Spinal cord imaging in multiple sclerosis

Filling the gap with the brain

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The use of advanced MRI modalities to study brain disease has provided new insights into the understanding of the pathophysiologic mechanisms of several neurologic disorders. It is notable that many of these modalities have not been widely applied to the spinal cord (SC), mainly because of the technical hurdles in performing high-confidence MRI acquisitions in this long, yet thin structure located deep to other structures with high magnetic susceptibility.[1] More recently, however, technical developments have improved MRI of the SC. Optimization of specific sequences (e.g., diffusion tensor imaging [DTI]) for SC anatomy,[2] higher field strength, and new coil technology have helped conventional and quantitative MRI of the SC to become more sensitive, specific, and accurate.[1]

In multiple sclerosis (MS), SC pathology has a particularly crucial role as a substantial portion of the accumulating patient's disability turns out to be related to the inflammation, demyelination, and neuroaxonal degeneration.[3] Because the SC is frequently affected in MS, the need for MRI modalities that are able to capture fully SC abnormalities is critical. Moreover, results of correlative studies with MRI and histopathology have shown that demyelination affects both the white and gray matter throughout the SC, and the consequent SC tissue loss seems to result only in part from local lesion size, likely reflecting diffuse damage of the entire normal-appearing tissue.[4] Coupled with the pragmatic challenges, the importance of information that can be gained from the SC in patients with SC damage strongly advocates for the use of nonconventional, quantitative MRI modalities to detect the full extent of pathologic changes occurring in the SC of patients with MS.

MS is the neurologic disease that has perhaps benefited most from the recent progress in advanced quantitative SC imaging techniques. Quantitative magnetic resonance approaches, such as SC atrophy measurements, DTI, magnetization transfer imaging, proton magnetic resonance spectroscopy, and fMRI, relate SC structure and function with improved specificity.[5] These studies have shown the potential of such methods to improve clinical diagnosis and monitoring of disease evolution and treatment in MS. However, despite these recent improvements and their wider application in MS research, the realization of methods able to provide clinical tools still requires further technological and strategic development. That is, there is still a need to simultaneously increase the signal-to-noise ratio and the spatial resolution while maintaining clinically relevant scan times. Furthermore, there are technical challenges common to all SC imaging methods such as the spatially inhomogeneous magnetic field environment, the small physical dimensions of the cord cross-section, and the physiologic motion, all of which mandate development of better postprocessing methods to provide sophisticated measurements reflective of tissue pathology, function, and ultimately prognosis.[1]

In this issue of *Neurology*®, Toosy et al.[6] describe a novel postprocessing method to assess SC DTI changes using a voxel-based analysis of a small group of patients (n = 11) with MS-related cervical myelitis. Using this innovative approach, the authors demonstrated that voxel-based fractional anisotropy and radial diffusivity of the cervical SC were closely associated with patients' disability as measured in the clinic. While the majority of previous quantitative MRI studies of the SC have utilized regions of interest or histogram-based analyses (which require an a priori hypothesis), the voxel-based approach described by Toosy et al.[6] allows for unbiased spatial localization of pathologically relevant areas (without an a priori hypothesis), providing greater statistical power and improving the ability to detect clinically relevant associations. Overall, the work highlights the importance of the combination of novel acquisition and analysis strategies targeted at the SC for providing insights into the tissue changes that occur in diseases such as MS.

Voxel-based analysis rarely has been applied to SC MRI data,[7,8] mostly because registration of the SC is challenging. Images of the brain usually contain

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thousands of voxels, and thus voxel-based analyses are often robust and accurate. This is much less true for the SC because of the presence of many fewer voxels than in the brain: the SC volume is approximately one-tenth to one-fifteenth that of the brain and therefore much less information is contained in the images to be used during registration. Partial volume effects, nonrigid spatial perturbations related to cardiac and CSF motions, and periodic field inhomogeneities due to the segmental structure of the SC all contribute to make registration of the SC more difficult. Lastly, unlike the brain, a routinely applied and globally appreciated SC atlas is not available. An improved SC registration comes with the method proposed by Toosy et al.[6] because of the use of axial (rather than sagittal) images, which can provide higher resolution with anisotropic voxels despite the relatively low field (e.g., 1.5 tesla) of MRI acquisition. This is particularly relevant in the light of the clinical implementation of such a method.

There are other issues and important limitations, such as the low spatial resolution of the SC DTI acquisition and the consequence of postprocessing procedures such as spatial smoothing (which may particularly affect the partial volume estimation at the gray matter–white matter interface), that deserve attention and must be faced in future studies. However, the field of SC imaging is moving forward, rapidly closing the gap with brain imaging: a further step toward the use of SC quantitative imaging biomarkers in the clinic to predict clinical outcome and monitor therapeutic treatments. The work by Toosy et al.[6] suggests that the clinical footprint of advanced SC MRI is getting larger and may be profound in evaluating patients and therapeutic advancements in the future.

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