SAS: Symmetric Analysis of Z-Spectra, a Method to Evaluate B0 Correction Techniques for CEST Data in Clinical Systems Using Non-Exchanging Phantoms

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Introduction: Chemical Exchange Saturation Transfer (CEST) data requires correction for B_0 variations, which alter the effective off-resonance applied frequencies on a voxel-by-voxel basis. Currently research groups worldwide use multiple methods of correcting for B_0 variations, which are often compared based on the resultant contrast values from the analysis method of choice. Here a new method for comparing the techniques deriving from external scans is proposed – a Symmetric Analysis of Z-Spectra (SAS) on phantoms containing no exchange effects or Magnetisation Transfer (MT) effects.

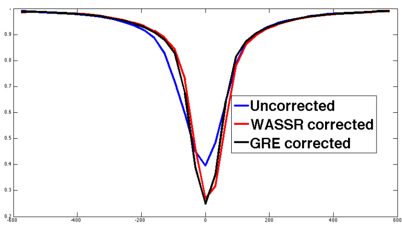

Fig 1. Effect of correction on ROI averaged CEST spectra (no shim condition)

Theory: *In-vivo* CEST data is inherently asymmetrical due to contributions to the z-spectrum from MT effects and exchange based CEST effects. In most experiments the z-spectrum is used to calculate a contrast value, such as the common MTR_{asym} metric. To obtain precise calculations based on the z-spectrum, there must be an accurate measure of the central frequency in each voxel, and therefore the effective applied off-resonance frequencies. Attempts to measure B_0 correction values have thus far failed to account for the underlying ground truth of the system to assess the validity and accuracy of each method. The SAS method proposed here designs a ground truth state by removing MT and CEST effects, which can be difficult to model accurately, allowing an objective assessment of the accuracy of each field correction method. The use of the SAS method is limited to B_0 correction techniques that rely on scans external to the CEST acquisition, and is not suitable for B_0 correction techniques based purely on fitting the z-spectrum. Here the SAS method is used to compare dual-echo Gradient Echo (GRE) B_0 field mapping, and WASSR[1] B_0 correction techniques, under a variety of field homogeneity conditions. The SAS value: the integral of the MTR_{asym} between 0.5 and 4.0 ppm, is proposed as a measure of the quality of field correction, as this covers conventional endogenous CEST imaging interests. A lower SAS value should correspond to an improved field correction, as no asymmetry should be present in the phantom.

Methods: Phantom: A cylindrical 2L liquid 12mM copper sulphate phantom was created with a similar T_2 to that of grey matter *in-vivo* at 3T[2] in order to create a direct saturation curve with a width similar to that expected *in-vivo*. Scanning: All scans were completed on a Philips Achieva 3T system (Philips, Best, The Netherlands) at 3x3x5mm^3 resolution with 192x192x100mm^3 FOV. CEST spectra were obtained from a 3D turbo gradient echo sequence TE 4.92 ms, TR 10.05 ms, T_{sat} 40ms, shot-interval 87 ms, with 4 lines of k-space acquired in each shot. 10% oversampling in the z-direction was used to allow the system to reach a steady state before significant portions of k-space were filled. 38 CEST offsets of 0 ± 0.25 ppm (32 Hz) to ± 4.5 ppm (576 Hz) including a normalisation image were acquired in 20 min with $B1_{rms}$ of 2.0μT, alternating positive and negative offsets from high to low. WASSR spectra were created with 63 offsets 0 ± 5Hz to ± 155Hz in order to account for large off-resonance frequencies in the non-ideal homogeneity conditions. WASSR spectra were obtained with 3D GraSE to allow fast acquisition of k-space following a short off-resonance pulse, with a long TR (3s) to prevent any steady-state magnetisation and TE 23.35ms, EPI factor 35, TSE factor 12, scan time 3 mins. Dual-echo GRE images for B_0 field mapping were taken with TE 4.6ms/6.9ms, TR 10.86ms, scan time 1 min. For each shim condition GRE images were followed immediately by the CEST and then WASSR acquisitions, with offset sampling orders chosen to minimise any effects of field drift. Shim conditions were varied in order to test methods at different field homogeneities, with scans completed with no shim, 1st order shimming over entire phantom, 2nd order "good" shimming over a volume covering the entire phantom, and 2nd order "poor" shimming over a small section at the edge of the phantom. Processing: WASSR field offset values were calculated by fitting a Lorentzian function to the acquired WASSR spectrum to find the central value in each voxel. All data sets – GRE corrected, WASSR corrected and uncorrected – were interpolated by a cubic spline to the input CEST offset values by addition of calculated field offset to the effective acquired CEST spectrum offsets. A singular ROI covering the whole phantom was drawn on the normalisation CEST image and applied to all data sets. For each B_0 correction technique, MTR_{asym} values were calculated at offsets used for conventional endogenous CEST species: 1.0 ppm for myo-inisotol, 1.5 ppm for GlucoCEST, 2.0 ppm for GluCEST, and 3.5 ppm for Amide Proton Transfer Imaging (APT). SAS values were also calculated by integrating MTR_{asym} between 0.5 and 4.0 ppm.

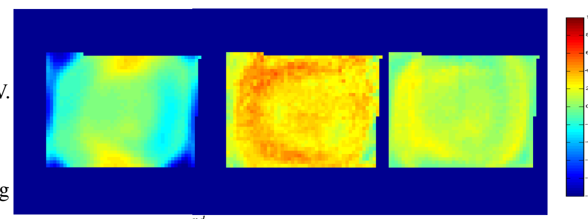

Fig. 2 SAS values 2nd order "good" shim, Uncorrected, WASSR and GRE corrected respectively

	None	Linear	2nd Order "good"	2nd Order "poor"
Uncorrected	-6.32 ± 28.45	-6.42 ± 27.74	-0.38 ± 3.30	-22.48 ± 76.30
WASSR	7.21 ± 5.72	5.60 ± 5.56	3.25 ± 1.72	-14.84 ± 58.9
GRE	1.54 ± 1.37	2.47 ± 1.37	0.99 ± 0.86	-14.50 ± 64.63

Table 1. SAS calculated means $\pm$ standard deviations for different conditions

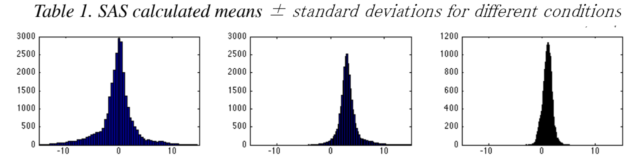

Fig 3. SAS value histograms – 2nd Order "good" shim. Uncorrected, WASSR and GRE respectively

Results: The SAS values are shown in Table 1. In all shim conditions except the "poor" GRE and WASSR correction methods significantly improved the MTR_{asym} and SAS values relative to uncorrected values, seen in either the histograms (Fig. 2), or the standard ddeviation in Table 1, with larger effects seen when less shimming was applied. Yet the WASSR seemed to introduce some bias in our data, as seen by the mean SAS value. In "poor" shim conditions clear effects of phase wrap can be seen in the GRE B_0 maps, which manifests in the MTR_{asym} and SAS values. The B0 field deviations also exceed the effective range of the WASSR acquisition, (±155Hz), leading to a smaller error on the SAS values.

Conclusions & Discussion: Here a new SAS method is presented to quantify the effects of B_0 correction techniques on CEST data. The SAS method is applicable when external scans are used to correct the CEST spectrum, but not when fitting methods are used for correction. This is because fitting methods will be heavily influenced by the function fitted; symmetrical fitting functions would give artificially high SAS values relative to correction methods relying on external scans. While the GRE correction method used here provides significant improvement relative to WASSR, the latter can potentially be improved through non-linear selection of offset frequencies to characterise the expected underlying field in typical scanning conditions.

References:[1]Kim, M et al, Magnetic Resonance in Medicine (2009); 61;1441-50. [2] Grenier, D et al, Magnetic Resonance Imaging (2002); 20,10;733-41.

Acknowledgements: MRC Training Grant MR/J500422/1. The MS Society in UK, NIHR UCL-UCLH BRC