CEST Imaging at 7 Tesla: Comparison of the WASSR and Higher Order Polynomial Fit to Determine Center Frequency

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INTRODUCTION Chemical exchange saturation transfer (CEST) imaging is a molecular MRI technique that detects endogenous mobile protons via saturation transfer. One type of CEST imaging, amide proton transfer (APT) enables MRI quantification of protein and peptide levels *in vivo* by probing amide protons in the peptide bonds through asymmetry in the z-spectrum. However, asymmetry analysis of the CEST z-spectrum is sensitive to magnetic field inhomogeneities causing the minimum of the CEST spectra to occur at frequency offsets up to 300 Hz away from the true minimum even in “well shimmed” imaging situations. This effect is exacerbated at higher field, in particular 7T. In order to resolve this shortcoming of CEST imaging, generally a polynomial fit to the CEST spectra is applied and the minimum of the polynomial fit is deemed the center frequency shift, and the CEST spectra are shifted accordingly. However, the robustness of this technique relies on sampling the minimum of the CEST spectra in sufficient detail, and therefore, one must sample the entire CEST spectra with high spectral resolution in order to obtain convincing CEST/APT/asymmetry results. Recently, a separate acquisition with low RF power, relying on direct water saturation imaging has been used to establish the frequency shift due to field inhomogeneities and is termed water saturation shift referencing (WASSR).[1] These WASSR spectra are symmetric with negligible interference from field inhomogeneities, MT, or CEST. Thus WASSR appears to be a robust method for determining the center frequency shift at 3T. An additional benefit is that in order for the WASSR method to be effective when shifting the CEST spectra, only a few points on the CEST spectra are necessary, which decreases the overall scan time. We have evaluated whether the WASSR technique works robustly well at higher field (7T) compared to high-order fitting for finding the center frequency of CEST data sets using a reduced sampling scheme for clinical APT imaging.

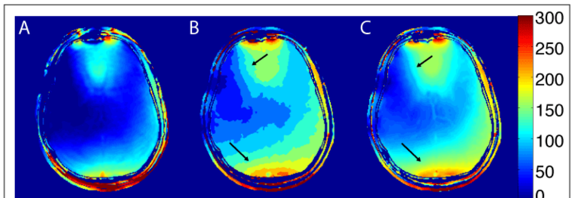

Fig. 1 - A) Bo map acquired from the scanner compared with frequency shift maps calculated by taking the minimum of a high order polynomial fit (B) and by taking the minimum of the WASSR z-spectra. the WASSR shift map is smoother and the transition zones are less profound (arrows). Color scale in Hertz.

METHODS Image acquisition: A total of six CEST experiments were performed on a Philips Achieva 7T scanner with a 16 channel NOVA head coil for signal reception. A 3D FFE sequence with single-shot TFE and a SENSE factor of 2.5 (AP) was used resulting in 2.1 x 2.1 x 3.0 mm resolution with eight slices acquired. WASSR data were acquired on the same volume using a 0.5 μT, 100 ms RF pulse at 26 offsets between ± 300 Hz (TR/TE = 50/2.4 ms, scan time = 5 mins). The CEST data were acquired using a 3.5 μT, 500 ms RF pulse at 25 offsets between ± 1350 Hz (TR/TE = 40/2.4 ms, scan time = 9 mins). A conventional B_o field map was also acquired for comparison (TR/TE = 48/3.9 ms, scan time = 44 sec). **Image analysis:** WASSR frequency shift maps through symmetry analysis of the center frequency. Results were compared to field maps calculated using the dual echo method.[2] Regions of interest (ROIs) were manually drawn and compared for both centering techniques. The CEST spectra were shifted using the WASSR shift and extrapolated back to the original RF offsets prior to asymmetry analysis. For comparison, the CEST data were interpolated to 100 points using piecewise cubic interpolation and fit to a high order (25^{th}) polynomial. The global minima of the polynomial fit were determined using the maximum symmetry algorithm[1] and used as the frequency shift for this method. In addition, the effects of reducing the number of offsets on the polynomial fitting method were examined by decreasing the points in the z-spectra, performing the high order fit, and using the calculated minima as the center frequency shift. Initially, 7 offsets were examined including ± 1050, 850, 200 and 0 Hz. Eliminating the 0 Hz frequency was also examined by fitting ± 1250, 1150, 1050, and 950 Hz.

RESULTS and DISCUSSION WASSR and CEST spectra were acquired from two healthy controls, shift maps (polynomial fit, B and WASSR-based shift map, C) are shown in Fig. 1 along with the B_o map (A) for comparison. Each map exhibits a similar trend and magnitude, but the WASSR shift map is smoother and the transition zones are less profound (arrows). Z-spectra for ROIs are shown in Fig. 2 prior to shifting (dashed line) and following shifts (solid lines) for both methods demonstrating the similar performance when sufficient RF offsets are acquired. However, Fig. 3 examines the effects of decreased RF offset sampling density for the polynomial fit method. The original 25 offsets with the results of WASSR (solid) and polynomial fit (dashed) shown in black. Application of the polynomial fit to a reduced the number of samples including a 0 Hz offset resulted in a miscalculation of the center frequency shift by 92 Hz (red dashed line), when removing 0 Hz, this miscalculation increased to 200 Hz (blue dashed line). Herein, we demonstrate that a fast WASSR imaging approach and achieve B_o with suitable accurate for CEST imaging in only 14 mins of scan time versus 9 mins for a traditional method. Such an approach will allow robust, quantitative CEST imaging at 7T in clinically feasible scan times (total protocol < 20 minutes).

REFERENCES 1. MRM 61(6):1441 **2.** MRM 37(4):628 **ACKNOWLEDGEMENTS** NIH T32 EB 001628 and NIH/NBIB K01-EB009120 for funding

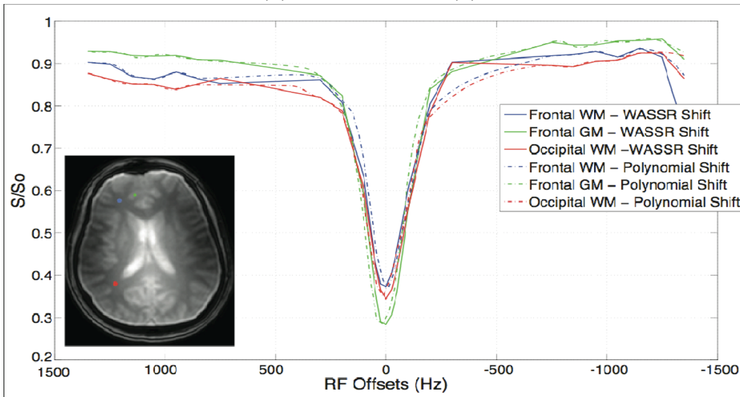

Fig. 2 - Region of interest analysis of CEST data desmonstrating the results of using the WASSR shift (solid lines) compared with the results of the higher order polynomial fit. These methods of centering the z-spectra perform simiarly when using 25 offsets between +/- 1350 Hz.

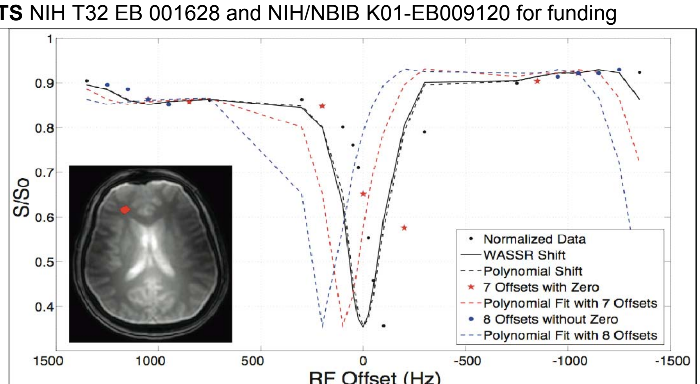

Fig. 3 - Effects of reducing the number of offsets on the center frequency determination using a higher order polynomial fit. The normalized data is shown in black with the results of WASSR shift and polynomial fit shift shown in solid and dashed black lines, respectivly. As the number of points is reduced, and the center offsets are removed, the polynomial fit shifting method does not perform as well as using the WASSR data to determine the center frequency.