Evaluation of lipid composition in patients with benign tissue and cancer using multiple gradient echo MRI

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TARGET AUDIENCE: Researchers (academic and industry) and clinicians interested in breast cancer risk assessment

PURPOSE: Obesity has been identified as a risk factor for the development of breast cancer[1]. Recent studies also demonstrated that lipid composition distant from lesions is different depending on the malignancy of the lesion[2] and its size[3]. While MR-visible lipids in the tumor microenvironment have been studied extensively[4], the relationship between lipid composition in breast adipose tissue and cancer development remains poorly understood. One of the challenges in investigating lipid composition of the breast in the clinical setting is the lack of rapid data acquisition methods that can cover a large portion of the breast with adequate spatial resolution for the complex structure of fibroglandular and adipose tissue. In this study, we use a multiple gradient echo MRI sequence to measure lipid composition in the breast within a clinical diagnostic imaging session.

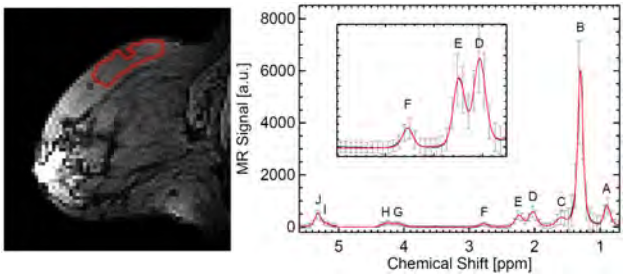

Figure 1. (left) Example image and user-drawn ROI (right) Example spectrum; fit shown in red.

METHODS: Unilateral 3D MR images with voxel-by-voxel spectroscopic information were acquired at 3T with IRB approval in 115 women undergoing diagnostic MRI between July 2013 and September 2014 (mean age 48 yrs, range 24-77 yrs, mean body mass index (BMI) 25.0, range 16.6-46.1, 54 pre- and 34 post-menopausal, 52 with benign tissue, 45 with malignant lesions, and 18 with a history of cancer). A 3D gradient echo sequence was used with 144 echoes (1.44ms echo spacing, 2.8mm isotropic resolution, 12-18 slices, 5min scan time). Regions of interest were drawn in adipose tissue by a single reader on randomized image slices (12-18 slices/patient).

Spectra were generated for each patient by performing a Fourier transform of the complex-valued image data along the echo dimension for voxels in the ROI. The fraction of saturated (SFA), monounsaturated (MUFA), and polyunsaturated fatty acids (PUFA) were calculated using previously published methods[5]. Spatial maps of the fatty acid fractions were generated across the entire acquired data set for 4 patients.

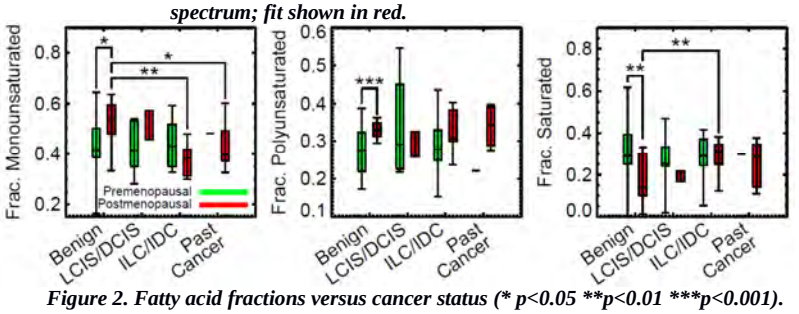

Figure 2. Fatty acid fractions versus cancer status (* p<0.05 **p<0.01 ***p<0.001).

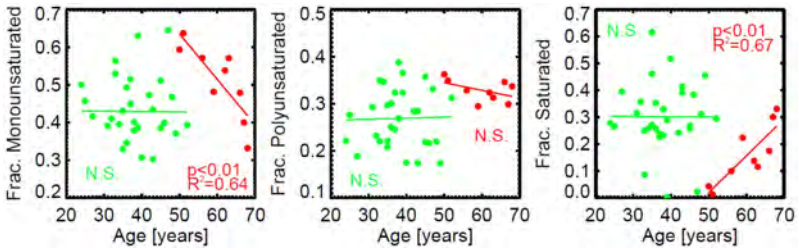

Figure 3. Fatty acid fractions versus age for benign cases (green=pre-menopausal, red=post-menopausal).

RESULTS: Post-menopausal women with invasive cancer had significantly lower MUFAs ($p<0.01$) and higher SFAs ($p<0.01$) than those with benign tissue. Post-menopausal women with a history of cancer also had lower MUFAs than women with benign tissue. There was no significant difference between fatty acid fractions for any of the cancer status groups for pre-menopausal women. Pre- and post-menopausal women with benign tissue had significantly different MUFA ($p<0.05$), PUFA ($p<0.001$), and SFA ($p<0.01$) values. For patients with benign tissue, MUFAs and SFAs in post-menopausal women decreased ($p<0.01$; $R^2=0.64$) and increased ($p<0.01$; $R^2=0.67$) significantly, respectively, with age (a risk factor for breast cancer development). No relationship with age was present for any of the fatty acids for pre-menopausal women. Post-menopausal women with invasive cancer had higher SFAs than those with *in situ* disease ($p=0.055$). While this was also true for pre-menopausal women in our sample, it was much less significant ($p=0.591$). Sample spatial maps showed no clear relationship between fatty acid fraction and distance from the lesion.

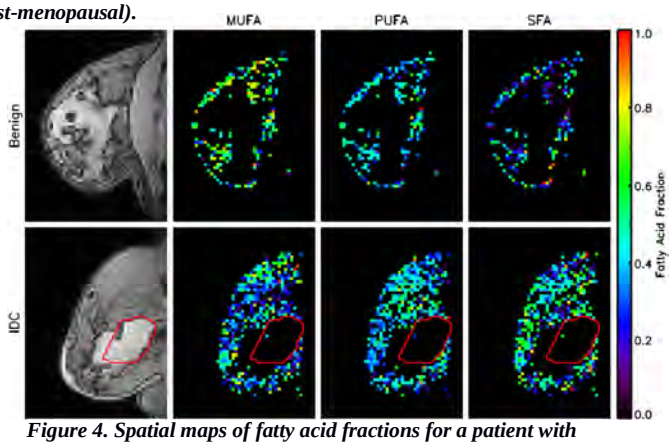

Figure 4. Spatial maps of fatty acid fractions for a patient with benign tissue and an invasive cancer. Maps are scaled from 0 to 1.

DISCUSSION: For post-menopausal women, the data suggest that lower MUFA and higher SFA levels may be related to the development of cancer and more invasive phenotypes, although additional research is necessary to determine if there is a causal relationship. Fatty acid levels do not seem to have a similar relationship for pre-menopausal women. Body mass index (BMI) is known to be an important risk factor for cancer and is believed to influence risk by increasing estrogen levels in the body, which lead to increased cell and tissue growth[6,7]. Estrogen levels in post-menopausal women correlate strongly with BMI, however, this is not true for pre-menopausal women since estrogen is synthesized via an independent mechanism. Therefore, it is not surprising that lipid composition may need to be interpreted differently for pre- and post-menopausal women. A more comprehensive analysis of spatial maps may provide additional information regarding the interaction of fatty acid composition and the presence of cancer.

CONCLUSION: Rapid, non-invasive evaluation of lipid composition may aid in breast cancer risk assessment, particularly for post-menopausal women, and provide insight into physiological mechanisms that facilitate cancer development.

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