Magnetization Transfer MRI measurements of Cervical Spinal Cord abnormalities in patients with Neuromyelitis Optica

M. Kim[1], A. Chan[1], H. Mak[1], Q. Chan[2], and K. Chan[3]
[1]Department of Diagnostic Radiology, The University of Hong Kong, Pokfulam, Hong Kong, China, People's Republic of, [2]Philips Healthcare, Hong Kong, [3]Department of Medicine, The University of Hong Kong, Hong Kong

Objective: Neuromyelitis optica (NMO) is an inflammatory and demyelinating disease of central nervous system that preferentially affects the optic nerve and spinal cord. NMO has long been thought of as a rare and severe variant of multiple sclerosis (MS), however, clinical, immunological and pathological characteristics that distinguish it from MS are now recognized [1]. As NMO involves recurrent and aggressive attacks of blindness and paralysis, unlike the attacks in MS, it is crucial to diagnose NMO in the early stages in order to especially provide the proper treatment [2]. However, current diagnostic criteria in routine practice using conventional T_1- (T_1w) and T_2-weighted (T_2w) images are not sensitive to early degenerative changes in NMO. Recent studies using diffusion tensor imaging have shown abnormality in normal appearing tissues of brain and spinal cord [3,4]. However, normal appearing tissue damage in cervical spinal cord has not been widely investigated due to technical limitations although understanding pathological mechanism in the cervical spinal cord is crucial in research of NMO. The goal of this research is to apply magnetization transfer-weighted (MTw) imaging for assessing the pathological mechanism of normal appearing cervical spinal cord tissue damage in patients with NMO.

Materials and Methods: Six NMO patients (five females and one male; mean age, 52 ± 11 years) diagnosed with NMO (mean EDSS = 3.2; range = 1-5) and four healthy volunteers (all females; mean age, 29 ± 3 years) were studied after signed, informed consent. All studies were approved by the local institutional review board. All scans were performed on a Philips 3T MRI system (Philips Health Care, Best, The Netherlands) with a body coil excitation and a 16-channel neurovascular coil for reception. Two imaging volumes covered C1-C3 (volume 1 (v1)) and C4-C6 (volume 2 (v2)). For T_1w and T_2w imaging, 30 multi-slices (slice thickness of 3 mm with 20 slices and 6 mm with 10 slices for v1 and v2, respectively) in axial plane were acquired with nominal in-plane resolution of 0.4x0.4 mm^2 and FOV of 180x121 mm^2. Other parameters for T_1w: repetition time (TR), 400-600 ms; echo time (TE), 10 ms; flip angle (FA), 90 degrees; multi-shot turbo spin echo (TSE) factor (number of refocusing pulses), 5; FOV, 180x121 mm^2; NSA, 2. For T_2w: TR, 2500-4000 ms; TE, 100 ms; FA, 90 degrees; TSE factor, 15; NSA, 2. For MTw imaging, same geometry as T1w and T2w were used. MTw images were obtained using an MT prepulse applied 1.5 kHz off resonance (15 ms, five-lobed sincgauss pulse with maximum amplitude 13.5 mT). Other parameters: TR, 145 ms; TE, 6 ms; FA, 7 degrees; 3D gradient echo sequence; sensitivity encoding acceleration factor, 2. The data were processed using a custom-written program in MATLAB (The Mathworks, Natick, MA, USA). In each slice, cerebrospinal fluid (CSF)-normalized MT (MTCSF, [5]) was calculated for three manually drawn regions of interest (ROIs) as illustrated in Fig. 1. The magnitude of the MT effect was quantified as MTCSF(ω) = $S(\omega)/S_0^{CSF}$ where $S(\omega)$ is the saturated signal intensity at offset frequency ω and S_0^{CSF} is the average voxel signal intensity of CSF segmented from a non-saturated image using an automated *k*-means clustering algorithm [6] in combination with threshold-based method.

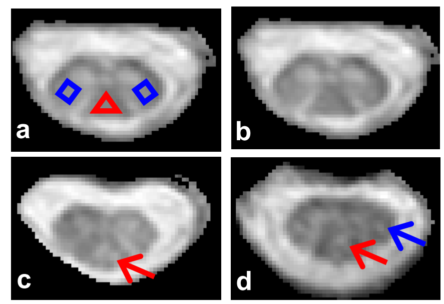

Fig. 1. MT-weighted images taken at the level of C3 and C4. (a) The placement of ROIs used for MTCSF analysis: lateral columns (blue) and dorsal column (red) white matter. (b) Healthy control. (c and d) Mildly affected NMO lesions in dorsal (red arrow) and lateral (blue arrow) columns.

Results and discussion: Fig. 1 shows representative MTCSF axial cervical spinal cord slices for one healthy control subject and one NMO patient with lesions. In an NMO patient, signal hyperintensity in the dorsal and lateral columns indicates lesions with tissues damage which appear as normal in T_1w and T_2w. Fig. 2 illustrates the a mean MTCSF values at the level of C2-C5 in healthy controls and NMO patients. MTCSF values were significantly greater in the NMO patients than in the control subjects for both dorsal and lateral regions ($p < 0.001$ at dorsal column and $p < 0.05$ at lateral column using two-tailed unpaired student's t-test). The locations of these MTCSF hyperintensities correspond well to areas of myelin loss that are visible in postmortem myelin stains of typical NMO patients [7]. This agrees with the expectation that disrupted structures due to demyelination will result in a less efficient MT exchange process, leading to increased intensity in MTw images as they contribute to the macromolecular semi-solid tissue content.

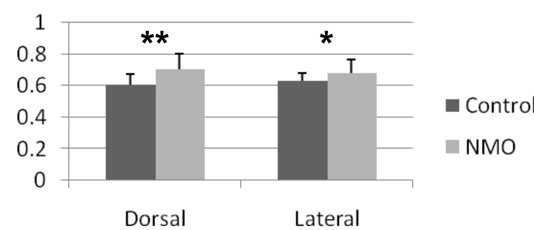

Fig. 2. Average MTCSF (1.5 kHz) values of dorsal and lateral columns at the level of C2-C5 in controls and NMO patients. The error bar represents the standard deviation. Significant differences between groups are indicated by * $p < 0.05$ and ** $p < 0.001$.

Conclusion: Our results show that it is feasible to obtain reliable measurements from MTCSF analysis of the cervical spinal cord from NMO patients. MTCSF values of NMO patients were significantly higher than those of control subjects. This suggests that the assessment of NMO cervical cord damage, using the quantitative capability of MT imaging in addition to existing clinical methods may lead to a better understanding of the clinical manifestations of the disease and may be a useful clinical tool in monitoring the effect of therapeutic intervention.

References: [1] Wingerchuk, D.M., et al., Lancet Neurol, 2007;6: p. 805-15. [2] Chan, K.H., et al., Eur J Neurol, 2009;16(3): p. 310-6. [3] Yu, C., et al., Radiology, 2008;246(1): p. 222-8. [4] Benedetti, B., et al, Neurology, 2006;11;67(1): p. 161-3. [5] Smith, S.A., et al., Magn Res Med, 2005;54: p. 201-6. [6] Kanungo, T., el al., IEEE Trans Pattern Anal Mach Intell, 2004;26(4): p. 520-4. [7] Misu, T., et al., Brain, 2007;130(Pt 5): p. 1224-34.

Grant Acknowledgment: URC Seed funding program for basic research.