High-Field Characterization of Spinal Cord Damage in Multiple Sclerosis

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Target Audience:
Physicians and clinicians interested in characterizing spinal cord damage in MS using high field (7T) imaging.

Purpose:
A paradox exists in the comparison of clinical evaluation of multiple sclerosis (MS) with imaging collected in a clinical setting: while patients exhibit disabilities with somatosensory stimulation and movement initiation, these issues are not always reflected in clinical (1.5T) MR images.[1] This is especially true in the spinal cord (SC) where, in contrast to MRI findings, nearly all patients with MS show lesions and spinal atrophy upon post-mortem examination.[2] Lower field MRI methods have demonstrated significant correlations between atrophy and clinical presentation, but the correlations between lesion volume/load and neurological dysfunction are often poorly correlated. We hypothesize the reasons for these are two-fold: 1) imaging resolution at clinical field strengths is insufficient to robustly characterize subtle and slowly progressing atrophy, and 2) the sensitivity to gray/white matter contrast and lesions with conventional, lower field MRI is poor. In addition, SC MRI poses a multitude of difficulties. For example, the physical size of the spinal cord and its location within a column of large bones complicate the demand for high-resolution MRI[2], while the constant surrounding motion of cerebrospinal fluid and the cardiac and respiratory systems causes artifacts obscuring the cord.[2] We hypothesize that a higher magnetic field (7T) can provide higher-resolution and sensitivity to lesions which can provide greater understanding of SC pathology in MS. To that end, we have developed novel, high-resolution MRI of the cervical SC at 7T and characterized lesion load and atrophy using a combined semi-automated and manual processing pipeline. We additionally compare across healthy and MS populations and the association with neurological disability.

Methods:
MR scans in 23 MS patients and 18 control participants were performed at 7T (Philips Healthcare) with a novel 16-channel cervical spinal cord receive coil (Nova Medical). High resolution T1- and T2*-weighted scans were acquired at 0.5x0.5x5mm3 resolution in 9 minutes with the following parameters: T1 - 3D fast-field echo (FFE), TR/TE/flip angle = 30ms/4ms/60°, T2*-weighted - multi-slice FFE, TR/TE/flip angle = 305ms/9ms/25°. Semi-automatic segmentation of the SC was performed utilizing MIPAV and FSL (FMRIB, Oxford UK). In MIPAV (NIH CIT, Bethesda MD), The T1-weighted image was cropped to show the spinal cord at the C2/C3 junction, and N3 bias-field correction was performed on the cropped image to minimize shading, with maximum iterations set to 100 and an end tolerance of 0.0001. The image was then automatically segmented using FSL FAST segmentation. The number of iterations for bias field removal was set to 10 and bias field smoothing was set to 5.0. From the segmented image, a VOI was selected over the segmented SC and the area, eccentricity, major axis length, and minor axis length were computed. Grey matter area was measured manually at the same level. T2*-weighted lesions were counted in the cervical SC and T2*-weighted lesion volume was estimated using MIPAV. 7T lesions were compared to the number of lesions observed using clinical standard of care at 1.5T and 3T. Descriptive statistics (two-sample unequal variance t-test) compared the patients with controls, while correlational statistics (two-tailed Spearman rank test) compared the imaging data with clinical data.

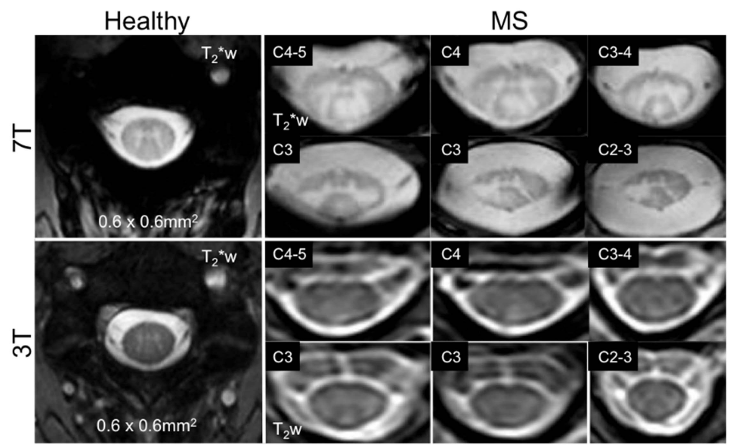

Figure 1. *Comparison of cervical SC T2*-weighted images in healthy volunteers and MS patients at high field (7T) and low field (3T).*

Results and Discussion:
An example comparing a 3T clinical standard of care and our 7T acquisition in one MS patient is shown in figure 1. It can be seen that at 7T, lesions are apparent on every slice compared to 3T. In sagittal T2 scans, 4.5 +/- 1.5 lesions were detected at 7T compared to 2.5 +/- 2.2 at 3T. Cord atrophy and lesions volumes at 7T were correlated with clinical outcomes. Cervical SC area (atrophy) inversely correlated with MS duration (R=-0.51 P=0.008), and disability (expanded disability status scale (EDSS) score (R=-0.42 P=0.04). GM area showed a trend to inverse correlation with MS duration (R=-0.45 P=0.058). Spinal cord lesion volume showed significant correlations with EDSS (R=0.75 P=0.001), and a trend to correlation with MS duration (R=0.47 P=0.07). T2*-weighted lesion number correlated with MS duration (R=0.52 P=0.046) and EDSS (R=0.81 P=0.003). The correlational statistics suggest a significant relationship between lesions and atrophy in the SC and the clinical assessment of MS patients, a correlation that is not well demonstrated at a lower field.

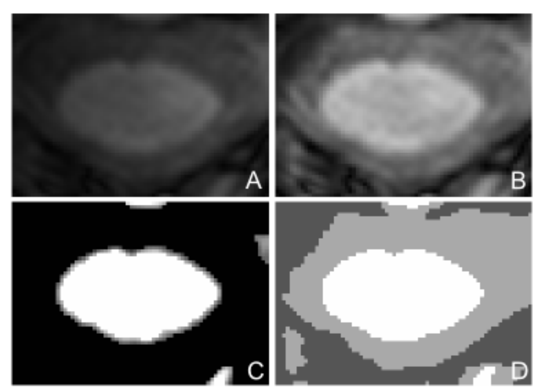

Figure 2. *Automatic Segmentation Procedure. The cropped C2/C3 junction image (A) is flattened using N3 correction (B). FSL FAST segmentation produces partial volume estimations (C) and a 3-class segmentation (D).*

Conclusion:
The implementation of 7T anatomical MRI in combination with a uniquely-designed SC receive coil resulted in an overall increase in the number of lesions detected, affirming our hypothesis that the clinical-radiological paradox can be attributed to the challenges at detecting lesions at lower field strengths. Additionally, we show a significant correlation between 7T SC MRI measures and clinical presentation which has been challenging at lower field strengths. As clinical medicine continues to advance, our findings pose a solution to resolving the clinical-radiological paradox by increasing the field strength at which peripheral effects of MS are detected.

References:
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2. Rocca, M. A. et al. Imaging Spinal Cord Damage in Multiple Sclerosis. Journal of Neuroimaging. October 2005;15(4): 298-304.

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