pH-Weighted Spinal Cord CEST in Degenerative Cervical Myelopathy

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INTRODUCTION: Degenerative cervical myelopathy (DCM) is a degenerative disease of the spine, causing compression and neurological dysfunction.[1] Recommended treatment is decompression surgery; however only ~1/3 of patients improve following intervention,[2] creating a need to develop predictors of surgical outcome. Although difficult to detect in humans, ischemia and hypoxia in the cord could impact recovery after surgery. Chemical Exchange Saturation Transfer (CEST) can produce pH-weighted contrast due to the pH-dependence of the amine and amide proton exchange rate. Specifically, amine/amide concentration-independent detection (AACID) is a ratiometric pH-weighted contrast with reduced sensitivity to tissue water and protein concentrations.[3] Since hypoxia alters tissue pH, AACID may be sensitive to ischemia and hypoxia. The objective of this study was to compare AACID values between the spinal cord of DCM patients and healthy controls.

METHODS: On a 3T Siemens MAGNETOM Prisma Fit MRI, a Siemens prototype 3D CEST sequence was used consisting of a saturation preparation period followed by a 3D gradient echo (GRE) readout. Saturation consisted of a train of 30 Gaussian-shaped RF pulses ($B_{1,mean}$ = 0.5 μT, pulse duration of 100 ms, interpulse delay of 1 ms, total saturation time = 3.03 s), applied at 45 offsets ranging from -6.5 to 6.5 ppm. A 2 s recovery time was employed after each readout. Other relevant imaging parameters included: TR/TE = 3.35/1.16 ms, nominal resolution = 2.0x2.0x5.0 mm^3, and matrix 96x96x14. A water saturation shift referencing (WASSR) spectrum was acquired to correct for B_0 inhomogeneities using five Gaussian-shaped saturation pulses ($B_{1,mean}$ = 0.5 μT, 25 offsets from -2.5 to 2.5 ppm). A B_1 correction was also applied (Windschuch *et al.*).[4] Six DCM patients (6 females, mean age (± SD) 53 ± 10 years), five healthy older controls (4 males, 56 ± 16 years), and twelve healthy controls (7 females, 26 ± 4 years) were scanned. In patients, the 3D CEST imaging volume was centered over the level of compression, while the volume was centered over the cervical 4 (C4) level in controls. A repeated one-way ANOVA was used to determine if AACID measurements differed above, below, and at the compression site of patients. To determine if AACID measurements in DCM patients were significantly different than controls, two Welch's t-tests ($p<0.05$) were used: (1) DCM AACID compression site mean vs younger control AACID mean from slices 6-8, and (2) DCM AACID compression site mean vs older control AACID mean from slices 6-8.

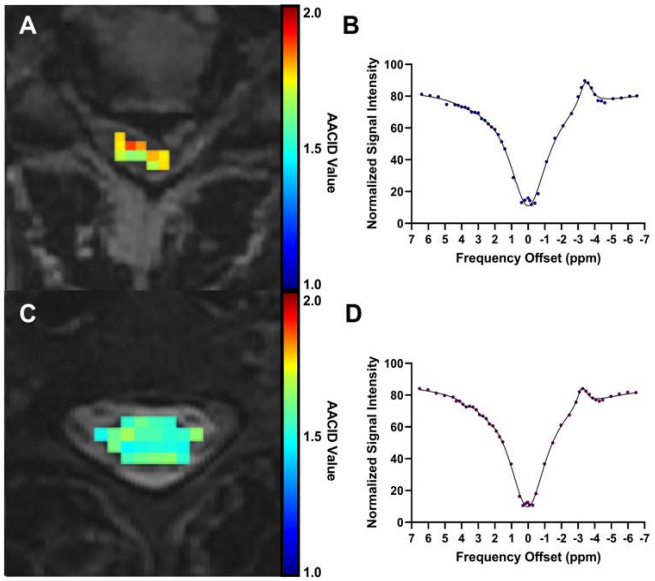

Figure 1: A. AACID map in the cord of slice corresponding to compression in DCM patient and **B.** corresponding average CEST spectrum. **C.** Center slice AACID map of age-matched healthy control and **D.** corresponding average CEST spectrum

RESULTS: Figure 1 demonstrates AACID maps and the corresponding average CEST spectrum from one DCM patient at the site of compression (top) and the corresponding age-matched control (bottom) at the center slice. When comparing AACID values along the cord of DCM patients, it was found that there were no significant differences between the compression site (mean AACID ± SD, 1.64 ± 0.07) and above (1.58 ± 0.19) (adjusted p = 0.85) or below (1.48 ± 0.17) (adjusted p = 0.15). The AACID measurements at the site of compression (1.64 ± 0.07) were significantly greater compared to younger controls (1.54 ± 0.10, $p<0.05$) but did not significantly differ from older controls (1.55 ± 0.08, p = 0.16).

DISCUSSION: Initial results suggest that hypoxia is occurring in the spinal cord of DCM patients due to the significantly greater AACID measurements at the site of compression compared to younger controls. Because the pH-weighted AACID measurements do not significantly differ throughout the cord of DCM patients, ischemic damage may not be localized at the site of compression and could influence recovery after intervention.

CONCLUSION: This preliminary work supports the hypothesis that spinal cord compression in DCM patients may result in ischemia and hypoxia and could potentially influence the result of decompression surgery. Future work includes increasing the sample size of both patients and controls, and linking AACID measurements to outcome measures following surgery to determine if AACID can be used as a predictor of functional outcome for these patients.

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