Characterizing anatomical variability in breast CT images

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Previous work [Burgess *et al.*, *Med. Phys.* **28**, 419–437 (2001)] has shown that anatomical noise in projection mammography results in a power spectrum well modeled over a range of frequencies by a power law, and the exponent (β) of this power law plays a critical role in determining the size at which a growing lesion reaches the threshold for detection. In this study, the authors evaluated the power-law model for breast computed tomography (bCT) images, which can be thought of as thin sections through a three-dimensional (3D) volume. Under the assumption of a 3D power law describing the distribution of attenuation coefficients in the breast parenchyma, the authors derived the relationship between the power-law exponents of bCT and projection images and found it to be $\beta_{\text{section}} = \beta_{\text{proj}} - 1$. They evaluated this relationship on clinical images by comparing bCT images from a set of 43 patients to Burgess' findings in mammography. They were able to make a direct comparison for 6 of these patients who had both a bCT exam and a digitized film-screen mammogram. They also evaluated segmented bCT images to investigate the extent to which the bCT power-law exponent can be explained by a binary model of attenuation coefficients based on the different attenuation of glandular and adipose tissue. The power-law model was found to be a good fit for bCT data over frequencies from 0.07 to 0.45 cyc/mm, where anatomical variability dominates the spectrum. The average exponent for bCT images was 1.86. This value is close to the theoretical prediction using Burgess' published data for projection mammography and for the limited set of mammography data available from the authors' patient sample. Exponents from the segmented bCT images (average value: 2.06) were systematically slightly higher than bCT images, with substantial correlation between the two ($r=0.84$). © 2008 American Association of Physicists in Medicine. [DOI: [10.1118/1.2977772](https://doi.org/10.1118/1.2977772)]

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I. INTRODUCTION

Mammography is the current clinical standard for breast cancer screening, but the use of projection mammography for breast imaging requires that abnormalities be identified against a background of normal anatomy integrated through the entire breast. This superimposition of breast tissues in projection mammography makes the identification of lesions more difficult.^{1–4} The appearance of variability in an image due to normal anatomy is sometimes referred to as “structured”⁵ or “anatomical” noise^{4,6} indicating its detrimental effect. Dual energy imaging,^{7–9} contrast enhanced imaging,¹⁰ and breast magnetic resonance imaging¹¹ all attempt to reduce the influence of anatomical noise by selectively enhancing the contrast of suspicious lesions relative to the surrounding normal anatomy.

Computed tomography of the breast^{12–15} (bCT) is another means of imaging the breast which substantially reduces the superimposition of breast tissue using the characteristics of tomographic imaging. Figure 1 shows a projection mammogram and several coronal sections from a three-dimensional (3D) reconstruction of the same breast acquired on a dedicated high-resolution breast bCT scanner. The use of such a scanner may help improve lesion detectability, however, only single observer unblinded scoring techniques have been used to document this to date.^{15,16} In the absence of more rigorous clinical validation (e.g., blinded ROC studies), the anatomical

noise properties of bCT images compared to mammography may provide guidance as to the theoretical potential of bCT to improve upon projection mammography.

Figure 2 shows example image regions from the projection mammogram and the bCT scan at approximately the same physical size. It is clear from these images that projection mammograms and bCT images have a different appearance and texture. In this investigation, we measure and analyze the image power spectrum (PS) to evaluate the characteristics of anatomical variability in bCT images under the assumption that the statistics associated with breast tissue are locally stationary in the regions sampled. A number of authors^{17–20} have shown that at spatial frequencies below about 0.5 cyc/mm, power spectra for projection mammography images are well-characterized by a power law: $S(f) = \alpha/f^\beta$, where f is the radial spatial frequency. The magnitude, α , and power-law exponent, β , are free parameters. Burgess and colleagues^{19,21} have also shown that the power-law exponent is a critical factor in determining the size at which a lesion reaches detection threshold, and thus characterizes the masking effect of normal anatomy. An important finding of that work is that a lower power-law exponent results in earlier detection of a growing lesion. In Sec. V, we discuss some of the issues that arise in trying to apply this result to bCT images, where lesion contrast is not directly related to lesion size.

FIG. 1. Projection mammogram and breast CT slices. A full field projection mammogram (a) is shown in the CC view. Six coronal slices from the corresponding bCT scan are shown (b) at various distances from the top of the field of view, which is approximately at the chest wall.

In this work we seek to extend Burgess' analysis to bCT images. Ignoring effects of breast compression, x-ray energy, and spatial sampling, standard mammography can be thought of as a projection of the 3D breast anatomy onto a two-dimensional (2D) image while a single bCT image can be thought of as representing a thin 2D section through the same volume. Under the assumption of a power law describing the 3D distribution of attenuation coefficients in the interior of the breast, we derive the relationship between power-law exponents of projections and thin sections of a volume. We find the power-law exponent (β) to be 1 less in sections compared to projections (i.e., $\beta_{\text{section}} = \beta_{\text{proj}} - 1$).

To evaluate the extent to which this relationship holds for clinical images of the breast, we have performed a PS analysis on 43 patient bCT images. We fit a power-law function over spatial frequencies where anatomical variability should dominate and use the exponent of the power law as an estimate of β . We then compare these to the published results of Burgess *et al.*¹⁹ for projection mammography. We also have a limited set of six mammograms digitized from film for this same patient sample. This gives us the opportunity to make a limited test of the predicted relationship for power-law exponents on mammography and bCT images from the same patients.

Furthermore, attenuation coefficients in the breast are often considered to be predominantly binary, representing either adipose or glandular tissue. This view would posit that the bCT image is effectively the binary texture of the breast

FIG. 2. Image texture in a mammogram and breast CT slice. A region from the interior of the same breast is shown for a projection mammogram (a) and for bCT slices (b). The regions have been magnified to be roughly at actual physical size.

at a limited spatial resolution and with additional acquisition noise. Therefore, at lower frequencies dominated by anatomical variability, the PS of this binary texture should follow that of the acquired (i.e., nonsegmented) bCT images ($\beta_{\text{seg}} = \beta_{\text{section}}$). We investigate this issue by evaluating power-law exponents from segmented bCT images, to assess if they match the exponent of the acquired bCT image. This allows us to evaluate the extent to which the statistical structure of the acquired images can be explained by a binary process.

II. THEORY

In this section we derive the relationship between the PS of thin sections through a stochastic 3D volume and line-integral projections through that volume. The analysis is similar to previous work on the Radon transform of a 2D stationary random field.^{22,23} Here we consider a single 2D projection of a 3D object. We also consider line integrals of limited length, which eliminates some technical problems with convergence of integrals in addition to more accurately representing the physical limitations of imaging systems.

The derivation is carried out in the framework of continuous functions and stationary processes because the result is most clear in this situation. Thin sections represent bCT images from a reconstructed volume, and projections represent x-ray mammography images. Under the assumption of an underlying 3D power-law process describing anatomical variability, we show that the power-law exponents of sections and projection images are related. A main goal of this work is to evaluate bCT images and projection mammograms to see if the relationship holds in practice. In this section we also describe the procedure used to estimate the PS from a set of randomly sampled regions of interest and to fit the power law.

II.A. Power spectra of sections and projections

A volumetric random function, $\mu(x, y, z)$, representing three-dimensional distribution of linear attenuation coefficients, is presumed to be a realization of a stationary random process. We denote the 3D Fourier transform (FT) of μ to be

$\hat{\mu}(u, v, w)$ and note that it is also a random function. One definition of the PS, $S(u, v, w)$, of a (wide sense) stationary process is the expectation

$$\langle \hat{\mu}(u, v, w) \overline{\hat{\mu}(u', v', w')} \rangle = \delta(u - u') \delta(v - v') \delta(w - w') S(u, v, w), \quad (1)$$

where the overline indicates the conjugate of a complex quantity. The delta functions enforce the constraint of zero crosstalk between spatial frequencies (i.e., the expectation is zero unless $u=u'$, $v=v'$, and $w=w'$). Infinite amplitudes of the delta functions reflect the assumption of an infinite spatial extent required for rigorous stationarity to hold.

Now we consider the projection of μ onto a plane using line integrals of length L . This transformation is accomplished by integrating in z over a length L for each xy pair. The choice of z is arbitrary. The 2D projection is given by

$$\mu_L(x, y) = \int_{-L/2}^{L/2} \mu(x, y, z) dz = \int_{-\infty}^{\infty} \mu(x, y, z) \text{rect}(z/L) dz, \quad (2)$$

where $\text{rect}(z)$ is the “rectangle” function that has a value of 1 from $-\frac{1}{2}$ to $\frac{1}{2}$, and is zero everywhere else. The one-dimensional FT of $\text{rect}(z/L)$ is $L \text{sinc}(\pi L w)$, where $\text{sinc}(x) = \sin(x)/x$. Using this FT pair, we find $\hat{\mu}_L(u, v)$, the 2D FT of μ_L , to be

$$\hat{\mu}_L(u, v) = L \int_{-\infty}^{\infty} \text{sinc}(\pi L w) \hat{\mu}(u, v, w) dw. \quad (3)$$

We will consider sectional images of a volume to be the limit of small L while projection images are represented by large values of L .

The PS of μ_L is defined by the 2D analog of Eq. (1), and we derive it by considering the expectation in $\hat{\mu}_L$. In this case we have

$$\begin{aligned} \langle \hat{\mu}_L(u, v) \overline{\hat{\mu}_L(u', v')} \rangle &= L^2 \left\langle \int_{-\infty}^{\infty} \text{sinc}(\pi L w) \hat{\mu}(u, v, w) dw \int_{-\infty}^{\infty} \text{sinc}(\pi L w') \overline{\hat{\mu}(u', v', w')} dw' \right\rangle \\ &= L^2 \int_{-\infty}^{\infty} \text{sinc}(\pi L w) \int_{-\infty}^{\infty} \text{sinc}(\pi L w') \langle \hat{\mu}(u, v, w) \overline{\hat{\mu}(u', v', w')} \rangle dw' dw. \end{aligned} \quad (4)$$

Using Eq. (1) for the 3D expectation we find

$$\langle \hat{\mu}_L(u, v) \overline{\hat{\mu}_L(u', v')} \rangle = \delta(u - u') \delta(v - v') L^2 \int_{-\infty}^{\infty} \text{sinc}(\pi L w)^2 S(u, v, w) dw. \quad (5)$$

This expectation shows that the PS of the projected image, $S_L(u, v)$, is related to the PS of the 3D object by

$$S_L(u, v) = L^2 \int_{-\infty}^{\infty} \text{sinc}(\pi L w)^2 S(u, v, w) dw. \quad (6)$$

II.B. Special cases

We now turn to two special cases of Eq. (6). We consider images made from a planar section through a 3D volume, and images made from projecting a thick volume onto a plane. A coronal bCT image typically has a section thickness of 0.2–0.4 mm, whereas a projection corresponds to a clinical mammogram in which the breast is compressed to a thickness of approximately 50 mm, a difference of more than two orders of magnitude.

II.B.1. Large L (projections)

As the length of projection, L , gets increasingly large (i.e., $L \rightarrow L_{\text{big}}$), $L \text{sinc}(\pi L w)^2$ in Eq. (6) becomes more like a delta function, therefore

$$S_{L_{\text{big}}}(u, v) \simeq L_{\text{big}} S(u, v, 0). \quad (7)$$

The 2D PS of the projection is therefore a 2D plane through the 3D PS, which is consistent with the well known projection-slice theorem of tomography.^{24,25} Note that the length dependence in the PS is linear in L . This is reasonable, since long integration paths allow some cancellation of variability to occur, thereby reducing power over the integration path in Eq. (6).

II.B.2. Small L (sections)

A section image from a 3D volume can be thought of as a projection over a very short path. In this case, the sinc function in Eq. (6) gets increasingly broad until it is effectively a constant assuming a finite region of support for the 3D PS. Hence, for short integration lengths (i.e., $L \rightarrow L_{\text{small}}$), the PS reduces to

$$S_{L_{\text{small}}}(u, v) \simeq L_{\text{small}}^2 \int_{-\infty}^{\infty} S(u, v, w) dw. \quad (8)$$

The leading term, L^2 in this case, reflects the fact that integrating over these small distances does not allow for any cancellation.

II.B.3. Example: Isotropic power law

Now we assume that the 3D object has an isotropic power law as its PS,

$$S(u, v, w) = \alpha(u^2 + v^2 + w^2)^{-\beta/2}, \quad (9)$$

where α is a scaling constant that indicates the magnitude of the PS. Under the large L (projection) approximation above, it is seen immediately that the NPS of the projection is also a power law, since

$$S_{L_{\text{big}}}(u, v) \approx L_{\text{big}} S(u, v, 0) = L_{\text{big}} \alpha(u^2 + v^2)^{-\beta/2}. \quad (10)$$

The small L (section image) approximation is computed from the integral

$$\begin{aligned} S_{L_{\text{small}}}(u, v) &\approx L_{\text{small}}^2 \int_{-\infty}^{\infty} S(u, v, w) dw \\ &= L_{\text{small}}^2 \alpha \int_{-\infty}^{\infty} (u^2 + v^2 + w^2)^{-\beta/2} dw. \end{aligned} \quad (11)$$

Assuming u and v do not both equal zero (where a pole exists), the right side of Eq. (11) can be rewritten as

$$\begin{aligned} S_{L_{\text{small}}}(u, v) &\approx L_{\text{small}}^2 \alpha (u^2 + v^2)^{-\beta/2} \\ &\times \int_{-\infty}^{\infty} \left(1 + \frac{w^2}{u^2 + v^2}\right)^{-\beta/2} dw. \end{aligned} \quad (12)$$

Using substitution of variables with $w' = w / \sqrt{u^2 + v^2}$ and $dw = \sqrt{u^2 + v^2} dw'$ gives the small L approximation as

$$S_{L_{\text{small}}}(u, v) \approx L_{\text{small}}^2 \alpha (u^2 + v^2)^{-\beta/2} \int_{-\infty}^{\infty} \sqrt{u^2 + v^2} (1 + w'^2)^{-\beta/2} dw' = L_{\text{small}}^2 \alpha (u^2 + v^2)^{-(\beta-1)/2} \int_{-\infty}^{\infty} (1 + w'^2)^{-\beta/2} dw'. \quad (13)$$

The remaining integral can be regarded as constant since it is now independent of u and w (for $\beta=2.8$ the constant is 2.135). Thus, the section image is also a realization of a power-law process, but the exponent β is now reduced by 1. Under the assumption of a power-law process, the relationship between exponents is

$$\beta_{\text{section}} = \beta_{\text{proj}} - 1. \quad (14)$$

Based on the above theoretical observation, the power-law exponents from computed tomography (CT) images of the breast are expected to be one less than power-law exponents of projection mammograms.

II.C. Estimation of power spectra from bCT and projection images

The derivations above specified the images as continuous functions and define a relation between the power-law exponents of sections and projections encompassed in Eq. (14). However, to verify this relationship in real clinical images, we will need to determine the PS from finite “pixelated” images that consist of an array of pixel or voxel intensities. This is done by randomly selecting regions of interest (ROIs) from sample images. The ROIs are then used to estimate a PS that is characteristic of the image.

Figure 3 illustrates the critical steps in estimating a power-law exponent from a set of ROIs. The approach is similar to one of the methods used by Burgess *et al.*^{18,19} for mammograms. In principle, we can simply compute the average magnitude squared of the finite Fourier transform (FFT) from the ROIs instead of the expectation and continuous Fourier transform used in Eq. (1). However, there are two potential problems with this approach. The first is that

the discrete sampling limits spectrum of the FFT to frequencies below Nyquist. This is not a substantial issue in this work since we are interested in frequencies which are dominated by anatomical variability, and hence, are well below the Nyquist limit. The second issue is that a PS based on the FFT implicitly assumes that spatial correlations between pixels are cyclic; that is they wrap around at the edge of the image. This is clearly violated in practice, and the result is excess power from discontinuities at the edges of the image. This situation is addressed by the use of a spatial window function that tapers the image to zero at the edges.^{26,27} Here, we use a radially symmetric Hanning window; $W(r) = 0.5 + 0.5 \cos(\pi r/R)$ with $W(r) = 0$ for $r > R$, where R is half the width of the image. Figure 3(a) shows a ROI before and after the window is applied. We note that the window is applied after the ensemble average—the value across all ROIs—has been subtracted. Figure 3(b) shows a contour plot of the average PS from a set of windowed ROIs. While noisy, contours are reasonably isotropic for frequencies below about 1 cyc/mm.

We fit a power law function, $S(f) = \alpha/f^\beta$, to the 2D PS over a range of frequencies by computing a linear fit of log-frequency to log-PS. Here we assume an N by N image with an isotropic pixel size of Δ_{pix} . Let $S[k, l]$ be the average discrete 2D PS at point k, l (both indices range from $-N/2$ to $N/2-1$), and the frequency spacing is given by $\Delta_f = 1/N\Delta_{\text{pix}}$. At each point, the radial frequency is defined as

$$f_{k,l} = \Delta_f \sqrt{k^2 + l^2}. \quad (15)$$

The power law fit is determined by a least-squares solution over some set of $[k, l]$ for the linear equations

FIG. 3. Procedure for generating power spectra. A sample ROI is shown (a) both without (top) and with (bottom) a radial Hanning window. A contour plot (b) of the average power over 50 sample ROIs shows relatively isotropic contours to approximately 1 cyc/mm. Average power as a function of frequency is plotted (c) along with a power law fitted over a range of frequencies (0.07–0.49 cyc/mm).

$$\log(S[k,l]) = \log(\alpha) - \beta \log(f_{k,l}), \quad (16)$$

where the parameters to be determined are $\log(\alpha)$ and β . Figure 3(c) shows a power-law fit to data. For presentation purposes, we have binned the data in the log-frequency domain (bin width is 0.075 log units) and the error bars represent the standard deviation for power-spectrum elements within the bins.

The main question in fitting the power law is how to decide on a range of frequencies to use for determining the fit. For the low frequency limit, we exclude frequencies less than or equal to $3\Delta_f$ because of possible contamination from the direct current component.^{19,21} The high frequency limit is somewhat more involved to find. It is clear from Fig. 3(c) that the linear regime of the PS ends somewhere near 0.5 cyc/mm, where quantum noise begins to dominate the PS. However, the extent of the linear regime varied in the images. This variation is likely due to breast size which has a substantial impact on the x-ray tube current and therefore the magnitude of the quantum noise component of the bCT images. We chose the high-frequency limit by using the frequency between 0.2 and 0.5 cyc/mm that maximized the fit of the line as determined by the R^2 statistic. The same approach was used for bCT images, segmented bCT images, and the limited set of projection mammograms described below.

III. MATERIALS AND METHODS

III.A. Patient selection

All patient studies were conducted under an IRB approved protocol at the authors' institution. Consent was obtained from women with positive mammographic findings (BIRADS 4 or 5), and the breast CT examination was performed prior to core biopsy. Both breasts were scanned for all patients, although for this study only the CT images of the left breast were used to maintain statistical independence between images. Of more than 100 patient scans acquired at the

time of the study, a subset of 44 was chosen on the basis of an artifact free scan and segmented image (see Sec. III C). Of these, one scan was excluded because of a poor power-law fit leaving a total of 43 scans for analysis.

III.B. bCT scans

Patients were scanned on a dedicated cone beam breast CT scanner developed at our institution.^{13,16–21} Subjects were positioned prone on a table-top that allowed a single breast to hang pendant into the field of view of the scanner. For each scan, 500 projection images were obtained at 80 kVp, and these images were acquired around the breast for over 360° coverage (some excess angular coverage was used as a safeguard in the event of patient motion during the scan). The mAs used for each patient depended on the size of the breast and was determined so that the mean glandular dose from a bCT scan was the same as it would be for a two view mammogram^{16,17,22} of the same breast. A PAXSCAN detector (model 4030CB; Varian Medical Systems, Palo Alto, CA) running at 30 frames per second was used in 2 by 2 pixel binning mode (0.388 mm pixels), resulting in projection images with a pixel dimension projected to isocenter of 0.205 mm × 0.205 mm. Breast CT images were reconstructed by filtered backprojection with a Shepp–Logan filter.^{28,29} The resulting CT images, reconstructed in the coronal plane, encompassed 512 pixels × 512 pixels, with a section thickness of 0.21 mm. The pixel dimensions for these images varied from patient to patient (range: 0.23–0.41 mm; average: 0.34 mm) as did the number of section images in a volume, which depended on the size of the breast.

III.C. Breast CT segmentations

Breast CT image segmentation was performed using an algorithm developed specifically for bCT.^{30,31} The algorithm first segments out the breast from the background using a histogram based two-means clustering algorithm. Two con-

FIG. 4. Power spectra for breast CT and corresponding mammogram. A slice from the bCT image (a) is shown with sample patches (squares) from multiple elevations overlaid. A standard projection mammogram of the same breast (b) is shown with sampling region (thick line) and sample patches overlaid. Log-log plots of normalized power spectra (c) are well fit by power-law functions over the range of frequencies dominated by anatomical variability. Power-law exponents (β) differ by approximately 1.

secutive iterative processes are then applied to segment glandular tissue from adipose tissue, both using percent glandularity as a convergence test. In the first iterative process, image noise is reduced by a seven-point 3D median filter. The histogram based two-means clustering algorithm is used to segment glandular and adipose tissue and estimate percent glandularity. In the second iterative process, final adipose segmentation is achieved by iteratively smoothing the adipose tissue with an adaptive smoothing filter that only smooths voxels below a threshold initially determined by the first iterative process. As the last step for the segmentation the skin was marked by scanning from the edges of the image inward.

Breast CT images were segmented into four categories: air (0), adipose tissue (1), glandular tissue (2), and skin (3). This segmentation allowed us to define the breast interior as the segmented voxels with values of 1 or 2.

III.D. Mammograms

For a subset of six patients, mammograms acquired on a film-screen system were available (left breast, CC view). While digital mammograms were acquired for many of the women, these were deemed unsuitable for this analysis since fully digital systems typically implement proprietary and potentially irreversible filtering operations that will alter the underlying anatomical structure of the breast. Film mammograms were digitized on a flatbed scanner using 0.1 mm sampling.

III.E. Region selection

Figure 4 shows examples of how ROIs were determined for a specific case. Power spectra in each condition and case were estimated from 50 ROIs. For the bCT images, coronal ROIs were constrained to a range of sections to avoid including any possible pectoral muscle near the chest wall and to avoid areas that were too small towards the nipple. The range

of sections used was determined manually for each image with an average of 122 sections (ranging from 24 to 200 in different cases). A random rejection method was used to uniformly sample ROIs within an image. In this approach, potential regions were generated over a large rectangular volume covering the area to be used for estimating the PS. Samples from a uniform distribution over this volume were produced from a random number generator. Each potential ROI was evaluated to see if it was completely contained in the breast interior. The check was done using the same ROI in the segmented image and verifying that the ROI was free of any voxels designated as skin (segmented value of 3) or air (segmented value of 0). If this constraint was satisfied, the ROI was used for estimating the PS, otherwise it was rejected and a new independent potential ROI was generated. This process continued until 50 ROIs were found. The rejection method will produce a uniform distribution of ROIs within the constraints on possible locations.

Figure 4(a) shows the spatial distribution of the selected ROIs against the bCT image closest to the chest wall. The ROIs actually come from many elevations, and are projected onto this image for display. ROIs were one section thick and 128 voxels on a side giving them an average physical size of 43.8 mm on a side.

For the mammograms, we followed Burgess' approach of using the interior of the image where compression forced the breast to approximately uniform thickness. For mammograms the regions were 256 by 256 pixels (25.6 mm on a side). We also wanted to avoid pectoral muscle near the chest wall. To accomplish this, we manually determined an irregular region in the interior of the breast that constrained the location of ROIs. A 2D rejection method was used to uniformly sample 50 ROIs within this region. Figure 4(b) shows the distribution of ROIs in the mammogram corresponding to Fig. 4(a). Figure 4(c) shows the radial plots of the two power spectra.

FIG. 5. Power spectra of bCT slices and segmentations. The panel shows a bCT ROI (a) and the corresponding segmentation (b) scaled to equate image intensity. The power spectrum (c) shows relatively close agreement between slices and segmentations up to frequencies around 0.4 cyc/mm.

Figure 5 shows sample ROIs from the bCT and segmented bCT images, along with plots of the spectra. As can be seen in Figs. 5(a) and 5(b) segmented bCT ROIs are taken from the same locations as the bCT images. We have also scaled the segmented image to match the intensity of the bCT image. Recall that the segmented image consisted of classification values for adipose and glandular tissue (assigned values of 1 and 2, respectively). We used the segmented values to determine the median intensity of adipose and glandular tissue across all ROIs from a scan, and then set the intensity voxels classified as 1 to the median of adipose tissue, and the intensity of voxels classified as 2 to the median of glandular tissue. Medians were used in order to be robust to misclassifications of the segmentation.

IV. RESULTS

Our main result is to report power-law exponents for bCT, segmented bCT slices, and a limited set of projection mammograms. We also present data showing the correlation between the bCT exponent and the proportion of glandular tissue in the ROIs as determined from the segmented bCT images. This shows the dependence of bCT exponents on breast density.

IV.A. Power-law exponents

The adaptive fitting procedure described in Sec. II C resulted in generally very good fits of a line in log-log coordinates for bCT images. For the full 44-patient sample, the

TABLE I. Power-Law exponent summary statistics. Sample size, average, and standard deviation are shown for estimates from Burgess *et al.* (Ref. 19) ($N=213$), the full sample ($N=43$), and the subset for which a digitized mammogram was available ($N=6$).

Modality	N	Average exponent	Standard deviation
Mammograms (Burgess <i>et al.</i>)	213	2.83	0.35
bCT Slices	43	1.86	0.38
Segmented bCT Slices	43	2.06	0.32
Mammograms	6	3.01	0.32
bCT Slices	6	1.99	0.33

median R^2 fit statistic was 0.9, and we note that when R^2 values were computed for the binned data [i.e., as plotted in Fig. 5(c)] they typically were above 0.99. However, in one case with a very low proportion of glandular tissue, the fit was quite poor relative to the rest of the cases ($R^2=0.41$), and this case was excluded from the subsequent statistics. On average, the low-frequency limit for fitting was 0.07 cyc/mm (standard deviation 0.01) and the high-frequency limit for fitting ranged from 0.22 to 0.5 cyc/mm with an average value of 0.45 cyc/mm. We note that the median value was 0.49 cyc/mm, and thus the distribution was relatively peaked near the upper limit of the frequency range with only a few cases skewed towards lower frequencies.

We also evaluated the effect of the number of ROIs used to estimate the power-law exponents. For each case, we computed the standard error of the bCT exponent by bootstrapping with 200 resamples per case. The average bootstrap standard error was 0.08, which when compared to the distribution of exponents explained less than 5% of the variance.

Table I summarizes the findings for power-law exponents on the patient samples. For reference, we have included the findings of Burgess *et al.*¹⁹ for projection mammography. For the 43 cases used, bCT slopes ranged from 0.9 to 2.6, with an average value of 1.86 and standard deviation of 0.38. Power-law exponents from segmented bCT images were somewhat higher than the bCT images with an average of 2.06 and standard deviation 0.32. On the subset of cases for which a film mammogram was available, the average bCT exponent was 1.99 and the average mammogram exponent was 3.01. For this subset, the relationship between exponents is very close to the theoretical prediction in Eq. (14).

Figure 6 shows the exponents for mammograms and segmented images as a function of the bCT exponent. We refer to the y axis as the comparison exponent since the plots consist of both segmented bCT exponents and mammography exponents, and they can be visually compared to predictions. For the mammograms, the theoretical prediction put forward in Eq. (14) can be interpreted as $\beta_{\text{mammo}} = \beta_{\text{bCT}} + 1$. For comparison with the segmented CT images, we plot the equivalence line corresponding to the prediction that segmented images have a statistically similar structure, specifically $\beta_{\text{seg}} = \beta_{\text{bCT}}$.

FIG. 6. Comparison of power-law exponents. A scatter plot of fitted exponents (β) show that on average exponents from segmentations are slightly elevated from the equivalence line for bCT exponent, and exponents from the corresponding mammograms are accurately predicted by theory [Eq. 2.14] in this limited sample.

IV.B. Dependence on breast density

Breast density is an important clinical property that can have a substantial influence on the effectiveness of mammography.^{32–34} Figure 7 demonstrates the relationship between breast density and power-law exponent. We plot the power-law exponent for bCT images, segmented bCT images, and the limited set of mammograms as a function of the proportion of glandular tissue in the bCT image samples. We note that the average density, approximately 30%, is consistent with other investigations of bCT.³¹ It is clear that the bCT exponents increase as a function of the glandular fraction. The Pearson correlation between this measure of breast density and the power-law exponent is 0.81 for bCT images and 0.74 for segmented bCT images. The mammogram exponents are too small of a sample to interpret the correlation coefficient.

V. DISCUSSION

V.A. Comparison of exponents

The average exponent for bCT images in our data is in good agreement with the theoretical predication that comes from applying Eq. (14) to Burgess' findings. The 95% confidence interval for the mean bCT exponent is 1.86 ± 0.11 and, hence, these data cannot reject the predicted bCT exponent of 1.83. The theoretical agreement is also very close in the limited set of six projection mammograms available for our cases. In this case, the confidence interval on the difference between the mammography exponent and the corresponding bCT exponent is 1.03 ± 0.26 , which cannot reject the predicted difference of 1. Thus, we find that the power-

FIG. 7. Exponents and breast density. Power-law exponents for bCT, segmented bCT, and mammographic images are plotted against the fraction of glandular tissue in the ROIs for 43 patients. Both bCT and segmented bCT images show a clear association between density and exponent (Pearson correlation coefficients are 0.81 for bCT and 0.74 for segmented bCT).

law exponent relationship is robust across different levels of breast compression, photon energies, ROI sizes, and spatial frequency ranges used for fitting. The accuracy and robustness of the prediction add further evidence to the idea put forward in Burgess' paper that the power-law spectra relates to a fundamental property of breast tissue that is captured in clinical images.

The implicit prediction of the segmented bCT images was that they should have the same exponent as the nonsegmented bCT slices. While the two exponents are clearly correlated with a Pearson correlation coefficient of 0.84, the difference in average values between them is significant ($p < 0.0001$, $df=42$, paired comparison t -test). Two possible explanations for this difference may apply. The first is that the difference between the exponents reflects some limitation in the accuracy of the segmentation algorithm. It is possible that our segmentation algorithm overclassifies glandular regions, thereby producing a segmented bCT image that is more "dense" than the original, and this would suggest a slightly increased exponent according to Fig. 7. A second possibility is that the bCT images may be violating the assumption of uniform attenuation within glandular and adipose regions. Subtle nonuniformities from calcifications, Cooper's ligaments, or blood vessels might also be affecting the power-law exponent. Further experimental work is needed to resolve these issues.

V.B. Implications for lesion detection

Burgess *et al.* have shown that power-law exponents have a strong and predictable impact on lesion detection in mam-

mograms and in computer-generated Gaussian textures as well.^{19,21} Using the generic parameters reported by Burgess *et al.*¹⁹ (see Fig. 10 of that work), the effect of an exponent going from 3 to 2 leads to approximately a 40% reduction (from 5 to 3 mm) in the diameter of a lesion at detection threshold. Thus, the reduction in the power law exponent found in bCT images predicts superior lesion detection potential for bCT images relative to mammography.

However, Burgess analysis is somewhat more complicated for breast CT. A fundamental assumption of Burgess' contrast-detail diagrams is that lesion contrast increases with lesion diameter. This is true for projection mammography where lesion contrast is based on integrated attenuation, and hence, is dependent on diameter. In breast CT slices, we would not expect the attenuation coefficients within the lesion to change with lesion size. However, this limitation may be offset by the fact that a larger lesion will be seen on multiple CT images. A more general measure of integrated lesion signal is needed to resolve this issue for breast CT. We anticipate exploring this approach and lesion detectability in general in future work.

It should also be noted that these observations are only applicable to mass lesions, which have spectral energy concentrated at much lower spatial frequencies than microcalcifications. Due to the elimination of higher spatial frequencies in the current analysis (where quantum noise dominates the PS), conclusions in regards to microcalcifications are not addressed in this study.

V.C. Limitations of the study

The analyses presented here rest on a number of assumptions. The description of anatomical variability by a power spectrum derived from a stationary process is itself an approximation.³⁵ There are clear departures from this assumption in the breast CT data. For example, in many of the images of larger breasts there is a border region between the skin and the breast interior that is composed almost entirely adipose tissue.³⁶ Another example is that the bCT images tend to become more glandular as the CT slice approaches the nipple region.³¹ However, the use of randomly chosen subregions masks this issue to some extent since the ROIs lose their gross reference to the breast, and thereby induce more stationarity than is likely present in the breast itself. A second limitation is the use of a second order statistic—such as the PS—to characterize anatomical variability. Higher order moments such as excess kurtosis are certainly present in the bCT slices, and have been reported recently.³⁶ The investigation presented here also does not include the scaling parameter of the power law, which will likely have an impact on diagnostic accuracy as well.

Thus, the current study represents a starting point for analysis of breast structure in 3D x-ray images. We anticipate future studies focusing on specific regions of the breast and exploring other parameters or higher order moments. For the purposes here, where we seek to demonstrate a relationship between the exponents of bCT images and mammograms, a stationary second-order analysis appears to suffice.

VI. CONCLUSIONS

We find that the PS of anatomical variability in bCT sections is well modeled by a power law for spatial frequencies up to approximately 0.45 cyc/mm. A rigorous and somewhat idealized derivation suggests that the exponent of this power should be one less than the exponent derived from a projection modality such as x-ray mammography. Our study of 43 patients appears to corroborate this relationship by comparison with Burgess' seminal work on this topic using clinical mammograms.¹⁹ We find the average power-law exponent is 1.86 (standard deviation 0.38), which is compared to the prediction of 1.83 from Burgess' work. The difference between the two is not significant and reflects good agreement considering that the data comes from an independent set of patients and different image-acquisition conditions as well. In the six cases where we have both a bCT scan and a (digitized) film-screen mammogram available, the relationship between exponents holds very well on average (average $\beta_{\text{bCT}} = 1.99$; average $\beta_{\text{Mammo}} - 1 = 2.01$).

We have also evaluated segmented bCT images as a way to determine the extent to which our findings can be explained as consequences of a binary texture, and for investigating the effect of breast density. The average power-law exponent derived from segmented slices is somewhat higher (2.06) than the bCT average (1.86). This 9.7% difference suggests the possibility that bCT images are capturing some variability of breast attenuation coefficients within adipose and glandular regions. However, we cannot yet rule out the possibility that there is spatial frequency dependence in the segmentation algorithm. The high Pearson correlation between bCT and segmented bCT exponents ($\rho = 0.84$) suggests that the patient-to-patient variability in this fundamental descriptor is well captured by the segmented images. Using the segmentation to define glandular and adipose tissue, we find a strong positive association between breast density (proportion of glandular tissue) and the power-law exponent ($\rho = 0.81$).

The results of Burgess *et al.*¹⁹ investigating detection thresholds in power-law noise show that the exponent is a critical factor for determining detection thresholds for lesions of different sizes. Of significance to this study is the prediction that a lower value of the exponent (β) leads to cancer detection at smaller lesion sizes, although this interpretation is based on the physical assumption that contrast increases with lesion size. In bCT images, the contrast will not likely increase as a lesion grows, but rather the lesion will spread over multiple adjacent images. While not a substitute for observer-performance studies, this finding is nonetheless encouraging in regards to the potential of dedicated high-resolution CT scanners for breast cancer screening and diagnosis.

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