New Concepts Related to Disease Appreciation in Multiple Sclerosis

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KEYWORDS

• Multiple sclerosis • MRI • Neuroimaging • Central vein imaging • Cortical lesions • Lesion probability mapping • Image subtraction • Brain volumetrics

KEY POINTS

- Central vein imaging, cortical lesion detection, and lesion probability mapping are emerging MRI techniques that have the potential to improve the accuracy of MRI in establishing a diagnosis of MS.
- Incorporating central vein imaging into clinical practice will require the adoption of a standardized and commercially available pulse sequence to detect central veins, a uniform definition of a central vein, and standard criteria to define the central vein sign as present or absent in an individual patient.
- Pulse sequences need to be optimized to ensure reliable detection of all cortical lesion types before incorporating cortical lesions into MS diagnostic criteria or clinical practice.
- The field needs to develop sophisticated image processing algorithms that are robust to large heterogeneity in MRI acquisition to derive useful information from the MRI scans that are collected in clinical practice.
- With some additional work, image subtraction and brain volumetrics are promising tools that could provide clinicians with quantitative metrics to monitor MS patients over time.

INTRODUCTION

In the past several decades, MRI has become an indispensable tool in the field of multiple sclerosis (MS) for clinicians and researchers alike. In addition to providing essential insights into MS pathophysiology, MRI plays an integral role in confirming

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diagnosis of MS as well as monitoring disease activity and response to treatment once a diagnosis is established. The utility of MRI as a diagnostic and monitoring tool is due, in large part, to its high sensitivity to detect inflammatory demyelinating white matter lesions, which have long been considered the pathologic and imaging hallmark of MS.

The past several decades of progress notwithstanding, MS clinicians and researchers still face several challenges. Although MRI is highly sensitive to detect white matter lesions caused by MS, it is not wholly specific to MS; in other words, MRI is also highly sensitive to detect white matter lesions from other etiologies (eg, migraine or small vessel disease). Discriminating MS from other conditions is a challenge that is routinely faced by clinicians and is not addressed by current MRI criteria for MS. Moreover, once a diagnosis of MS has been established, clinicians lack standardized, quantitative methods to reliably measure changes in the disease over time, which may help guide treatment decisions.

This review highlights promising MRI and postprocessing techniques that have potential applications in these areas. With some further study, these tools could be usefully integrated into clinical care.

THE ROLE OF MRI IN ESTABLISHING A DIAGNOSIS OF MULTIPLE SCLEROSIS

MRI plays a fundamentally important role in establishing a diagnosis of MS. In the current version of the MS diagnostic criteria,[1] MRI can support, or even replace, clinical criteria for dissemination in space and time in patients with a clinical presentation suggestive of a demyelinating event. Dissemination in space can be demonstrated on MRI by the presence of greater than or equal to 1 T2 lesion in greater than or equal to 2 of 4 areas consistent with demyelination (periventricular, juxtacortical, infratentorial, and spinal cord). Dissemination in time can be satisfied by the simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time, or by a new T2 or gadolinium-enhancing lesion on any follow-up MRI. Compared with earlier versions of the MRI criteria,[2,3] the current version is simplified because it emphasizes lesion location rather than lesion counts, making it easier to apply in practice, and because it often allows a diagnosis of MS to be made with a single MRI scan rather than requiring a follow-up MRI after an arbitrary amount of time as in previous versions.[2,3]

When applied to patients who present with a clinical syndrome consistent with inflammatory demyelination of the central nervous system (CNS) (ie, optic neuritis, partial myelitis, or brainstem syndrome), the current version of the MRI criteria has been shown to have a sensitivity of 72% to 85% and a specificity of 67% to 92% to diagnose MS.[4–6] It has been emphasized that the MRI criteria are meant to be applied only in such patients with an appropriate clinical presentation,[1,7] and that they were not developed to differentiate MS from other conditions. The misinterpretation of MRI findings, including the inappropriate application of MRI criteria to patients with symptoms that are atypical or nonspecific for CNS demyelination, has been cited as a common cause of MS misdiagnosis,[8] an emerging area in the current MS literature. Cases in which white matter abnormalities are detected on an MRI that was obtained for atypical, nonspecific, or completely unrelated symptoms present a particular challenge for clinicians and highlight the need for advanced imaging techniques to be incorporated into clinical practice to aid the differentiation of inflammatory demyelination from other conditions. Central vein imaging, cortical demyelinating lesion detection, and lesion probability mapping are emerging MRI techniques that have the potential to improve the accuracy of MRI in establishing a diagnosis of MS.