Reduction of Breast Density Following Tamoxifen Treatment Evaluated by 3-D MRI

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Background and purpose: For women diagnosed with breast cancer, the risk of developing secondary cancer in the ipsilateral or contralateral breast is increased. The current standard of care treatment for pre-menopausal patients with hormonal positive breast cancer is to give Tamoxifen for 5 years. Tamoxifen can reduce the cancer risk by as much as 50%. A few studies assessing the change of breast density after adjuvant hormonal therapy using mammography have been reported. However, mammography acquires projection images and the measured density may be affected by the positioning of the patent as well as the technical factor such as compression angle, compression level, kVp and mAs. It has been shown that in patients receiving Raloxifene, MRI is more sensitive to detect the changes in breast density than mammography [Eng-Wong et al. Cancer Epidemiol Biomarkers Prev. 2008; 17:1696-701]. MRI provides a 3-dimensional view of the breast and does not suffer from the problems in mammography. This study analyzed the change of breast density in women receiving tamoxifen treatment using 3-D MRI.

Materials and Methods: Sixteen women (age 33-51, mean 43) were studied. Each woman received breast MRI before and after tamoxifen treatment at 1.5T. The duration between pre-treatment and follow-up studies ranged from 8 months to 26 months (17.5 ± 5.7 months). The quantification of breast density was performed using a 3D MRI-based method developed earlier by our group. The breast and the fibroglandular tissue were segmented using a computer-assisted algorithm, based on non-fat suppression T1-weighted images. For fibroglandular tissue segmentation, the adaptive FCM was applied for bias field correction to remove image intensity non-uniformities, and for segmentation of the fibroglandular tissue from the surrounding fatty tissue. The fibroglandular tissue volume (FV) and breast volume (BV) were measured and the ratio was calculated as the percent breast density (%BD). The changes in breast volume (ΔBV), absolute fibroglandular tissue volume (ΔFV), and absolute percent density (Δ%BD) at F/U relative to the baseline values were analyzed and correlated with treatment duration and baseline breast density. FV was not normally distributed, and the square root (sqrt) transformation was applied before performing statistical analyses.

Results: All 16 patients showed reduction in the fibroglandular tissue volume (ΔFV). The change of BV, FV, and %BD between the baseline and the follow-up MRI for each patient was calculated, and the range and the group mean are summarized in Table 1. The mean reduction of Δ%BD was 5.8% (STD 3.8%). Seven subjects showed Δ%BD less than 5%; 7 were between 5-10%; and 2 showed larger than 10%. Overall, the group mean of BV, FV, and %BD between the baseline and the follow-up MRI all show significant reduction. The reduction of FV is significantly correlated with baseline FV ($P<0.001$) (Fig. 1) and treatment duration ($P=0.03$). Patients with higher baseline FV showed greater reduction, and patients who were on treatment longer showed a greater reduction. When normalized to the baseline FV, the %ΔFV reduction ranged from 9.0% to 72.0%, which was correlated with duration ($P=0.049$) (Fig. 2). Fig.3 shows a case example.

Table 1: The changes in breast volume, fibroglandular tissue volume and the percent density between the baseline and the follow-up MRI.

	Range (median)	Mean±STD 95% CI	P-value
BV(B/L) – BV(F/U) cm^3	-17.8-94.6 (25.6)	26.7 ± 35.5 [7.7-45.6]	P=0.01
FV(B/L) – FV(F/U) cm^3	4.7-97.0 (14.7)	26.6±24.8 [13.0-40.3]	P<0.001
BD(B/L) – BD(F/U) %	0.3-11.9 (5.5)	5.8 ± 3.8 (%) [3.7-7.8]	P<0.001

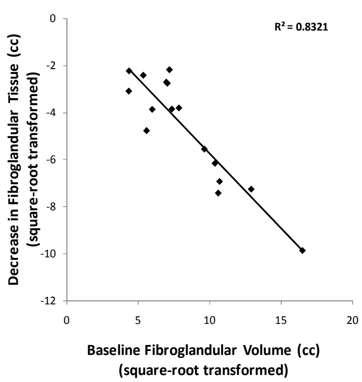

Fig. 1: The reduction of FV was positively correlated with baseline FV.

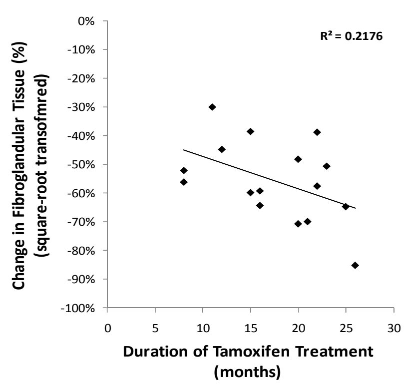

Fig. 2: The percentage reduction in FV was significantly correlated with the duration of treatment.

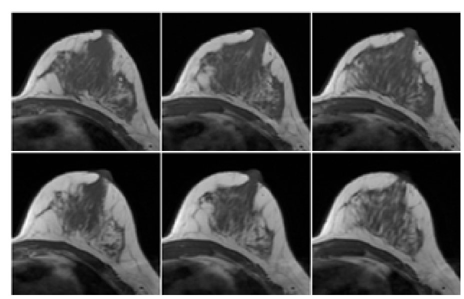

Fig. 3: The baseline and F/U images from the normal breast of a 38-year-old patient. The upper row shows 3 baseline images from the mid-section of the breast, and the lower row shows the corresponding images 25 months after the tamoxifen treatment. The fibroglandular tissue volume is 114 ml at baseline and 67 ml at F/U, with a reduction of 47 ml (41.8%).

Conclusion: We have demonstrated that the breast density analyzed based on a 3D MR method can be used to investigate the changes associated with tamoxifen treatment. We found a significant reduction in FV and %BD after treatment, and the density reduction was positively correlated with the baseline density and treatment duration. Women with higher baseline density had greater reduction. Since breast density is affected by many variables, it is difficult to estimate a woman's risk based on the measure of density at one time point. When the baseline density of a woman is known to serve as her own control, a reliable method, such as 3D MRI, may be used to measure changes over time. For a patient receiving adjuvant hormonal therapy, such a method may be very helpful to evaluate her own benefit in terms of reducing breast density, thus cancer risk.

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