“Spinal cord MR imaging in Multiple Sclerosis”

Àlex Rovira
Unitat de Neurorradiologia. Servei de Radiologia
Hospital Vall d’Hebron
Barcelona
alex.rovira@idi.gencat.cat
Disclosures

I have no disclosures in relation to the content of this presentation
Summary

- Introduction
- Technical features
- MR imaging features
- Spinal cord MRI for the diagnosis and prognosis of MS
- Spinal cord MRI for monitoring MS
- Conclusions
T2 and CE T1-WI

- Highly sensitive for detecting MS plaques
- Provide quantitative assessment of inflammatory activity and lesion load
- Most important paraclinical tool for diagnosing and monitoring MS
Spinal cord MRI imaging in MS

Spinal cord MRI is not performed as commonly as brain MRI, mainly because of certain technical difficulties and the increase in total acquisition time.

**Technical issues**

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

35-48 mm transverse diameter

Ghosting artefacts from swallowing

Absence of artefacts
Solutions

• Cardiac gating (SE)
• Presaturation slabs
• Fast imaging sequences
• Phased-array coils

Fast double-echo and STIR sequences obtained with phase-array coils covering the entire spinal cord
Selection of T2w MR sequences

Cord almost isointense with surrounding CSF
Easy identification of any increase in signal

Higher sensitivity compared to T2 SE
More susceptible to artifacts (false positive)
Use it in combination with T2

Selection of T2w MR sequences

Single echo heavily T2 weighted\textsuperscript{1-2}:
\begin{itemize}
\item limited sensitivity in depicting signal abnormalities\textsuperscript{1-2}
\item should not be obtained as a stand-alone sequence\textsuperscript{3}
\end{itemize}

Combination of at least two T2w sequences\textsuperscript{3}: T2, PD, STIR

Heavily T1-weighted sequences, such as PSIR (phase-sensitive inversion recovery) or MPRAGE /MP2RAGE (two inversion-contrast magnetization-prepared rapid gradient echo), improve MS lesion detection.

**Field strength:** 1.5 or 3.0T

**Sequences:**

**Mandatory**
- Axial proton density; 2D /3D T2-FLAIR; T2-weighted
- Axial 2D or 3D contrast-enhanced T1-weighted (single dose, minimum delay 5 min)

**Optional**
- Unenhanced 2D or high-resolution isotropic 3D T1-weighted (brain atrophy)
- 2D/3D double inversion recovery (cortical lesions)
- Diffusion-weighted imaging (PML)
- Spinal cord imaging:
  - Sagittal contrast-enhanced T1-weighted
  - Sagittal proton density (STIR) / T2-weighthed
  - Axial T2-weighted
Typical MR imaging findings: spinal cord

- No cord swelling (unless active)
- Unequivocal hyperintense T2 or Gd-enhancing; focal lesions
- ≥3mm in size; <2 vertebral segments long
- Peripheral location, cigar shaped
- Occupying only part of cord cross-section (less than 50%)

Typical MR imaging findings: spinal cord

Weier et al. Mult Scler 2012;18:1560-9
Distribution of focal lesions in the spinal cord

- Focal lesions primarily located in the cervical cord: **59%**
- Only in 16% of patients the lesions are exclusively located in the cervical cord.
- Lesions are also quite frequently (20%) in the lower thoracic spinal segments (Th7–12).
- In 8% of patients, lesions are found either exclusively, or at least one of only two lesions, below the level of the Th5.
Lesion patterns in spinal cord MRI

Typical MRI patterns
- unifocal
- multifocal

Atypical MRI patterns
- tumefactive
- diffuse
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.
Lesion patterns in spinal cord MRI

**Diffuse pattern**

Diffuse abnormality in brain and spinal cord, but no focal lesions

Zwemmer et al. Mult Scler J 2008
Distribution of diffuse lesions in the spinal cord

Diffuse signal changes seen in 15% of patients and extended along 4–17 vertebral segments (mean=10.2 segments)
Prevalence of spinal cord lesions in Multiple Sclerosis

- Spinal cord lesions in **30%** of subjects with RIS
  - 84% progressed to CIS or PPMS (median time 1.6 years)
  - OR of clinical progression: 75.3

- Subclinical lesions in **27-53%** of patients with CIS

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

- Spinal cord lesions in **74-92%** of patients with MS and in **6%** of patients with non-MS white matter diseases

# Indications of spinal cord MRI in Multiple Sclerosis

<table>
<thead>
<tr>
<th>Situation</th>
<th>Objective</th>
</tr>
</thead>
</table>
| Clinically isolated syndrome with spinal cord symptoms                    | Detect symptomatic lesion
|                                                                            | Rule out alternative diagnosis                                            |
| Clinically isolated syndrome with/without spinal cord symptoms            | Predict risk of conversion to MS                                           |
|                                                                            | Predict disability                                                          |
| Clinically isolated syndrome with inconclusive / non specific brain MRI findings | Increase specificity of diagnosis                                         |
| Negative brain scan, but strong clinical suspicion of MS                  | Increase sensitivity of diagnosis                                           |
| Primary progressive MS                                                    | Required for diagnosis (McDonald criteria for dissemination in space)      |
|                                                                            | Rule out alternative diagnosis                                             |
| Radiologically isolated syndrome                                           | Predict risk of conversion to MS                                           |
| Monitoring MS (If clinical activity or disease progression cannot be explained by brain MRI findings) | Detect disease activity                                                   |

Rovira A, De Stefano N. Curr Op Neurol 2016 in press
**BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>N=1015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females: N (%)</td>
<td>686 (67.6)</td>
</tr>
<tr>
<td>Age at onset (mean, SD)</td>
<td>31.1 (8.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CIS topography N (%)</th>
<th>N=1015</th>
</tr>
</thead>
<tbody>
<tr>
<td>ON</td>
<td>373 (36.7)</td>
</tr>
<tr>
<td>BS</td>
<td>271 (26.7)</td>
</tr>
<tr>
<td>SC</td>
<td>261 (25.7)</td>
</tr>
<tr>
<td>Other</td>
<td>110 (10.8)</td>
</tr>
</tbody>
</table>

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

Indications of spinal cord MRI in Multiple Sclerosis
32 year old woman
Unilateral optic neuritis

**Table 1:** 2010 McDonald MRI Criteria for Demonstration of DIS

- **Periventricular** ✔
- **Juxtacortical** ✓
- **Infratentorial** ✓
- **Spinal cord** ✓

Basis: Swanton et al 2006, 2007.\(^{22,27}\)
- Gadolinium enhancement of lesions is not required for DIS.
- If a subject has a brainstem or spinal cord syndrome, the symptomatic lesions are excluded from the criteria and do not contribute to lesion count.
- MRI = magnetic resonance imaging; DIS = lesion dissemination in space; CNS = central nervous system.

**Table 2:** 2010 McDonald MRI Criteria for Demonstration of DIT

- **DIT Can Be Demonstrated by:**
  1. A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI -
  2. Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time -

Based: Montalban et al 2010.\(^{24}\)
- MRI = magnetic resonance imaging; DIT = lesion dissemination in time.
32 year old woman
Unilateral optic neuritis

Two asymptomatic spinal cord lesions

Added value of spinal cord MRI in the diagnosis of MS
Non spinal CIS not fulfilling McDonald brain MRI criteria

- 7 MRI scans needed to diagnose 1 more patient
- Prognostic value: identifies a subgroup that has a very low risk of developing MS

**Spinal cord MRI in CIS:**

- All patients with SC presentation
- Non SC patients who do not meet McDonald criteria on brain MRI

---

**Prognostic value of spinal cord MRI in CIS**

**Amsterdam cohort**

<table>
<thead>
<tr>
<th>1. Spinal CIS fulfilling McDonald brain MRI criteria</th>
<th>No. of patients</th>
<th>No. of patients with SC lesions</th>
<th>No. of patients without SC lesions</th>
<th>OR for patients with SC lesions to develop CDMS vs patients without SC lesions (95% CI)</th>
<th>Hazard ratio for time to develop CDMS, using Cox regression (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>79 patients</td>
<td>20</td>
<td>18</td>
<td>2</td>
<td>NA&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.69 (0.14-3.36), p = 0.65</td>
</tr>
<tr>
<td>2. Spinal CIS not fulfilling McDonald brain MRI criteria</td>
<td>43</td>
<td>33</td>
<td>10</td>
<td>1.33 (0.29-6.14)</td>
<td>1.08 (0.29-4.06), p = 0.92</td>
</tr>
<tr>
<td>3. Nonspinal CIS fulfilling McDonald brain MRI criteria</td>
<td>16</td>
<td>12</td>
<td>4</td>
<td>1.67 (0.11-25.4)</td>
<td>0.89 (0.21-3.71), p = 0.87</td>
</tr>
<tr>
<td>4. Nonspinal CIS not fulfilling McDonald brain MRI criteria</td>
<td>42</td>
<td>19</td>
<td>23</td>
<td>14.4 (2.60-80.03)</td>
<td>51.38 (5.54-476.33), p = 0.001</td>
</tr>
</tbody>
</table>

---

Sombekke et al. Neurology 2013
Prognostic value of spinal cord MRI in CIS
The Barcelona inception cohort

- Study design: single-center, observational
- Sample size: 207 CIS patients (31% with a spinal cord syndrome)
- Follow-up: mean 35.7 (15.8) months.
- Outcomes: conversion to MS (CDMS, McDonald)

Presence of SC lesions is an independent risk factor for evolving to MS

Covariables considered:
- Brain T2 lesion number
- OCB in CSF
- Age
- Gender
- CIS topography
- Treatment with DMT

Arrambide G et al. Poster presentation (P996) ECTRIMS 2015
Brain MRI with equivocal findings

Primary progressive MS

• One year disease progression
• Normal brain MRI
• Positive CSF analysis

Normal brain in MRI in MS patients: 1-3%, 50% are PPMS. Most have an abnormal SC MRI
• First proposed in **2009** (Okuda et al. Neurology 2009)

• Incidental MRI anomalies within the CNS suggestive of multiple sclerosis
Radiologically Isolated Syndrome (RIS)

RIS Cases = 451 (20 databases, 5 countries)

Kaplan-Meier survival analysis with the endpoint of time to the first acute or progressive event at 5-years for the entire RIS cohort.

Kaplan-Meier survival analysis with the endpoint of time to a first clinical event by the presence of spinal cord lesions.

Spinal cord lesions presence

- YES
- NO

HR = 2.92, [1.92-4.34], p<0.001

Okuda et al. Plos One 2014
Radiologically Isolated Syndrome (RIS)

- No risk factors: females, >35 yoa, no spinal cord lesions
- 1 risk factor
- 2 risk factors
- 3 risk factors: males, <35 yoa, spinal cord lesions

0: 116 subjects, 5-year probability of a first clinical event = 10%
1: 163 subjects, 5-year probability of a first clinical event = 34%
2: 96 subjects, 5-year probability of a first clinical event = 53%
3: 8 subjects, 5-year probability of a first clinical event = 100%

Okuda et al. Plos One 2014
Radiologically Isolated Syndrome (RIS)

Male, 43 years

5-year probability of a first clinical event = 53%
Prognostic value of spinal cord MRI in CIS
The Barcelona inception cohort

- Study design: single-center, observational
- Sample size: 207 CIS patients (31% with a spinal cord syndrome)
- Follow-up: mean 35.7 (15.8) months.
- Outcomes: reach significant disability EDSS ≥ 3.0

<table>
<thead>
<tr>
<th>Presence of SC lesions: n (%)</th>
<th>All CIS n=207</th>
<th>SC CIS n=64</th>
<th>Non-SC CIS n=143</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of SC lesions: n (%)</td>
<td>93 (44.9)</td>
<td>50 (78.1)</td>
<td>43 (30.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EDSS ≥3.0: n (%)</td>
<td>13 (6.3)</td>
<td>6 (9.4)</td>
<td>7 (4.8)</td>
<td>0.171</td>
</tr>
</tbody>
</table>

Presence of at least one SC lesion was associated with an EDSS ≥ 3.0: 11.8% (vs 1.8%) p=0.003

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>aHR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No SC lesions</td>
<td>114</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC lesions</td>
<td>93</td>
<td>5.7</td>
<td>0.9-36.0</td>
<td>0.067</td>
</tr>
<tr>
<td>SC CIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No SC lesions</td>
<td>14</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC lesions</td>
<td>15</td>
<td>0.5</td>
<td>0.04-7.9</td>
<td>0.647</td>
</tr>
<tr>
<td>Non-SC CIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No SC lesions</td>
<td>100</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC lesions</td>
<td>43</td>
<td>36.2</td>
<td>1.5-880.4</td>
<td>0.028</td>
</tr>
</tbody>
</table>

aHR for reaching an EDSS ≥3.0.

The presence of at least one SC lesion at the time of the CIS is associated with short-term disability and further contributes to estimate the risk of disability accumulation, particularly in non-SC CIS.
Spinal cord MRI in CIS
Diagnostic and prognostic value

• It is recommended performing a SC MRI in non-SC CIS who do not fulfill the McDonald criteria with brain MRI alone for diagnostic purposes.

• However, acquiring a baseline SC MRI in all CIS patients is useful to estimate their prognosis.
• Serial spinal MRI shows considerably fewer new lesions than serial brain MRI
• Most are symptomatic
• Difficult to detect
• A relationship exists between development of new lesions in the brain and the development of new lesions in the spinal cord
103 RRMS patients: clinically stable
Median interval between scans: 17 months

New asymptomatic lesions

- 43.7% brain
- 25.2% spinal cord
- **9.8% only asymptomatic SC lesions**

A significant proportion of disease activity only in the SC, a fact that could have important implications in assessing and predicting treatment response

Zecca et al. Mult Scler J 2015
A lesion topography-based approach
To predict treatment response to IFNB

• Study design: Independent, single-centre, post-marketing analysis
• Sample size: 390 RRMS patients starting IFNB and reassessed one year after
• Follow-up: 1-4 years after treatment start
• Outcomes: relapses, sustained disability progression

...clinical relapses (n=160, 41%)

<table>
<thead>
<tr>
<th>Independent Predictor</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (each year)</td>
<td>0.98 (0.96-0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>Relapses 1Y</td>
<td>1.7 (1.1-2.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>New T2 lesion count 1Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.4 (0.7-2.7)</td>
<td>0.29</td>
</tr>
<tr>
<td>2</td>
<td>1.7 (1.0-2.8)</td>
<td>0.06</td>
</tr>
<tr>
<td>3+</td>
<td>2.6 (1.5-4.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Lesion location did not contribute to fit the model

...sustained disability worsening (n=65, 16%)

<table>
<thead>
<tr>
<th>Independent Predictor</th>
<th>HR (95% CIs)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>1.9 (1.1-3.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>EDSS score (each step)</td>
<td>2.1 (1.6-2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relapses 1Y</td>
<td>2.9 (1.6-5.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>New infratentorial lesions 1Y</td>
<td>2.6 (1.2-5.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>New spinal cord lesions 1Y</td>
<td>2.3 (1.1-4.8)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Lesion count did not contribute to fit the model

Galassi et al. Mult Scler 2015;23 (11 Suppl):307 (abs P634)
• MR imaging of the spinal cord is more challenging than imaging of the brain in MS patients, and a meticulous standardized MR technique is essential to enable acquisition of high-quality images.

• Spinal cord MR imaging provides additional useful information to brain MR imaging to establish a prompt and accurate diagnosis of MS, to provide valuable prognostic information, and in certain cases for monitoring the disease course and treatment response.

• Quantitative MR-based measures, in particular spinal cord atrophy measurements, have proven valuable for assessing the type and degree of spinal cord damage, although their assessment is technically challenging and cannot still be currently incorporated into the daily clinical setting.
Special thanks to:

MR Unit
- Cristina Auger
- Raquel Mitjana
- Elena Huerga
- Xavier Aymerich
- Deborah Pareto
- Juan F. Corral

Neurology department
- Xavier Montalban
- Jaume Sastre-Garriga
- Carmen Tur
- Mar Tintoré
- Jordi Río