Comparison of Breast Density in the Contralateral Normal Breast of Patients with Different Types of Breast Cancer Measured on MRI

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Background and Purpose

Many studies have shown that mammographic density is associated with the risk of breast cancer (1). The association is slightly weaker for DCIS than for invasive breast cancer (2). This raises a curious question about the differential cancer risk between patients who have different types of cancer that may be associated with breast density. In this study we investigated the breast density in 4 groups of patients, invasive ductal cancer (IDC), ductal carcinoma in situ (DCIS), and estrogen receptor (ER) positive and negative cancer. Risk factors for ER-positive and ER-negative breast cancers are known to be different. Postmenopausal hormonal replacement therapy is associated with an increased risk of developing an ER-positive tumor (3). If estrogen is associated with an increased risk of ER positive breast cancer, and also associated with breast density, it may be possible to find a higher density in patients who develop ER-positive cancer than ER-negative cancer. The evaluation of breast density based on mammogram may not accurately analyze the density due to projection imaging thus the tissue-overlapping problem. MRI, however, provides strong soft tissue contrast distinguishing between fibroglandular and fatty tissues and a 3-dimensional view of breast tissues without compression. We have developed a comprehensive method to analyze breast density based on MRI. In this study we measured breast density in patients with IDC and DCIS, also between patients with ER-positive and ER-negative cancer and compared the results to investigate whether they show significant differences.

Materials and Methods

Totally 141 pathologically proven patients, including 100 subjects of invasive cancer and 41 subjects of DCIS, were included in the IDC-DCIS group. 80 (45 ER positive and 35 ER negative) out of the 100 IDC subjects were studied in the ER group. The breast density was measured from the contra-lateral normal breast of each subject, assuming symmetric bilateral breast density. In this study we used 3D MR-based method for measurement of breast density. All MR studies were performed at a 1.5 T scanner. Non-contrast-enhanced 3D SPGR (RF-FAST) T1 weighted imaging without fat suppression (TR= 8.1 ms, TE= 4.0 ms, flip angle=20°, slice thickness = 3-4 mm) were used for calculation of the breast density. After segmenting the breast the total breast volume is calculated. For fibroglandular tissue segmentation, the adaptive FCM was applied for bias field correction to remove image intensity non-uniformity, and for segmentation of the fibroglandular tissue from the surrounding fatty tissue. The breast density is defined as the ratio of the volume of the fibroglandular tissue over that of the whole breast. Since breast density is known to be age-dependent, the age information f all patients were obtained and used as a control variable in the analysis.

Results

Figure 1 shows 4 case examples in patients with IDC and DCIS, and ER+ and ER- breast cancer. The mean age was 53 years old in the invasive cancer group and 58 years old in the DCIS patients group. Overall, the measured breast density did not show significant difference between the two groups of patients (10.9 ± 8.4% for invasive cancer group vs. 10.4 ± 6.2% for the DCIS group, P = 0.73) (**Table 1**). The mean age was 54 years old in the ER-positive group, and 47 years old in the ER-negative group (significantly younger, P< 0.005). In the ER-positive group, 20 patients were ≥ 55 y/o and 25 were < 55 y/o. Overall, the measured breast density did not show significant difference between the ER +/- patient groups (9.9 ± 7.2% for ER-positive group vs. 12.6 ± 8.9% for the ER-negative group, P = 0.14) (**Table 1**). **Figures 2** show the scattered plot between the % breast density and the age for the 4 groups of patients. Visually it was also noted that there were no obvious differences among patients with different cancer types. However, the age dependence was clearly noted, higher density with younger age. A logistic model was applied to analyze the difference in density, controlling for age, and the results show no significant difference between IDC vs. DCIS, or ER +/- cancers.

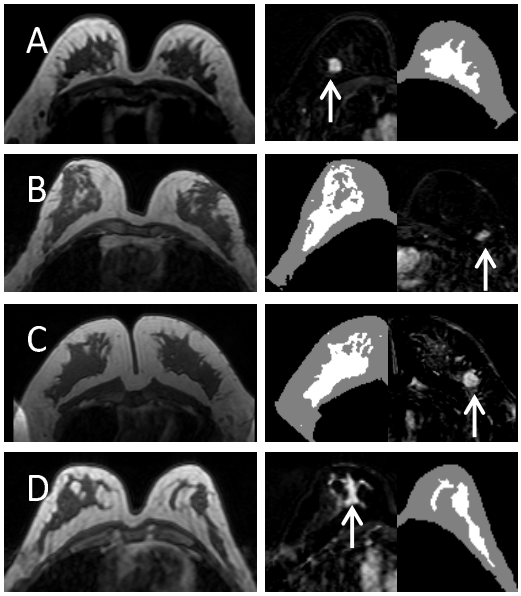

Figure 1. A: 50 y/o with IDC; B: 50 y/o with DCIS; C: 41 y/o with ER+ cancer; D:50 y/o with ER- cancer. IDC, DCIS, and ER+ cancer are mass lesions, and ER- cancer is a non-mass lesion, indicated by arrows. The segmented fibroglandular density is shown for the normal breast. The measured breast densities in the contralateral breast were 17.3%, 16% ,12% and 11.9%, respectively.

Table 1. Breast volume and density in 4 patient groups

	Volume (cm^3)	Density (%)
Invasive breast cancer (N= 100)	**807 ± 352**	**10.9 ± 8.4%**
Ductal carcinoma in situ (N= 41)	**861 ± 311**	**10.4 ± 6.2%**
ER-positive cancer (N= 45)	**791 ± 373**	**9.9 ± 7.2%**
ER-negative cancer (N= 35)	**787 ± 320**	**12.6 ± 8.9%**

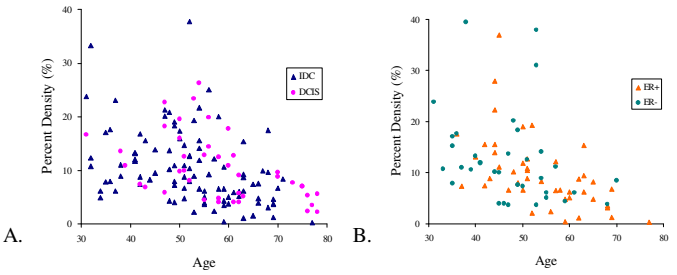

Figure 2. Scatter-plot of percent breast density vs. age in patients with IDC and DCIS (A) and with ER+ and ER- breast cancer (B). A clear age-dependence is noted, but not between different cancer types.

Discussion

In this study, the overall comparison between IDC and DCIS did not showed any significant difference in the breast density. Our results suggest that although literature has showed that both invasive cancer and DCIS are related to density, density alone might not predict differential risk for patients who will develop IDC vs. DCIS. Our results also did not show significant differences in density between ER-positive and ER-negative patients suggesting that the link between breast density and breast cancer may be due to factors other than or in addition to estrogen exposure.

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References **1.** Boyd NF, et al. N Engl J Med. 2007 Jan 18;356(3):227-36. **2.** Gill JK, et al. Breast Cancer Research 2006; 8(3):R30. Epub 2006 Jun 23. **3.** Ziv E, et al. Cancer Epidemiol Biomarkers Prev 2004;13(12):2090–5.