

## Comparison of Fibroglandular Tissue Density Evaluated by MRI in Three Different Racial Groups

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### Purpose

Higher breast density has been reported to be associated with increased breast cancer risk. Most published studies in the literature reported mammographic density (that is, density measured on mammogram). Since mammography takes projection image, several factors may lead to different images thus variable results in the measurement of density. These factors include the level of breast compression, the projection angle and the position of the breast, and x-ray intensity. Breast MRI takes a three-dimensional view of the breast without compression, and provides superior soft tissue contrast differentiating between fibroglandular and fatty tissues. Therefore, compared to mammography it may provide a more precise method for density measurements. To date only a few studies have investigated breast density measurements using MRI, mainly reporting methodological development using a small number of selected subjects. So far no study has reported the measurement of breast density using MRI-based method from a large cohort of consecutive patients. We have published a method that utilized computer algorithms based on body landmarks of each individual woman and fuzzy-c-means clustering segmentation to quantitatively measure the fibroglandular density in the whole breast [1]. In the last ISMRM meeting we presented preliminary results from a cohort of 168 patients [2]. In this study, we expanded the case number to 321. With the large dataset we could further evaluate the age- and race-dependence among three racial background (Caucasians, Hispanics, and Asians) using a logistic regression model. Since breast density is known to be age-dependent, age was controlled in the analysis. The Asian women were reported to have denser breasts compared to others, and in this study we evaluated the breast volume, the fibroglandular tissue volume and the calculated percentage, to further understand the origin of the finding.

### Methods

A total of 321 consecutive patients with confirmed age and race information were included in this study. The cases were selected from our breast MRI research database, including patients with suspicious lesions referred for diagnosis and patients with biopsy-confirmed lesions referred for pre-treatment staging. The pathology reports were reviewed to make sure that the contralateral breast did not have any abnormal findings, and only the normal breast was analyzed. The patients were separated into three age groups: <45 (N=77), 45 to 55 (N=97), and > 55 y/o (N=147); and three race groups: White (N=180), Asian (N=71), and Hispanic (N=70). The mean age was 54 in White, 55 in Hispanic, and 52 in Asian. The breast and fibroglandular tissue regions were segmented using our previously published method [1]. Fig.1 shows the segmentation results from three case examples with different parenchymal patterns: (a) fatty breast, (b) with mixed fatty and fibroglandular tissues, (c) with centrally confined fibroglandular tissue surrounded by fat. The segmented breast and fibroglandular tissue on each slice were combined, and the total breast volume and the total fibroglandular tissue volume were calculated. To understand whether the breast density difference was related to age, race, or breast volume, multivariate linear regression analyses were performed with adjustment for these covariates. All variables were transformed to normally distribute for significance test using ANOVA.

### Results

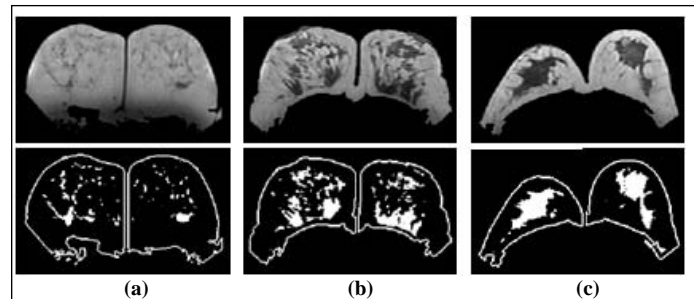
Fig.2 showed the distributions of the mean fibroglandular tissue volume and mean percentage density among the three age groups in White, Asian and Hispanic women. It demonstrates a strong age-dependence relationship. In all 3 racial groups, both fibroglandular tissue volume and the percent density decreased significantly with age. Regarding the racial difference, while the fibroglandular tissue volume did not show obvious difference among 3 groups (Fig.2a), the Asian was noted to have much higher percent density (Fig.2b). The mean density was 15.1% in the Asian women, and the White and Hispanic women had the similar density of 11.6% and 11.5% respectively, significantly higher in the Asian group ( $p = 0.003$ ). To further understand whether the higher density in the Asian women was related to younger age (52 vs.54 (White) and 55 (Hispanic)), or smaller breast volume, three multivariate linear regression analyses were performed with unadjusted, age-adjusted, and age and breast volume-adjusted. The results are summarized in Table 1. After adjusting for age, the estimated percent density decreased from 15.1% to 14.6% in the Asian women, which was still significantly higher than that in the White women (11.9%) and the Hispanic women (11.4%) with  $p = 0.01$ . However, after further adjustment for differences in breast volume, there was no significant difference in mean transformed percent density among racial groups ( $p = 0.25$ ).

### Discussion

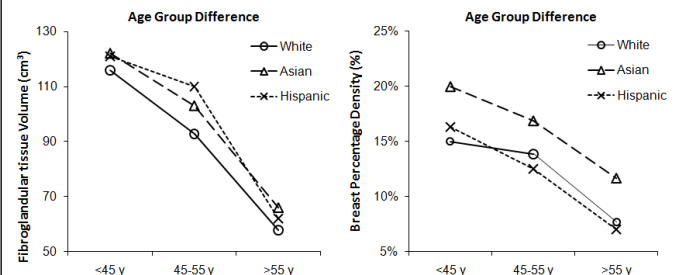
This study measures the breast density in the whole breast based on 3D MRI, and to further investigate the age- and race-dependence in a large cohort of 321 consecutive patients. The fibroglandular tissue volume and the percent density showed a strong age-dependence. On average, the Asian women had higher percent density compared to the White and Hispanic women, but the differences were found to come from the smaller breast volume in the Asian women containing comparable fibroglandular tissue volume. Our age- and race-dependence results were consistent with larger series analyzed based on mammography, supporting that the breast density analyzed based on MRI may provide a feasible quantitative analysis method. With the small measurement variation using MRI-based method [1], this may provide a means to evaluate the small changes after therapy, which cannot be reliably measured by mammography. Given the established relationship between the increased and decreased breast density with increased and decreased breast cancer risk, the density measured on MRI may be applied to evaluate the change of risk after drug interventions (such as hormonal replacement therapy and chemoprevention).

**References:** [1] Nie et al. 2008 ISMRM proceedings, program #3163, or Med Phys. 2008 (in press). [2] Nie et al. 2008 ISMRM proceedings, program #3752.

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**Fig. 1** Three case examples of fibroglandular tissue segmentation results. In (a) the total breast volume = 841cm<sup>3</sup>, and the percent density = 3%. In (b) the total breast volume = 660 cm<sup>3</sup>, and the percent density = 17%. In (c) the total breast volume = 529 cm<sup>3</sup>, and the percent density = 16%.



**Fig.2** The age dependence of fibroglandular tissue volume and the percent density in women <45, 45-55, and > 55 years old. The three race groups have comparable fibroglandular tissue volumes, but it is clearly noted that the Asian group has a higher percent density.

**Table 1.** Comparison of percentage density in 3 race groups

	Mean Percent Density in % (95% CI)			P-Value
	White	Asian	Hispanic	
Unadjusted	11.6 (10.4-12.8)	15.1 (13.3-17.0)	11.5 (9.5-13.4)	<b>0.003*</b>
Age Adjusted	11.9 (10.8-13.0)	14.6 (12.8-16.3)	11.4 (9.7-13.2)	<b>0.01*</b>
Age, BV Adjusted	12.1 (11.0-13.1)	13.7 (12.0-15.5)	11.8 (10.1-13.5)	0.25