mm	40.28	Y	Y	50.21	Y	Y	60.55	Y	Y
0.36 mm	23.43	Y	Y	35.44	Y	Y	42.74	Y	Y
0.24 mm	18.95	Y	Y	23.63	Y	Y	28.1	Y	Y
0.16 mm	12.63	N	N	15.75	Y	Y	18.9	N	Y
0.11 mm	8.68	N	N	10.83	N	N	13.06	N	N
0.06 mm	4.73	N	N	5.90	N	N	7.12	N	N

Table 7

The ratio $CNR_{AKN/I}$ calculated for three disc diameters of 4.82 mm, 3.50 mm and 2.32 mm along 0.73 mm,, 0.51 and 0.36 mm milled depths for the image acquired at 100 kVp in M = 2.5.

	4.82 mm disk	3.50 mm disk	2.32 mm disk
0.73 mm	3.26	3.30	3.21
0.51 mm	3.25	3.27	3.61
0.36 mm	3.10	3.32	3.51