MRI Morphology of Multiple Sclerosis

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Multiple sclerosis

- chronic inflammatory demyelinating disease of the Central Nervous System
- inflammatory demyelinating diseases encompass a broad spectrum of disorders
- represent profound heterogeneity in clinical course, neuroimaging appearance of lesions, and response to therapy.
**MS:** a chronic inflammatory demyelinating disorder

**Histologic hallmarks:**

<table>
<thead>
<tr>
<th>Inflammation and demyelination</th>
<th>Axon loss and gliosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>⇒ account for the lesion pattern of <strong>acute MS</strong>!</td>
<td>⇒ responsible for progressive, irrevocable disability of <strong>chronic MS</strong>!</td>
</tr>
</tbody>
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New MR criteria

<table>
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<tr>
<th>Dissemination in space</th>
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<td><strong>McDonald (2001)</strong></td>
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| Three or more of the following:  
  Nine T2 lesions or one Gd-enhancing lesion; three or more periventricular lesions; one or more juxtacortical lesion; one or more posterior fossa lesion  
*One spinal cord lesion can replace one brain lesion |
| **McDonald (2005)**    |
| Three or more of the following:  
  Nine T2 lesions or one Gd-enhancing lesion; three or more periventricular lesions; one or more juxtacortical lesion; one or more posterior fossa lesion or spinal cord lesion  
*A spinal cord lesion can replace an infratentorial lesion  
**Any number of spinal cord lesions can be included in total lesion count |
| **New criteria**        |
| One or more lesion in each of two or more characteristic locations: periventricular, juxtacortical, posterior fossa and spinal cord  
All lesions in symptomatic region excluded in brainstem and spinal cord syndromes |

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<tr>
<td>A Gd-enhancing lesion three or more months after clinically isolated syndrome; a new T2 lesion with reference to a baseline scan obtained 30 days or more after onset of clinically isolated syndrome</td>
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<td><strong>New criteria</strong></td>
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<tr>
<td>A new T2 lesion on follow-up MRI irrespective of timing of baseline scan</td>
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Performance of MRI criteria for development of clinically definite multiple sclerosis (CDMS)

<table>
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<tr>
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<th>DIS +DIT</th>
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<th>McDonald 2005</th>
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<tr>
<td>Specificity</td>
<td>87%</td>
<td>88%</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>72%</td>
<td>60%</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>81%</td>
<td>76%</td>
<td>73%</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>79%</td>
<td>77%</td>
<td>78%</td>
<td></td>
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New criteria

• → simpler without compromising specificity and accuracy.

• dissemination in space (DIS) and in time (DIT) from 2 MRI scans
  ⇒ higher specificity for CDMS than either DIS or DIT alone.

Technical considerations:

Supratentorial: FLAIR > PD

Infratentorial: PD > FLAIR

Change of paradigm: addition of 3D sequences ⇒
3D Flair Space, 3D DIR (double inversion recovery), 3D T1
→ improved spatial + inherent contrast resolution

3D sequences ⇒
conspicuity of lesions ↑
Monosymptomatic demyelinating diseases (CIS) are commonly the first manifestations of MS.

<table>
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<tr>
<th>Optic neuritis</th>
<th>Brainstem-cerebellar syndromes</th>
<th>Partial transverse myelitis</th>
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clinically isolated syndrome (CIS)
MRI → identify patients at risk of conversion to CDMS

- Longitudinal study (Ø14.1 years) 71 patients with CIS
  - abnormal MRI results at presentation ⇒ 88% CDMS
  - normal MRI at presentation ⇒ 19% CDMS


- After CIS: Ø 20.2 years f-up in 107 pats: CDMS 63%
  - abnormal baseline MR 60/73 ⇒ 82% CDMS
  - normal baseline MR 7/34 ⇒ 21% CDMS

MR morphology:
One or more lesions in each of two or more characteristic locations (=DIS):

- perivenular ventriculo-petal
  = Dawson fingers
- juxtacortical
- posterior fossa
- spinal cord

**MR morphology:**

One or more lesions in each of two or more characteristic locations (=DIS):

- Periventricular lesions
- Juxtacortical
- Posterior fossa
- Spinal cord

Periventricular lesions → higher specificity than juxtacortical lesions

- C. callosum + forceps major/minor
- Splenium + optic radiation
- Demyelination plus neurodegeneration
MR morphology:

One or more lesions in each of two or more characteristic locations (=DIS):

Perivenular (occasionally → grey matter)

periventricular
juxtacortical
posterior fossa
spinal cord

Lucchinetti C et al.
MR morphology:

One or more lesions in each of two or more characteristic locations (=DIS):

- periventricular
- juxtacortical
- posterior fossa
- spinal cord

Images:

- 4th ventricle, brainstem
- Subpial pons
- Trigeminal fibers
- Middle cerebellar peduncle
- Medial longitudinal fasciculus
**MR morphology:**

One or more lesions in each of two or more characteristic locations (=DIS):

- periventricular
- juxtacortical
- posterior fossa
- spinal cord

Related to venous density, insertion of denticulate ligament

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**Spinal MR:**

- Useful in depicting dissemination in space when brain MRI brain is normal or equivocal
- 30-40% of pts w. CIS → addit. cord lesions
- Sensitivity ↑ from 66% to 84% for CDMS
  - focal lesion(s) T2 ↑ or Gd +,
  - > 3mm, ≤2 vertebral segments!
  - only part of cord cross section involved

Midline FOV 28cm

C2/3: post. column + centromedullary

C3/4: lat. column

C4: lat. column

C6: lat. column bilat + anterior

Lateral column left
MR morphology: assessment of acuity
⇒ Gd enhanced delayed T1 sequences

Contrast enhancement

• tissue vascularity/
• fractional blood volume
• transendothelial diffusion

*At 5` delay: no of active lesions increased: 10→18 with 0.5mol/L Gd
16→24 with 1.0mol/L Gd

** Short delay 15-20`: no Gd lesions ↑ w. single dose:  plus 47%

„Detection was not significantly further improved by a longer delay”.

* Uysal E et al. Sensitivity of immediate and delayed gadolinium-enhanced MRI after injection of 0.5 M and 1.0 M gadolinium chelates for detecting multiple sclerosis lesions. AJR Am J Roentgenol 2007;188:697–702

**Silver NC et al. Sensitivity of contrast enhanced MRI in multiple sclerosis: Effects of gadolinium dose, magnetization transfer contrast and delayed imaging. Brain 1997; 120;1149-1161
Acute lesions - contrast enhancement

Pattern:
- solid punctate
- curvilinear
- open ring !!
- ringlike

represents initial stage of inflammation by T lymphocytes and macrophages
→ Gd enhancement lasts for 3.1 weeks on average (untreated)
Acute lesions – DWI nonrestricted, ADC high

common: b1000 normal / (↓)
ADC ↑

rare: b 1000 ↓
ADC ↓

High ADC values in acute MS lesions:
~increase of extracellular space by
eextracellular edema or demyelination

Low ADC values in acute MS lesions:
~release inflammatory cytokines
→mitochondrial dysfunction → cytotoxic edema

Rosso C et al. Diffusion-Weighted MR Imaging Characteristics of an Acute Stroke like Form of Multiple Sclerosis
AJNR 2006; 27:1006-1008
Acute lesions – $H^+$spectroscopy

Metabolites: ↑↑ cholin, ↑ lactate + lipids, ↓NAA
⇒ tumefactive/pseudotumoral demyelination
Inflammatory demyelinating disease with restricted topographic manifestation

optic neuritis & transverse myelitis; cord lesions extending ≥ 3 vertical segments, brain MR does not meet criteria for MS; IgG AQ4 antibody positive status in 70-90%

Nakamura M et al. Preferential spinal central gray matter involvement in neuromyelitis optica. J Neurol 2008; 255 ;163-170
Dissemination in Time (DIT)

Simultaneous presence of asymptomatic Gd enhanced and non-enhanced lesions at any time

or a new T2 and/or gadolinium-enhanced lesion on f-up MR irrespective of timing of baseline study

Filippi M et Rocca MA Radiology 2011;259;659-81
Relapsing remitting course (RRMS)

most frequent clinical course of MS (~80%)

- T2 lesion load ~ age at onset, relapse rate, EDSS and Gd enhancement
- plateauing relationship between T2 lesion load and disability (EDSS>4.5).

Li DKB et al. MRI T2 lesion burden in multiple sclerosis : A plateauing relationship with clinical disability – NEUROLOGY 2006;66:1384-1389
Benign course of MS (~10-20% of RRMS)

**Predictors:**
- **Clinical:** onset <40y, with ON, lack of pyramidal signs at presentation, duration of first remission >1 year, only one relapse within 5 years
- **MR:** few new or enlarging lesions, low incidence of Gd + lesions!
Secondary progressive course (SPMS)

After several years of RRMS course ~ 50% of untreated patients will develop SPMS

Axonal loss, gliosis & neurodegeneration

• over 20 y, the rate of lesion growth was 2.89 cm³/year → SPMS (42%) compared to 0.80 cm³/year in those who remain RRMS (58%)

patients are older, m=f, present w slowly progressive spastic paraparesis
MR: lower T2 lesion load, slower rate of new T2 and Gd + lesions,
→ diffuse wm changes , cortical and spinal cord lesions
# Diagnostic Criteria – Key Principles

- **2 or more lesions in characteristic locations of CNS**  
  (dissemination in space DIS)
- **2 or more episodes of CNS dysfunction**  
  (dissemination in time DIT)  
  or (chronic) progression for defined observation time  
  (> 6 or 12 months)
- **exclusion of other diagnoses**

* No single diagnostic test is a definitive proof !

⇒ synthesis of neurological findings,  
MR imaging morphology & addit.investigations

* Kappos L.  
MS in MRI - A learning CD-ROM by Bacelar O, De Vera A, Radue E-W