Digital Breast Tomosynthesis Parenchymal Texture Analysis for Breast Cancer Risk Estimation: A Preliminary Study

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Abstract. Studies with mammograms have demonstrated a relationship between parenchymal texture and breast cancer risk. Although promising, texture analysis in mammograms is limited by the effect of tissue superimposition. Digital Breast Tomosynthesis (DBT) is a novel tomographic x-ray breast imaging modality that alleviates the effect of tissue superimposition. We explore the potential advantages of DBT texture analysis for breast cancer risk estimation. We analyzed bilateral DBT and DM images from 39 women, and compared the performance of the computed texture features in (i) reflecting characteristic parenchymal properties, and (ii) correlating to mammographic breast density, an established surrogate of breast cancer risk. Strong texture correlation was observed between contralateral and ipsilateral breasts, indicating that parenchymal properties are potentially inherent to an individual woman. Compared to DM, DBT texture features demonstrated a stronger correlation with breast density. Although preliminary, our results show that DBT texture analysis could potentially improve breast cancer risk estimation.

Keywords. Digital breast tomosynthesis, digital mammography, parenchymal pattern analysis, breast cancer risk estimation.

1 Introduction

Growing evidence suggests that mammographic breast density is an independent risk factor for breast cancer [1]. While the relationship between mammographic breast density and breast cancer risk has been clearly demonstrated [1], studies have also shown that a potential relationship exists between mammographic parenchymal texture and the risk of breast cancer [2, 3]. Computerized analysis of digitized mammograms has shown the potential to distinguish the parenchymal patterns of BRCA1/2

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gene mutation carriers using parenchymal texture features particularly from the retroareolar breast region [2, 3]. These studies suggest that computer-extracted texture features could provide fully-automated, objective and reproducible methods to identify parenchymal patterns that are associated with increased levels of risk.

Mammograms, however, are projection images in which the breast tissue layers are superimposed. For this reason, mammographic texture features reflect mixed properties of superficial skin and subcutaneous tissue overlapping deeper fibro-glandular (*i.e.,* dense) and fatty (*i.e.,* non-dense) tissues. Knowing that the risk of breast cancer is mainly associated with properties of the fibro-glandular tissue (*i.e.,* breast density), superficial layers of skin or subcutaneous fat could be considered irrelevant to cancer risk estimation, and therefore reduce the predictive value of the computed texture features. To overcome these limitations of mammography, tomographic breast imaging could offer the ability to selectively analyze the fibro-glandular tissue texture, and ultimately provide more accurate measures to estimate risk.

Digital breast tomosynthesis (DBT) is a novel 3D x-ray imaging modality in which tomographic images of the breast are reconstructed from multiple low-dose x-ray source projection images acquired at different angles of the x-ray tube [4] (Fig. 1). By filtering out adjacent anatomical structures, DBT alleviates the effect of tissue superimposition and offers the ability to selectively analyze the texture of characteristic fibro-glandular tissue regions (Fig. 2). Our long-term hypothesis is that DBT will provide more relevant measures to characterize the fibro-glandular texture, in comparison to mammography, and therefore ultimately yield more accurate measures of risk.

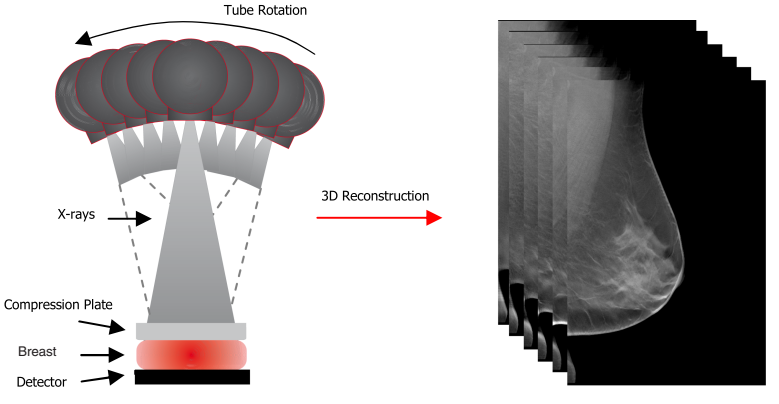

Fig. 1. An example of DBT acquisition geometry with rotation of the x-ray tube

In this paper, we explore the potential advantages of DBT texture analysis for breast cancer risk estimation. We compare the performance of DBT and digital mammography (DM) texture features in (i) reflecting characteristic parenchymal properties, and (ii) correlating to mammographic breast density, an established surrogate of breast cancer risk. Although preliminary, our study intends to offer instrumental evidence for the design of larger clinical studies on DBT texture analysis for breast cancer risk estimation.

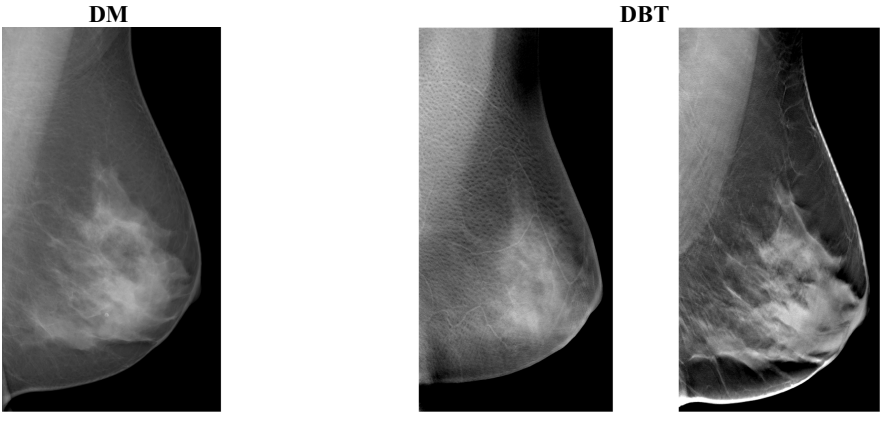

Fig. 2. Differences in parenchymal texture in (a) a DM and (b-c) the DBT tomographic slices for the same breast: (b) the superficial skin layer and (c) a deeper fibro-glandular tissue layer

2 Methods

We analyzed DBT and DM images from 39 women with recently detected abnormalities and/or previously diagnosed breast cancer (age range 31-80 yrs, mean age 51.4 yrs, normal distribution Lilliefors test, at α=0.05). The images were retrospectively collected under IRB approval and HIPAA regulations from a breast imaging clinical trial at the Radiology Department of the University of Pennsylvania. DBT and DM acquisition was performed on the same day with a GE Senographe 2000D (General Electric Medical Systems, Milwaukee, WI) FFDM system modified to allow positioning of the x-ray tube at 9 locations by varying the angle from -25^o to +25^o with increments of 6.25^o. The breast was compressed in an MLO position and the source projection images were acquired with spatial resolution of 0.1mm/pixel. Filtered-backprojection was used to reconstruct DBT tomographic planes in 1mm increments with 0.22mm in-plane resolution. Retroareolar (2.5 cm)^3 regions of interest (ROIs) were manually segmented from the DBT reconstructed images; corresponding (2.5 cm)^2 ROIs were segmented from the *Premium View*™ DM images. Figure 3 shows examples of such ROIs from our study population.

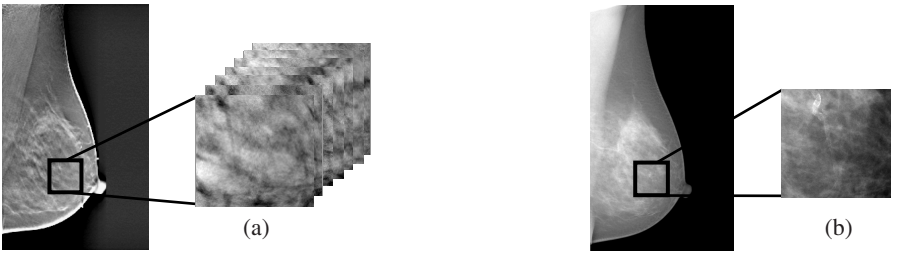

Fig. 3. An example of (a) a 3D ROI segmented from a reconstructed DBT image and (b) the corresponding 2D ROI from the DM of the same breast

We computed texture features that have been shown in previous studies with mammograms to distinguish the parenchymal patterns of women at different risk levels [2, 3]. For DBT texture analysis, we implemented a 3D extension of the texture descriptors, similarly to Chen *et al.* [5], in which a 3D neighborhood of voxels was considered, rather than a 2D neighborhood of pixels, when computing gray-level texture statistics. Grey-level quantization was also implemented to optimize the computation [6].

Skewness was computed as the third moment of the gray-level histogram

$$skewness = \frac{w_3}{w_2^{3/2}}, \quad w_k = \sum_{i=0}^{g_{\max}} n_i (i - \bar{i})^k / N, \quad N = \sum_{i=0}^{g_{\max}} n_i, \text{ and } \bar{i} = \sum_{i=0}^{g_{\max}} (i n_i / N),$$

where n_i represents the number of times that gray level value i takes place in the ROI volume, g_{max} is the maximum gray-level value and N is the total number of voxels.

Coarseness is a texture feature that reflects the local variation in image intensity and is based on the Neighborhood Gray Tone Difference Matrix (NGTDM) [7]:

$$coarseness = \left(\sum_{i=0}^{g_{\max}} p_i v(i) \right)^{-1}, \text{ where } v(i) = \begin{cases} \sum | i - \bar{L}_i | \; for \; i \in \{n_i\} \; if \; n_i \neq 0 \\ 0 \quad otherwise \end{cases},$$

and g_{max} is the maximum gray-level value, p_i is the probability of gray level i to take place, and $v(i)$ is the 3D NGTDM. For computing $v(i)$, $\{n_i\}$ is the set of pixels having gray level value equal to i, and $\bar{L}_i$ is computed as

$$\bar{L}_i = \frac{1}{S-1} \sum_{k=-t}^{t} \sum_{l=-t}^{t} \sum_{q=-t}^{t} j(x+k, y+l, z+q)$$

where $j(x,y,z)$ is the voxel located at (x,y,z) with gray level value i, $(k,l,z) \neq (0,0,0)$ and $S=(2d+1)^3$ with d specifying the 3D voxel window around (x,y,z).

Contrast and **Energy** require the computation of a gray-level co-occurrence matrix [8],

$$contrast = \sum_{i}^{g} \sum_{j}^{g} |i - j|^2 C(i,j), \text{ and } energy = \sum_{i}^{g} \sum_{j}^{g} C(i,j),$$

where g is the total number of different gray levels and C is the normalized co-occurrence matrix defined by a voxel displacement $d = (dx, dy, dz)$ along x, y, and z dimensions [5] .

Mammographic breast percent density (PD) was also estimated for all women in our study population, as a measure of their individual risk [1], using *Cumulus* (Ver. 4.0 2006, University of Toronto), the widely validated software for breast percent density estimation [1]. PD was estimated as the percentage of the total breast region occupied by fibro-glandular (*i.e.,* dense) tissue.

To evaluate the degree to which parenchymal texture is inherent in an individual woman, the Pearson correlation coefficient ρ was computed between the texture features of the contralateral and ipsilateral breasts. To investigate the potential value of texture features for breast cancer risk estimation, the correlation ρ was estimated

between the parenchymal texture features and the corresponding PD estimates. To further examine differences in texture patterns between groups of women at different risk levels, linear regression was performed to model the association between increasing breast PD and parenchymal texture features; corresponding regression beta *b* coefficients and R^2 were estimated.

3 Results

Strong texture correlation was detected between the contralateral and ipsilateral breast of each woman for both DBT and DM ($p \leq 0.05$); overall the DBT correlations were stronger (Table 1). When investigating the correlation between texture features and PD, DBT demonstrated higher and statistically significant correlations ($p \leq 0.05$), for coarseness, contrast and energy (Table 1). Figure 4 shows representative scatter-plots of parenchymal features versus the corresponding breast PD estimates. Figure 5 shows representative box-plots of the texture feature distributions within the groups of increasing breast PD. Fitted regression lines are shown with corresponding regression beta *b* coefficients and R^2 estimates. In general, the association between breast density and texture features was stronger for DBT than for DM, as evidenced by fitted regression lines with steeper slopes and more strongly significant *p*-values.

Table 1. Pearson correlation coefficient (ρ) between texture features from contralateral and ipsilateral breasts (* for $p \leq 0.05$, ** for $p \leq 0.01$)

	Pearson correlation coefficient (ρ)			
	Contralateral vs. Ipsilateral		**Texture vs. Breast Percent Density**	
	DBT	**DM**	**DBT**	**DM**
Skewness	0.58 **	0.55 **	0.18	-0.18
Coarseness	0.47 **	0.59 **	0.46 **	0.15
Contrast	0.80 **	0.77 **	-0.31 *	-0.25
Energy	0.88 **	0.64 **	-0.36 *	-0.29

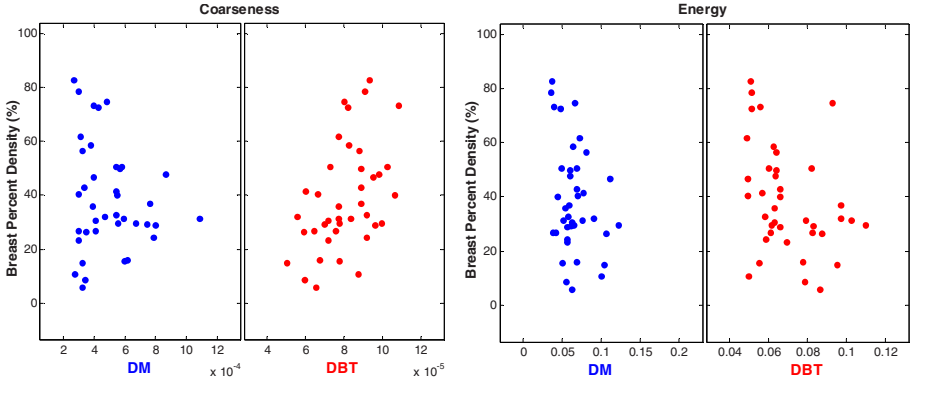

Fig. 4. Scatter-plots of the texture features versus breast percent density estimates for digital-mammography (DM) and digital breast tomosynthesis (DBT)

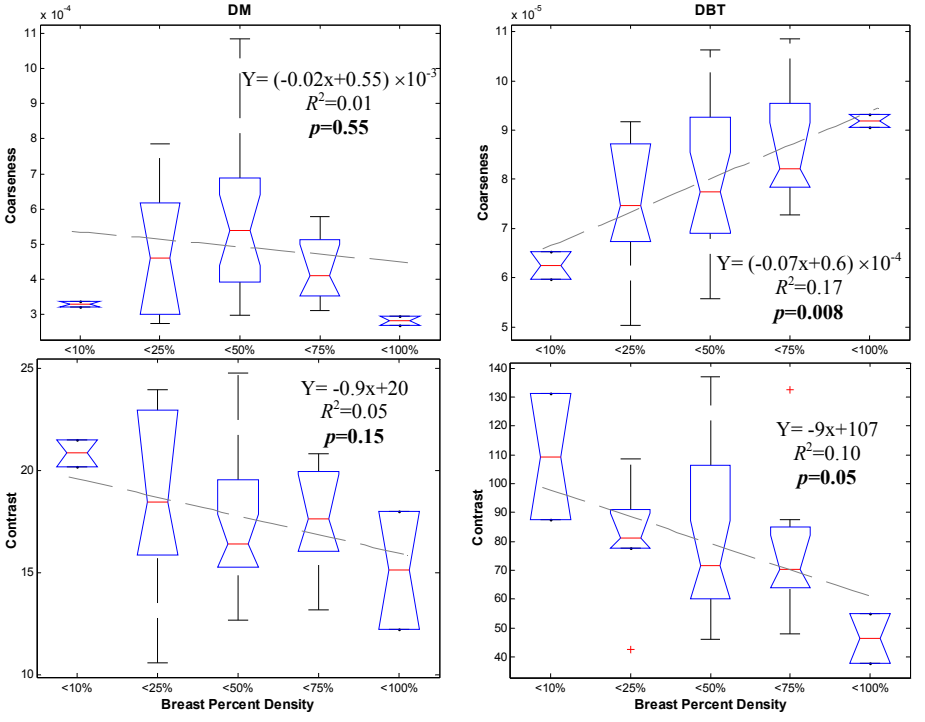

Fig. 5. Box-plots with fitted regression lines for coarseness and contrast features versus five groups of increasing breast percent density (<10%, 10 to <25%, 25 to <50%, 50 to <75%, and ≥75%)

4 Discussion

The strong texture correlation between a woman's breasts indicates that characteristic parenchymal properties are inherent to an individual woman. This is an essential assumption for breast cancer risk estimation: the increasingly supported hypothesis is that inherent biological factors associated with breast cancer risk are expressed in a woman's parenchymal tissue and subsequently manifested in her mammographic parenchymal patterns [9]. The strong texture correlation between contralateral and ipsilateral breasts indicates that texture of the unaffected breast could be used as a surrogate of risk.

Our analyses also suggest a potential association between parenchymal texture features and breast density, one of the strongest factors associated with breast cancer risk [1]. Our findings are consistent with previous studies on mammograms. We observed a positive correlation between coarseness and breast percent density; Huo, Li, et al. have reported that BRCA1/2 gene mutation carriers, a population known to be at very high risk, appear to have coarser mammographic texture patterns with increasing breast density [2, 3]. We also observed that contrast and energy appear to have a negative correlation with breast density; these results also agree with the previous

reports of Huo and Li [2, 3], who showed that high-risk women had mammographic texture patterns with lower contrast.

Our results demonstrate the potential of DBT to provide more discriminative measures to characterize the fibro-glandular texture, in comparison to DM, as evidenced by the detected stronger association between DBT texture features and breast density. DBT offers the ability to perform spatially localized analysis of parenchymal patterns within characteristic areas of the breast volume, such as the retroareolar breast region, which has been shown to be particularly discriminative for breast cancer risk assessment [2, 3]. By excluding irrelevant breast tissue layers such as the skin and the subcutaneous fat, DBT offers the ability to selectively analyze the fibro-glandular texture and potentially yield more accurate measures for breast cancer risk estimation.

To date, mammographic breast density has been used as the main radiographic marker of risk [1]. Previous studies have shown the potential to increase the accuracy of the current epidemiological breast cancer risk estimation models by including breast density descriptors [10, 11]; nevertheless, these improvements have been minimal, mostly due to the subjective nature of breast density estimation [12, 13]. DBT texture descriptors could provide fully-automated, objective, and reproducible methods to characterize breast density patterns, and ultimately provide more reliable measures of risk.

To the best of our knowledge our study represents the first report on parenchymal texture analysis in DBT, with the intention to offer instrumental evidence for the design of larger clinical studies. Although preliminary, our results suggest a potential advantage of DBT texture analysis for breast cancer risk estimation. The improved performance and low cost of DBT will likely fuel the rapid and broad dissemination of DBT as a breast cancer screening modality [4], making available larger datasets for analysis. Our ultimate goal is to develop DBT Computer-Assisted Risk Estimation (CARe) methods for improving breast cancer estimation in clinical practice.

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