

Evaluation of Bilateral Breasts Response to the Hormonal Fluctuation of Menstrual Cycle Using 3D MRI

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Background and Purposes:

The normal breast tissue responds to the fluctuation of endogenous hormones during the menstrual cycle (MC) and shows structural and morphological alterations [1]. The histological changes of fibroglandular tissue can be assessed with imaging. Previous mammographic and MRI studies have focused on the difference of breast density between follicular and luteal phase [2, 3], mainly for investigating their influence on cancer detection and the optimal timing to image patients. Among the many studies, none has investigated the symmetry of functional response between the bilateral breasts during MC. Morphologically, bilateral breasts in a healthy woman are thought to be symmetrical. Functional symmetry is less known. Asymmetrical change in mammography may indicate the potential abnormality in one breast. In this study we used 3D MRI to investigate how the bilateral breast tissues of healthy women respond to the hormonal fluctuations during a menstrual cycle.

Materials and Methods:

Twenty-four healthy premenopausal Asian women (age range 23-48, mean 29 y/o) were studied. All the 24 subjects were slim, and the BMI ranged narrowly from 17.2 to 25.8 (mean 20.6 ± STD 2.1). Each subject received four consecutive weekly breast MRI examinations from the first week of their menstruation. The breast MRI scan was performed on a 1.5T MR scanner (Siemens, Somatom, Erlangen, Germany) with a 4-channel dual mode breast coil. Breast density was analyzed on non-contrast-enhanced 3D non-fat-suppressed gradient echo T1 weighted images. The segmentation was performed by two independent operators to measure the fibroglandular tissue volume (FV), breast volume (BV), and percent breast density (PD) using our previously developed computer-based algorithm [4, 5]. After completing the segmentation from all two-dimensional imaging slices, FV is calculated. PD was defined as the ratio of FV over BV (x 100%). Regarding morphological patterns, three parameters, including circularity, convexity, and irregularity, were analyzed to quantify the three dimensional spatial distribution of the fibroglandular tissue within the breast. The fluctuation of these six measured parameters among the four MR studies through MC was evaluated using the coefficient of variation (CV), defined as the ratio of standard deviation over the mean value of the four MR measurements. The maximal percent difference of FV, defined as $[(FV_{max} - FV_{min}) / \text{average of } (FV_{max} + FV_{min})] \times 100\%$, measured among the four breast MRI studies in each of the bilateral breasts of each woman was also calculated. The obtained CV and maximal percent difference of FV in the left and the right breast of all subjects were compared using Pearson's correlation.

Results:

All density parameters measured from the bilateral breasts are highly correlated, with $r > 0.93$, indicating their static morphological symmetry. Regarding functional symmetry, the correlation of CV within the MC between the left and the right breasts by the two operators were, $r=0.77$ and $r=0.91$ for FV, $r=0.67$ and $r=0.60$ for BV, and $r=0.56$ and $r=0.40$ for PD, respectively. Figure 1 shows the correlation of the maximal percent difference of FV measured from the left and the right breasts. The results analyzed by the two operators are shown separately. The correlation coefficient (r) was 0.93 for Operator-1, and 0.66 for Operator-2. Figures 2 and 3 illustrate two examples, from two subjects showing small and large fluctuation of FV during the MC. The measured parameters from these 2 cases are summarized in Table 1. It can be seen the changes in fibroglandular tissue volume between the left and right breasts are symmetrical. For the three analyzed morphological parameters during MC, the mean CV was in the range of 1.5%-4.1%, which was smaller compared to the CV of the fibroglandular tissue volume. The CV measured from the left and the right breasts were not significantly different, where p-values are 0.43, 0.36, and 0.77 for circularity, convexity, and irregularity, respectively.

Discussion:

The results demonstrate a high correlation in all parameters (dense tissue volume and morphology) measured from the left and right breasts of healthy women. For the functional fluctuation during the MC, the CV of the fibroglandular tissue volume measured from the left and the right breasts shows a strong correlation ($r > 0.7$), so as the maximal changes of FV. The fluctuations of the morphological parameters between the left and the right breasts were not significantly different. As shown in the 2 case examples, the change of dense tissue seems to be concentric, while the morphological patterns are preserved. Since most of breast cancers occur unilaterally, it would be interesting to investigate whether the functional response of tissues in bilateral breasts to hormonal stimulation is associated with different risks in developing cancer.

References: [1] Ramakrishnan et al. Mod Pathol. 2002; 15:1348-56. [2] White et al. J Natl Cancer Inst. 1998; 90:906-10. [3] Graham et al. JMIR 1995; 5:695-701. [4] Nie et al. Medical Physics 2008; 35:5253-62. [5] Lin et al. Medical Physics 2011;38:5-14.

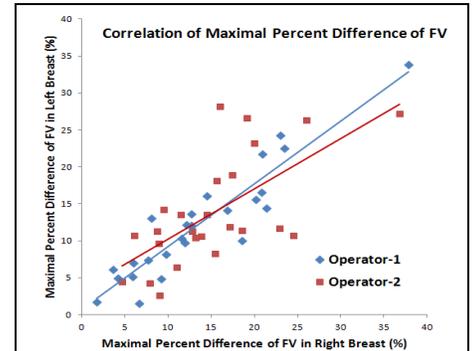


Fig 1. Correlation of the maximal percent difference in fibroglandular volume measured during the menstrual cycle between the bilateral breasts.

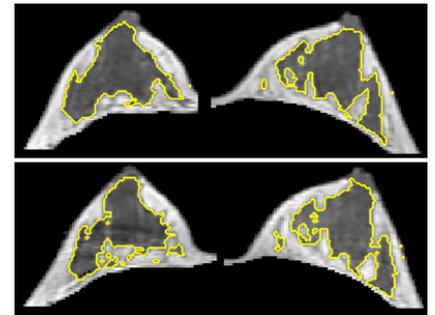


Fig 2. A 23 y/o woman showing symmetrical small fluctuation of FV during her MC. The maximal percent difference of FV was 4.9% for the left and 4.2 % for the right breast.

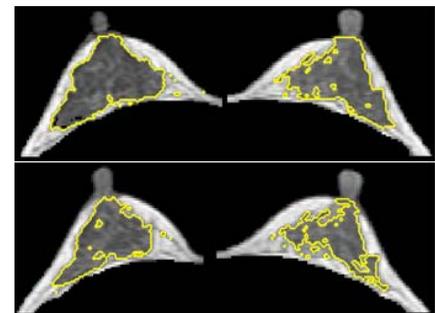


Fig 3. A 45 y/o woman showing symmetrical large fluctuation of FV during her MC. The maximal percent difference of FV was 33.8% for the left and 37.8 % for the right breast. The fibroglandular volume was apparently smaller on the bottom images compared to the top.

Table 1. The right/left breast density parameters measured from the 2 cases shown in Fig.2 & Fig.3

	FV (cc)	BV (cc)	PD (%)	Circularity	Convexity	Irregularity
Fig.2 top	45.9/58.7	170.4/206.6	27.0/28.4	0.65/0.61	0.66/0.66	0.61/0.62
bottom	44.0/55.9	173.4/196.2	25.4/28.5	0.67/0.62	0.65/0.64	0.62/0.63
Fig.3 top	50.1/43.9	178.5/167.7	28.1/26.2	0.61/0.59	0.60/0.52	0.62/0.70
bottom	34.2/31.2	147.7/148.4	23.1/21.0	0.61/0.58	0.58/0.55	0.63/0.70