Repeatability of magnetization transfer ratio measurements in the healthy breast at 3T
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Introduction
Magnetization transfer (MT) imaging is sensitive to changes in the macromolecular content of tissue and is, therefore, gaining increased attention as a noninvasive approach to probe the complex tumor environment in cancer [1-2]. We have previously demonstrated the feasibility of performing MT imaging of the breast at 3T in healthy controls [3]. The aim of this study is to explore the repeatability of MT ratio (MTR) measurements of fibroglandular (FG) tissue in healthy controls at 3T.

Methods
Twelve women with no history of breast disease were scanned twice within a 24-hour period. Images were acquired with a 3T Achieva MR scanner equipped with the MammoTrak table, including a dedicated 16-channel sensitivity encoding (SENSE) receive double-breast coil (Philips Healthcare, Best, The Netherlands). MT images were acquired with a 3D gradient echo (GE) sequence with TR = 82 ms, TE = 5.7 ms, flip angle = 10°, SENSE parallel imaging (acceleration factor = 2), signals averaged = 2, and a 1:3:3:1 binomial excitation pulse was applied for fat suppression. A sagittal volume was acquired with FOV = 192 x 192 x 60 mm³ and voxel size = 1.33 x 1.33 x 5 mm³. Two image volumes were acquired in a total scan time of 1 min 40 s: a reference image (MTRref) with no saturation pulse applied and an MT-weighted image (MTRw) with a saturation pulse applied (RF offset = 1.25 kHz, duration = 20 ms, effective flip angle = 1200°).

MT ratio (MTR) maps were calculated: \( \text{MTR} = 1 - (\text{MTRw} / \text{MTRref}) \). Regions of interest (ROIs) encompassing the FG tissue were defined for each slice in the MTRref image using a semi-automated thresholding scheme to exclude skin, muscle, and voxels with severe partial volume averaging. The individual ROIs were combined to generate a single volume of interest (VOI), and the mean MTR (mMTR) value was calculated for the VOI for each scan for each subject. Repeatability statistics were performed with the methods outlined by Galbraith et al. [4].

Results
Representative results from the central slice of a single subject are shown: MTRref (A), MTRw (B), and an overlay of the corresponding masked FG MTR map (C). FG MTR values are plotted for each data set, with the mean and standard deviation (SD) values denoted by the red solid and blue dashed lines, respectively (D). The difference between the mMTR values between scans is plotted against the average of the mMTR values for the two scans for each subject (E). The mean difference for all subjects (-0.007) was not significantly different from zero, and the individual difference values were not dependent upon the average mMTR value. The 95% confidence interval limits were ±0.013 (\( \alpha = 0.05 \)) and the repeatability measure (2.77 x within-subject standard deviation) was 0.044.

Discussion
We were able to reliably produce MTR maps of healthy FG tissue with good fat suppression. The results from this study indicate that a change in mMTR larger than ±0.044 for an individual or ±0.013 for a group of 12 patients would be statistically significant (\( \alpha = 0.05 \)).

MT imaging is potentially sensitive to microstructural changes that occur prior to macroscopic changes in gross morphology and traditional contrast mechanisms, such as T1 and T2 relaxation rates. In particular, the magnitude of the MT effect depends on the interaction between large, relatively immobile, semi-solid like macromolecules and bulk water. If there is a change in the macromolecular concentration of the tissue, then the MTR may reflect the change. The assessment of the variability of breast MTR imaging at 3T in healthy volunteers will allow for further studies of pathology. Future work includes studying the effects of menstrual cycle and age (potential sources of changes in breast water content) on FG MTR values and applying the technique in an ongoing longitudinal, multiparametric study of treatment assessment in breast cancer.

References
1) Bonini et al., MRM 2008; 59:1030. 2) Kim et al., ISMRM 2010, 4745. 3) Arlinghaus et al., ISMRM 2010; 1005. 4) Galbraith et al., NMR Biomed 2002; 15:132. Funding NCI 1R01CA129961 and NCI 1U01CA142565