Detection of subpial cortical demyelinating lesions in multiple sclerosis in vivo

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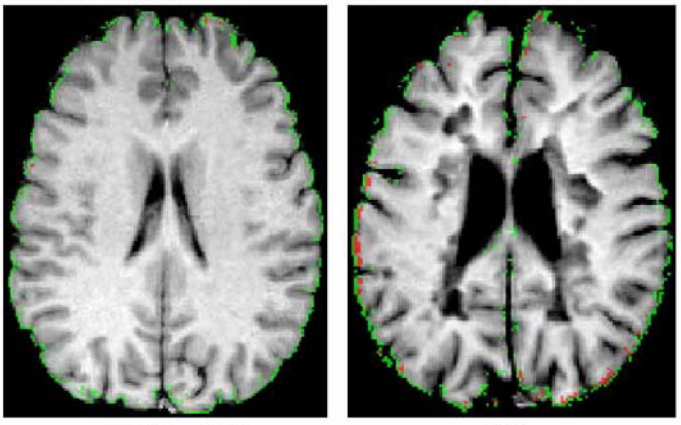
Abstract: Multiple sclerosis (MS) patients often have a substantial burden of demyelinating lesions in their cortical grey matter (cGM) on post-mortem examination. The vast majority of these lesions are subpial, band-like lesions that can extend over several gyri. These lesions, which are associated with very little inflammation or edema, are not seen on conventional MRI. We used a combination of T1-weighted (T1w) structural images and magnetization transfer ratio (MTR) images to improve our ability to detect demyelination just under the surface of the cortex. Using T1-weighted MRI to define the boundary between the extra-cerebral cerebrospinal-fluid (eCSF) and the cGM, and using MTR to define a boundary between sparsely myelinated and normally myelinated cortex, we could detect abnormal regions of subpial demyelination that extended into the deeper layers of the cortex with a pattern and prevalence consistent with the cortical subpial demyelinating lesions that have been observed previously by immunohistopathology. To estimate the burden of cortical pathology, we quantified the percentage of the cortical surface that had a sparsely myelinated outer layer greater than 1 mm in thickness based on the distance between the maximal intensity gradients orthogonal to the cortical surface in the T1w and MTR scans. The range in the MS patients was 5.3 to 26.0 %, with a median value of 10.2 %. In control subjects it was approximately 5%. Our results suggest that image-processing combining T1w and MTR images can detect and quantify subpial demyelinating lesions in cGM in vivo.

Introduction: Although cortical pathology in MS is detectable by post-mortem histopathology [1], it remains difficult to quantify on MRI. In vivo imaging that has demonstrated cortical pathology is often most sensitive to juxta-cortical lesions at the grey-matter/white-matter interface [2]. However, the majority of cortical lesions are subpial and remain undetected on MRI despite extending over several gyri [3]. Although the outermost layers of normal cortex are relatively sparsely myelinated [4], the subpial lesions extend beyond these normally sparsely myelinated outer layers, resulting in a thicker sparsely myelinated outer cortical layer.

Methods: *Subjects:* We studied 2 control subjects and 15 MS patients who were scanned as part of the Canadian MS/BMT trial. *MRI acquisition:* Proton-density, T2-weighted, imaging with and without a magnetization transfer (MT) saturation pulse, and T1-weighted imaging, were acquired at a 1 mm in-plane resolution and a 3 mm thickness. *Image analysis:* This method is an extension of previous work quantifying neocortical thickness [5]. All images were linearly registered to the T1w, and the MTR was calculated. To provide starting conditions for the orthogonal intensity profiles, a Bayesian tissue segmentation was performed. For each neocortical surface voxel, the boundary between the eCSF and the cGM was determined, by finding the maximum of the derivative of the T1w intensity profile orthogonal to the surface of the cortex. Along the same orthogonal, the boundary between sparsely myelinated cortex and normally myelinated cortex was determined by finding the maximum of the derivative of the co-registered MTR intensity profile. The distance between the maxima, which depends on the thickness of the outer cortex that is sparsely myelinated, was calculated to sub-voxel accuracy by quadratic interpolation of the cross-correlation of the derivatives of the intensity profiles. Since the outermost layers of normal cortex are normally sparsely myelinated, we quantified the percentage of the cortical surface that had a greater than 1 mm distance between the maxima, corresponding to a sparsely myelinated outer layer greater than 1 mm in thickness.

Results: In the control subjects, approximately 5 % of cortex had more than 1 mm difference in the distance between the maximal intensity gradients defined on T1w versus MTR images. The range in the MS patients was 5.3 to 26.0 %, with a median value of 10.2 % .

Using T1w and MTR images to detect subpial demyelination.
The eCSF/cGM boundary is shown in green, and the sparsely myelinated regions that were more than 1 mm in thickness are shown in red.



Conclusion: We describe a method that makes it possible to detect regions of cortical subpial demyelination in MS in vivo on standard resolution images obtained at 1.5 T using a combination of T1w and MTR images and advanced image-processing techniques.

Acknowledgements: The Canadian MS/BMT trial is funded by the Multiple Sclerosis Scientific Research Foundation.

References: [1] Brownell and Hughes, J Neurol Neurosurg Psychiatry, 1962. [2] Geurts et al, AJNR AM J Neuroradiol, 2005. [3] Peterson et al, Ann Neurol, 2001. [4] Vogt and Vogt, J Psychol Neurol, 1919. [5] Chen et al, Neuroimage, 2004.