Effect of Neoadjuvant Chemotherapy on the Fibroglandular Tissue Volume and Breast Density in the Contralateral Normal Breast: Evaluate at 3T MRI

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Background and Purpose:

Systemic chemotherapy administered to treat breast cancer will also affect normal breast tissues and suppress ovarian function. The results from our previous MRI monitoring study had shown reduction of breast density in patients receiving Doxorubicin and Cyclophosphamide (AC) followed by taxane-based neoadjuvant chemotherapy (NAC). The effects were already significant after initial treatment with one to two cycles of the AC regimen [1]. The taxane treatment was given after AC, and we did not observe further significant density reduction during the taxane regimen. Because a great reduction in density had already occurred during the AC regimen, the effect of taxane on the change of breast tissue is still not clear. Due to the concern of the cardiac toxicity of AC, as well as the availability of targeted therapy and effective hormonal therapy, since early 2008 we have changed the order of the regimen by first administering taxane-based agents for 12 weeks, with optional AC as the second line. This new NAC protocol hence allows us to examine the effect of taxane-based drugs on the change of breast tissue.

Materials and Methods:

In a period of three years (early 2008- mid-2011), 49 women (age 28-82, mean 48) who had received NAC and breast MRI for response monitoring were studied. The MRI studies were performed using a 3.0 T MR scanner. The non-contrast T1W images without fat suppression were used for measurement of the breast density. All patients had a baseline MRI prior to NAC and follow-up MR studies during the course of treatment. The NAC regimens include Abraxane and Carboplatin, plus Herceptin for patients with Her-2 positive cancer or Avastin for patients with Her-2 negative patients. Breast segmentation and fibroglandular tissue segmentation was based on our developed N3+FCM algorithm [2, 3]. The volume of fibroglandular tissue (FV) was calculated, and the percent density (PD) was obtained by normalizing to the total breast volume. The percent reduction of FV and PD measured at MRI during (4 weeks of treatments) and after (12 weeks of treatment) NAC, compared to baseline MRI, was calculated. The effect of age and treatment duration on the reduction of FV and PD was investigated.

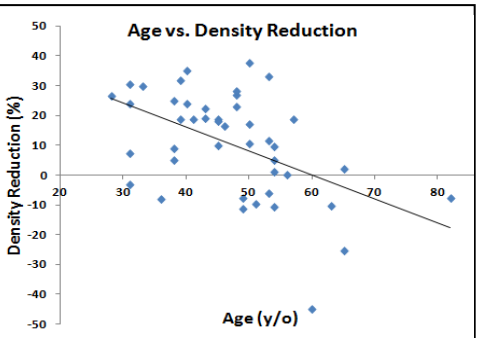

Figure 1. Correlation of decreased percent breast density with patient's age.

Results:

Of the 49 subjects, 33 were pre-menopausal (≤50 y/o) and 16 were post-menopausal (>50 y/o) women. Forty-five subjects had MRI follow-up after 4 weeks and 12 weeks of NAC treatment. Four women had only received 4 weeks of treatment and one MRI follow-up. To examine the age effect on the percent reduction of FV and PD, those 45 patients with MRI follow-up after 12 weeks NAC were studied. The results showed a trend (r=0.5) that patients of younger age showed a higher percent reduction of PD than patients of older age (Figure 1). Table 1 shows the comparison of reduction of FV and PD after 4 weeks and 12 weeks of NAC treatment between pre- and post-menopausal women. Significant difference of FV and PD percent reduction between the two groups in both treatment durations was noted (all p values <0.05). For pre-menopausal women, the percent reduction of FV and PD after 4 weeks, compared to that of 12 weeks, was significant (7.6%±12.3% vs. 15.8%±15.3% for FV, p=0.02; 8.5%±11.9% vs. 18.7%±14.9% for PD, p=0.004). In the post-menopausal women, the change of density is smaller, and the difference after 4 weeks and 12 weeks of treatment was not significant (p=0.08 for FV; and p=0.99 for PD). Figure 2 shows examples of three pre-menopausal women with remarkable FV reduction after NAC, and one post-menopausal woman with a smaller reduction in FV.

Table 1 Breast Density Reduction in Pre- and Post-menopausal Women

	Premenopausal (N=33)	Postmenopausal (N=16)	P values
4 wks' treatment			
Percent reduction of FV	7.6%±12.3%	-2.5%±10.3%	P <0.005
Percent reduction of PD	8.5%±11.9%	-3.0%±14.4%	P <0.05
12 wks' treatment			
Percent reduction of FV	15.8%±15.3%	5.2%±13.7%	P <0.05
Percent reduction of PD	18.7%±14.9%	-3.0±36.7%	P <0.001

Discussion:

The results show that NAC using Abraxane and Carboplatin also had similar effect on the reduction of FV and PD as did AC in our previous study [1]. The effect is age-related and duration-related. For patients with cancer in one breast, the risk of developing another cancer in the contralateral breast is increased, and they are followed as a high-risk population. Since quantitative measures of FV and PD can be obtained on MRI, the reduction of these two parameters after NAC may potentially be used an imaging biomarker to correlate with future cancer risk occurring in the contralateral normal breast.

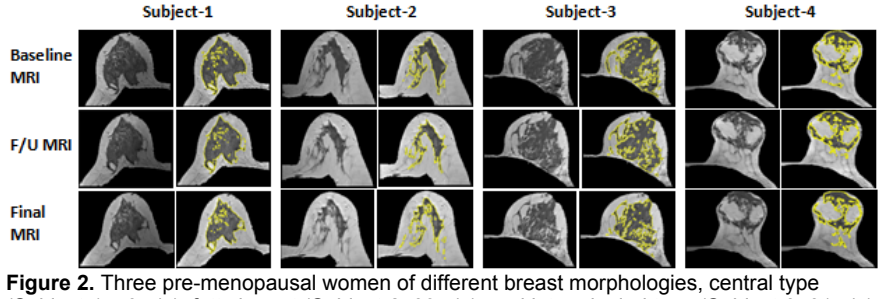

Figure 2. Three pre-menopausal women of different breast morphologies, central type (Subject-1, 40 y/o), fatty breast (Subject-2, 39 y/o), and intermingled type (Subject-3, 31 y/o), and a post-menopausal women (Subject-4, 54 y/o). The pre-menopausal patients showed decreased FV (30%, 43%, 35%, and 4.9% respectively for Subjects 1, 2, 3, and 4) and decreased PD (35%, 32%, 30%, and 9.4 %) after NAC treatment.

References: [1] Chen et al. Radiology 2010;255:44-52. **[2]** Nie et al. Medical Physics 2008;35:5253-62. **[3]** Lin et al. Medical Physics 2011;38:5-14.