Parenchymal Enhancement in the Contralateral Normal Breast of Patients Undergoing Neoadjuvant Chemotherapy Measured by DCE-MRI

Jeon-Hor Chen[1,2], Hon J. Yu[1], Christine Hsu[1], MuQing Lin[1], Rita S. Mehta[3], and Min-Ying Su[1]

[1]*Center for Functional Onco-Imaging,Department of Radiological Sciences, University of California Irvine, Irvine, CA, United States,* [2]*Department of Radiology, E-Da Hospital and I-Shou University, Kaohsiung, Taiwan,* [3]*Department of Medicine, University of California Irvine, Irvine, CA, United States*

Background and Purposes: Contrast enhancements in normal fibroglandular breast tissue of women are commonly observed in dynamic contrast enhanced (DCE)-MRI. Multiple factors, including age, menstrual or menopausal status, and hormone can affect glandular tissue enhancement kinetics. A recent study examining the relationships between breast cancer and both the amount and the contrast enhancement level of normal fibroglandular tissue at MRI has found that increased background tissue enhancement is strongly predictive of breast cancer odds [1]. This background tissue enhancement is usually evaluated by visual inspection and categorized into low, moderate, or strong; however, a low enhancement may be truly reflecting low contrast enhancement in a dense breast (e.g. **Figure 1**), or it may be related to a low amount of fibroglandular tissue thus cannot show a strong enhancement (e.g. **Figure 2**). In order to separate these two effects, in the present study we applied a computer-aided segmentation program to segment the fibroglandular tissue first, and then calculate the mean enhancement by averaging the signal intensities from all pixels in the segmented fibroglandular tissue. The calculated percent enhancement by referencing to the pre-contrast signal intensity is termed "Background Parenchymal Enhancement (BPE)" in this study. The BPE was measured from patients undergoing neoadjuvant chemotherapy, and the results in follow-up MRI studies were compared to the baseline values measured in pre-treatment MRI. In a previous study we have reported the decrease of breast density in patients receiving NAC (doxorubicin and cyclophosphamide (AC) followed by taxane) [2]. By using the proposed analysis methods, we can further investigate whether the background tissue enhancement is also affected by NAC. The association with age was also investigated.

Materials and Methods: Forty-five subjects (30 y/o - 72 y/o, mean 48 y/o) were analyzed in this study. Thirty-three women were younger than 55 y/o, and twelve were ≥ 55 y/o. Each patient had a baseline MRI scan and at least 2 follow-up MRI studies. After the first 2 cycles of AC, the patients continued to receive 2 additional cycles of AC or were switched to a taxane-based regimen. All HER-2 positive patients also received trastuzumab with taxane. Some HER-2 negative patients also received bevacizumab with taxane. The FU-1 MRI was performed after one or two cycles of AC. The FU-2 MRI was performed after 2 months of therapy when the patients had finished four cycles of AC or two cycles of AC plus one month of taxane. The breast MRI study was performed by using a 1.5 Tesla MR scanner. A total of 16 DCE frames (4 pre and 12 post) were acquired with a temporal resolution of 42 seconds. In this study, only the contralateral normal breast of the patient was analyzed. The segmentation of the fibroglandular tissue was performed by an experienced operator using a comprehensive program based on computer algorithms [3]. A mean signal intensity time course was generated by averaging over all segmented fibroglandular tissue pixels. A mean percent enhancement was calculated from all 12 post enhancement time points in the entire DCE period; also the mean percent enhancement in 3 DCE time segments were separately calculated, defined as "early" (the first 4 post-contrast frames, 1-3 min), "middle" (the next 4 frames, 3-5 min), and "late" (the last 4 frames, 5-7 min).

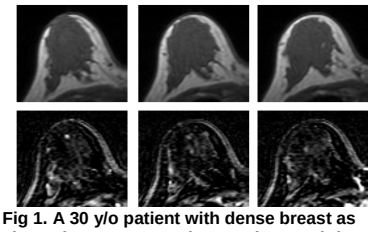

Fig 1. A 30 y/o patient with dense breast as shown in pre-contrast images (top row), but the tissue shows a low contrast enhancement on subtraction images (bottom row). The percent density is 25.3%, and the mean background parenchymal enhancement is 13.2%.

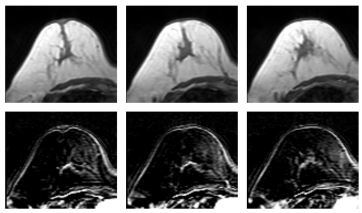

Fig 2. A 56-year-old patient with fatty breast. The percent density is only 2.2%, but it has a similar BPE of 13.8% comparable to Fig.1.

Results: The enhancement kinetics measured from the normal fibroglandular tissue shows a persistent enhancing pattern. As shown in **Figure 3**, the mean enhancement in early to middle to late DCE time segments shows a clear increasing trend. The mean percent enhancement from the entire DCE period was higher in the < 55 y/o group compared to ≥ 55 y/o group (20.1±7.4 vs. 12.1±5.1, p=0.01 for B/L MRI; 18.8±6.9 vs. 11.0 ±3.8, p=0.02 for FU-1 MRI; and 13.3±5.7 vs. 11.8±4.8, p=0.6 for FU-2 MRI). The BPE in the baseline MRI had a weak negative correlation with age, with r = - 0.3. In the group of women < 55 y/o (Fig.3a), the mean BPE shows a clear decreasing trend with chemotherapy. The reduction in BPE at FU-2 compared to B/L was significant (p=0.0002), and also significant compared to FU-1 (p=0.0004). The percent BPE reduction at FU-2 compared to the baseline value is -30%±40%, -24%±35%, and -23%±37% for early, middle and late DCE time segments, respectively. In contrast, there is no significant change in the group of women ≥ 55 y/o. **Figure 4** shows the correlation of percent density (PD) with BPE measured in baseline MRI before the treatment. **Figure 5** illustrates two case examples: a 41 y/o woman with triple negative cancer, who showed a strong BPE in the normal breast at baseline MRI and decreased BPE in F/U MRI; and a 56 y/o woman diagnosed with HR(+)/HER2(-) cancer, who showed unremarkable BPE in all 3 MRI studies.

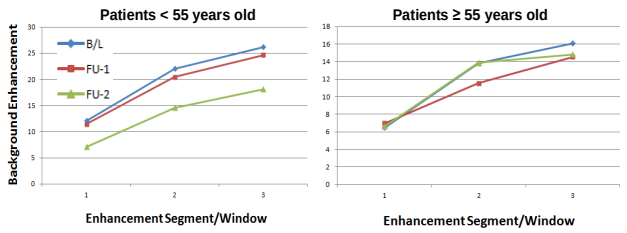

Fig 3. BPE before and after NAC in women < 55 y/o (left) and ≥ 55 y/o (right). The enhancement scale is different, higher in < 55 y/o group. A clear decreasing trend with NAC is noted in < 55 but not in ≥ 55 y/o groups.

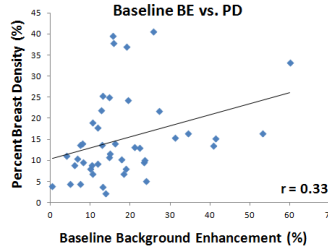

Fig 4. The BPE only shows a weak correlation with the percent density.

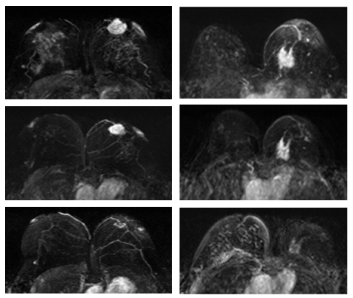

Fig 5. Two cases from top down showing baseline, FU-1 and FU-2 MRI. Right breast is the normal side. In a 41 y/o woman (left panel), BPE is decreased in FU compared to baseline MRI. In a 56 y/o woman (right panel), scattered background enhancements are seen in all three MRI studies, and no change.

Discussion: In this study we measured the background tissue enhancement from the segmented fibroglandular tissue. Most previous studies investigating background tissue enhancement did not use segmentation, thus not able to differentiate the effect coming from the amount of dense tissue versus the true tissue enhancement (reflecting blood perfusion in the fibroglandular tissue). We found a weak correlation between the percent density and the BPE, suggesting that although they were associated but not highly correlated. Using this quantitative method for measuring BPE, we found that women of younger age tended to have higher BPE than older women. Also, younger women were more likely to show decreased BPE after chemotherapy. The effect of BPE reduction in younger women was most likely due to the ovarian ablation induced by chemotherapeutic agents, thus it may be used as a risk predictor for development of contralateral breast cancer. Further studies are needed to evaluate the role of reduction in the dense tissue volume and the BPE after NAC to serve as a biomarker for the assessment of cancer risk in the contralateral normal breast.

References: [**1**] King V. Radiology. 2011; 260(1):50-60. [**2**] Chen JH. Radiology 2010; 255(1):44-52. [**3**] Nie K. Med Phys 2008; 35 (12): 5253-5262.

Acknowledgement: This work was supported in part by NIH/NCI Grant No. R01 CA127927 and R03 CA136071.