Magnetization Transfer Ratio variations in malignant breast lesions and parenchyma

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Target Audience: Researchers with an interest in magnetization transfer changes resulting from malignancy.

Purpose: Breast cancer remains the second leading cause of cancer death in women and the primary cause of death in women aged 45-55. Dynamic contrast enhanced (DCE) MRI is widely used for pre-surgical planning, screening high-risk patients, evaluating implants and response to neoadjuvant therapy. Magnetization Transfer imaging measures the interactions of water protons with different macromolecular environments. This technique exploits interactions between the "free" water protons which yield the conventional MRI signal and "restricted" protons which are typically bound to macromolecules. By applying an off-resonance RF preparation pulse, MT effects can be observed as attenuation in the bound proton pool. Magnetization Transfer Ratio (MTR) is calculated as the ratio of signal intensity with and without the off-resonance saturation pulse. Previously in breast imaging, Heller, et al has demonstrated how MTR can distinguish malignant and benign breast lesions[1], and Bonini, et al has shown how MTR combined with DCE can improve the accuracy of predicting malignancy[2]. To date, there are no reports in the literature of regional variation in MTR within functional parenchyma or on the difference in MTR between malignant breast tumor types. The purpose of this study is therefore to report on changes in MTR in tissue proximal to the malignancy and compare these with respect to the contralateral breast. This study also investigates the differences in MTR between type and grade of malignancy.

Methods: Thirty female patients (aged 55.8±11.0, range 32 to 80 years) were recruited with biopsy-confirmed malignant breast cancer for the purpose of pre-surgical planning. Imaging was performed on a 3T scanner (GE MR750, GE Healthcare, Waukesha, WI) using an eight channel receive-only breast coil. The following 3D spoiled gradient echo sequence was acquired (TE/TR: 2.1/30ms, FA=5°, matrix size=256×256×56, FOV=35cm) with and without a magnetization transfer preparation pulse (400°, offset frequency 2.2kHz). The B_1 field variation was measured using the Bloch-Siegert method as described by Sacolick[3]. MTR was calculated as the difference between MT-on and MT-off divided by MT-off. B_1 maps were derived in MATLAB (v8.0, The MathWorks, Inc., Natick, MA) and spatial convolution was performed using a 7×7 median filter and the resulting B_1 maps were spatially interpolated to match the MTR maps. MTR were corrected for RF transmit field variations using the B_1 maps using empirical validation similar to that previously reported by Samson[4]. The MTR maps were imported into OsiriX (version 5.5.2, Pixmeo, Bernex, Switzerland) and regions of interest (ROIs) were defined to encompass the pectoralis major muscle, parenchyma contralateral to the lesion, parenchyma ipsilateral and proximal to the lesion (within 2cm from the lesion) and tumor. Spatially matched post-contrast T_1W images were used to assist. Normalized Magnetization Transfer Ratio (NMTR) was calculated by dividing each respective measurement by the pectoralis muscle measurement, since others have reported this to reduce inter-individual variation[1]. Shapiro-Wilk's tests were used to investigate if the distributions were normally distributed. One-way ANOVAs were used to assess group differences. A p-value <0.05 was deemed statistically significant.

Results: The biopsies identified a range of grades and invasive types: grade I (n=3), grade II (n=19), grade III (n=8); ductal (n=6), lobular (n=19), mucinous (n=2), tubular (n=2) and papillary (n=2). The MTR and NMTR were significantly lower in proximal parenchyma relative to the contralateral parenchyma ($p<0.001$ for both), however, no difference was noted with either MTR or NMTR between contralateral parenchyma and tumor ($p=0.397$ and 0.370 respectively). There was no statistically significant difference in MTR and NMTR between tumor grades ($p=0.872$ and $p=0.901$). However, the difference in MTR and NMTR between tumour types was statistically significant ($p=0.013$ and $p=0.004$).

Discussion: This is the first study to report on regional variations in MTR within parenchyma associated with malignancy and differences in MTR between tumor types. Tumor stromal changes have been closely associated with the pro-fibrotic 'desmoplastic' reactions in breast cancer[5]. With an increased expression of collagen fibers and myofibroblasts, connective tissue remodeling takes place around the tumor which may contribute to our observed MTR changes.

Conclusions: In this study we noted how the MT effects in invasive mucinous type appear lower than the other tumor types. This is likely to be a result of the high mucin component surrounding the breast cancer cells. We also noted significantly lower MTR values in parenchyma proximal to malignant lesions which may be linked to desmoplastic reactions.

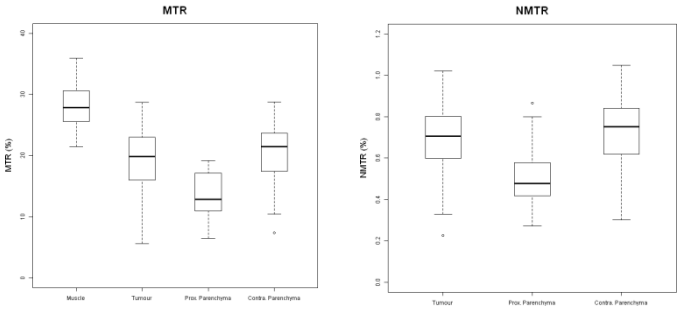

Fig 1: MTR and NMTR distributions illustrating how malignant tumor MT was equivalent to the contralateral parenchyma, however, proximal parenchyma was systematically lower.

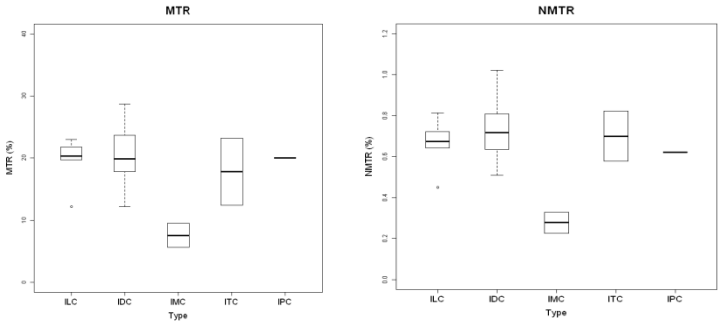

Fig 2: MTR and NMTR distributions for the respective tumor types: Lobular (ILC), Ductal (IDC), Mucinous (IMC), Tubular (ITC) and Papillary (IPC)

References

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