MR imaging of the Spinal Cord in Multiple Sclerosis

A. Rovira¹, C. Auger¹, R. Mitjana¹, Corral JF¹, A. Rovira-Gols²

¹Hospital Vall d’Hebron, Barcelona. SPAIN.
²UDIAT-CD Parc Taulí, Sabadell. SPAIN

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alex.rovira@idi-cat.org
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# 1370-ECR

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MR imaging of the spinal cord in Multiple Sclerosis

Summary

- **Technical issues**
- Clinical and MRI correlations
- Indications of spinal cord MR imaging
- Spinal cord MR imaging features
MRI of the spinal cord: a technical challenge

Technical issues

The spinal cord is a small and mobile structure, which makes MRI difficult. Furthermore, image quality may be degraded by ghosting artifacts from heart and great vessels and truncation artefacts.

- Small, long and mobile structure
- Ghosting artefacts from heart and great vessels
- Truncation artefacts (tissue interface)
- Patient movement artefacts

35-48 mm transverse diameter

Ghosting artefacts from swallowing (arrows)

Absence of artefacts

35-48 mm transverse diameter
MRI of the spinal cord: a technical challenge

Solutions

These difficulties are largely overcome by technical improvements such as:

- Cardiac gating
- Presaturation slabs
- Fast imaging sequences
- Phased-array coils

Fast double-echo sequence obtained with phased-array coils covering the entire spinal cord
For sagittal imaging, conventional dual echo spin echo is the gold standard

**PD:**
- cord almost isointense with surrounding CSF
- easy identification of any increase in signal

**T2:**
- CSF signal is higher
- facilitates depiction of the anatomical location of the cord / lesions

**Single echo heavily T2 weighted:**
- limited sensitivity in depicting signal abnormalities
- should not be obtained as a stand-alone sequence

*Geert Lycklama et al. Lancet Neurol 2003*
Spinal cord MRI technique
Sagittal imaging: STIR

- May depict additional lesions compared to PD SE
- *More susceptible to artefacts*
- *Not recommended as a stand-alone sequence*

Spinal cord MRI in MS

Use of gadolinium

Contrast-enhancing lesions in the spinal cord:

- rarer than in the brain
- usually small, single, no or little edema or swelling
- usually associated with clinical symptoms
MR imaging of the spinal cord in Multiple Sclerosis

Summary

• Technical issues
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• Indications of spinal cord MR imaging
• Spinal cord MR imaging features
Clinical relevance of spinal cord lesions

Multiple Sclerosis

- Frequent location for lesions causing relapses

- Spinal cord damage is likely to be one of the major determinants of disability in patients with MS

  • *Progressive spastic paraparesis: SPMS, PPMS*
  • *Sphincter dysfunction*
  • *Sensory disturbance / pain*
Spinal cord MRI to understand disability and monitor the course of MS

- Only a mild correlation between the extent of cord MRI abnormalities and clinical disability in MS patients

- Serial spinal MRI shows considerably fewer new lesions than serial brain MRI

Negligible power gain for proof-of-concept trials of immunomodulation
New cord lesions more likely to be symptomatic

Lycklama et al. Brain 1998
Filippi et al. J Neurol Sci 1996
Clinico-radiological paradox

Discrepancy between conventional MRI and clinical measures

- Limited sensitivity in detecting spinal cord focal lesions
- No clear relationship between the number of spinal cord lesions and the number of brain lesions
- Non specificity of the underlying lesion substrate
- Insensitivity to precisely quantify the extent of damage
- Insensitivity to reveal abnormalities in the normal appearing cord tissue
Spinal cord MR abnormalities in MS

Discrepancy between T2 lesion load in the brain and in the spinal cord is particularly relevant in primary progressive MS phenotype, which has smaller T2 lesion loads, despite similar spinal cord T2 lesion load compared to the relapsing MS forms.

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<tr>
<th></th>
<th>RR</th>
<th>SP</th>
<th>PP</th>
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<tbody>
<tr>
<td>Brain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2 focal lesion load (cm³)</td>
<td>4.1 (0–23.6)</td>
<td>11.0 (0.1–49.2)†</td>
<td>3.2 (0.4–32.1)</td>
</tr>
<tr>
<td>T1 focal lesion load (cm³)</td>
<td>0.3 (0–3.4)</td>
<td>2.0 (0–27.2)†</td>
<td>0.3 (0–11.5)</td>
</tr>
<tr>
<td>T1 : T2 load ratio</td>
<td>0.09 (0–0.45)</td>
<td>0.17 (0–0.71)</td>
<td>0.12 (0–0.54)</td>
</tr>
<tr>
<td>Spinal cord</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2 focal lesion load</td>
<td>2.25 (0–6.5)</td>
<td>2.0 (0–9)</td>
<td>2.4 (0–13)</td>
</tr>
<tr>
<td>T1 focal lesion load</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Lycklama et al. Brain 1998
How can we overcome limits of conventional spinal cord MRI in MS?

- Development of new sequences with higher sensitivity to detect focal pathology
- Application of non-conventional MR techniques that indirectly detect diffuse and irreversible pathology in the normal appearing spinal cord tissue
Spinal cord MRI in MS

MR techniques that indirectly detect diffuse and irreversible pathology in the normal appearing spinal cord tissue

Focal T2 lesions:
- demyelination, edema
- variable degree of axonal loss
- poor correlation with clinical disability
- axonal loss occurs outside visible focal lesions
- axonal loss occurs independently of T2 lesions

Non conventional MR measures

Imaging irreversible and diffuse cord damage
Spinal cord atrophy and disability

- Significant, but weak correlation between disability and:
  Number of spinal cord T2 lesions

- Good correlation with:
  Cord area (measure of atrophy)

\[ r = 0.7 \text{ (Losseff et al. Brain 1996)} \]
Spinal cord atrophy and disability

Correlation between change in upper cervical cord area and change in expanded disability status scale (EDSS)

$r = 0.4$ (Constantinescu et al. JNNP 2003)
Valvasina et al. demonstrated using a multivariate linear regression model that average cord FA was independently associated with disability, with a correlation coefficient of 0.73 (p<0.001), supporting the ability of DTI in revealing cervical cord tissue loss in MS patients.

Valvasina et al. Neuroimage 2006
MR imaging of the spinal cord in Multiple Sclerosis

Summary

- Technical issues
- Clinical and MRI correlations
- **Indications of spinal cord MR imaging**
- Spinal cord MR imaging features
Spinal cord MRI in MS
Prevalence of spinal cord lesions

- Subclinical lesions in **27-40%** of patients with CIS
  - 20% in optic neuritis
  - 33% in brainstem syndromes
  - 36% in hemispheric or multifocal syndromes

- Spinal cord lesions **83%** of patients with early relapsing MS

- Spinal cord lesions in **74-92%** of patients with MS

## Indications of Spinal cord MRI in MS

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<th><strong>Situation</strong></th>
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Modified from Bot and Barkhof. *Neuroimage Clin N Am* 2009
Role of MR imaging of the spinal cord in Clinically Isolated Syndromes

1. In patients with spinal cord syndrome

   - Identify the demyelinating lesion that cause the clinical symptoms
   - Rule out non-demyelinating lesions responsible for the clinical symptoms

   Typical demyelinating cervical cord lesion involving the posterior columns

   Microcystic spinal cord degeneration secondary to cervical disk herniation
Role of MR imaging of the spinal cord in Clinically Isolated Syndromes

2. In all patients with spinal cord syndrome

Identify subclinical spinal cord lesions, when brain MRI findings are non conclusive, to demonstrate demyelinating lesions disseminated in space, according to the 2010 version of the McDonald criteria

Diagnostic Criteria for Multiple Sclerosis: 2010 Revisions to the McDonald Criteria

Chris H. Polman, MD, PhD,1 Stephen C. Reingold, PhD,2 Brenda Banwell, MD,3 Michel Clanet, MD,4 Jeffrey A. Cohen, MD,5 Massimo Filippi, MD,6 Kazuo Fujihara, MD,7 Eva Havrdova, MD, PhD,8 Michael Hutchinson, MD,9 Ludwig Kappos, MD,10 Fred D. Lublin, MD,11 Xavier Montalban, MD,12 Paul O’Connor, MD,13 Magnhild Sandberg-Wollheim, MD, PhD,14 Alan J. Thompson, MD,15 Emmanuelle Waubant, MD, PhD,16 Brian Weinshenker, MD,17 and Jerry S. Wolinsky, MD,18

New evidence and consensus has led to further revision of the McDonald Criteria for diagnosis of multiple sclerosis. The use of imaging for demonstration of dissemination of central nervous system lesions in space and time has been simplified, and in some circumstances dissemination in space and time can be established by a single scan. These revisions simplify the Criteria, preserve their diagnostic sensitivity and specificity, address their applicability across populations, and may allow earlier diagnosis and more uniform and widespread use.

Dissemination in space (DIS)

DIS Can Be Demonstrated by ≥1 T2 Lesion in at Least 2 of 4 Areas of the CNS:

- Periventricular
- Juxtacortical
- Infratentorial
- Spinal cord


aGadolinium enhancement of lesions is not required for DIS.
bIf a subject has a brainstem or spinal cord syndrome, the symptomatic lesions are excluded from the Criteria and do not contribute to lesion count.
Added value of spinal cord MRI in the diagnosis of MS

Dissemination in space (DIS)

Swanton (Swanton et al. J NNP 2006)

DIS ≥1 subclinical lesion in each of ≥2 characteristic locations:
- Periventricular
- Juxtacortical
- Posterior fossa
- Spinal cord

35 year old woman: optic neuritis

Brain MRI: only 1 Swanton criteria fulfilled (at least one subclinical periventricular lesion)

Spinal cord MRI: showing subclinical lesions

Spinal cord MR imaging is specially recommended in CIS patients when the brain MR findings are not conclusive (i.e. not fulfilling criteria for dissemination in space)
# Indications of Spinal cord MRI in MS

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Modified from Bot and Barkhof. *Neuroimag Clin N Am 2009*
Normal brain MRI in patients with clinically definite MS
2-3% of all MS patients

- 50% are PPMS
- Most have an abnormal spinal cord MRI
- A normal brain and spinal cord MRI requires reconsideration of a clinical diagnosis of MS

Thorpe et al. Brain 1996

43 year old man with a clinical diagnosis of primary progressive MS. Brain MRI was normal, but spinal cord MRI showed multifocal demyelinating lesions that supported the clinical diagnosis.
## Indications of Spinal cord MRI in MS

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Brain MRI with equivocal findings: added value of spinal cord MRI

Diagnostic certainty can be increased in patients with non-specific brain findings, particularly those >50 years old, because asymptomatic cord lesions are relatively frequent in MS but rare with other white matter diseases.

51 year old man presenting with diplopia and brain multifocal white matter lesions, some of them periventricular.

A demyelinating disease (multiple sclerosis) was clinically suspected.

Absence of subclinical lesions on spinal cord MRI was against the clinical diagnosis. A vascular origin of brain lesions was the most likely etiology.

According to Bot et al. Radiology 2002, subclinical spinal cord lesions are rare in patients with non-MS white matter diseases.
Brain MRI with equivocal findings: added value of spinal cord MRI

Diagnostic certainty can be increased in patients with non-specific brain findings, particularly those >50 years old, because asymptomatic cord lesions are relatively frequent in MS but rare with other white matter diseases.

48 year old man presenting with diplopia and brain multifocal white matter lesions.
A demyelinating disease (multiple sclerosis) was included in the differential diagnosis.
Presence of subclinical lesions on spinal cord MRI (arrows) supported the diagnosis of multiple sclerosis.

According to Bot et al. Radiology 2002, subclinical spinal cord lesions are common (92%) in patients multiple sclerosis.
# Indications of Spinal cord MRI in MS

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Spinal cord MRI in MS patients with atypical new spinal cord symptoms

34 year old man diagnosed of MS. Brain MRI showed typical white matter demyelinating lesions.

New symptoms, considered atypical (lower limb weakness associated with cervical radicular pain), indicated a cervical spine MRI, that showed a compressive myelopathy related to disk disease, that required surgical decompression. Observe the spinal cord demyelinating plaques (arrows).
## Indications of Spinal cord MRI in MS

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Modified from Bot and Barkhof. *Neuroimag Clin N Am* 2009
Added value of spinal cord MRI in primary progressive MS

• Primary progressive forms comprises approximately 10% of MS cases. The most common presentation of this MS phenotype is slowly progressing spastic paraparesis, and less frequently, progressive cerebellar, brainstem, visual, hemiplegic and cognitive syndromes.

• The presence of extensive spinal cord damage may partially explain the discrepancy between the MR abnormalities and the severity of the clinical disease in this form of MS.

Primary progressive MS
47 year old man, with progressive spastic paraparesis. Brain MRI showed minimal signal abnormalities in the right hemisphere periventricular white matter and in the brainstem (arrows). Spinal cord MRI showed multiple focal lesions (arrows), which supported the diagnosis and explain the severity of the clinical symptoms.
Compared to patients with the more frequent relapsing forms of MS (relapsing-remitting and secondary progressive MS), patients with primary progressive MS have smaller T2 lesion loads, smaller T2 lesions, despite similar spinal cord T2 lesion load. Therefore, spinal cord MRI is specially required in the initial diagnosis of primary progressive MS patients, when brain MR findings are not conclusive.
Rule out other diagnosis

40 year old woman, with mild and slowly progressive spastic paraparesis. Primary progressive multiple sclerosis?

Brain MRI was normal. Spinal cord MRI showed a transdural spinal cord herniation (arrows) that could explain the clinical symptoms.
Summary

• Technical issues
• Clinical and MRI correlations
• Indications of spinal cord MR imaging
• **Spinal cord MR imaging features**
Spinal cord MR imaging features

MRI lesions patterns

In addition to the typical unifocal or multifocal pattern, a tumefactive and diffuse patterns can also be found in the spinal cord of patients with MS.

Typical MRI patterns

- unifocal
- multifocal

Atypical MRI patterns

- tumefactive
- diffuse
Spinal cord MRI
Typical imaging features in MS

MS lesions of the spinal cord resemble those in the brain. The lesions can be focal (single or multiple) or diffuse, and mainly affect the cervical cord segment. On sagittal scans, the lesions characteristically have a cigar shape and rarely exceed two vertebral segments in length. On cross-section they typically occupy the lateral and posterior white-matter columns, and rarely occupy more than one half the cross-sectional area of the cord.

- **No cord swelling**
- **Unequivocal hyperintense T2 or Gd-enhancing; focal lesions (not diffuse)**
- **≥3mm in size; <2 vertebral segments long**
- **Occupying only part of cord cross-section**
Spinal cord MRI
Focal spinal cord lesions: axial imaging

Transverse T2 imaging should be added in the spinal cord MRI protocol as they increase the sensitivity of MRI in detecting focal spinal cord lesions, which commonly have a marginal location that limits their identification on the sagittal plane.

Relapsing-remitting MS patient with multifocal demyelinating lesions involving the spinal cord. The lesions were initially overlooked with the heavily T2-weighted sagittal image, but depicted on the proton density images (arrows). Transverse T2 images confirmed the presence of the lesions, and precisely showed their marginal location (arrows).
Spinal cord MRI
Role of transverse imaging in the differential diagnosis

Transverse T2 imaging should be added in the spinal cord MRI protocol as they clearly depict the topography of the lesions, an imaging feature that helps in establishing an accurate differential diagnosis with other diseases that may present with focal spinal cord lesions.
Spinal cord MR imaging features in MS

Diffuse pattern

The diffuse pattern (diffuse areas of slightly increased signal intensity on T2-weighted images) can be identified in all MS phenotypes, although is far more frequent in the primary progressive form.

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<tbody>
<tr>
<td>Spinal cord</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>6</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>with diffuse</td>
<td>(21%)</td>
<td>(31%)</td>
<td>(61%)</td>
</tr>
<tr>
<td>abnormalities (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lycklama et al. *Brain* 1998
Spinal cord MR imaging features in MS

Diffuse pattern

MR demonstration of a diffuse pattern requires an adequate technique, with high contrast-resolution T2 and proton density images in the sagittal plane. The use of a heavily T2-weighted sequences (single echo) commonly overlooks this pattern.

Primary progressive MS

42 year old man, with severe spastic paraparesis. Spinal cord MRI showed diffuse high signal intensity of the whole cervical spinal cord, better depicted on the proton density images (arrows). Spinal cord atrophy is also seen.

Observe, on a normal subject, that the normal spinal cord is isointense to CSD on the proton density image.
The tumefactive pattern represents a diagnostic challenge, as in addition to spinal cord tumors, different non-MS inflammatory diseases may present with expansive spinal cord lesions, particularly involving the spinal cord.
In patients over 50 years old, the tumefactive pattern should include in the differential diagnosis vascular malformations, particularly if there is slowly progressive evolution of a sensorimotor transverse lesion.

56 year old man, with subacute and progressive spinal cord syndrome. MRI showed a tumefactive spinal cord lesion.

Selective intraarterial angiography of the suboccipital artery demonstrated a dural fistula with venous drainage into the perimedullary venous system.
Spinal cord MR imaging features in MS

Tumefactive pattern

**Neuromyelitis optica (NMO) or Devic’s disease** should be considered in the differential diagnosis in patients presenting with extensive/tumefactive spinal cord lesions.
Devic Neuromyelitis optica (NMO)

Diagnostic criteria

Optic neuritis
Acute myelitis

At least two of three supportive criteria:

Contiguous MRI spinal cord lesions extending over ≥ 3 vertebral segments
Brain MRI findings not typical for MS
NMO-IgG seropositive status

Wingerchuck et al. Neurology 2006
Devic Neuromyelitis optica (NMO)  
Spinal cord MRI features

MR imaging of the spinal cord in symptomatic NMO shows extensive cervical or thoracic tumefactive myelitis, involving more than three vertebral segments on sagittal and much of the cross-section on axial T2-weighted images, which sometimes enhance with gadolinium for several months.
Spinal cord MRI in NMO

Role of transverse imaging in the differential diagnosis with MS

Devic Neuromyelitis optica

Preferential spinal central gray matter (>50% of cross-sectional area) involvement in NMO

Multiple Sclerosis

Preferential marginal white matter involvement (<50% of cross sectional area) in MS

Nakamura et al. J Neurol 2008
Clinical and radiological differences between NMO and MS

<table>
<thead>
<tr>
<th></th>
<th>MS</th>
<th>NMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex %</td>
<td>70</td>
<td>90</td>
</tr>
<tr>
<td>Age at onset</td>
<td>20-40</td>
<td>30-50</td>
</tr>
<tr>
<td>Topography</td>
<td>Any</td>
<td>Optic nerve/spinal cord</td>
</tr>
<tr>
<td>Symptomatic brain involvement</td>
<td>Common and early</td>
<td>Uncommon and late</td>
</tr>
<tr>
<td>Attack severity</td>
<td>Usually mild</td>
<td>Usually severe</td>
</tr>
<tr>
<td>Brain MRI</td>
<td>Abnormal</td>
<td>Normal/atypical for MS</td>
</tr>
<tr>
<td>Spinal cord MRI</td>
<td>&lt;1 segment, marginal</td>
<td>&gt;3 segments, central</td>
</tr>
</tbody>
</table>

[Images of MRI scans for MS and NMO]