Novel CEST MRI processing pipeline in pilot study of MCI patients with biomarkers of AD vs Controls

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INTRODUCTION: Current diagnostic methods for Alzheimer's Disease (AD) are invasive (CSF analysis) or costly (PET imaging). Chemical Exchange Saturation Transfer (CEST) MRI could offer a low cost and non-invasive complimentary modality for evaluating patients being considered for or receiving anti-amyloid treatments. Specifically, given the need to repeat serial monitoring MRIs while undergoing treatment, CEST could serve as a response monitoring tool, a current unmet need in this population. Here, first, we develop a novel CEST MRI pipeline utilizing established neuroimaging processing tools. Next, we demonstrate its use in the pilot study of Mild Cognitive Impairment (MCI) patients (i.e. early AD) vs normal controls (NC).

METHODS: Four MCI patients with CSF-biomarker confirmed AD pathology and 4 age-matched cognitively healthy individuals were recruited and scanned using a 3 Tesla MR unit (Philips Ingenia). Multi-slice CEST GRE mDixon sequence was acquired with in-plane resolution=2x2 mm, slice thickness=5mm. For Z-spectrum, 23 frequency points were acquired between ±6 ppm with a total scan time ~12 min. Water-only images were rigidly motion corrected using Advanced Normalization Tools (ANTs) [1]. Custom Matlab routines were used to generate voxelwise MTR_{asym} maps at 1ppm, 2ppm and 3.5ppm. 3D T1w images were processed with Freesurfer 6.0 to generate ROIs common to all subjects [2]. ANTs was then used to co-register the Freesurfer ROIs to the CEST data. Additionally, a six pool multi-Lorentzian model (water, MT pool, 1 ppm, 2 ppm, 3.5 ppm and -3.5 ppm) was fit to average Fressurfer ROI Z-spectrum data for each subject. Average group CEST effects (MTR_{asym} and Lorentzian Amplitudes) across each ROI for the AD and NC groups were evaluated. A summary of the pipeline can be found in Figure 1.

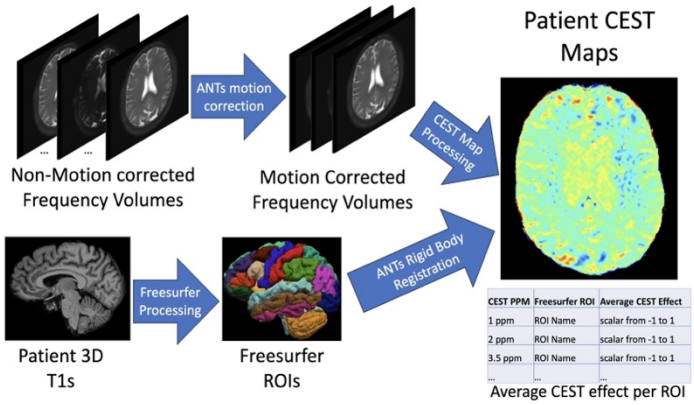

Figure 1

RESULTS: An evident reduction of erroneous signal along gyral borders was noted with motion corrected data shown in Figure 2 where A is non-motion corrected and B is motion corrected. Figure 3 shows axial slices from a representative patient's T1w MRI overlaid with 3D representations of the Freesurfer ROIs that were identified as having p-values less than 0.05 for the comparison of Lorentzian amplitude differences within the hydroxide, amine, and amine pools. Figure 3 shows views from superior to inferior (left) and inferior to superior (right).

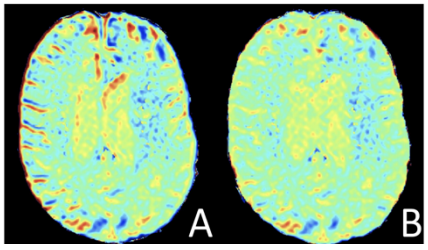

Figure 2

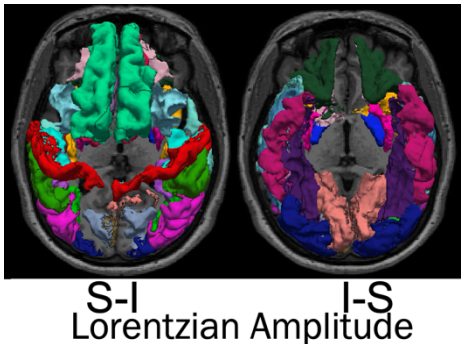

Figure 3

DISCUSSION: Regions with p-values less than 0.05 coincide with known AD-involved brain regions such as the cingulate [3], precuneus [4], putamen [5], orbitofrontal [6], and temporal regions [7] with a similar distribution to previous amyloid histopathology studies [8]. Lorentzian fit identified more differences between AD and NC groups. With the ctx-lingual, ctx-supramarginal, ctx-superiortemporal, putamen, pallidum, and wm-postcentral regions with p-values less than 0.05 in both analyses.

CONCLUSION: Here, we introduced a novel CEST MRI pipeline to probe regional differences in AD. Detecting molecular AD changes in a cost-efficient and non-invasive manner could lead to more timely interventions, guide therapeutic strategies, improve access to AD treatments, and improve patient outcomes.

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