Introduction:
The tissue composition of the breast is affected by sex hormone exposures and continually varies throughout a woman’s lifetime. Mammographic density is a well-established risk factor for breast cancer, but is not well characterized in healthy young women, because mammograms are not recommended for average risk women under the age of 40. The purpose of this study was to assess if MRI could be used to monitor breast volume and density changes during the menstrual cycle. MRI analysis methods developed for this study may be useful for future studies assessing the effects of hormonal medications (e.g. oral contraceptives) on breast density in young premenopausal women.

Materials and Methods:
MRI data were acquired using a whole body Siemens 3T Tim Trio system and a 7-element breast coil. Three-point Dixon imaging was performed using a 3D FLASH sequence with TR=7.6 ms, FA=10º, iPat=2, bandwidth = 680 Hz/pixel, and spatial resolution = 0.9 x 0.9 x 1.5 mm covering the entire breast. This sequence was run three times with three different TEs; 3.37 ms, 4.17 ms, and 4.96 ms. The water and fat images were reconstructed using Iterative Decomposition of Water and fat with Echo Asymmetry and Least-squares (IDEAL) method (1). The total scan time for Dixon imaging was approximately 6 min in total. The breast was mildly immobilized by side plates built in the coil to minimize motion artifact. In addition, relative phase shifts of the raw images due to motion were removed by adjusting the phases estimated from the voxel with the highest signal intensity in the raw images. A software tool was developed for semi-automatic segmentation of the breast. On axial images, the software detects the skin boundary based on the edge detected by Canny operator. The boundary between the breast and pectoralis major muscle is detected using active contour (2). For each slice, the boundary of the breast generated by the software is examined by an operator and corrected if not satisfactory. The fibroglandular (FG) density is measured as the average of water fraction in the segmented breast.

Reproducibility of the volume and density measurement was assessed with data from four subjects. Each subject had two scans on the same day. After the first scan, the subject took a two minute break outside of the scanner and was repositioned for the second scan. The amount of breast compression by the side plates was randomly determined by the operator for the first scan, but the amount of immobilization was recorded and applied for the subsequent scans. For one subject, the first scan was done without immobilization and the second one with a large compression as shown in Fig.1. In order to select a same portion of the breast from the two scans, segmentation of the breast was performed for the first scan data, and then was co-registered to the second data set using SPM5 (UCL, UK) normalization.

The above method was applied to monitor the longitudinal changes of the breast volume and density during menstrual cycle. Five healthy premenopausal women (ages 24-31) were scanned once a week for four weeks. In order to select a same portion of the breast for all scans, segmentation of the breast was performed using data from one visit and was co-registered to the other ones using SPM. The institutional review board approved this study, and written informed consent was obtained from all subjects before the scans.

Results and Discussion:
Fig.2 shows the result of the reproducibility test. The mean difference of the volume between two scans was 1.3 ± 0.5 %. The difference of the FG density was 3.2 ± 1.0 %. The larger difference in FG density measurement may be due to residual motion artifact related to breathing as well as partial volume effect. Table 1 summarizes the breast volume and density changes of five healthy control subjects over a four-week period. Data measured at the follicular phase were used as reference to measure relative percent differences at the subsequent weeks corresponding to the ovulatory, the late luteal, and menstrual phases. The median breast volume was smallest in the ovulatory phase and largest in the late luteal phase. FG density was lowest at the follicular phase and highest in the late luteal phase; consistent with the established data that breast tissue proliferation peaks during the late luteal phase and reaches a minimum during the follicular phase (Going et al, 1988; Navarrete et al, 2004; Potten et al, 1988; Ferguson et al, 1981, and others). While this preliminary result demonstrates the feasibility of monitoring physiological changes of the breast, the data have relatively large ranges and the median differences are not substantially larger than the measurement errors estimated from the reproducibility test.

We plan to further refine these methods to reduce sources of random error and apply future analyses to a larger number of women.