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Presented at: SPIE Medical Imaging Conference, Orlando, US, 2013.

Published at: Proc. SPIE 8668, Medical Imaging 2013: Physics of Medical Imaging, 86680Y (March 19, 2013);

doi: 10.1117/12.2008333

Link: <u>http://proceedings.spiedigitallibrary.org/proceeding.aspx?articleid=1669657</u>

Simulation of 3D DLA masses in digital breast tomosynthesis

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ABSTRACT

Digital breast tomosynthesis (DBT) is suggested to have superior performance compared to 2D mammography in terms of cancer visibility, especially in the case of dense breasts. However, the overall performance of tomosynthesis for screening applications, and the manner in which tomosynthesis should be optimally used for screening remains unclear. This motivates the development of software tools that can insert user-defined synthetic pathology of realistic appearance into clinical tomosynthesis images for subsequent use in virtual clinical trials. We present a method for inserting lesions grown using Diffusion Limited Aggregation, previously validated in 2D mammograms, into clinical DBT images. A preliminary pilot study was used to validate the realism of the masses, wherein three readers each viewed 19 cases and rated the realism of the inserted masses. Each case included a simulated mass inserted in the tomosynthesis projections and can produce visually authentic DBT images containing synthetic pathology. These results will be used to further optimize the appearance of these masses in DBT for an upcoming validation.

Keywords: Simulation, Breast lesion, Diffusion limited aggregation, Fractal growth, Digital breast tomosynthesis, Digital mammography, validation

1. INTRODUCTION

Two-dimensional X-ray mammography is currently the primary imaging modality used in breast screening programs for early detection. However, there are known limitations to this modality which include difficulty in detecting small lesions, due to over- and underlying breast architecture (inherent in 2D planar projection geometry) and limited sensitivity in breasts with high glandularity.^{1,2} However, digital breast tomosynthesis (DBT) has been suggested to have superior performance compared to 2D mammography in terms of cancer visibility, especially in dense breasts, as much of the obfuscating architecture is removed.^{2,3} While DBT appears promising, there remain a number of variables in the design of DBT systems and their usage that are expected to affect the quality of reconstructed images and cancer detection.¹ Clinical trials can be conducted to study such systems and the attendant issues of application and imaging methodology. However these trials are costly, time consuming and limited to commercially-available system design. Alternatively, a simulation framework where synthetic breast cancer pathology is inserted into tomosynthesis projections could be used to expedite comparisons of multiple systems and investigate the influencing variables on the detection task.

A number of previous studies have used simulation tools to study these modalities. Gong *et al.*³ and Timberg *et al.*⁴ compared digital mammography and DBT using simulated masses. However, the realism of the mass models used in their work was unclear. In this study we are extending our previous work^{5,6} which validated the use of 3D masses grown using diffusion limited aggregation (DLA) for 2D planar mammography, to the use of these masses in tomosynthesis.

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2. MATERIALS AND METHODS

The overall framework for simulation of masses in 2D digital mammograms and DBT projections is shown in Figure 1, which starts by generating a 3D mass using the DLA method described in section 2.2. The same simulated mass was then inserted in both modalities at the same location. The insertion location was determined by manually identifying an insertion location for the mass on the 2D mammogram based on local morphology and visual appearance. The depth of insertion was arbitrarily selected within the breast thickness. The simulated DLA mass was inserted in a 2D mammogram using the method developed by Rashidnasab *et al.*^{5,7} which used a degradation model of the imaging system, taking into account the polychromatic nature of the X-ray spectra, local glandularity and the scatter around the insertion site. The corresponding insertion location and local glandularity estimation were then calculated for the DBT 0° projection. Ray tracing was then undertaken on fifteen DBT projections for calculation of primary transmission using the method developed by the addition of detector blur using the system modulation transmission function (MTF). The mass was then inserted into the clinical projections and reconstructed into planes using the manufacturer-specific tomosynthesis reconstruction package. Further details of this process are described below.



Figure 1. Overall frameworks for inserting simulated masses into 2D digital mammograms and DBT projections. Each numbered block is described further in the text.

2.1 Materials

For the purpose of this study, images acquired by a Hologic Selenia Dimension system were used. This system can operate in two modes: 2D mammography and tomosynthesis. An anti-scatter grid was used in 2D mode and the detector pixel size was 70 μ m, while in tomosynthesis mode there was no anti-scatter grid and the pixels were re-binned to 140 μ m. When operating in tomosynthesis mode, 15 projections were acquired by moving the X-ray source over the angular range of +7.5° to -7.5°. Images, which were acquired in both modes for each patient, were collected from the Jarvis Breast Screening Centre, Guildford, UK. The DBT images in this centre were acquired for patients with a family history of the disease.

2.2 Simulation of 3D masses using diffusion limited aggregation

A new method to simulate 3D masses based on random fractal-like appearance of real breast cancers was previously developed by our group.^{5,6} Diffusion limited aggregation (DLA) was used to simulate these masses which includes two main steps: first diffusion of particles in a random walk manner and then rule-based aggregation of the particles to form a cluster.

Initially the DLA growth starts by incrementing the value of the centre voxel of a 3D binary array representing the mass aggregation centre. Particles are then randomly launched from launching sites, which, in this case, are in the form of concentric spheres about the aggregation centre. The launched particle moves using a random walk process. The particle stops at the adjacent point of contact to the mass cluster and may then become part of the cluster, depending on a heuristic sticking rule. The fractal and irregular shape of masses is achieved by addition of random particles to the adjacent voxels lining the mass cluster. If a random moving particle misses the mass cluster and travels further than a given distance it will be discarded. More detail on DLA growth parameters and their effect on the resultant mass volume can be found in [19]. A voxel size of 35 μ m was used in simulating mass volumes. These mass volumes were then used, as explained in the next steps, for insertion into both 2D mammograms and DBT projections.

2.3. Insertion of simulated masses in 2D mammograms

Simulated masses were inserted into 2D mammograms using the method developed by Rashidnasab *et al.*^{5,7} as shown in Figure 1(left). The primary photon flux was calculated at each pixel before and after insertion using polychromatic X-ray spectra model (block 3). This uses the work of Boone *et al.*⁹ for spectral matching of the associated mammogram acquisition settings, in terms of target/filter combination, tube voltage, filter thickness and half-value layer derived from the associated DICOM header. The composition of breast tissues was taken from the work of Hammerstein *et al.*¹⁰ and the linear attenuation coefficients were calculated using data from NIST¹¹. The breast attenuation coefficient was calculated using an estimate of the local glandularity of the breast over each image pixel (block 2). For this purpose, the Volpara¹² software tool was used on the mammograms for volumetric breast composition estimation.

The process of image degradation caused by the 2D imaging system's acquisition process was modelled using a method proposed by Mackenzie *et al.*¹³ This includes filtering the primary 2D array by the system MTF and then downsampling to the associated system detector pixel size of 70 μ m (block 4). The scatter was taken into consideration in the insertion process with the following steps: removal of the estimated local scatter in the clinical image (around the insertion site) to facilitate local adjustment of the primary transmission due to the DLA mass, and then re-instatement of the local scatter⁵ (block 5 and 6). The scatter to primary ratio (SPR) was calculated using the validated Monte Carlo model of Diaz et al.¹⁴ which is based on the Geant4 toolkit¹⁵. Finally, the resultant raw mammogram with the inserted mass was processed by the manufacturer's post acquisition image processing package (LORAD FFDM Selenia v 5.0), (block 7).

2.4. Insertion of simulated masses in DBT

2.4.1. Ray tracing and MTF filtering

Figure 1(right) shows the steps in insertion of masses into DBT projections using the method developed by Elangovan *et al.*⁸. A voxelised insertion volume of known length, width and thickness (estimated from DICOM header of the raw clinical projection) was created (block 10). The tissue composition of this volume was set as that of the local glandularity estimated at the insertion site. Then, the insertion volume was modified by placing a lesion at an arbitrary depth location. A ray tracing tool based on the Siddon algorithm¹⁶ was implemented⁷ which computes the path length for each type of tissue traversed via a line of response from the source to the image receptor. Using this ray tracing tool, primary transmission estimates were acquired for each of the 15 angles for the appropriate mammographic X-ray spectral model using the same material as described in section 2.3 (block 11). During ray tracing, the pixel size of 140 μ m at detector plane was used to account for Hologic detector pixel size in DBT mode.

A local estimation of glandularity was used in the calculation of the breast attenuation coefficient at the insertion site assuming that the local glandularity changed insignificantly with projection angle. The local glandularity on tomosynthesis 0° projection was produced by scaling the local glandularity estimate of the counterpart 2D digital mammogram (block 9). However, a study of use of pixel by pixel glandularity versus average local glandularity in simulations showed insignificant change is the results; hence for minimizing computation time the average local glandularity at the DBT 0° projection insertion site was used.

Degradation associated with the DBT imaging system was accounted for by filtering these primary projection arrays with the tomosynthesis system MTF by Mackenzie *et al.*¹³ (block 12). An idealized (point) focal spot was used in the simulation to reduce computational complexity.

2.4.2 Insertion and reconstruction

The insertion was then performed in the same manner as in 2D mammograms. The scatter to primary ratio used here was calculated using the validated Monte Carlo Model of Diaz *et al.*¹⁷ for the Hologic Selenia Dimension Tomosynthesis system geometry for a set of breast thicknesses, glandularity and different projection angles. The resulting values were tabulated so that the SPR for any breast thickness, glandularity, and projection angle could be found by interpolation (block 13, 14). The manufacturer's reconstruction software was used to reconstruct the tomographic breast image planes from the raw projection images (block 15).

2.5. Validation

A pilot study was used to initially validate the appearance of the simulated masses in tomosynthesis images. Nineteen DBT set each containing a simulated mass were reviewed by three radiologists with 2D mammogram reading experience of 5-20 years and up to maximum eighteen months experience in reading DBT images. The radiologists were asked to evaluate the realism of the simulated masses by ranking them on a scale of 1 to 10, with descriptors ranging from 'looks definitely simulated' (1) through to 'looks definitely real' (10). Score 0 was used for inserted masses that were considered not visible to the radiologist. They were also asked to rank the counterpart 2D mammograms with the simulated masses in the same manner.

3. RESULTS AND DISCUSSION

3.1. Simulation results

Figure 2(a) and 2(c) show 3D render of the DLA masses simulated by the method described in section 2.2. Figure 2(b) and 2(d) show the parallel projection of these masses prior to the insertion in the 2D mammogram. Figure 3(a) and 3(d) display the initial normal mammograms and the yellow square defines the selected ROI for mass insertion. Figure 3(b) and 3(e) show the mammograms with the inserted simulated mass using the mass in Figure 2(a) and 2(b), respectively. The magnified view of the selected ROI after mass insertion is shown in Figure 3(c) and 3(f).

Figure 4 and Figure 5 show results of inserting these masses in DBT projections. Figure 4(a-d) displays different reconstructed planes from the tomographic projections with the inserted mass using the mass in Figure 2(a). Figure 5(a-d) shows different reconstruction planes with the inserted mass using the mass in Figure 2(b). The magnified view of the inserted mass at each plane is shown in Figure 4(e-h) and Figure 5(e-h), respectively. The tomosynthesis results can be compared with the mass insertion results in 2D digital mammogram in Figure 3.



Figure 2. Examples of simulated DLA mass before insertion, (a) and (c) 3D rendering of the mass, (b) and (d) projection of the mass in 2D.



Figure 3. Insertion of simulated masses into 2D mammograms, (a) the processed normal digital mammogram before inserting the mass, (b) processed mammogram after insertion using the mass in Figure 2(a); (d) the processed normal digital mammogram before inserting the mass, (e) processed mammogram after insertion using the mass in Figure 2(b). The mass is located at the centre of the yellow box, (c) and (f) magnified view of the inserted masses.

3.2 Validation results

Table 1 shows the summary of the ranking results from three observers used in this pilot study for both 2D mammograms and DBT planes. Here score 5 was used as a threshold to classify the results to more realistic and more simulated appearance masses. As seen in the table the DLA masses produce promising results in 2D. However in DBT half of the masses were ranked as real. The number of invisible cases was reported less in 2D compared to DBT except for observer 3 who is the least experienced in reading 2D mammograms. Masses in DBT have more

cases reported as not visible due to lack of margin or dense centre. Figure 6 shows the boxplot of scores for each observer in each modality for better comparison of inter- and intra- observer variability. The comparison of the median of scores (shown in red line) suggests that insertion of these masses in 2D mammograms tends to produce a more realistic result than insertion into DBT images. DLA masses in DBT have larger variability of scores for each observer, yet all of the observers scored 50% of the cases as looking realistic.



Figure 4. Example of simulation of masses in DBT, (a-d) several reconstructed planes from clinical projections after insertion using the mass in Figure 3(a), the mass is located at the centre of the yellow box; (e-h) magnified view of the inserted mass at each plane.

Observer	Modality	# Looks more real	# Looks more simulated	# Not visible	# Total cases
1	2D mammogram	17	2	0	19
	DBT	10	9	0	19
2	2D mammogram	17	1	1	19
	DBT	10	4	5	19
3	2D mammogram	12	0	7	19
	DBT	10	4	5	19

Table1. Summary of each observer scores for simulated masses inserted in 2D mammograms and DBT.



Figure 5. Example of simulation of masses in DBT, (a-d) several reconstructed planes from clinical projections after insertion using the mass in Figure 3(b), the mass is located at the centre of the yellow box; (e-h) magnified view of the inserted mass at each plane.



Figure 6. Comparison of ranking of the simulated masses in DBT and 2D mammograms for each observer. Red line indicates the median of the ranking score (1: looks definitely simulated- 10: looks definitely real; 0: Not visible).

4. CONCLUSION AND FUTURE WORK

Diffusion limited aggregation (DLA), a type of fractal growth, was used to simulate 3D breast masses for insertion into clinical tomosynthesis projection images. The DLA mass was successfully inserted into clinical tomosynthesis projections using ray tracing. Previously, these simulated masses were validated in 2D digital mammograms. In this latest work we present a method for inserting such masses into tomosynthesis projections. A preliminary pilot study was performed where radiologists were asked to feedback on the realism of the simulated masses. The results from pilot study show that some DLA masses can produce realistic pathology in DBT. Prior to undertaking a full ROC study we will further optimise the appearance of our DLA masses, as their appearance whilst entirely satisfactory in 2D, does not reliably infer satisfactory appearance in DBT. The results of this pilot study will be used to improve the simulation model and to further optimise parameter selection for a forthcoming detailed ROC validation study.

ACKNOWLEDGMENTS

This work is part of the OPTIMAM project and is supported by the CR-UK & EPSRC Cancer Imaging Programme in Surrey, in association with the MRC and Department of Health (England). The authors thanks Hologic for granting access to DBT reconstruction software and Ralph Highnam for granting access to the Volpara breast volume measurement tool and providing technical assistance. The authors would also like to thank colleagues at NCCPM, the clinical observers Dr. Julie Cooke and Dr. Victoria Cooke at Jarvis Breast Screening Centre, Guildford and Dr. Matthew Wallis at Addenbrookes Hospital, Cambridge.

REFERENCES

[1] Young, K. C. and Dance, D. R., [Contemporary issues in cancer imaging: Breast cancer- Chapter4: Advances in x-ray mammography], Cambridge Uni. Press, 46-69 (2010).

[2] Gur, D., Abrams, G. S., Chough, D. M., Gannot, M. A., Hakim, C. M., Perrin, R. L., Rathfon, G. Y., Sumkin, J. H., Zuley, M. L. and Bandos, A. I., "Digital breast tomosynthesis: Observer performance study," Am. J. Roentgenol. 193, 586-591 (2009).

[3] Gong, X., Glick, S. J., Liu, B., Vedula, A. A. and Thacker, S., "A computer simulation study comparing lesion detection accuracy with digital mammography, breast tomosynthesis, and cone-beam CT breast imaging," Med. Phys. 33(4), 1041-1052 (2006).

[4] Timberg, P, Bath, M., Andersson, I., Mattsson, S., Tingberg, A., Ruschin, M., "In-plane visibility of lesions using breast tomosynthesis and digital mammography," Med. Phys. 37(11), 5618-5626 (2010).

[5] Rashidnasab, A., Elangovan, P., Yip, M., Diaz, O., Dance, D. R., Young, K. C. and Wells, K., "Simulation and assessment of realistic breast lesions using fractal growth models," Submitted to Phys. Med. Biol., (2012).

[6] Rashidnasab, A., Elangovan, P., Yip, M., Diaz, O., Dance, D. R., Young, K. C. and Wells, K., "Modeling Realistic Breast Lesions using Diffusion Limited Aggregation," Proc. SPIE 8313, Medical Imaging 2012: Physics of Medical Imaging, 83134L (2012).

[7] Rashidnasab, A., Elangovan, P., Dance, D. R., Young, K. C., Yip, M., Diaz, O. and Wells, K., "Realistic simulation of breast mass appearance using random walk", Proc. SPIE 8313, Medical Imaging 2012: Physics of Medical Imaging, 83130L (2012).

[8] Elangovan, P., Mackenzie, A., Diaz, O., Rashidnasab A., Dance, D. R., Young, K. C., Warren, L. M., Shaheen E., Bosmans, H. and Wells, K., "A modeling framework for evaluation of 2D mammography and breast tomosynthesis systems," Proc. IWDM, 338-345 (2012).

[9] Boone, J. M., Fewell, T. R. and Jennings, R. J., "Molybdenum, rhodium, and tungsten anode spectral models using interpolating polynomials with application to mammography," Med. Phys. 24(12), 1863-1874 (1997).

[10] Hammerstein, G. R., Miller, D. W., White, D. R., Masterson, M. E., Woodard, H. Q. and Laughlin, J. S., "Absorbed radiation dose in mammography," Radiology 130, 485-489 (1979).

[11] Berger, M. J., Hubbell, J. H., Seltzer, S. M., Chang, J., Coursey, J. S., Sukumar, R., Zucker, D. S. and Olsen, K., "XCOM: Photon cross sections database (version 1.5)," National Institute of Standards and Technology, Gaithersburg, MD, (2010), http://physics.nist.gpv/xcom>.

[12] Highnam, R., Brady, S. M., Yaffe, M. J., Karssemeijer, N. and Harvey, J., "Robust breast composition measurement VolparaTM," Proc. IWDM, 342-344 (2010).

[13] Mackenzie, A., Dance, D. R., Workman, A., Yip, M., Wells, K. and Young, K. C., "Conversion of mammographic images to appear with the noise and sharpness characteristics of a different detector and x-ray system," Med. Phys. 39(5), 2721-2734 (2012).

[14] Diaz, O., Yip, M., Cabello, J., Dance, D. R., Young, K. C. and Wells, K., "Monte carlo simulation of scatter field for calculation of contrast of discs in synthetic CDMAM images," Proc. IWDM, 628-635 (2010).

[15] Agostinelli S. et al., "GEANT4: A simulation toolkit," Nuclear Instruments and Methods in Physics Research A506, 250-303, (2003).

[16] Siddon, R. L., "Fast calculation of the exact radiological path for a three dimensional CT array," Med. Phys. 12(2), 252-255 (1985).

[17] Diaz, O., Dance, D. R., Young, K. C., Elangovan, P., Bakic, P. R. and Wells, K., "A fast scatter field estimator for digital breast tomosynthesis," Proc.SPIE 8313, Medical Imaging 2012: Physics of Medical Imaging, 831305 (2012).