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**Should spinal cord MRI be systematically performed for diagnosis and follow up of
multiple sclerosis? Yes**

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Introduction

Spinal cord MRI is currently performed far less frequently than brain MRI in patients with multiple sclerosis (MS), mainly owing to technical limitations, such as the time required to perform the acquisition and the artefacts affecting this small and mobile structure. However, as we explain below, spinal cord involvement is frequently observed in patients with MS, and has a diagnostic and above all a prognostic value. These factors, together with recent improvements in MRI acquisition protocols, should lead to the growing use of spinal cord MRI in clinical practice within the near future.

Spinal cord involvement is frequently observed in patients with MS, and efficient MRI sequences are now available for visualizing it.

Over many years, imaging and anatomopathological studies have consistently shown a high frequency of spinal cord lesions in patients with MS (1-3). These lesions have been described in 75-92% of patients, depending on the study and the disease phenotype. Patients with the secondary progressive (SPMS) or primary progressive (PPMS) form of the disease have a higher spinal cord lesion count and volume than patients with relapsing-remitting MS (RRMS), who in turn have a higher count and volume than those with clinically isolated syndrome (CIS) (4, 5).

In the axial plane, the lesions are mainly found in the lateral and posterior columns, rather than the anterior part of the spinal cord (6). The lateral corticospinal and proprioceptive tracts are therefore frequently impaired by MS lesions, causing motor and gait dysfunction in patients. In the sagittal plane, lesions are more frequent in the cervical rather than thoracic spinal cord, and more frequent in the upper rather than lower cervical cord (7). However, in a recent MRI study featuring systematic sagittal and axial coverage of the cervical and thoracic spinal cord, lesion frequency was only slightly higher in the cervical cord than in the thoracic spinal cord (8). Combined analyses of the sagittal and axial planes, as opposed to the sagittal sequence alone, resulted in the identification of 22% additional lesions, mainly ones with small axial diameters. Thus, spinal cord lesions are probably underestimated in clinical practice when only sagittal acquisition is performed. New 3D sequences such as phase-sensitive inversion recovery (3D PSIR) have also recently been developed to improve lesion detection (9). However, the use of 3D sequences and axial sequences with full spinal cord coverage is not yet widespread in clinical routine. An optimum imaging sequence for spinal cord lesion identification had been recently defined, comprising at least two sagittal sequences (STIR, T2, PD, PSIR or 3DT1 MPRAGE) or two different planes (i.e. sagittal + axial) to be confident that the identified spinal cord lesions are not artefacts (10). Acquisition should cover both the

cervical and thoracic spine. Figure 1 illustrates the visualization of spinal cord MS lesions using different conventional sequences that are potentially available in clinical practice.

Spinal cord MRI is important for MS diagnosis

The spinal cord is one of the four areas where typical MS lesions are scored to fulfill the dissemination in space criterion (11). Since the publication in 2017 of the revised McDonald criteria, both symptomatic and asymptomatic spinal cord lesions can be counted. Spinal cord MRI is also important for the differential diagnosis of MS, as spinal cord lesions are not observed in either normal aging, migraine, or cerebrovascular disease (12). Moreover, in MS, spinal cord lesions are typically small (fewer than two vertebral segments and less than half the cord area), contrary to neuromyelitis optica spectrum disorders (13). Thus, spinal cord MRI is currently recommended for i) patients with CIS whose clinical symptoms are suggestive of myelitis, ii) patients with CIS whose clinical symptoms are not suggestive of myelitis, but where there is no evidence of dissemination in space on brain MRI, iii) patients with a suspicion of primary progressive MS, and iv) patients with inconclusive brain MRI lesions (11). However, as explained below, spinal cord MRI also has a strong prognostic value that potentially justifies its use in each new patient with CIS or MS.

Spinal cord MRI is important for MS prognosis

First, in radiologically isolated syndrome (RIS), spinal cord lesions are associated with conversion to MS and an increased risk of developing PPMS (14). Thus, 100% of RIS patients who go on to develop PPMS have spinal cord lesions prior to the progressive phase, compared with 64% for those who convert to CIS or RRMS, and 23% for those who remain asymptomatic. Other MRI characteristics in the preprogressive phase of PPMS are indistinguishable from CIS/MS. Similarly, in patients with CIS, spinal cord lesions are independently associated with conversion to clinically definite MS, disability progression, and conversion to SPMS (15–18). These results were recently confirmed in a long-term (15 years) follow-up study of 178 patients with CIS. Spinal cord lesions at baseline were the strongest independent factor associated with SPMS at 15 years (odds ratio = 4.71, $p < 0.01$) (17). It should, however, be noted that the impact of asymptomatic spinal cord lesions alone on subsequent disability progression remains more ambiguous (19). Finally, in patients with confirmed MS, spinal cord lesions are associated with disability scored on the EDSS (20) and with an increased risk of mid-term disability progression (21).

Spinal cord MRI may be important for the follow up of patients with MS

To date, owing to the lack of longitudinal data, systematic spinal cord MRI for the follow up of patients with MS cannot be formally recommended in clinical practice. However, recent

research has yielded several arguments in favor of this practice. First, although spinal cord lesions are more likely to be symptomatic than brain lesions, asymptomatic spinal cord lesions commonly occur. Thus, in patients with stable RRMS, 25% had new asymptomatic spinal cord lesions (vs. 44% for asymptomatic brain lesions) after a median interval of 17 months, while 10% had asymptomatic spinal cord lesions but no asymptomatic brain lesions (22). Similarly, in another study, 31% of spinal cord lesions were asymptomatic in patients with CIS or RRMS (23). These asymptomatic spinal cord lesions were the only sign of disease activity in 12% of patients (no clinical or brain radiological activity). Second, in a study including patients with CIS (16), both the number of spinal cord lesions at baseline and the change in cord lesion number during follow up were independently associated with EDSS at 5 years. Including brain T2 lesion load and change in brain T2 lesion load only modestly increased the model's predictive power. These results were recently confirmed in a 15-year follow-up study of patients with CIS (17). Both spinal cord lesion number at baseline and new spinal cord lesions at 1 and 3 years were associated with conversion to SPMS at 15 years.

Conclusion

Spinal cord lesions are frequent in patients with MS, and are increasingly being visualized, as a result of improvements in MRI acquisition. There is strong evidence in favor of performing a first spinal cord MRI in patients with CIS and early RRMS, for both diagnostic and prognostic purposes. This spinal cord MRI should include at least two different sagittal sequences or two different planes (sagittal + axial), to be sure that the spinal cord lesions identified are not artefacts, and should cover both the cervical and thoracic spine. The use of systematic spinal cord MRI in addition to systematic brain MRI for monitoring disease progression in asymptomatic patients with MS needs further evaluation.

Conflict of interest

The authors have not declared links of interest in relation to this article.

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Figure 1. Example of MRI sequences used to visualize spinal cord lesions in patients with MS: (A) sagittal T2 FSE; (B) sagittal PSIR; (C) axial T2*; (D) 3D PSIR. Source: personal data, except for (D) from (6).