Repeatability of chemical exchange saturation transfer measurements in healthy fibroglandular breast tissue at 3T

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Introduction

Chemical exchange saturation transfer (CEST) MRI is sensitive to solute/water proton exchange at specific resonance frequencies, such as the amide protons, and modulation of this exchange by the hydrogen ion concentration. Amide proton transfer (APT) CEST MRI has been applied to brain tumors both in animals [1] and humans [2-3], and has shown the potential to distinguish between inflammation and pathological tissue. We have previously demonstrated the feasibility of performing CEST imaging at 3T in human breast [4]. The goal of this study is to determine the repeatability of CEST MRI applied to human fibroglandular (FG) of the breast at 3T.

Methods

Image acquisition Ten 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). Images were acquired with a 3D gradient echo sequence with TR/TE = 7.1/3.5 ms, flip angle = 10^0, single-shot turbo-field echo fast imaging with TFE factor of 42, SENSE parallel imaging (acceleration factor of 2 in both RL and AP directions), and a 1-3-3-1 binomial pulse for fat suppression. Ten unilateral sagittal slices were acquired (FOV = 192 x 192 x 50 mm^3) with in-plane resolution of 2.5 x 2.5 x 5.0 mm^3. The pulsed CEST saturation was achieved with a 35 sinc-Gauss 25 ms, 0.5 mT pulses with a 90% duty cycle. The offset was swept between ± 6 ppm in 0.3 ppm increments with a total scan time of 6 min 42 s.

Image analysis The data, ($S(\Delta\omega)$), were non-rigidly co-registered using diffeomorphic demons with diffusion regularization criteria as implemented in Medical Image Processing, Analysis, and Visualization (MIPAV). Data were normalized using the average of $S(\omega=\pm 6\ ppm)$ =S0. The data, $S(\Delta\omega)/S0$, were fit to a Lorentzian and the minima of the fit were used as the center frequency. Data were shifted accordingly and extrapolated to the acquired frequencies to account for field inhomogeneities. The magnitude of the CEST effect was calculated as the residuals between the acquired CEST saturation spectra and the Lorentzian fit on a voxel-by-voxel basis. This technique accounts for spurious asymmetric MT effects, fat contamination, or simply noise. To quantify the CEST effect caused by the presence of amide protons (typically termed the amide proton transfer asymmetry), the magnitude of the difference between the fitted Lorentzian and the shifted CEST spectrum at the amide resonance, $\Delta\omega$ = 3.5ppm was calculated and designated the $APT_{residual}$. Regions of interest (ROIs) were defined for each slice using a semi-automated thresholding scheme to exclude skin, muscle, and voxels with severe partial volume averaging. Repeatability statistics were performed with the methods outlined by Galbraith et al. [5].

Results

Representative $APT_{residual}$ maps from the FG tissue of the same healthy control are shown in Panel A and B while the spectral results of the FG tissue are shown in Panel C. The difference between the ROI $APT_{residual}$ values between scans is plotted against the average of the $APT_{residual}$ values for the two scans Panel D. The mean difference for all subjects (0.6738) was not significantly different from zero, and the individual difference values were not dependent upon the average $APT_{residual}$ value. The 95% confidence interval limits ±0.418 (α = 0.05) and the repeatability value was 1.321.

Discussion

We were able to reliably produce $APT_{residual}$ maps of healthy FG tissue with good fat suppression. The results from this study indicate that a change in $APT_{residual}$ larger than $\pm$1.321 for an individual or ±0.418 for a group of 10 patients would be statistically significant (α = 0.05). CEST imaging is potentially sensitive to microstructural molecular changes that occur prior to macroscopic changes in gross morphology and traditional contrast mechanisms, such as T_1 and T_2 relaxation times. In particular, the magnitude of the CEST effect depends on the interaction between relatively mobile macromolecules, such as those associated with the amides, and bulk water. If there is a change in the mobile macromolecular concentration of the tissue, then the CEST saturation spectrum will reveal the change. The assessment of the variability of breast CEST 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 $APT_{residual}$ values and applying the technique in an ongoing longitudinal, multiparametric study of treatment assessment in breast cancer.
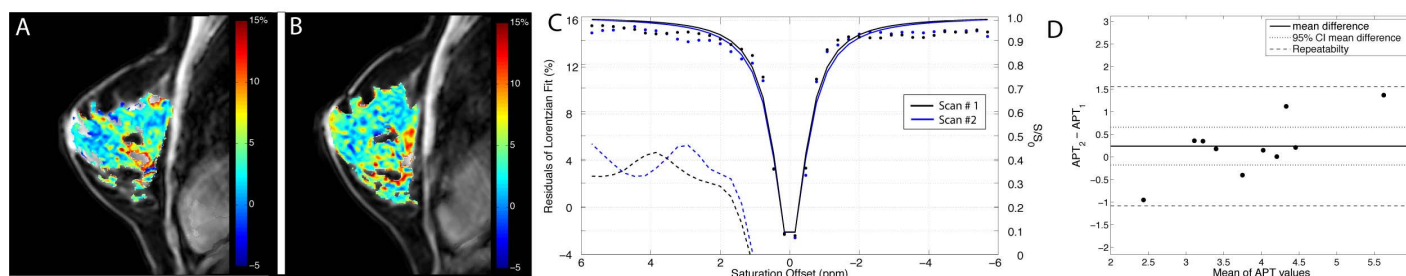
References 1) Salhotra et al. NMR Biomed 2008. 2) Zhou et al. MRM 2008. 3) Zhou et al. MRM 2003. 4) Dula et al., ISMRM 2011. 5) Galbraith et al., NMR Biomed 2002.