On the selection of reference images used for registration in CEST imaging

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Target audience: Researchers using image registration in chemical exchange saturation transfer (CEST) imaging.

Purpose: CEST is an emerging imaging modality, which can provide valuable molecular information through the bulk water signal used for clinical imaging. It typically requires multiple images to be repetitively acquired at various dynamic saturation or unsaturation frequencies. Conceivably, motion can occur between dynamics, especially for human applications where anesthesia is seldom used. Image registration has been widely used as an important preprocessing procedure for ensuring high-quality CEST images[1-7]. In many of these cases[1-4], the unsaturated images (S_0) were used as the reference during image registration. However, there is no report on the proper choice of reference images. As shown in this abstract, the selection of reference images can have significant impact on results.

Methods: Five normal volunteers with informed consent were recruited for CEST imaging on a 3T dual-transmit Philips Achieva system. Thirty-two sinc-gauss-shaped pulse elements were alternated between the two transmit channels to achieve an effective continuous saturation[8] (32x50ms=1.6s) with an average B1 power of 2uT. Nine saturation frequencies were used, i.e. 3.0, -3.0, 3.5, 3.5, -3.5, -3.5, 4.0, -4.0 ppm and S_0, for amide proton transfer (APT) imaging[5]. The 3D imaging readout (FOV: 212x186x66mm, acquisition resolution: 2.2x2.2x4.4mm) was done with TFE (turbo factor: 110; flip angle: 10^0), TSE (turbo factor: 55) and GRASE (SE factor: 22; EPI factor: 7) sequences, respectively. As for B_0 correction, a separate WASSR[9] sequence was used employing TSE readout (turbo factor: 183) with an average saturation power of 0.5uT and a saturation duration of 0.2s (=4x50ms).

Image registration was performed with AFNI[10] by setting the reference as each of the 9 saturation dynamics and the mean of all dynamics. The cost function was normalized mutual information, the resampling method was sinc and the registration algorithm was 12-degree-of-freedom affine transformation.

Eleven sets (10 registered sets and 1 original non-registered set) of APTw images for each of the 3 different readout sequences of each of the 5 volunteers were generated after the normalization to S_0 and correction for B_0[5]. To evaluate the different sets of APTw images quantitatively, a uniformity index (UI) was computed based on the standard of National Electrical Manufactures Association, as $UI = 100(1 - 1/N/\bar{Y} \times \sum_{i=1}^{N}|Y_i - \bar{Y}|)$, where Y_i is the intensity of i^{th} voxel, $\bar{Y}$ is the mean intensity of all voxels and N is the number of voxels. The rationale is that a higher UI is expected for better motion-corrected APTw images, which are supposed to be uniform across the whole brain for normal volunteers at 3T. Paired t-test was performed to determine the statistical difference in UIs between registered images compared to original non-registered (n.r.) images.

Fig. 1: APTw images after registration using different reference images.

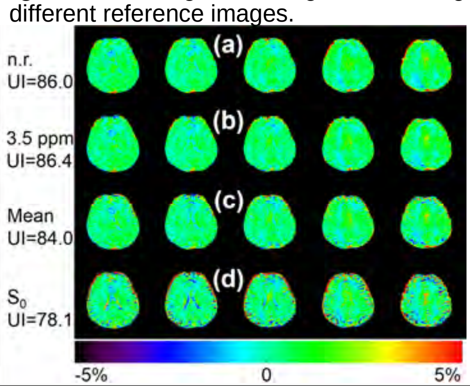


Fig. 2: APTw images after registration using different reference images.

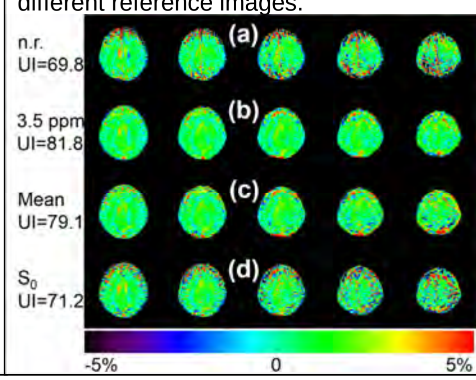
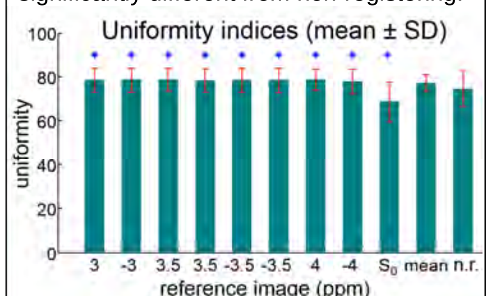


Fig. 3: Uniformity indices from all volunteers and all readout sequences by using different reference images. Blue stars denote significantly different from non-registering.



Results: **Fig. 1** shows that the UI increases slightly after registering to the 3.5ppm dynamic (1b) compared to that from the original non-registered images (1a). On the contrary, the UI decreases after registering to the mean of all dynamics (1c), and along with noticeable worse uniformity after registering to the unsaturated dynamic (1d). **Fig. 2** shows that the APTw images (2a) are significantly improved after registration to the 3.5ppm (2b) or the mean of all dynamics (2c). However, improvement is barely seen if registering to S_0 (2d). **Fig. 3** shows that registering to S_0 is significantly worse than non-registering. Registering to the first 3.5ppm dynamic generates the highest average UI though it's not significantly different from others except those from S_0, the mean and non-registering. Compared to non-registered UI, registering to the 3.5ppm dynamic increases UI by 6% while registering to S_0 decreases UI by 8%.

Discussion and Conclusion: APTw images can be significantly different in terms of visual appearance and quantitative UIs (Figs. 1-3) when different reference images are chosen during registration. Differing from usage of S_0 as the reference in many reports[1-4], it's shown here that S_0 is actually the worst reference while the 3.5ppm dynamic generates the highest UI and the best visual uniformity.

References: [1] Johns CK, et al. MRM 2012. [2] Johns CK, et al. NeuroImage 2013. [3] Scheidegger R, et al. NeuroImage 2014. [4] Tee YK, et al. NMR Biomed 2014. [5] Zhou J, et al. JMRI 2013. [6] Tietze A, et al. NMR Biomed 2013. [7] Togao O, et al. NeuroOncolgy 2014. [8] Keupp J, et al. ISMRM 2011. [9] Kim M, et al. MRM 2009. [10] Cox RW. Comput Biomed Res 1996.