Short T2* components in the normal murine mammary gland and pre-invasive carcinoma may aid in detection of early breast cancer.

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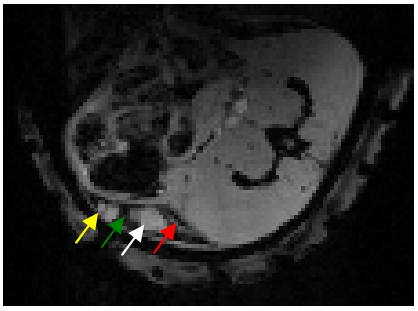
Introduction: Ductal carcinoma *in situ* (DCIS) is the earliest stage of breast cancer, where cancer cells are still confined by mammary ducts. While dynamic contrast enhanced MR imaging (DCEMRI) of the breast has demonstrated excellent sensitivity for early invasive breast cancers, improvements in the diagnostic accuracy of DCEMRI for DCIS is highly desirable. Relaxometry of pure DCIS is important to improve diagnosis of these lesions; however this is difficult to perform in women due to the challenge of isolating and identifying ducts with DCIS. Recently, we have reported for the first time that noncontrast MR imaging techniques can reliably detect early mammary cancer in mice, including single ducts with DCIS. Here, we use transgenic mouse models to perform relaxometry of murine DCIS and normal tissue.

Methods: Female C3(1) SV40 Tag transgenic mice (n=8) were used under IACUC compliance. MR imaging was performed on a 9.4T Bruker magnet. Initially, gradient echo images were acquired for lesion localization (1). Three slices containing normal tissue, DCIS, tumors and lymph nodes were then selected for measurements of T_1 (RARE with variable TR, 4 RARE partitions, TE=12.3 ms, FOV = 3.0×3.0, NEX=2, slice thickness= 1.00 mm, in plane resolution=234 microns), T_2 (spin SE with variable TE, TR/min TE=4000/14.1 ms, FOV=3.0×3.0 cm, NEX=1, slice thickness=1.00, in plane resolution 234 microns) and T_2* (MGE, variable TE, TR/min TE: 400/1.5ms, FOV=3.0×3.0 cm, NEX=1, slice thickness=1.00, in place resolution 234 microns). Signal intensity vs. time curves were generated for several regions of interest: ducts with DCIS, early invasive tumors, normal mammary tissue, and lymph nodes. To calculate T_2 and T_2*, the curves were fit to $S(t) = A_1 \exp(-t / A_2)$ and to test for biexponential decay $S(t) = A_1 \exp(-t / A_2) + A_3 \exp(-t / A_4)$; to calculate T_1 curves were fit to: $S(t) = A_1(1 - \exp(-t / A_2))$.

Results: The average relaxation parameters are displayed in Table 1 for DCIS, normal tissue, tumors and lymph nodes. Normal mammary tissue and DCIS displayed biexponential T_2 and T_2*decay (Figure 1), with short T_2* components: below 3.0 ms for DCIS and 1.0 ms for normal tissue, on average. In comparison, lymph nodes and early invasive tumors exhibited monoexponential decay, with longer T_2 and T_2* decay times. DCIS lesions were better appreciated on shorter TE images, at TE=1.5ms compared to TE=5.0 ms, in terms of morphology, size and signal-to-noise ratio.

ROI	T_1(ms)	T_2 (ms)	T_2* (ms)
DCIS (n=5)	649	36.7	2.4/11.7
Normal tissue (n=8)	1140	90.7	0.7/9.9
Tumor (n=5)	1331	36.5	12.1
Lymph node (n=8)	1480	41.3	11.7

Table 1: Average values of T_1, T_2 and T_2* in various regions of interest. For DCIS and normal tissue, the T_2* decay was bi-exponential, and both low and high T2* components are indicated.



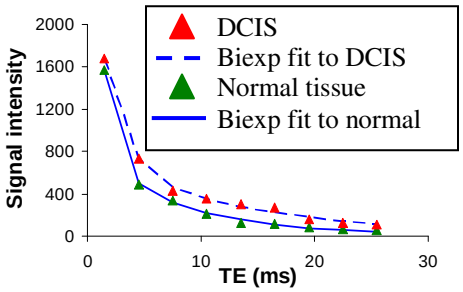


Figure 1: *Left*. Axial GE image demonstrating lymph node (white arrow), small tumor (yellow arrow), duct with DCIS (red arrow) and normal tissue (dark area, green arrow). *Right*. T_2* decay curves of normal tissue and demonstrating bi exponential decay and short T_2* components.

Discussion: These results represent the first direct measurements of the tissue relaxation parameters of early mammary cancer, including DCIS. We found that normal tissue and the earliest stage of breast cancer, DCIS, exhibited biexponential T_2 and T_2* decay, and short T_2* components. Furthermore, the lengthening of T_2* and the loss of biexponential decay accompanied tumorigogensis, and may be a predictive marker identifying when DCIS will progress. Due to the short T_2* components, shorter TE images allow for improved visualization of early cancer and normal tissue. Although further studies are needed in larger numbers of mice, these results do imply that imaging at shorter TE may allow for improved imaging of DCIS and improved characterization of normal breast parenchyma in women, even at lower field.

References: 1.Jansen SA, Conzen SD, Fan X, et al. Detection of in situ mammary cancer in a transgenic mouse model: in vitro and in vivo MRI studies demonstrate histopathologic correlation. Phys Med Biol 2008; 53:5481-5493.

Acknowledgements: We would like to thank the Segal Foundation and Florsheim Foundation for financial support.