Correlation of 3D MR-Based Percent Breast Density with Apparent Diffusion Coefficient of the Breast Fibroglandular Tissue

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Background and Purpose: Mammographic density is a strong risk factor for breast cancer. Mammographically dense areas of the breast differ histologically from non-dense areas, reflected in greater proportions of stroma and/or epithelium and lesser proportions of fat in the dense compared to non-dense breast tissue [1, 2]. Within the stroma are numerous systems that are all capable of modulating epithelial function. It is noted the epithelial-stromal interactions play a crucial role in cancer initiation, progression, and invasion. Mammographically dense tissues are also associated with increased collagen-1 deposition in the stromal tissue. A higher collagen levels in the mammary gland increase tumor formation and invasive behavior. Studies of both epithelial and stromal components thus are important in understanding the association between mammographic density and breast cancer risk. Characterization of breast density by mammography has several limitations, and the uses of breast density in risk prediction and breast cancer prevention may be improved by other methods of imaging, such as magnetic resonance imaging (MRI). The aims of this study were to investigate the association of 3D MR-based breast density with apparent diffusion coefficient (ADC) acquired from diffusion weighted imaging (DWI). Epidemiological studies have noted that women with higher breast density, i.e., Asian women, do not necessarily have higher breast cancer risk than Western women. Thus the clinical question to be addressed is whether women with higher breast density will have higher macromolecular stromal tissue, which can be assessed using ADC.

Materials and Methods: MR images from 47 women (mean age 49, range 32-79) diagnosed with unilateral breast cancer were retrospectively reviewed. With the exclusion of 9 women due to issues of imaging quality, eventually 38 subjects were studied. In this study, only the contralateral normal breast was analyzed. MR imaging was acquired with a dedicated 7-channel breast coil at a 3.0T MR scanner. The non-enhance T1-weighted images (spin echo axial, TR/TE; 620/10 msec, matrix 332 x 332, field of view 200x340 mm, slice thickness 3 mm, and gap 1 mm), used for segmentation of breast and fibroglandular tissue, and quantification of breast density, and DWI (TR/TE 1864/77 msec, FA 90 degrees, matrix 128x127, field of view 350x350, and b-factor 1000), used for ADC quantification, were analyzed. The MR density measurement was based on our well-established template-based automatic segmentation method [3]. With the method, the chest body region on a middle slice was used as the template. Within the chest template, an initial V-shape cut using three body landmarks (thoracic spine and bilateral boundary of the pectoralis muscle) was performed to determine the posterior lateral boundary of the breast. The chest template was mapped to each subject's image space to obtain a subject-specific chest model for exclusion. The chest and muscle boundaries determined on the middle slice were used as a reference for the segmentation of adjacent slices, and the process continued until all 3D slices were segmented. The segmentation of fibroglandular tissue and fatty tissue was based on N3+FCM algorithm [3]. Percent breast density (PD) was defined as the ratio of the fibroglandular tissue volume over the breast volume. Using SPM package in Matlab (Mathworks, Natick, MA), all ADC maps were coregistered to respective T1W images by affine transformation and normalized mutual information to have the same voxel-size as that of T1W. ADC values below 100 (considered as noise or that of fatty tissue) and above 3200 (that approaching that of 'free-water') were filtered out.

Results: Figure 1 was a 34 y/o woman with left breast cancer -- left upper: T1WI, left lower: DWI, right upper: segmented image, and right lower: co-registration image. The percent density measured in the right breast was 36.4%. The mean ADC was 1821 (x10^{-6}mm^2/sec). The cut-off value for the top 90% pixels of ADC was 2344 (x10^{-6}mm^2/sec). **Figure 2** contained two cases showing the histogram distribution of ADC values for all pixels of the fibroglandular tissue in a 45 y/o woman with higher breast density (upper panel, PD=47.6%) vs. a 58 y/o woman with lower breast density (lower panel, PD=3.5%). It was clear that the subject with lower PD had lower ADC distribution and the mean/median ADC values were also lower than the subject with higher PD. The mean ADC were 1795 and 724 (x10^{-6}mm^2/sec), and the cut-off values for the top 90% pixels of ADC were 2262 and 1204 (x10^{-6}mm^2/sec) respectively. For the whole study, overall, the mean ADC measured from the whole fibroglandular tissue pixels, the cut-off ADC values for the top 90% and the lowest 10% pixels were positively correlated with the PD (r=0.70, r=0.50, and r=0.79 respectively) (**Figure 3**).

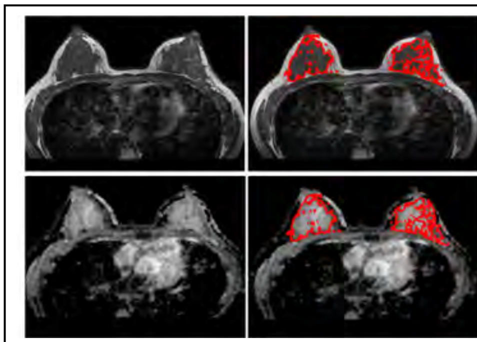

Figure 1

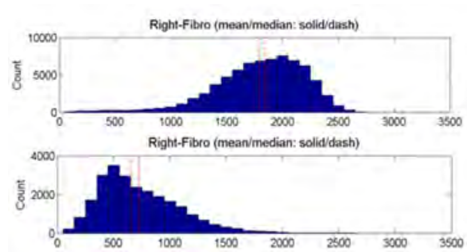

Figure 2

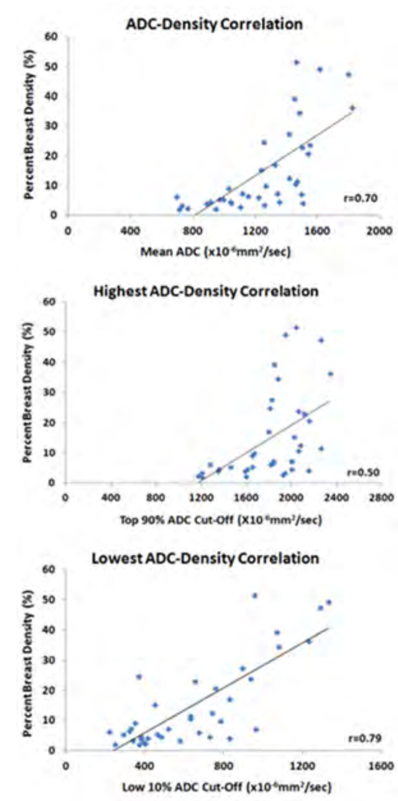

Figure 3

Conclusion: The results from our study noted a positive correlation of ADC values with MR-measured PD. Our results were consistent with histological findings [1] that the differences in tissue proportions were greater for stroma than for epithelium (46.1% vs. 4.8%) comparing dense and non-dense tissue. This study proved that women with higher breast density had higher stromal tissue, which can be assessed using ADC. The significance of the more freedom of water protons motion in the extracellular matrix-rich microenvironment related to carcinogenesis in women with higher PD should be further investigated.

References: 1. Ghosh K. Breast Cancer Res Treat. 2012 Jan;131(1):267-75. ; 2. Lin SJ. Breast Cancer Res Treat. 2011 Jul;128(2):505-16. ; 3. Lin M. Med Phys. 2013 ;40(12):122301.

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