# Age- and Race- Dependence of the Percent Fibroglandular Breast Density Evaluated by MRI

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### Purpose:

Extensive mammographic density is strongly associated with the risk of breast cancer. It is reported that in women with density greater than 75% the risk is approximately 3-4 times that of women with less than 25% density [1]. On mammogram, the BI-RADS (Breast Imaging Reporting and Data System) category of 1-4 is the only established method for evaluation of breast density. The majority of women fell within BI-RADS 2 and 3 and the ranges of densities were broad, making mammographic density unable to provide a sensitive measure. Other quantitative method has also been developed to calculate the percent density, however, it is based on projection image with overlapping tissue components, and it may be affected by the calibration of the x-ray system. MRI provides soft tissue contrast differentiating between fibroglandular and fatty tissues; and it provides 3-dimensional view of the breast without compression. Therefore, it may be used for accurate assessment of breast density, if a reliable analysis method can be developed. For women who have high risk for breast cancer, whether to consider chemoprevention is a difficult decision to make. Similarly, for women who are considering hormonal replacement therapy, the increased risk for breast cancer is a major concern. If a reliable quantitative method for evaluating breast density can be developed to measure subtle changes with a high sensitivity, it may provide an individualized monitoring method for a woman to evaluate her benefits or risks when considering chemoprevention or hormonal replacement therapy. In this study we developed a method to measure the percent fibroglandular density on breast MRI, and evaluated the age- and race-dependence.

### Methods:

All patients enrolled into a breast MRI study from Mar. 2004 to June 2006 using a Phillips Eclipse 1.5T scanner were included in this study. The pathology report was reviewed for each patient to identify the concerned breast. Only the normal breast was analyzed. All together a total of 168 subjects with confirmed age and race information were selected. The initial breast region was determined using each individual subject's body landmarks (V-shape cutting in Fig.1). For each MR image slice, the breast was automatically segmented using clustering based algorithm in conjunction with dynamic searching followed by the b-spline curve fitting. Then the fuzzy c-means method was utilized to perform background uniformity correction and fibroglandular tissue segmentation. An example of segmentation result is shown in Fig 1. The detailed method and reliability test results are presented in another abstract. The resulted images were combined together to obtain a 3-D breast volume and the fibroglandular volume to calculate the fibroglandular tissue percentage. The patients were separated into three age groups, < 45 years old, between 45 to 55 yo, and > 55 yo. For race-association, 3 major groups: White, Asian and Hispanic were identified. The age and race distribution of 168 subjects is summarized in Table 1.

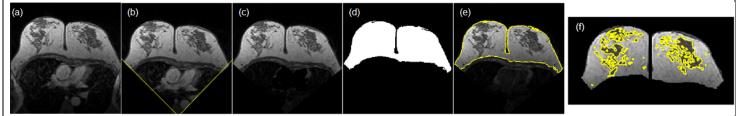
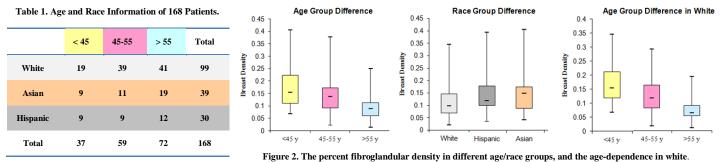


Figure 1: Breast and fibroglandular tissue segmentation process (a) original image, (b) initial v-shape cut result c) heart removal d) breast mask obtained using our segmentation procedures, (e) overlay of breast mask on the image to segment out the breast, (f) the fibroglandular tissue analyzed using FCM algorithm, separately for right & left breasts.

#### Results:

Fig. 2 shows the percent density results in different age and race groups. The percent fibroglandular density was  $15.5\pm7.0\%$  for women <45 yo;  $13.7\pm6.1\%$  for 45-55 yo; and decreased to  $8\pm3.7\%$  for women >55 yo. Kruskal-Wallis H-test was used for group comparison, which was statistically significance with p < 0.0001. For race-dependence, the Asian women have the highest density  $14.9\pm8.1\%$ , and the White women had the lowest density  $10.1\%\pm6\%$ . The Hispanic women had the density of  $13.2\pm6.9\%$ . The difference only reached marginal significance level with p=0.05 in H-test. Since the majority was White, we also evaluated the age-dependence in this subgroup. The breast density was  $15.5\pm7.0\%$  for <45 yo;  $11.7\pm6.1\%$  for 45-55 yo; and decreased to  $6.4\pm2.1\%$  for >55 yo. The H-test showed significant difference between these three groups (p < 0.0001).



#### Discussion:

We have developed a quantitative method for evaluation of fibroglandular breast density based on 3-dimensional MR imaging. The method was applied to a retrospective database to analyze the age and race dependence. The percent density showed age-dependence, as expected, the lowest for women over age of 55 after entering menopause. White women showed a relatively lower breast density when compared to Asian or Hispanic. However, for women younger than 45, the density in the White was the same as the group mean (15.5%), i.e. not showing race dependence at younger age. Increased breast density is a well known risk factor associated with development of breast cancer. Breast density is affected by many variables, thus it is difficult to evaluate the risk based on one cross-sectional measure. A reliable quantitative analysis method, such as the one presented here, may be applied to measure the change after a women starting chemoprevention, to evaluate her benefit in terms of reducing breast density, thus cancer risk. Conversely, it may be applied to evaluate the increase of density after starting hormonal replacement therapy, to evaluate the increased risk. This may help each individual woman to evaluate her own risk/benefit ratio when considering drug interventions.

<u>References:</u> [1] Barlow et al. J Natl Cancer Inst. 2006;98(17):1204-14. <u>Acknowledgement:</u> This work was supported in part by NIH CA90437 and CBCRP 9WB-0020.