MRI quantitative changes of breast tissue composition with short-term tamoxifen treatment in cancer patients.

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Introduction: Fifteen to twenty five percent of all newly diagnosed breast cancers are cases of Ductal Carcinoma in Situ (DCIS), a highly heterogeneous group of pre-invasive, cancerous lesions of the ducts. These lesions have great potential for progression to invasive breast cancer [1]. It has been shown that breast density at time of DCIS diagnosis is a risk factor for developing invasive cancer following lumpectomy for DCIS [2]. Tamoxifen is a selective estrogen receptor modulator that has been shown to decrease breast density [3]. The purpose of this retrospective study was to measure the quantitative effects of a 3-month course of tamoxifen treatment on tissue composition in women with DCIS. The changes related to DCIS lesions will be reported in a separate analysis.

Materials and Methods: Our retrospective study involved 16 patients with biopsy proven DCIS who underwent 2 breast MRI exams at our institution - at the beginning of tamoxifen treatment and at the conclusion of the 3-month course - and then underwent surgery. Patient history and pathology results were available. All patients signed an informed consent.

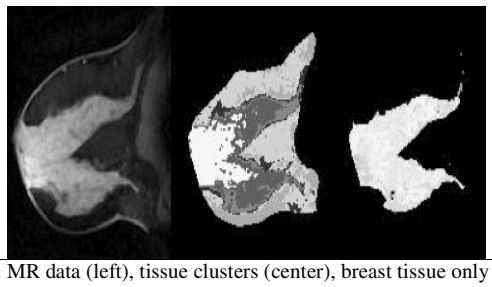

Fig. 1. MR data (left), tissue clusters (center), breast tissue only (right).

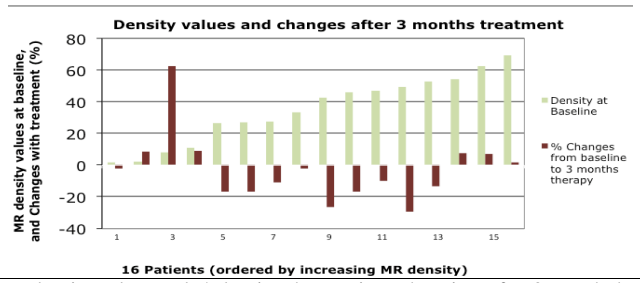

Fig. 2. Breast density values and % density changes in each patient after 3-month therapy

The 16 patients were premenopausal women with mean age 46.5, range [41, 53]. All exams were performed on a 1.5T Signa system (General Electric Medical Systems, Milwaukee, WI) using an 8-element phased array breast coil (Sentinelle Vanguard System), and gadopentetate dimeglumine (Magnevist, Schering, Berlin Germany) was injected at a dose of 0.1mmol/kg of body weight. A high-resolution fat suppressed T1-weighted 3D fast gradient echo sequence was used, and data were acquired before contrast injection and at two time points after injection. The MR exam parameters were 20 cm field of view, 2 mm slice thickness and 256x192 acquisition matrix. The resulting in-plane resolution was approximately 0.78x0.78mm and 60 slices were acquired in the sagittal orientation. In order to distinguish fibroglandular breast tissue volume from fat regions in the breast, we used a semi-automatic segmentation technique based on fuzzy clustering using the precontrast MRI data [4]. The technique segments the entire breast into tissue clusters. The final segmentation step provides a map of breast fibroglandular tissue only (see figure 1). We defined the volumetric breast density or "MR Breast Density" as the ratio of breast fibroglandular tissue volume within the entire breast over the total breast volume. We defined 3 groups of MR density: fatty (less than 25% MR density), mixed density (25 to 50% MR density) and dense (>50% MR density) breasts.

Results: We showed that the group of mixed densities had a significant reduction in breast density (mean 13.4%) after 3 months of treatment compared to baseline. Figure 2 presents the patients' MR densities arranged in increasing order, as well as the percentage mean change in MR density between baseline and 3 months of therapy. All women with mixed density breasts (25-50% MR density) exhibited a significant decrease in MR density with treatment. Variations in the dense category (>50% MR density) were negligible. Large variations in the fatty population were also observed.

Discussion: The segmentation of breast density was more difficult for fatty breasts due to the large amount of partial voluming. This may explain the difference in results from those obtained in the mixed density group, who all exhibited reductions in MR density. While a decrease in trend was not seen in the dense category group it could become apparent with longer therapy. These results suggest that quantifying MR breast density can provide important information on treatment effects and that MR density (independent of enhancement) could potentially be used as a potential marker of treatment response. Future studies will test this hypothesis.

References: [1] Hetelekidis S. Cancer J. Clin 1995:45,244-253, [2] Hwang ES et al. Cancer Epidemiol Biomarkers Prev. 2007 Dec;16(12):2587-93, [3] Atkinson C et al. Cancer Epidemiol Biomarkers Prev. 1999 Oct;8(10):863-6, [4] Klifa C et al. Conf Proc IEEE Eng Med Biol Soc. 2004;3:1667-70. Funding Acknowledgments: R01 CA116182.