A statistically defined anthropomorphic software breast phantom

Beverly A. Lau,^{a)} Ingrid Reiser, and Robert M. Nishikawa^{b)}
Department of Radiology, The University of Chicago, Chicago, Illinois 60637

Predrag R. Bakic

Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania 19104

(Received 18 July 2011; revised 4 April 2012; accepted for publication 30 April 2012; published 24 May 2012)

Purpose: Digital anthropomorphic breast phantoms have emerged in the past decade because of recent advances in 3D breast x-ray imaging techniques. Computer phantoms in the literature have incorporated power-law noise to represent glandular tissue and branching structures to represent linear components such as ducts. When power-law noise is added to those phantoms in one piece, the simulated fibroglandular tissue is distributed randomly throughout the breast, resulting in dense tissue placement that may not be observed in a real breast. The authors describe a method for enhancing an existing digital anthropomorphic breast phantom by adding binarized power-law noise to a limited area of the breast.

Methods: Phantoms with $(0.5 \text{ mm})^3$ voxel size were generated using software developed by Bakic *et al.* Between 0% and 40% of adipose compartments in each phantom were replaced with binarized power-law noise ($\beta = 3.0$) ranging from 0.1 to 0.6 volumetric glandular fraction. The phantoms were compressed to 7.5 cm thickness, then blurred using a 3×3 boxcar kernel and up-sampled to $(0.1 \text{ mm})^3$ voxel size using trilinear interpolation. Following interpolation, the phantoms were adjusted for volumetric glandular fraction using global thresholding. Monoenergetic phantom projections were created, including quantum noise and simulated detector blur. Texture was quantified in the simulated projections using power-spectrum analysis to estimate the power-law exponent β from $25.6 \times 25.6 \text{ mm}^2$ regions of interest.

Results: Phantoms were generated with total volumetric glandular fraction ranging from 3% to 24%. Values for β (averaged per projection view) were found to be between 2.67 and 3.73. Thus, the range of textures of the simulated breasts covers the textures observed in clinical images.

Conclusions: Using these new techniques, digital anthropomorphic breast phantoms can be generated with a variety of glandular fractions and patterns. β values for this new phantom are comparable with published values for breast tissue in x-ray projection modalities. The combination of conspicuous linear structures and binarized power-law noise added to a limited area of the phantom qualitatively improves its realism. © 2012 American Association of Physicists in Medicine.
[http://dx.doi.org/10.1118/1.4718576]

Key words: anthropomorphic breast phantom, phantom, simulation, power-law noise

I. INTRODUCTION

The need for realistic digital anthropomorphic breast phantoms has emerged in the past decade because of recent advances in 3D breast x-ray imaging techniques for breast cancer screening and diagnosis (such as MRI, CT, and tomography). With the increased interest in these new modalities, it has become essential to use anthropomorphic computer phantoms to optimize these systems in clinically relevant tasks.

Many groups are working on creating three-dimensional breast phantoms, including ones based on mastectomy specimens,¹ breast CT patient data,² and entirely computer-generated models.^{3–10} While phantoms based on patient data and mastectomy specimens have a higher chance of appearing more realistic, those phantoms require one patient per unique phantom. Moreover, phantoms made by imaging objects are limited by the pixel size of the imaging device

and are subject to physical effects of the system, such as blurring and noise. Entirely computer-generated phantoms require no radiation exposure to patients, while also allowing a large number of unique samples to be generated in a reasonable amount of time with no imaging artifacts and at the desired resolution.

One such entirely computer-generated anthropomorphic phantom was designed by Bakic *et al.*^{3–6} The version of these phantoms⁶ discussed in this paper are generated using a region-growing algorithm, which assigns voxels to a tissue type: adipose, fibroglandular, or skin. Simulated Cooper's ligaments separate the phantom into tissue compartments.

While the original Bakic phantom is realistic from a large-scale perspective, it lacks small-scale structures. The absence of small-scale structures causes linear patterns in the spatial frequency domain. The periodograms (squared

FIG. 1. ROIs from projection view images (top) with corresponding periodograms (bottom). The left two columns are from the original Bakic phantom and rightmost column is from the center projection of a clinical tomosynthesis dataset, shown for comparison. Pixel size is $0.1 \text{ mm} \times 0.1 \text{ mm}$ in the ROI images.

modulus of the 2D FFT) of extracted regions of interest (ROIs) have “spurious” structure that is not seen in a periodogram from a typical x-ray image of the breast (see Fig. 1).

In addition, the resolution of the original Bakic phantom was inadequate for simulating x-ray based modalities. Ideally the phantom could be used for simulating any x-ray-based modality: mammography, CT, tomosynthesis, among others. The detectors used in these modalities have pixel sizes that range from 0.05 to 0.3 mm. To avoid artifacts when projecting the phantom onto an x-ray detector, the phantom should have resolution at least as good as that of the detector. If this is not the case, artifacts can be observed in the spatial frequency domain (see Ref. 11).

Finally, slices through the phantom⁶ have little resemblance to slices through a breast imaged with breast CT, which produces fully resolved 3D breast images.¹²

Other groups have incorporated power-law noise into computer breast phantoms,^{7,10} which adds higher-frequency structures. While these phantoms also include branching ductal structures, the branching structure is often inconspicuous in the projection view images. And, since power-law noise is added to the entire breast in one piece, the simulated

fibroglandular tissue is distributed randomly throughout the breast, resulting in dense tissue placement that is unlikely to occur in a real breast.

In this paper, we describe a method to produce 3D breast models that combine the large-scale features of the Bakic phantom with the small-scale features of power-law noise to create a new phantom that has anthropomorphic structures at many different scales. We calculate β , a measure of tissue structure complexity, for simulated zero-degree projection view images to suggest the suitability of this phantom for x-ray imaging models.

II. MATERIALS AND METHODS

An overview of the method used to generate a phantom is given in Fig. 2. Briefly, we began with a base phantom that was constructed with voxel size $(0.5 \text{ mm})^3$. The base phantom was a semi-ellipsoid separated into irregularly shaped compartments. A fraction of these compartments were selected and replaced with binarized power-law noise, after which the phantom was deformed using a finite-element deformation method to simulate mammographic compression. The phantom was smoothed, up-sampled, and divided into distinct tissue types.

FIG. 2. A flowchart for phantom generation.

Completed phantoms underwent simulated cone-beam projection through ray tracing. Noise and blur were added based on procedures used in the literature. Regions of interest were extracted from the uniform-thickness area, and β was calculated for $25.6 \text{ mm} \times 25.6 \text{ mm}$ ROIs chosen with 50% overlap.

II.A. Base phantom creation

The first step in the production of the phantom was to create a base phantom, which consisted of a shell of skin that has adipose compartments delimited by simulated Cooper's ligaments [see Fig. 3(a)]. Unlike the original Bakic phantom, this base phantom did not include a "predominantly fibroglandular tissue region," which is a geometric shape consisting of uniform glandular tissue with spherical adipose inclusions.⁶

The base phantom was constructed using software by Bakic *et al.*, which generates Cooper's ligaments with thickness of a single voxel. In order to obtain base phantoms that have Cooper's ligaments 0.5 mm in thickness, all base phantoms were generated with $(0.5 \text{ mm})^3$ voxels. Compartments were formed through a region-growing algorithm,^{6,8} with the number of compartments equal to the number of seed points. Compartment size depends on the number of seed points and the ellipsoidal shell size. The number of compartments (n_c) was chosen to be 150, 200, or 300.

Skin thickness has been demonstrated to be approximately 1.5 mm for both healthy and diseased breasts.¹³ Phantoms were constructed with 1.5 mm skin thickness.

II.B. Power-law noise addition

In order to simulate structures in the breast such as terminal ductal lobular units,¹⁴ which are approximately 0.5–1 mm in size, uniform adipose tissue was replaced with binarized power-law noise [see Fig. 5(b)] in a subset of compartments. The fraction of compartments to be filled (f_c) was user-defined.

The compartments to be filled were selected strategically to create fibroglandular tissue structures that project out from the nipple into the breast, leaving a layer of adipose compartments immediately under the skin layer. To accomplish this, a rectangular pyramid of grid of points through the phantom was created along lines joining a 2D grid on a coronal plane at the chest wall and a point designated to be the nipple (see Fig. 4). Compartments were selected from seed points on this 3D grid, starting at the nipple and continuing proximally, until the user-defined number of compartments to fill was satisfied. Selected compartments were labeled in numerical order, to facilitate power-law noise addition [see Fig. 3(b)].

Power-law noise volumes were generated as described in Ref. 11 with $\beta = 3$. The volumes were binarized by selecting a threshold and setting all pixels below the threshold equal to 0 and setting all pixels above the threshold equal to 1. The threshold value was selected to yield a specified volumetric glandular fraction (VGF). A compartment was filled by overlapping the empty adipose compartment with a binarized noise volume and replacing the overlapping adipose voxels with the noise voxels [see Figs. 3(c) and 5].

Since structures in the breast are around 0.5–1 mm in size, binarized power-law noise with 0.5 mm resolution was added to the $(0.5 \text{ mm})^3$ voxel size phantom, before resolution adjustment to $(0.1 \text{ mm})^3$ voxel size. Power-law noise was added to 0%–40% of the compartments, with between 0.1 and 0.6 volumetric glandular fraction (f_g) in each noise volume. The f_g for each volume was randomly selected from a uniform distribution.

II.C. Compression

The breast deformation due to mammographic compression was simulated using a finite elements model^{15,16} on the $(0.5 \text{ mm})^3$ voxel size phantoms. The final compressed phantom had volume equal to 1500 mm^3 and thickness equal to 7.5 cm [see Fig. 3(d)].

II.D. Resolution adjustment

Projection of voxels onto pixels of smaller size leads to artifacts in both the spatial and spatial frequency domains.¹¹ Therefore, in order to create a phantom suitable for projection

FIG. 3. Steps for phantom creation: (a) construction of base phantom with empty compartments, (b) labeling requested number of compartments, (c) replacing filled compartments with binarized filtered noise, (d) compression, and (e) smoothing and resolution adjustment.

onto a detector with 0.1 mm pixel size, the $(0.5 \text{ mm})^3$ voxel phantom was up-sampled to have $(0.1 \text{ mm})^3$ voxel size.

Before up-sampling, the phantoms were blurred using a 3×3 boxcar kernel to smooth any rough edges. Next, the

phantoms were trilinearly interpolated to a coordinate grid with five times as many samples in each dimension, resulting in a phantom with voxel size equal to 0.1 mm in each dimension [see Fig. 3(e)].

FIG. 4. Schematic of compartment selection method. Three-quarter view to show rectangular pyramid grid (left) and sagittal view showing grid points between nipple and chest wall (right).

II.E. Volumetric glandular fraction adjustment

Following interpolation, the phantom had floating point values that were problematic for simulating a polychromatic x-ray beam, which required each voxel to be designated a particular tissue type. In order to return the phantom to its original discrete values, global thresholding was used. Threshold values were determined empirically to produce phantoms with percent volumetric glandular fraction within the range for real breasts. The range of volumetric breast densities was measured to be 13.7%–25.6% (average 19.3%) accord-

TABLE I. Typical input parameters for phantoms.

Symbol	Parameter	Range
n_c	Total number of compartments	150–300
f_c	Fraction of compartments filled	0.1–0.4
f_g	Glandular fraction of noise volumes	0.1–0.6

ing to a study by Yaffe *et al.*¹⁷ and confirmed by Huang *et al.*¹⁸

Since blurring followed by thresholding eliminated the Cooper's ligaments that extend to the skin, the resolution of the skin was adjusted separately from the rest of the breast. Once the up-sampled phantom was divided into distinct tissue types, the up-sampled and thresholded skin was added back to the rest of the phantom.

II.F. Volumetric glandular fraction determination

VGF_{sk} of the completed phantoms was calculated as the fraction of glandular and skin voxels, combined, in the phantom. The following equation was used to calculate VGF_{sk} :

$$\text{VGF}_{sk} = \frac{n_g + n_{sk}}{n_g + n_a + n_{sk}}, \quad (1)$$

where n_g , n_a , and n_{sk} are the number of voxels designated glandular, adipose, and skin, respectively. For these phantoms, the Cooper's ligaments were considered glandular tissue.

II.G. Projection

Phantoms were created and compressed to mimic medio-lateral oblique positioning. To visualize a mammogram-like image of the phantom, a simulated cone-beam projection onto a 10 cm × 30 cm detector with pixel size equal to 0.1 mm × 0.1 mm was performed, assuming a 20-keV mono-energetic x-ray beam. Attenuation coefficients were taken from the literature.^{19,20}

Following ray-tracing projection, detector blur was simulated by convolution with a Gaussian kernel with width to match MTF data from the literature.²¹

FIG. 5. Method for filling compartments with binarized power-law noise, displayed simplified in 2D. Power-law noise was generated using $\beta = 3.0$ [shown in (a)], then it was binarized using a threshold to achieve a given glandular fraction [shown in (b)]. A labeled compartment (c) was overlapped with the binarized noise, and that region of noise was extracted for use in the phantom [shown in (d)].

FIG. 6. A single (central) slice through the phantom (top) and simulated projection of the full phantom (bottom). Parameters chosen were $n_c = 300$, $f_c = 0.10$, and $f_g = 0.3$ – 0.6 . The VGF_{sk} was calculated to be 0.089, including skin and Cooper's ligaments as glandular tissue. All phantom projection view image figures are displayed with the same window and level setting. Note that the skin is not visible in the projection view image because of the window and level setting used.

Quantum noise was added to these images using stochastic noise filtered by a measured noise power spectrum (NPS), following methods in Ref. 22.

II.H. β calculation

β was calculated for these phantoms in the zero-degree projection view images, following methods used in the literature,^{23,24} as we have done before.²⁵ Nonuniformly thick areas of the log-transformed image of the projected

breast were removed by erosion using a circular structuring element with 9.7 mm diameter. ROIs were extracted with 50% overlap and size equal to 25.6 mm $\times$ 25.6 mm. This ROI size was chosen because we previously found that smaller ROI sizes lead to systematically lower β values.²⁶

The modulus-squared 2D FFT (periodogram) was calculated from the mean-subtracted ROIs and averaged radially to yield an estimate of the 1D power spectrum. The data in range [0.15, 0.7] cycles/mm were fit to a power-law to determine

FIG. 7. A single (central) slice through the phantom (top) and simulated projection of the full phantom (bottom). Parameters chosen were $n_c = 300$, $f_c = 0.20$, and $f_g = 0.3$ – 0.6 . For this phantom, $VGF_{sk} = 0.159$. All phantom projection view image figures are displayed with the same window and level setting. Note that the skin is not visible in the projection view image because of the window and level setting used.

FIG. 8. A single (central) slice through the phantom (top) and simulated projection of the full phantom (bottom). Parameters chosen were $n_c = 300$, $f_c = 0.3$, and $f_g = 0.3$ – 0.6 . For this phantom, $\text{VGF}_{sk} = 0.235$. All phantom projection view image figures are displayed with the same window and level setting. Note that the skin is not visible in the projection view image because of the window and level setting used.

the power-law exponent β for each ROI. The range for fitting was chosen to be independent of quantum noise, as we have done previously.²³ Average β was calculated for each set of acquisition parameters (f_c , f_g , and n_c) from 1500 ROIs (20 phantom projections yielding 75 ROIs each).

To show the variation of β across the breast, beta maps were constructed by computing beta from ROIs centered at each image pixel. For these maps, $25.6 \text{ mm} \times 25.6 \text{ mm}$ ROIs

were extracted at every location within the uniform-thickness area, with no restriction on overlap with other extracted ROIs. These were visually compared among phantom images.

III. RESULTS

A variety of phantoms were generated with different volumetric glandular fractions (see Table I for typical input

FIG. 9. Simulated projections of six phantoms using the same base phantom ($n_c = 300$) with different input parameters. The left column has $f_g = 0.1$ – 0.3 and the right column has $f_g = 0.3$ – 0.6 . Rows from top to bottom have $f_c = 0.10$, 0.20 , and 0.30 , respectively. Dimensions of each image are identical to those in the projection view images in Figs. 6–8. Values for VGF_{sk} are shown for each phantom. All phantom projection view image figures are displayed with the same window and level setting. Note that the skin is not visible in the projection view image because of the window and level setting used.

FIG. 10. Simulated projection images of six different base phantoms with the same input parameters ($n_c = 200$, $f_g = 0.1$ – 0.3 , and $f_c = 0.20$). Dimensions of each image are identical to those in the projection view images in Figs. 6–8. All phantom projection view image figures are displayed with the same window and level setting. Note that the skin is not visible in the projection view image because of the window and level setting used.

parameters). Sixty (60) base phantoms were generated: 20 with 150 compartments, 20 with 200 compartments, and 20 with 300 compartments. For each base phantom, binarized filtered noise was added to 10%, 20%, and 30% of the compartments, using volumetric glandular fraction ranges f_g in two ranges: (0.1, 0.3) and (0.3, 0.6). Binarized filtered noise was also added to 40% of the compartments in the $n_c = 300$ base phantoms using $f_g = 0.3$ – 0.6 , in an effort to explore higher-volumetric glandular fraction phantoms. In total, 380 phantoms were constructed from 60 base phantoms.

Using the same base phantom and altering just the number of compartments filled, we were able to create controlled variations in both phantom glandularity and simulated parenchymal tissue pattern (see Figs. 6–8). The displayed base phantom has 300 compartments. The three phantoms had 10%, 20%, and 30% compartments filled with $f_g = (0.3, 0.6)$, which resulted in VGF_{sk} of 0.089, 0.159, and 0.235, respectively.

To demonstrate the variety of phantoms that can be obtained using this method, multiple phantoms were made using a single base phantom and a variety of input parameters (see Fig. 9). For each phantom shown, the Cooper's ligament structure is exactly the same, but the number of compartments filled with power-law noise and the power-law noise volumes are different.

To demonstrate the possible range of textures, many phantoms were created using different base phantoms, using constant n_c , f_c , and f_g (see Fig. 10).

The effect of varying the construction parameters (n_c , f_c , and f_g) can be appreciated from the mean VGF_{sk} values shown in Table II. The average volumetric glandular fraction ranged from 0.029 to 0.239. Phantoms may be generated with higher VGF_{sk} by using different construction parameters and a different threshold value to separate the up-sampled phantom into distinct tissue types.

TABLE II. Mean VGF_{sk} data and standard deviation for 20 phantoms generated using each set of input parameters (f_c , f_g , and n_c). Twenty unique base phantoms were generated for each n_c .

f_c	f_g	Number of compartments (n_c)		
		150	200	300
0.10	0.1–0.3	0.029 ($\sigma = 0.005$)	0.031 (0.006)	0.036 (0.005)
0.20	0.1–0.3	0.052 (0.008)	0.054 (0.008)	0.060 (0.005)
0.30	0.1–0.3	0.070 (0.007)	0.077 (0.009)	0.083 (0.007)
0.10	0.3–0.6	0.063 (0.012)	0.063 (0.011)	0.068 (0.010)
0.20	0.3–0.6	0.118 (0.015)	0.121 (0.018)	0.127 (0.012)
0.30	0.3–0.6	0.173 (0.022)	0.175 (0.018)	0.183 (0.015)
0.40	0.3–0.6	—	—	0.239 (0.022)

FIG. 11. ROIs from simulated projection view images (top) of the statistically defined anthropomorphic phantom with corresponding periodograms (bottom). Pixel size is $0.1 \text{ mm} \times 0.1 \text{ mm}$ in the ROI images. Values for β in these ROIs were 2.81 (left) and 2.97 (right).

Periodograms were calculated for $25.6 \text{ mm} \times 25.6 \text{ mm}$ ROIs within the uniform-thickness region. An example of two ROIs and their periodograms are shown in Fig. 11. The corresponding radially averaged periodograms are shown in Fig. 12. The average β values for simulated projection view images of phantoms with different parameters are listed in Table III. Average β values ranged from 2.67 to 3.73.

Beta maps were calculated for a random selection of phantoms for comparison among phantoms constructed using different parameters (see Fig. 13).

IV. DISCUSSION

This phantom can be controlled in a number of ways in order to affect the overall glandular fraction and texture properties. Since the phantom is divided into closed compartments, the spatial distribution of simulated fibroglandular tissue can be controlled. The total volumetric glandular fraction of the phantom can be increased in three ways: (1) by increasing the number of compartments filled with power-law noise, (2) by increasing the glandular fraction of the binarized power-law noise volumes that replace selected adipose compartments, and (3) by increasing the total number of compartments, which increases the total volume of Cooper's ligaments. The effect of varying these parameters

can be appreciated from the mean VGF_{sk} values for different n_c and f_c shown in Table II.

It should be noted that the fraction of compartments filled with binarized power-law noise is not equivalent to the VGF_{sk} of the final phantom. The quantity VGF_{sk} includes the Cooper's ligaments and skin as glandular tissue, and the selected compartments are not entirely replaced by voxels identified as fibroglandular tissue. The base phantom and parameters n_c , f_c , and f_g do not determine the exact VGF_{sk} either, because although the binarized power-law volumes have f_g for each volume, only the part that overlaps with the empty adipose compartment will be used in the phantom (see Fig. 5).

Average values measured for β per projection view in this statistically defined anthropomorphic breast phantom ranged from 2.67 to 3.73, which is comparable to values measured for x-ray projection view images of real breasts (2.83 for mammography²⁷ and 3.06 for tomosynthesis).²³ From Table III, it appears that β increases with increasing fraction of compartments filled. This can be attributed to a larger percentage of the projection view image spanned by fibroglandular tissue, which is evident from the beta map images in Fig. 13.

Power-law noise alone lacks linear structures, which includes ducts, connective tissue, and blood vessels. Moreover, power-law noise included in a breast model as one

FIG. 12. Radially averaged periodograms for ROIs shown in Fig. 11. β was calculated using data points between 0.15 and 0.7 cycles/mm (shown as circles). (a) $\beta = 2.81$ and (b) $\beta = 2.97$.

TABLE III. Average β values for 20 phantoms using each set of input parameters (f_c , f_g , and n_c). Twenty unique base phantoms were generated for each n_c .

f_c	f_g	Number of compartments (n_c)		
		150	200	300
0.10	0.1–0.3	2.83 ($\sigma = 0.08$)	2.87 (0.06)	2.90 (0.08)
0.20	0.1–0.3	3.14 (0.11)	3.16 (0.11)	3.18 (0.06)
0.30	0.1–0.3	3.36 (0.09)	3.39 (0.07)	3.42 (0.07)
0.10	0.3–0.6	2.92 (0.09)	2.93 (0.06)	2.96 (0.08)
0.20	0.3–0.6	3.25 (0.12)	3.26 (0.10)	3.28 (0.07)
0.30	0.3–0.6	3.47 (0.10)	3.50 (0.07)	3.52 (0.07)
0.40	0.3–0.6	—	—	3.65 (0.04)

contiguous volume leads to unrealistic fibroglandular tissue distributions throughout the breast (see Fig. 14). However, when combined with an anthropomorphic breast phantom that includes linear structures such as Cooper's ligaments, strategically placed binarized power-law noise can improve the appearance of the overall breast phantom by providing simulated small-scale tissue structures.

V. CONCLUSION

We have developed a new way of enhancing an existing anthropomorphic breast phantom to include both large-scale and small-scale structures, and we have shown that this new phantom can yield radially symmetric periodograms, suitable for power spectral analysis. Moreover, we have shown average β values from projection view images of this phantom to be similar to reported values from real breast images. Matching β is a necessary, but not sufficient, condition for validating an anthropomorphic phantom, since many natural

FIG. 13. Projection views (left) and corresponding beta map images (right). One base phantom with $n_c = 300$, with $f_g = 0.1$ –0.3 and three different f_c : (a) 0.10, (b) 0.20, and (c) 0.30. Values for VGF_{sk} (left) and beta map average β (right) are shown for each phantom. For each beta map, 1 207 616 ROIs were extracted.

FIG. 14. Example projections of phantoms with binarized filtered noise added as a single contiguous volume. These phantoms were generated using the same methods as the compartmentalized version, except the entire breast was treated as a single compartment. Figures are displayed with the same window and level setting as projection view images shown previously.

scenes yield similar β values. With improvements in the phantom generating software, it will be possible to make phantoms with smaller voxel size and user-defined Cooper's ligament widths.²⁸ Validation studies are ongoing for this phantom.

ACKNOWLEDGMENTS

This work was funded in part by grants: DOD W81XWH-08-1-0353, NIH R21 EB008801, S10 RR021039, S10 RR029030, and P30 CA14599. The contents of this paper are solely the responsibility of the authors and do not necessarily represent the official views of any of the supporting organizations. The authors thank Andrew Maidment and Robert Schmidt for helpful discussions, and Lorenzo Pesce for assistance in running our code on the supercomputer. RM Nishikawa is a shareholder in and receives royalties from Hologic, Inc.

^{a)}Electronic mail: beverly@uchicago.edu

^{b)}Electronic mail: r-nishikawa@uchicago.edu

¹J. O'Connor, M. Das, C. Didier, M. Mah'D, and S. Glick, "Development of an ensemble of digital breast object models," in *Digital Mammography (IWDM)*, Lecture Notes in Computer Science, edited by J. Martí, A. Oliver, J. Freixenet, and R. Martí (Springer-Verlag, Berlin, Heidelberg, 2010), Vol. 6136, pp. 54–61.

²C. Li, W. Segars, G. Tourassi, J. Boone, and J. Dobbins III, "Methodology for generating a 3D computerized breast phantom from empirical data," *Med. Phys.* **36**, 3122–3131 (2009).

³P. R. Bakic, M. Albert, D. Brzakovic, and A. D. A. Maidment, "Mammogram synthesis using a 3D simulation. I. Breast tissue model and image acquisition simulation," *Med. Phys.* **29**, 2131–2139 (2002).

⁴P. R. Bakic, M. Albert, D. Brzakovic, and A. D. A. Maidment, "Mammogram synthesis using a 3D simulation. II. Evaluation of synthetic mammogram texture," *Med. Phys.* **29**, 2140–2151 (2002).

⁵P. R. Bakic, M. Albert, D. Brzakovic, and A. D. A. Maidment, "Mammogram synthesis using a three-dimensional simulation. III. Model-

ing and evaluation of the breast ductal network," *Med. Phys.* **30**, 1914–1925 (2003).

⁶P. R. Bakic, C. Zhang, and A. D. A. Maidment, "Development and characterization of an anthropomorphic breast software phantom based upon region-growing algorithm," *Med. Phys.* **38**, 3165–3176 (2011).

⁷K. Bliznakova, Z. Bliznakov, V. Bravou, Z. Kolitsi, and N. Pallikarakis, "A three-dimensional breast software phantom for mammography simulation," *Phys. Med. Biol.* **48**, 3699–3719 (2003).

⁸C. Zhang, P. R. Bakic, and A. D. A. Maidment, "Development of an anthropomorphic breast software phantom based on region growing algorithm," *Proc. SPIE* **6918**, 69180V (2008).

⁹A. Ma, S. Gunn, and D. Darambara, "Introducing DeBRa: A detailed breast model for radiological studies," *Phys. Med. Biol.* **54**, 4533–4545 (2009).

¹⁰B. Chen, J. Shorey, R. S. Saunders, S. Richard, J. Thompson, L. W. Nolte, and E. Samei, "An anthropomorphic breast model for breast imaging simulation and optimization," *Acad. Radiol.* **18**, 536–546 (2011).

¹¹I. Reiser and R. M. Nishikawa, "Task-based assessment of breast tomosynthesis: Effect of acquisition parameters and quantum noise," *Med. Phys.* **37**, 1591–1600 (2010).

¹²K. Lindfors, J. Boone, T. Nelson, K. Yang, A. Kwan, and D. Miller, "Dedicated breast CT: Initial clinical experience," *Radiology* **246**(3), 725–733 (2008).

¹³S.-Y. Huang, J. M. Boone, K. Yang, A. L. C. Kwan, and N. J. Packard, "The effect of skin thickness determined using breast CT on mammographic dosimetry," *Med. Phys.* **35**, 1199–1206 (2008).

¹⁴L. Tabár, T. Tot, and P. B. Dean, *Breast Cancer: The Art and Science of Early Detection With Mammography: Perception, Interpretation, Histopathic Correlation*, 1st ed. (Thieme, New York, NY, 2005), p. 48.

¹⁵S. Xia, F. Liu, A. D. A. Maidment, and P. R. Bakic, "Refinements to the deformation model of an anthropomorphic computer generated breast phantom," *Med. Phys.* **37**, 3131 (2010).

¹⁶N. V. Ruiter, C. Zhang, P. R. Bakic, A.-K. Carton, J. Kuo, and A. D. A. Maidment, "Simulation of tomosynthesis images based on an anthropomorphic software breast tissue phantom," *Proc. SPIE* **6918**, 69182I (2008).

¹⁷M. J. Yaffe, J. M. Boone, N. Packard, O. Alonzo-Proulx, S.-Y. Huang, C. L. Peressotti, A. Al-Mayah, and K. Brock, "The myth of the 50-50 breast," *Med. Phys.* **36**, 5437–5443 (2009).

¹⁸S.-Y. Huang, J. M. Boone, K. Yang, N. J. Packard, S. E. Mckenney, N. D. Prionas, K. K. Lindfors, and M. J. Yaffe, "The characterization of breast anatomical metrics using dedicated breast CT," *Med. Phys.* **38**, 2180–2191 (2011).

¹⁹G. R. Hammerstein, D. W. Miller, D. R. White, M. E. Masterson, H. Q. Woodard, and J. S. Laughlin, "Absorbed radiation dose in mammography," *Radiology* **130**, 485–491 (1979).

²⁰P. C. Johns and M. J. Yaffe, "X-ray characterisation of normal and neoplastic breast tissues," *Phys. Med. Biol.* **32**, 675–695 (1987).

²¹C. Ghetti, A. Borriani, O. Ortenzia, R. Rossi, and P. L. Ordóñez, "Physical characteristics of GE Senographe Essential and DS digital mammography detectors," *Med. Phys.* **35**, 456–463 (2008).

²²R. Saunders, Jr. and E. Samei, "A method for modifying the image quality parameters of digital radiographic images," *Med. Phys.* **30**, 3006–3017 (2003).

²³E. Engstrom, I. Reiser, and R. Nishikawa, "Comparison of power spectra for tomosynthesis projections and reconstructed images," *Med. Phys.* **36**, 1753–1758 (2009).

²⁴A. Burgess, "Mammographic structure: Data preparation and spatial statistics analysis," *Proc. SPIE* **3661**, 642–653 (1999).

²⁵P. Bakic, B. Lau, A.-K. Carton, I. Reiser, A. Maidment, and R. Nishikawa, "An anthropomorphic software breast phantom for tomosynthesis simulation: Power spectrum analysis of phantom projections," in *Digital Mammography (IWDM)*, Lecture Notes in Computer Science, edited by J. Martí, A. Oliver, J. Freixenet, and R. Martí (Springer-Verlag, Berlin, Heidelberg, 2010), Vol. 6136, pp. 452–458.

²⁶B. A. Lau, I. Reiser, and R. M. Nishikawa, "Issues in characterizing anatomical structure in digital breast tomosynthesis," *Proc. SPIE* **7961** (2011).

²⁷A. Burgess, F. Jacobson, and P. Judy, "Human observer detection experiments with mammograms and power-law noise," *Med. Phys.* **28**, 419–437 (2001).

²⁸D. D. Pokrajac, A. D. A. Maidment, and P. R. Bakic, "Optimized generation of high resolution breast anthropomorphic software phantoms," *Med. Phys.* **39**, 2290–2302 (2012).