

Correlation of Breast Density Measured by MRI and Diffuse Optical Spectroscopic Imaging (DOSI) in the Contralateral Normal Breast of Patients During Neoadjuvant Chemotherapy

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Purpose:

Chemoprevention offers an effective intervention strategy to reduce the risk of developing breast cancer. However, given the possible side effects, it is only recommended in high-risk women who are more likely to achieve a favorable benefit to risk ratio. One main difficulty in assessing the benefit-risk ratio is the lack of an appropriate method that can be used to predict whether chemoprevention can reduce an individual's breast cancer risk. A recent study has shown that in a primary prevention study using tamoxifen, only those women who exhibited >10% reduction in percent mammographic density had a protective effect in decreased cancer incidence, whereas women in the treated group who showed <10% decreased density had exactly the same cancer rates compared to the control group [1]. These findings and other related studies suggest that breast density, in addition to being a risk factor, may also provide a surrogate imaging biomarker for monitoring, predicting, and optimizing individual response to hormonal therapies. In addition to hormonal therapy, we have also shown that the density of the contralateral normal breast is reduced significantly during neoadjuvant chemotherapy (NAC) [2], presumably due to hormonal suppression from compromised ovarian function. These results suggest that the change of breast density in NAC patients may also have prognostic value. Most breast density studies in the literature are measured on mammography, and in recent years MRI-based analysis has also attracted attention. Optical imaging technology is also evolving rapidly, and several devices have been used in clinical studies. In this work we applied breast MRI and a laser breast scanner based on broadband diffuse optical spectroscopic imaging (DOSI) [3, **Figure 1**], to measure the density in the contralateral normal breast of patients undergoing NAC. DOSI provides a quantitative measure of tissue functional components (blood, lipid, and water). The water concentration measured by DOSI is a marker of breast density, and the results were compared to fibroglandular tissue volume measured by MRI.

Methods:

We analyzed 22 studies from seven NAC patients who were measured with DOSI and MRI (within a week) at different times. None of the patients had disease or symptoms in the contralateral breast. MRI was performed on a 3.0T Philips scanner before, during and after completion of NAC, in a prone position. For DOSI, subjects were measured in a supine position (**Figure 1**). The DOSI probe was placed against the breast tissue, and sequential measurements were taken in a rectangular grid pattern using 10-mm spacing. DOSI measurement regions did not include the full breast, but were taken to mirror the area of the underlying tumor on the ipsilateral breast, with a minimum of 32 grid points. Tissue concentrations of oxyhemoglobin (ctO₂Hb), deoxyhemoglobin (ctHHb), water, and lipid were calculated at each measurement point, and these data were used to construct 2D maps using a linear interpolation between measurement points. The fibroglandular tissue was segmented on MRI, and the volume was calculated for comparison.

Results:

Of the 7 subjects, five were premenopausal and two were postmenopausal, and there were a total of 22 corresponding DOSI+MRI measurements done at different times during the NAC. Of all measured DOSI parameters, the MRI fibroglandular tissue volume had a high correlation with water concentration ($r=0.671$, $p=0.0006$) and total hemoglobin ($r=0.658$, $p=0.0009$), and weaker correlation with bulk lipid concentration ($r=-0.512$, $p=0.015$). The correlation was better with deoxyhemoglobin ($r=0.675$, $p=0.0006$) than with oxyhemoglobin ($r=0.597$, $p=0.0034$), but not with oxygen saturation ($r=0.1542$, $p=0.4932$). **Figures 2 and 3** illustrate the MR images and the DOSI water concentration map measured from a pre-menopausal and a post-menopausal patient, respectively. The correlation between the fibroglandular tissue volume and the mean DOSI water concentration from 22 studies is shown in **Figure 4**. The measurements were taken at different times before and after NAC.

Discussion:

Because fibroglandular tissue has a greater water concentration than adipose tissue, we see a clear correlation between fibroglandular density measured with MRI and tissue water concentration measured with DOSI. Greater hemoglobin concentration in patients with dense breast tissue confirms a greater vascular density. We see a much greater reduction in water and therefore tissue density in younger women after treatment, implying that the reduction in breast density during NAC is due to hormonal reduction because of ovarian suppression. This finding may be examined further by looking at water concentration of control tissues with fewer hormone receptors. Suppressed ovarian function may lead to favorable prognosis, and the results suggest that the change of breast density measured by imaging may provide a prognostic marker. Compared to MRI, DOSI may offer a less expensive bed side imaging device for this purpose. The preliminary results obtained in this study are encouraging, and larger studies need to be performed to further understand the correlation of parameters measured by these two breast imaging modalities.

Reference: [1] Cuzick et al. J Natl Cancer Inst. 2011; 103:744-752. [2] Chen et al. Radiology 2010; 255:44-52. [3] Cerussi et al. Acad Radiol. 2010; 17:1031-1039.



Fig.1: DOSI measurements using the laser breast scanner.

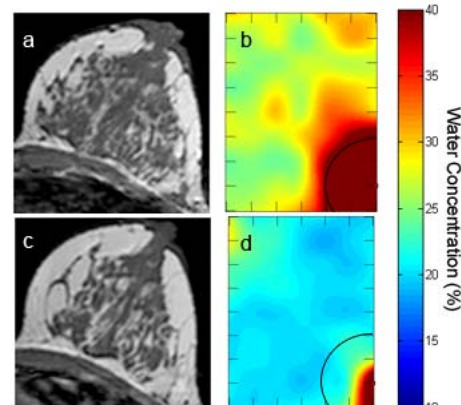


Fig.2: MR images (a, c) and corresponding DOSI water concentration maps (b, d) at baseline and after NAC, respectively in the contralateral normal breast of a pre-menopausal patient. The DOSI maps depict water concentration as a function of position (each tick mark represents 1 cm). The illustrated maps are taken from a 8 x 6 cm area from the upper-inner region of the left breast. The areolar region is the red-color zone, marked by the semi-circle. This region has a high water concentration, and it is excluded from the calculation of mean water concentration. The decreased density after NAC is clearly visible. MRI shows 30.4% reduction in fibroglandular tissue volume and DOSI shows 24.4% reduction in tissue water.

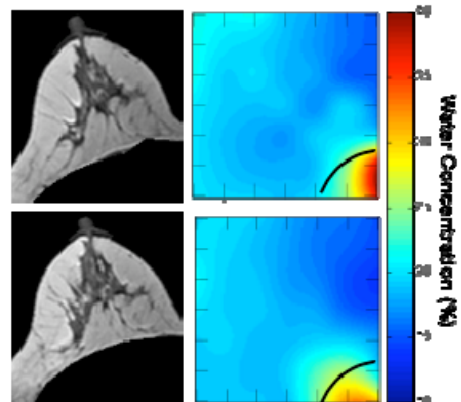


Fig. 3: A post-menopausal woman at baseline (top) and after NAC (bottom). Both the MRI fibroglandular tissue and the DOSI water maps showed little change.

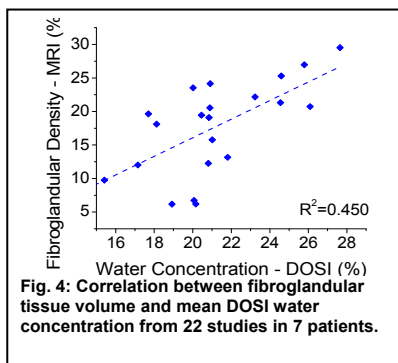


Fig. 4: Correlation between fibroglandular tissue volume and mean DOSI water concentration from 22 studies in 7 patients.