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Synthesizing Mammogram from Digital Breast Tomosynthesis

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Abstract

Our purpose is to develop a new method for generating synthesized mammogram (SM) from digital breast tomosynthesis (DBT) and to assess its potential as an adjunct to DBT. We first applied multiscale bilateral filtering to the reconstructed DBT slices to enhance the high-frequency features and reduce noise. A maximum intensity projection (MIP) image was then obtained from the high-frequency components of the DBT slices. A multiscale image fusion method was designed to combine the MIP image and the central DBT projection view into an SM and further enhance the high-frequency features. We conducted a pilot reader study to visually assess the image quality of SM in comparison to full field digital mammograms (FFDM). For each DBT craniocaudal or mediolateral view, a clinical FFDM of the corresponding view was retrospectively collected. Three MQSA radiologists, blinded to the pathological and other clinical information, independently interpreted the SM and the corresponding FFDM side by side marked with the lesion locations. The differences in the BI-RADS assessments of both MCs and masses between SM and FFDM did not achieve statistical significance for all 3 readers. The conspicuity of MCs on SM was superior to that on FFDM and the BI-RADS assessments of MCs were comparable while the conspicuity of masses on SM was degraded and interpretation on SM was less accurate than

that on FFDM. The SM may be useful for efficient prescreening of MCs in DBT but the DBT should be used for detection and characterization of masses.

Keywords

breast cancer; digital breast tomosynthesis (DBT); synthesized mammography (SM)

1. INTRODUCTION

Breast cancer remains one of the leading causes of death among women of age 40 and older (American Cancer Society, (2017). Mammography is a cost-effective method for early detection of breast cancer despite the recent controversy on the benefits of screening and early detection. However, the accuracy of mammography can be affected by the overlapping fibroglandular tissue, patient age, and histologic tumor type that can cause substantial differences on both false negative diagnosis and false positive recalls.

In 2011, the Food and Drug Administration (FDA) in the United States approved the first system using digital breast tomosynthesis (DBT) as an adjunct to full-field digital mammography (FFDM) for breast cancer screening. DBT (Niklason *et al* 1997, Dobbins and Godfrey 2003) is built upon FFDM technology to overcome the limitations of mammography. In DBT, a series of projection view (PV) images is acquired as the x-ray source is moved over a limited range of angles. The total dose required for a DBT scan is kept at nearly the same or only slightly higher than that of a mammogram. Tomosynthesized slices of the imaged volume are reconstructed from the series of PV images. Although DBT can only provide quasi-3D information with limited resolution along the depth direction, the reduced overlap of breast tissue provides superior conspicuity and detectability of subtle lesions, and fewer false positive lesions due to summation artifacts in comparison with conventional projection mammograms. A number of studies found that the combination of DBT with DM ("combo mode") could increase the cancer detection rate and reduce recall rate compared to DM alone (Rose *et al* 2013, Skaane *et al* 2013a, Skaane *et al* 2013b, Friedewald *et al* 2014, Greenberg *et al* 2014, Durand *et al* 2015, Bernardi *et al* 2016, Conant *et al* 2016, Sharpe *et al* 2016). Studies also showed that wide-angle DBT alone increased cancer detection and diagnosis compared to DM alone (Lang *et al* 2016, Chan *et al* 2017)

The visibility of breast lesions in DBT often depends on its physical properties. Although DBT has strong potential to improve the detection of masses as compared to FFDM, the detection of grouped microcalcifications (MCs) on DBT may range from comparable to somewhat inferior (Poplack *et al* 2007, Andersson *et al* 2008, Kopans *et al* 2011, Spangler *et al* 2011, Tagliafico *et al* 2015, Clauser *et al* 2016). MCs are more sensitive to the reconstructed image quality because of the small size and low contrast of subtle MCs. The reconstructed image quality is affected by many factors, including those related to the DBT system design and the reconstruction techniques (Sechopoulos 2013a, Sechopoulos 2013b, Chan *et al* 2014, Goodsitt *et al* 2014). In particular, the conspicuity of grouped MCs could be reduced due to factors such as blurring by oblique incidence to the detector and the reconstructed voxels, the inaccuracy in the geometry for reconstruction, and focus spot

motion, if any, during acquisition of each projection. The separation of the MCs in a subtle MC cluster into several slices further reduces its conspicuity. One of the advantages of using the combo mode is to alleviate the effort for searching subtle MCs in the DBT volume.

Although the combo mode can increase cancer detection rate while reducing recall rate, it increases the radiation dose to the patient. Synthetic 2D mammography (SM) has the potential to replace FFDM in the combo mode and thus eliminate the additional radiation exposure (Skaane *et al* 2014, Zuley *et al* 2014, Bernardi *et al* 2016). An SM is a 2D mammogram-like image generated from the DBT data to mimic the FFDM. A few studies have reported methods for generating SMs. One method (Dennerlein *et al* 2013) computed a virtual projection image directly from the set of low-dose projection data without involving the reconstruction of a DBT volume or the forward-projection process. Another method (Homann *et al* 2015) used an edge-weighting approach in which a weighting function was computed from the response of an edge-detection filter applied to the reconstructed DBT volume. However, both studies were very preliminary and only one or two DBT volumes, respectively, of real breasts were shown to demonstrate the performance of the method. A third method (van Schie *et al* 2013) used a computer-aided detection system to identify relevant points of interest in the DBT volume and rendered a mammogram from the intersection of a surface fitted through these points; a pilot observer study showed that there was no significant difference between the localization accuracy of masses in the SM and that in the corresponding FFDM.

In this study, we developed a novel method in which a re-projected 2D image from 3D DBT volume and one of the PVs were used to generate the SM. To evaluate the feasibility of using the SM synthesized with our method as an adjunct to DBT, we conducted a reader study to compare lesion visibility and BI-RADS assessments with FFDM. (ref. Wei et al. RSNA abstract)

2. Generation of 2D Synthetic Mammogram (SM)

Figure 1 illustrates the schematic overview of the proposed method to generate an SM at the projection angle of the central PV. The method uses the projection view images and the reconstructed DBT slices as input. Note that our approach could generate an SM at any angle using the corresponding PV; the central PV was used in this study because it corresponds to the projection geometry of DM (i.e., central ray of x-ray beam perpendicular to the detector). Multiscale bilateral filtering (MSBF) is first applied to the reconstructed DBT slices. Each slice is decomposed into a series of multiscale high-frequency images (Laplacian pyramid) and a series of multiscale low frequency images (Gaussian pyramid) by the Laplacian pyramid decomposition (LPD) method (Burt and Adelson 1983). The high-frequency images in the Laplacian pyramid are denoised by bilateral filtering and recomposed into a high-frequency image at full resolution. A 2D maximum intensity projection (MIP) view is then generated from the high-frequency components of the DBT slices. The PV and the MIP image are decomposed by LPD and the corresponding levels of the Laplacian pyramids from the MIP image and the PV are combined nonlinearly. Finally, the Gaussian pyramid from the PV and the combined Laplacian pyramid are recomposed using the reverse LPD process to generate the SM. Details are described below.

2.1 DBT reconstruction and extraction of high-frequency MIP image

In this study, the DBT was reconstructed by the simultaneous algebraic reconstruction technique (SART) (Zhang *et al* 2006) but the proposed SM method is applicable to DBT reconstructed with other methods. SART is an iterative reconstruction algorithm to solve a set of linear equations for the unknown tissue attenuation coefficients using the system matrix and the measured projection data. The linear attenuation coefficient of each voxel is updated simultaneously using all rays in one projection. The number of updates in each SART iteration is therefore equal to the number of projections in the DBT. Our previous studies showed that 1 to 3 iterations are sufficient for reconstruction of DBT with good image quality (Zhang *et al* 2006). For the purpose of generating an SM, we experimentally chose 2 iterations.

We previously developed the MSBF method to improve the contrast-to-noise ratio (CNR) of MCs without compromising the quality of masses and soft tissue background structures in DBT reconstruction, as detailed in (Lu *et al* 2015). Briefly, at the end of an iteration, each DBT slice is decomposed into several frequency bands via LPD (see Section 2.2 below). With the multiscale structure, bilateral filtering is applied to the high-frequency bands to reduce noise while no regularization is applied to the low frequency band. After bilateral filtering, the high-and low-frequency bands of each slice are recomposed into a regularized DBT slice. The stack of recomposed slices is used for the next iteration.

Bilateral filtering is a nonlinear edge-preserving and noise-reducing filter, defined as

$$\begin{aligned}\hat{I}(x) &= \frac{1}{W_x} \sum_{x_i \in \Omega} I(x_i) f_r(\|I(x_i) - I(x)\|) g_s(\|x_i - x\|), \text{ and} \\ W_x &= \sum_{x_i \in \Omega} f_r(\|I(x_i) - I(x)\|) g_s(\|x_i - x\|),\end{aligned}\quad (1)$$

where W_x is the normalization factor, $\hat{I}$ is the filtered image intensity at the 2D coordinates x of the targeted pixel on the slice, Ω is a local region centered at x . f_r and g_s are Gaussian functions with standard deviation of σ_r and σ_s , respectively. f_r is the range filter with weights determined by the differences in intensities between x and a pixel at x_i in the local region, and g_s is the domain filter with weights determined by the spatial distances between the pixels. Based on our previous study (Lu *et al* 2015), σ_s is selected to be 3 and the value of σ_r is adaptively estimated by the noise of the DBT to be reconstructed as follows. The breast region on each DBT slice is divided by non-overlapping 20×20 pixels ROIs. The noise level of each slice is estimated as the average of the root-mean-square (RMS) variation of pixel values within each ROI in the same slice. The σ_r value for the whole volume is then determined to be the mean RMS variation of all slices.

For our SM generation, after the DBT reconstruction is completed at the second iteration, multiscale decomposition is applied to each DBT slice to extract the high-frequency bands, which undergo bilateral filtering to reduce noise. After denoising, instead of recomposing a DBT slice with all frequency components, only the bilateral filtered high-frequency bands are used to recompose a slice with high-frequency features. A MIP image is then generated

from the stack of high-frequency slices of the DBT volume by projecting along the angle of the chosen projection view. This is accomplished by using a ray-tracing technique to identify the x-ray path from each pixel on the 2D projection view to the x-ray source and the maximum intensity is found along the x-ray path.

In the process described above, the multiscale decomposition and bilateral filtering are applied to the DBT slices independently after reconstruction. The same methods can therefore be applied to DBT slices reconstructed with any other techniques to extract the high-frequency images for the subsequent SM generation.

2.2. Multiscale enhancement of projection view image

A projection view is a 2D low-dose FFDM. We use a multiscale method to enhance the contrast of the projection view. Since a multiscale method processes the information from different frequency bands extracted from the image adaptively, it is more flexible and versatile than commonly used image enhancement methods. The multiscale method also allows the manipulation of different frequency bands by adding information from other sources. Previous studies (Chan *et al* 1996, Dippel *et al* 2002, Wei *et al* 2005) have shown that using the LPD method can successfully enhance medical images while controlling artifacts. We therefore chose the Laplacian pyramid method for multiscale contrast enhancement.

For a given projection view, we first use an inverse logarithmic function to transform the raw data. The inverse logarithmic function is defined as

$$S_x = \ln \left(\frac{X_{\max}}{X} \right) \quad (2)$$

where X is the gray level of the raw data, $X_{\max}$ is the maximum of the digital gray scale. The transformed image is then linearly scaled to 12-bit pixel values. The Laplacian pyramid method is used to decompose the log-transformed image into different frequency bands. The Laplacian pyramid is a sequence of high-frequency images $L_0, L_1, \dots, L_n$, each of which is the difference between two consecutive levels of the Gaussian pyramid. The decomposition of the image from level k to level $k+1$ can be expressed by the following equation:

$$L_k = g_k - \text{Expand}(g_{k+1}) \quad (3)$$

Where

$$\text{Expand}(g_{k+1}) = 4 \sum_{m=-2}^2 \sum_{n=-2}^2 w(m, n) g_{k+1} \left(\frac{i-m}{2}, \frac{j-n}{2} \right) \quad (4)$$

$$g_k(i, j) = \sum_{m=-2}^2 \sum_{n=-2}^2 w(m, n) g_{k-1}(2i + m, 2j + n) \quad (5)$$

The same LPD process is applied to the MIP image from the high-frequency images of the DBT slices, which is generated by ray-tracing with cone-beam geometry, decomposing it into the same number of levels as the projection view image. We generate an enhanced image $r(k)$ at the k th level of the Laplacian pyramid by combining the k th level Laplacian image obtained from the projection view (L_k) and that from the MIP image (ML_k) using the following equation:

$$r(k) = \alpha \text{Expand}(g_{k+1}) + \beta (\text{Expand}(g_{k+1}))^p (L_k + ML_k) \quad (6)$$

where α , β , and p are constants. In our previous study, we compared LPD to the GE preprocessing method for lesion detection on DMs (Wei *et al* 2005). We found that the LPD method was superior for the lesion detection task in a CAD system. In this study, we used the previously selected values for each pyramid level. These parameters have been applied to DMs and DBT projection views of different imaging parameters, with the goal to enhance the high frequency structures at the lower levels and the high density background tissue and masses at higher levels. The parameters were chosen independent of both breast type and DBT geometry. Table I summarized the parameters at different levels in the Laplacian pyramid used in this study. A reverse process of the LPD is then used to recompose a synthesized mammogram from the highest level of the Gaussian pyramid and the enhanced Laplacian pyramid.

3. Reader Study

A GE second generation prototype DBT system at the University of Michigan was used to acquire DBT scans. The system has a CsI phosphor/a:Si active matrix flat panel digital detector with dimensions of 19.20 cm $\times$ 23.04 cm and a pixel pitch of 0.1 mm $\times$ 0.1 mm. The system has a Rh-anode/Rh-filter x-ray source combination and its rotation plane is parallel to the chest wall edge of the detector. The detector is stationary during image acquisition. The system uses a step-and-shoot design and acquires PV images from a total of 21 angles in 3° increments over a $\pm 30^\circ$ range within 8 seconds.

This study was IRB approved and HIPAA compliant. Human subjects who were recommended for biopsy of breast lesions (Breast Imaging Reporting and Data System, BI-RADS 4 and 5) in our Breast Imaging Division according to findings in their clinical FFDMs were recruited with written informed consent. DBTs in craniocaudal (CC) and mediolateral (MLO) views of the affected breast were acquired.

A data set of 56 patients with DBTs and corresponding clinical FFDMs was collected for the reader study. The FFDMs were acquired with GE Essential systems and the “for presentation” images were used. The time intervals between the DBT and the corresponding FFDM studies ranged from 3 to 76 days (17.8 $\pm$ 15.2). A total of 105 pairs of DBT and

FFDM views (CC or MLO) were collected, including 68 grouped microcalcifications (MCs) on 60 views from 31 cases and 48 masses on 45 views from 25 cases. Of the 68 grouped MCs and 48 masses, respectively, were biopsy-proven to be malignant and the rest were benign. The longest diameters of MC clusters and masses ranged from 2.2 to 58.1 mm (mean 17.6 mm, standard deviation 15.8 mm) and from 7.4 to 32.3 mm (mean 16.6 mm, standard deviation 6.8 mm), respectively. An experienced Mammography Quality Standards Act (MQSA) radiologist marked the location of the biopsied MC or mass by a 2D box in each FFDM based on all available clinical and imaging information. The corresponding lesion was marked by a 3D box in each DBT volume. The 3D box in the DBT volume was projected onto the SM based on the DBT system geometry.

Three experienced MQSA radiologists with 32, 28, and 11 years of experiences in breast imaging participated as readers in the reader study. They were asked to provide a visual assessment of each biopsied lesion. During the visual assessment, a pair of SM and FFDM of the same view were displayed side by side and the locations of the lesions were marked on two DICOM-calibrated 21" 5M-pixel (2048 × 2560) display monitors (model EIZO SMD 21500 D). The specifications of the monitors were similar to those of clinical FFDM review workstations. An in-house developed graphic user interface (GUI) was used to display the pair of SM and FFDM images in randomized order. The GUI allowed the reader to apply windowing, zooming and panning to the displayed images if needed. The reader ratings and BI-RADS assessments for the lesions were recorded electronically by the GUI. Each reader independently assessed the visual quality of SM and FFDM, and provided ratings of: 1) conspicuity of the known lesion on a 10-point scale (10 = most conspicuous). 2) BI-RADS assessment of lesion on a 7-point scale (1, 2, 3, 4a, 4b, 4c, 5) excluding BI-RADS 0. This forced BI-RADS scale is often used in observer studies so that the reader will need to provide a decision based on the available information without deferring to additional imaging. The BI-RADS assessment may be considered a surrogate of detailed lesion features because the degree of suspicion of a lesion depends on its appearance. 3) Using FFDM as reference, readers also rated the acceptability of overall image quality on SM on a 10-point scale. The radiologists were instructed that the 10-point scale was defined as unacceptable (<5), acceptable (5–8), similar to FFDM (>8), and 10 being the same as FFDM. Before the study, each reader underwent a training session to become familiar with the GUI using FFDMs with lesions that were not part of the data set. No time limit was imposed to assess each pair of SM and FFDM. The Student's two-tailed paired t-tests were used to estimate the statistical significance in the visual differences between the SM and the FFDM.

4. Results

Figure 2 shows four pairs of image examples with SM and FFDM side by side, one from each breast density category, assessed by our reference radiologist on FFDM. Figure 2(a) shows a case with fatty breast (BI-RADS density category A). It contained a group of microcalcifications that could be seen on both FFDM and SM. Individual microcalcifications appeared slightly larger on SM, probably due to the blurring caused by reconstruction from the projection views at different angles and the MIP from the reconstructed volume with limited depth resolution. The overall image quality on SM was

considered similar to FFDM with an average rating of 8.4 from the three radiologists. Figure 2(b) shows a case with scattered areas of fibroglandular density (BI-RADS density category B). An invasive ductal carcinoma (IDC) was seen overlapping with the pectoral muscle on both FFDM and SM. A few microcalcifications were clearly seen on SM while those on FFDM were very subtle. The overall image quality on SM was acceptable with an average rating of 6.5. Figure 2(c) shows a case with heterogeneously dense breast (BI-RADS density category C). An irregular spiculated mass representing IDC was also seen overlapping with the pectoral muscle. The spiculations were enhanced on the SM with noticeable microcalcifications on top of the mass. The microcalcifications and spiculations were less visible on the FFDM. The overall image quality on SM was similar to FFDM with an average rating of 8.6. Figure 2(d) showed a case with a dense breast (BI-RADS density category D). The overall image quality on SM was acceptable with an average rating of 6.2, probably because a large proportion of dense tissues was not reproduced well on SM and the breast appeared less dense than FFDM. A small group of microcalcifications was seen overlapping with fibrous tissue in the upper breast. The individual MCs were larger on SM compared to those on FFDM. For our data set of 105 SMs, the average ratings of overall image quality by the three readers were 8.6, 8.0, and 8.8, respectively. Figure 3 shows the histogram of overall image quality ratings assessed by the three readers.

Figures 4(a) and 4(b) compared the average conspicuity ratings of each lesion by the three radiologists on SMs and DMs for MCs and masses, respectively. Table II summarizes the mean conspicuity ratings by radiologists' visual assessment for the MCs and masses. The mean conspicuities of MCs on SMs were 7.7, 7.0, and 8.0 while the ratings on FFDM were 5.8, 5.5, and for the three readers, respectively. The differences between the conspicuity ratings on SMs and FFDMs were statistically significant by paired t-tests (p-value <0.0001 for all three readers). On the other hand, the conspicuity ratings of masses were 4.3, 4.5, and 5.0 on SMs in comparison to 4.9, 5.0, and 5.9 on FFDMs for the three readers, respectively. These differences were also statistically significant by paired t-tests (p-values: 0.007, 0.022, 0.004, respectively). Figure 5 shows the histograms of the differences in the conspicuity ratings for masses and MCs between DMs and SMs for the three readers.

For either MCs or masses, the difference in the BI-RADS assessments between SM and FFDM did not achieve statistical significance for all 3 readers. Of the 348 BI-RADS assessments from 3 readers, 4 (3 benign masses and 1 malignant MC) were upgraded from 3 on FFDM to 4a on SM, and 17 (11 benign and 3 malignant masses, 2 benign and 1 malignant MCs) were downgraded from 4a on FFDM to 3 on SM. Note that a BI-RADS assessment of 4 and above (4a) is generally recommended for biopsy so that a change in BI-RADS assessment across the threshold of 4a represents a change of potentially higher clinical significance. Figure 6 shows the histograms of all relative changes in BI-RADS assessments for MCs and masses for the three readers.

5. Discussion

In this study, we developed a novel multiscale method for the generation of an SM from the 3D DBT volume and a 2D projection view image. We apply multiscale Laplacian pyramid decomposition to the DBT slices and bilateral filtering to the high-frequency components to

reduce noise and enhance subtle microcalcifications. A MIP image with high frequency information including microcalcifications is then generated from the stack of denoised and recomposed high-frequency images of the DBT slices. We further use the Laplacian pyramid decomposition method to decompose the 2D projection view and the high-frequency MIP image from the 3D DBT volume, combine the corresponding levels of the two Laplacian pyramids nonlinearly, and recompose the multiscale images into an SM. Although each of the individual projection views is a low-dose version of an FFDM, the generated SM with enhanced high-frequency information obtained from the DBT volume is found to be acceptable in comparison to DM by a reader study with experienced breast radiologists.

The overall image quality of the SMs was similar to that of the corresponding views of FFDM. For MCs, the conspicuity on SM was superior and their BI-RADS assessment was comparable to that on FFDM. For masses, the interpretation on SM may be affected by the degraded conspicuity. Detection of MCs in the DBT volume is a challenging task for radiologists so that it may be more efficient to use DM, or a comparable SM, to guide the search for MC. Our results suggested that SM by our method has the potential to be used in place of FFDM to search for MCs but assessment of masses should be performed in 3D DBT volume. Since a large number of previous studies have shown that the 2D DM is inferior to DBT in detection of soft tissue lesions (e.g., masses and architectural distortion), radiologists should not rely on the SM for detection or characterization of soft-tissue lesions regardless of whether its quality is comparable to DM; otherwise the incremental cancer detection benefit of DBT may be defeated. Therefore, the SM being inferior to DM for masses may not be a problem for the purpose of generating SM.

Although we used DBT acquired with our prototype system due to our accurate knowledge of its geometry and easy access to the raw projection data, we expect that the proposed method can be applied to DBT from other systems or different reconstruction methods. As a demonstration, we simulated a DBT geometry of 24-deg scan angle at 3-deg increments by using the central 9 PVs from the DBT acquired with 60-deg scan angle and 21 PVs at 3-deg increments, which is close to the commercial GE DBT system with the geometry of 25-deg scan angle and 9 PVs at 3-deg increments. In addition, our prototype DBT system had been upgraded with an advanced mode that allows DBT imaging with a wide range of combinations of scan angle, number of PVs and angular increment between PVs (Chan *et al* 2014, Goodsitt *et al* 2014). With the advanced mode, we had previously acquired a small set of human subject DBTs for another project using the geometry of 16-deg scan angle and 17 PVs at 1-deg increments, which is close to the geometry of a Hologic DBT system of 15-deg scan angle and 15 PVs. The total radiation dose of the 16 deg-17 PV DBT scans was set at about 50% of the 60 deg-21 PV DBT scans, and the simulated 24 deg-9 PV DBT scan was about 43% of the 60 deg-21 PV DBT scans due to the removal of 12 PVs in reconstruction. We generated the SM using our proposed method and parameters for an example in each geometry as shown in Fig. 7. We applied SART to all DBT images to avoid changes in image quality due to reconstruction techniques. These examples show that there is no visible blurring due to the application of our SM generation method to the different scan geometries. The SMs from the lower dose scan is noisier, which is an inherent property in imaging physics. These examples show that our method can work with different DBT geometries and imaging conditions, as long as the DBT scan geometry is accurately known.

With our method, we could also generate an SM at any given projection angle. For the purpose of our reader study, we used the central projection view to generate the SM since it was close to the projection angle as the clinical FFDM. The 2D SM is a simulated projection of overlapping breast tissues at a given projection angle. The central projection angle may not be the optimal projection for breast lesions at different locations in a DBT volume. A future topic of interest is to study whether the flexibility of selecting the projection angle of the SM or their combinations may provide some advantages or additional applications for SMs.

A previous study (van Schie *et al* 2013) proposed to use the detection results of computer aided detection system (CAD) for generation of SM. Such an approach is also used in some commercial software. When breast masses and architectural distortions were properly detected on the DBT volume, the CAD approach could improve the visibility of masses and architectural distortions on SM. However, it could potentially enhance false lesions when the CAD system finds false positives, as well as the more clinically significant problem of false negatives when the CAD system misses the true lesions with potential radiologist over-reliance on CAD generated synthetic images. In our SM approach, it is also possible to utilize CAD detection results to guide lesion enhancement and image weighting if desired. In the current study, we focused on evaluation of our SM as a potential replacement of DM for the purpose of navigation or preview while reducing dose. If CAD is incorporated into our SM scheme to further enhance mass lesions, it may increase the utility of such SM for initial search of masses, which should be further evaluated by a reader study. Nevertheless, regardless of SM generation methods with or without using CAD, overreliance on the SM for detection or characterization of breast lesions should not be advocated because of the limitations on the detection sensitivity in a 2D projection image or by CAD.

There are limitations in our study. First, the sample size in the study is limited although the important observations did reach statistical significance. Second, we used DBT acquired with our prototype system at 60-degree scan angle and the DBT was reconstructed with SART for this study. However, we expect that the proposed method can be applied to DBT from other systems or different reconstruction methods. We have demonstrated the application of our method to two other narrow-angle DBTs at 24 degrees and 16 degrees. For DBT reconstructed with different methods, the SM generation process is basically the same, except that some of the multiscale enhancement parameters may need to be adjusted according to the contrast and frequency characteristics of the DBT slices that are influenced by the reconstruction technique. We will evaluate the proposed method on DBTs from other systems in future studies if data sets become available. Third, we did not exhaustively evaluate different combinations of the enhancement parameters because of the large number of possible combinations and there is no simple figure-of-merit to objectively calculate the quality of the SMs for different types of lesions and guide the optimization. It is also impractical to have images processed with many sets of parameters for the radiologists to compare in a reader study due to their limited time available. Rather, we adjusted the parameters based on our experience from previous studies using DMs (Wei *et al* 2005), and subjectively compared the appearance of MCs and masses of the SMs from a small set of representative images to select the parameters. The final set of parameters was then used for processing the entire set of images and assessed by the experienced radiologists in the reader

study. The selected set of parameters therefore may not be optimal; nevertheless, the radiologists' ratings (8) indicated that the overall image quality of the SMs, on average, was acceptable. Fourth, our reader study focused on the comparison of image quality with DM. How the SM will affect the detection and diagnosis of the different types of lesions in a DBT-plus-SM reading mode in comparison to the DBT-plus-DM reading mode is an important question and needs to be addressed by an extensive observer or clinical study. This and other workflow or cost-benefit issues due to replacing SM with DM are out of the scope of this preliminary study and future follow-up studies are warranted.

6. Conclusion

In this study, we developed a novel approach to generate a synthesized 2D mammogram from a reconstructed 3D volume. We proposed a fusion method in which multiscale enhancement was employed to extract high-frequency information from the DBT volume, which was then re-projected to a 2D image and combined with a 2D projection view in a second multiscale process. A reader study was conducted to assess the image quality of SM in comparison to DM. We found that the conspicuity of MCs on SM was superior to that on FFDM and the MC appearance was acceptable for BI-RADS assessment. Since detection of MCs is more challenging in the reconstructed 3D DBT volumes, the SM may be useful for guiding radiologists in search of grouped MCs. However, the search of masses on the SM may be affected by the degraded conspicuity and thus necessitates careful review of DBT images that have been shown to be superior to 2D projections for lesion visualization.

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Figure 1.
The pipeline for the generation of synthetic 2D mammography (SM) from the DBT slices and a projection view (PV). MIP: maximum intensity projection.

Figure 2.

Image examples with pairs of FFDM (for presentation image) and SM of the same view with BI-RADS density categories A to D. FFDM is shown on the left and SM on the right. A close-up view of the lesion of interest is shown at the upper left corner of each image. (a) BI-RADS fatty density A breast with a group of microcalcifications – ductal carcinoma in situ (DCIS) (b) BI-RADS scattered density B breast with an invasive ductal carcinoma. (c) BI-RADS heterogeneously dense density C breast with an invasive ductal carcinoma. (d) BI-RADS extremely dense density D breast with a group of microcalcifications - DCIS. The two white spots on the FFDM are markers on the breast.

Figure 3.

Overall image quality ratings of SM relative to the corresponding FFDM assessed by three MQSA radiologists (R1, R2, and R3) in a 10-point scale: unacceptable (<5), acceptable (5–8), similar to FFDM (>8), and 10 being the same as FFDM.

Figure 4. Scatter plots of conspicuity ratings of lesions visually assessed on SMs and DMs averaged over three MQSA radiologists: (a) grouped microcalcifications (MCs), (b) masses. The diagonal line is a reference where the DMs and SMs have equal ratings.

(a)

(b)

Figure 5. Differences in conspicuity ratings of lesions visually assessed on digital mammogram (DM) and synthesized mammogram (SM) by the three MQSA radiologists, where positive value indicates conspicuity on DM is higher than that for SM.: (a) grouped microcalcifications (MCs), (b) masses.

Figure 6. Changes of BI-RADS assessments from digital mammogram (DM) to synthesized mammogram (SM) by the three MQSA radiologists, where positive change indicates higher BI-RADS category in SM than DM. (a) grouped microcalcifications (MCs), (b) masses.

Figure 7.

Synthetic mammogram examples with different DBT scan geometries. (a) From left to right: DM, SM generated from the 60 deg-21 PV DBT (same example as that shown in Fig. 2(c)), and SM from the 24 deg-9 PV DBT obtained by using the central 9 PVs from the 21-PV scan. (b) From left to right: DM, and SM generated from the 16 deg-17 PV DBT. Both cases had an invasive ductal carcinoma as marked by the box.

Table I.

Parameters used to generate the enhanced images at different levels in the Laplacian pyramid for recomposing the synthesized mammogram (SM).

Scale k	α	β	p
1	1.0	2.0	1.0
2	1.0	2.0	1.0
3	1.0	2.0	1.0
4	1.0	1.0	2.0
5	1.0	1.0	2.0
6	0.4	1.0	2.0
7	0.2	1.0	2.0

Table II.

Mean conspicuity ratings of lesions visually assessed by three MQSA radiologists.

Lesion Type	Microcalcifications			Mass		
	R1	R2	R3	R1	R2	R3
Readers						
FFDM	5.8	5.5	7.2	4.9	5.0	5.9
SM	7.7	7.0	8.0	4.3	4.5	5.0
<i>P</i> value	<0.0001	<0.0001	<0.0001	0.007	0.022	0.004