Study of breast density using Magnetic Resonance Imaging and Diffuse Optical Spectroscopy

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Introduction: Mammographic breast density is a strong marker for cancer risk. Since the biologic basis of the strong association between breast density and breast cancer risk is still unknown, we hypothesize that tissue features of the breast closely associated with density are the relevant risk factors. Mammography suffers from many limitations including the 2-dimensional projection of the breast and limited applicability to the population of women with dense breasts, and does not provide information on the underlying biology of the breast. Magnetic Resonance Imaging (MRI) presents very high soft-tissue contrast and allows three-dimensional characterization of breast tissue. Near-infrared Broadband Diffuse Optical Spectroscopy (DOS) is a new non-invasive modality that can characterize breast tissue composition and function [1]. The purpose of this study was to use a combination of MRI and DOS to quantify breast composition on normal volunteers and evaluate parameters that may contribute to radiological breast density. The overall goal of our research is a better understanding of the biological basis of the relation between mammographic breast density and cancer risk. If we can explain what biological components in the breast are linked to breast density, using our combination of MRI and DOS, then we will be able to better monitor breast cancer risk by monitoring these components. Alone MRI and DOS are not specific enough to become routinely used screening tools for breast cancer, but combined in a new screening modality, they could provide unique sensitivity to breast tissue function and lead to improved breast cancer management.

Materials and Methods: We recruited 16 healthy volunteers who underwent one breast MRI followed by one breast DOS scan at our center. The volunteers were premenopausal females between 24 and 53 years, (mean 38 years). All MRI exams were performed on a 1.5T Signa system (General Electric Medical Systems, Milwaukee, WI) using a bilateral phased array breast coil. For each volunteer we acquired a high resolution fat suppressed T1-weighted 3D fast gradient echo sequence (3DFGRE) (TR=8.4ms, TE=4.2ms, NEX=2, 256x256matrix, FOV 20cm, Slice thickness 2mm, no gap) and a bilateral axial diffusion-weighted MR sequence (TR/TE=6.2/6.1, 5mm thickness, b=600, FOV 35cm). To help co-localize DOS measures on MR data, vitamin A fiducials (visible on MR data, see figure 1) were placed at 8 specific locations around the breast. DOS measurements were obtained at each fiducial location on the breast, with the patient in the same prone position as used for the MRI exam. DOS measurements were used to quantify lipid content, water content, deoxy- oxy- and total hemoglobin (THC) and hemoglobin oxygen saturation. In addition tissue scattering and scatter power (SP, related to the distribution of scatter particle size in tissue) were obtained at each measurement location. A composite index of DOS parameters related to the overall metabolism of the tissue, the Tissue Optical Index (TOI = (THC)(water)/(lipid)(oxygen saturation)) was also calculated. We also quantified the following: 1) MR breast density using a Fuzzy C-Means technique [2] allowing total breast tissue segmentation within the entire breast volume, 2) Mean Apparent Diffusion Coefficient (ADC) from diffusion-weighted slices displaying DOS fiducials, 3) Gray-level distribution of intensities in the breast, using co-occurrence matrices (averaged orientations, distance: 3 and 5 pixels) from which 4 features were extracted to quantify breast tissue texture, 4) MR fat and tissue thickness (cm) along rays perpendicular to the skin under each fiducial (figure 1). We classified the data into 3 groups of MR breast density: low (<20%), medium (20-50%), and high (>50%). To take into account the distance separating the optical measures from breast tissue within the breast, we multiplied each DOS parameter with a "MR weighting coefficient" obtained using MR fat and breast tissue thickness at all locations. For MR fat thickness (distance skin surface to breast tissue) around zero cm, the weighting coefficient is set to 1, since breast tissue composition is then the total contributor to DOS measures. For higher MR fat thickness, the weighting factor becomes smaller than 1 to attenuate the DOS information describing breast tissue composition. This simplified model takes into account the amount of fat that light needs to cross before getting to breast tissue. We applied a multivariate linear regression technique to investigate the association of MRI and DOS parameters with breast density.

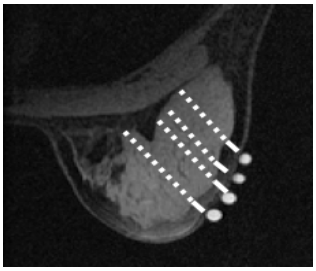

Figure 1: Axial T1-weighted image with thickness measures at fiducials (white circles): fat thickness (solid), tissue thickness (dotted)

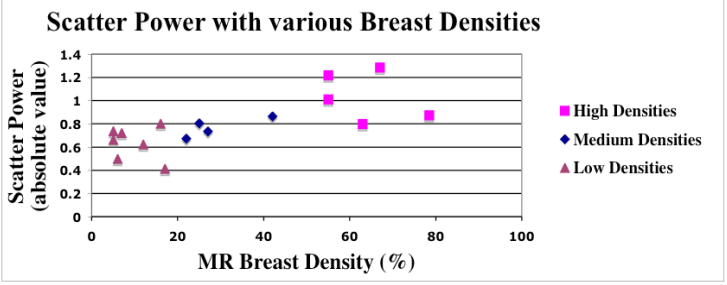

Figure 2: Scatter power in different groups of MR breast density.

Results: Figure 2 shows the absolute value of SP for all volunteers, presenting a clear separation in scatter power for the 3 breast density groups. Scatter Power has shown to be higher in women with a greater proportion of glandular tissue and may therefore be related to breast density since collagen and glandular epithelium have smaller scattering particles than adipose tissue as described in [1,3]. Similarly, we found a significant difference between low-medium vs high density groups for the TOI. The multivariate linear regression technique showed that MR breast density can be predicted ($p<0.0001$) using a combination of 1) ADC ($p<0.0001$), 2) textural feature describing the non-uniformity of breast tissue (entropy sensitive to fat involvement) ($p=0.011$) and 3) THC ($p=0.0002$), after using "MR weighting factors" at each fiducial location.

Conclusion: In this study a combination of tissue properties measured using MRI and DOS were very strongly associated with breast density, suggesting an association between underlying physiological tissue properties and breast density. This is an important innovation that we expect to test further on larger populations of women undergoing treatment known to change breast density. This study was funded by the American Cancer Society, ACS-0702.

References: [1] **Cerussi A.** et al, 2001:" Sources of absorption and scattering contrast for near infrared optical mammography", Acad. Radiol. 8:211-218, [2] **Klifa C.** et al, 2004:"Quantification of breast tissue index from MR data using fuzzy clustering", IEEE EMBS, 1667-1670. [3] **Cerussi A**. et al, 2002:"Spectroscopy enhances the information content of optical mammography", J.Biomedical.Optics, Vol. 7, (1) 60-71.