Application of chemical exchange saturation transfer (CEST) to the spinal cord at 7 Tesla

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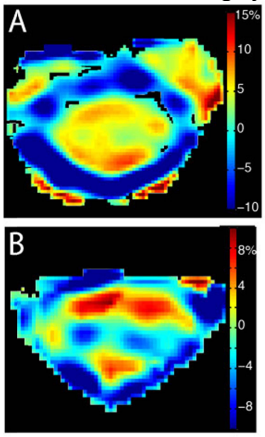
Introduction: Chemical exchange saturation transfer (CEST [1,2]) is sensitive to solute/water proton interactions of exchangeable protons, which resonate at specific spectral resonant frequencies. Since these protons are in direct chemical exchange, it is possible to detect low concentrations of metabolites, proteins, peptides, and ultimately determine the pH of the tissue without the use of exogenous contrast agents. However, for the CEST effect to be realized, the exchanging spins must be in the slow to intermediate regime on the NMR time scale, the SNR must be sufficiently high, and the field inhomogeneities minimized. Significant improvement of the CEST measurement can be obtained at 7T since the exchange rate is more favorable and the SNR higher. CEST measurements of the spinal cord have not been reported in the literature due to limited SNR and variable field inhomogeneity compared to the brain. However, if the latter can be corrected with "centering methods", transitioning to higher B0 can combat the former. We apply this knowledge to the development of a 7T CEST acquisition scheme for the healthy cervical spinal cord and compare the results with our previous studies at 3T. We hypothesize that development of spinal cord CEST could reveal the health of the spinal cord and its relationship to disease earlier than conventional MRI methods.

Methods: Data Acquisition: Five healthy volunteers were imaged using a 7T Philips MR scanner at the level of C3. Signal excitation and reception were achieved using a novel surface quadrature transmission and 16-channel receive coil (Nova Medical). CEST data were obtained using a single-shot Turbo Field Echo (TFE factor = 63, shot duration = 1.1s) over 8 slices (5mm) with nominal in-plane resolution = 1.5x1.5mm^2 (FOV = 180x180mm^2). Other parameters were: TFE echo spacing/TE/α = 4.8ms/3ms/25, SENSE = 2, and one average. Saturation was achieved with a train of 25, single-lobed Gaussian pulses (1μT, duration = 25ms, 80% duty cycle) leading to a saturation train of 500ms. The offset frequency ($\Delta\omega$, w.r.t. to water) was obtained from -5 to 5ppm over 48 offset values (0.2ppm spacing).

Data Analysis: Prior to analysis, all CEST data were registered to a reference (mean of $\pm$5ppm) using a 12-degree of freedom affine registration algorithm. Data were normalized using the average of $S(\omega = \pm 5\ ppm) = S0$ and the CEST saturation spectra was fit to a Lorentzian and the offset frequency of the minima of the fit were used as the center frequency, voxel-by-voxel. Data were shifted accordingly and extrapolated to the acquired frequencies to account for field inhomogeneities. Deviation from a Lorentzian fit has been shown (ISMRM 2011) to be an accurate reference from which to calculate the magnitude of the CEST effect, and thus, we calculated 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 increase SNR, the integral of the signal difference between the fit Lorentzian and the CEST spectra from 3.1-3.9ppm was calculated and reported as a measure of the APT effect (similar to the APT_{asym} used in the literature, though the values will be different) and denoted $APT_{redisual}$.

Results and Discussion: Representative *integrated APT effect* maps ($APT_{residual}$) from the described 7T acquisition (Panel A) and from 3T (Panel B)[3] are shown. The 7T results reveal values and white/gray matter contrast comparable to that found in the brain [4]. Panel C shows the CEST spectra (points) from regions of interest in the gray matter and lateral white matter (WM), the Lorentzian fit (solid lines, right y-axis), and residual between this fit and the data (dashed lines, left y-axis). The integrated residuals around the amide resonance ($APT_{residual}$) were quantified for each of the 5 subjects with results shown in Table 1. Although there is apparent WM/gray matter separation seen in the $APT_{residual}$ map in Panel A, the $APT_{residual}$ values (Table 1) did not exhibit a significant difference (p = 0.21) using the Kruskal-Wallis test. Finally, there are apparent peaks at 3.5 and 2.25ppm in the residual plot (dashed lines). The former is known to relate to the amide proton exchange, but the latter may be more reflective of subtle tissues differences in spinal cord relative to the brain where it is not seen. Further optimizations of sequence design and reproducibility comparisons are necessary.



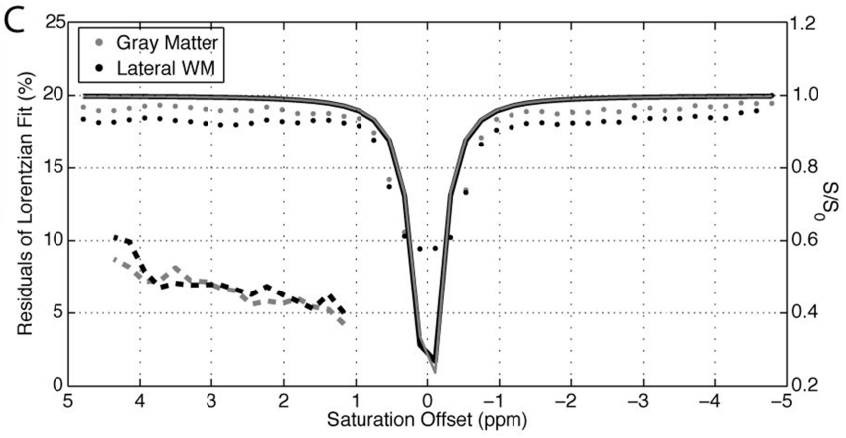


Table 1 - Integrated area between Lorentzian fit and CEST spectra

	GM		Dorsal White Matter		Lateral White Matter	
	mean	std	mean	std	mean	std
1	6.21	± 2.84	6.78	± 4.34	5.55	± 3.48
2	6.72	± 3.27	8.79	± 5.32	10.86	± 5.05
3	6.68	± 3.25	8.74	± 5.28	10.79	± 5.02
4	6.72	± 3.27	6.44	± 3.51	6.05	± 3.67
5	4.90	± 1.99	7.88	± 4.66	7.15	± 4.37
Group Mean	6.25	± 0.78	7.73	± 1.09	8.08	± 2.57

References 1) Wolff et al. MRM 1989. 2) Van Zijl et al. MRM 2003. 3) Dula et al. ISMRM 2011. 4) Dula et al. MRM 2011.

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