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MRI in MS

- MRI lacks specificity but has high sensitivity; established as a most important “paraclinical test”
- Important in the new diagnostic criteria
- Many new MR technologies have been first applied for MS
  - Ex. FLAIR, MTR, double IR
- Biomarker
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• Hyperintense: edema, inflammation, demyelination, axonal loss can be hyperintense; lacks specificity

• Slightly hyperintense: dirty-appearing WM
  Vrenken, et al. *AJNR* 2010;31:541-8

• Isointense: normal-appearing WM: microscopical demyelination and/or axonal loss

• Hypointense: iron deposition? (putamen, thalamus)
• Hyperintense (free radical? Foam cell? Ferritin?)
  – Periphery of active lesions
  – Dentate nucleus
• 20% of MS patients (esp., SPMS) (Roccataglitata, et al. *Radiology* 2009;251:503-10)
• Isointense: 80-90% of T2 lesions
• Hypointense: “T1-black hole” (10-20% of T2 lesions): Axonal loss of severe demyelination
Gd-enhanced MRI

- BBB breakdown; active lesions
- 5-10 times > clinical relapse
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McDonald criteria


- Symptoms suggestive of MS
- Dissemination in space
  - Clinical information
  - MR abnormality
- Dissemination in time
  - Clinical information
  - MR abnormality
- No better explanation than MS
MRI Criteria for Brain Abnormality (Dissemination in Space)

- Three of four of the following:
  1. One Gd-enhancing lesion or nine T2-hyperintense lesions if there is no Gd enhancing lesion
  2. At least one infratentorial lesion
  3. At least one juxtacortical lesion
  4. At least three periventricular lesions
- A spinal cord lesion can be considered equivalent to a brain infratentorial lesion; an enhancing cord lesion to an enhancing brain lesion.

MRI Criteria for Dissemination of Lesions in Time

- Detection of an enhancing lesion at least 3 months after the onset of the initial clinical event, not at the site corresponding to the initial event
- Detection of a new T2 lesion if it appears at any time compared with a reference scan done at least 30 days after the onset of the initial clinical event
Swanton criteria

Swanton et al. *JNNP* 2006;77:830-3

- Intended to increase the sensitivity for clinically isolated syndrome (CIS)
- Dissemination in space
  - $\geq 2$ of the followings
    - Subcortical WM, periventricular WM, posterior fossa, spinal cord
- Dissemination in time
  - New T2 lesion on follow-up MRI
- Higher sensitivity, almost equal specificity
- Hesitation among most clinicians to adopt
  (Loevblad et al. *AJNR* 2010;31:983)
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MS in Asia

• 1/3 of patients have optic-spinal MS or Devic disease
  – Most of these patients are probably neuromyelitis optica (NMO).

• Fewer brain lesions than Caucasians

• Much fewer cerebellar lesions

• Fewer chronic progressive (primary or secondary progressive) MS patients

• More lesions with atypical MR finding

• Lower rate of positive CSF oligoclonal bands
  – Patients with negative oligoclonal bands have more frequent atypical lesions, such as tumefactive MS or diffuse white matter lesions
• Clinical symptoms more important than MRI for RRMS
• Same with McDonald criteria for PPMS
• Additional definitions for CPMS, Devic disease, optic-spinal MS and Balo’s concentric sclerosis
Proposed modifications to the McDonald criteria for use in Asia

<table>
<thead>
<tr>
<th>McDonald criteria</th>
<th>Proposed modifications for Asians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal MRI</td>
<td></td>
</tr>
<tr>
<td>Spinal cord lesion should be under two vertebral bodies in height</td>
<td>No restriction to length of spinal cord lesion</td>
</tr>
<tr>
<td>No swelling of the spinal cord lesion</td>
<td>No restriction to spinal cord lesion with swelling</td>
</tr>
<tr>
<td>Spinal cord lesion should occupy part of the cross section</td>
<td>No restriction to spinal cord lesion involving complete cross section</td>
</tr>
<tr>
<td>Brain MRI</td>
<td></td>
</tr>
<tr>
<td>Nine T2-hyperintense lesions or one gadolinium-enhancing lesion</td>
<td>Four or more brain MRI T2-hyperintense lesions in patients less than 60 years of age or one gadolinium-enhancing lesion; or more than one lesion in two or more typical sites (juxtacortical, periventricular, posterior fossa, and spinal cord)</td>
</tr>
</tbody>
</table>
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MR variations in MS

- Ovoid lesion
- Enhancing lesion
- Callosal-septal interface lesion
- Isolated U-fiber lesion
- Tumefactive MS lesion
- Balo’s concentric sclerosis
- Spinal cord lesion
Ovoid lesions
(Dawson's finger)

- Ovoid-shaped deep WM lesions perpendicular to the lateral ventricular wall
- Represent perivenous inflammation
- Frequent but not specific

Callosal-septal interface lesions (Subcallosal striations)

- Intracallosal lesions perpendicular to the ventricular wall
- High sensitivity and specificity
- Thin, sagittal FLAIR useful for MS diagnosis

Isolated U-fiber lesions (Juxtacortical lesions)

- MS lesions extending along the subcortical U-fibers
- About half of MS patients have at least one isolated U-fiber lesion
- Representing inflammation along the subcortical U-fibers?
- May be a cause of subcortical dementia
- Relatively specific for MS; adopted in McDonald’s criteria


Pathology (PAS stain), Okazaki
Fundamentals of Neuropathology
Tumefactive MS

- Glioma (GBM)-like MS lesion
  - Large size (>2 cm)
  - Mass effect
  - Ring enhancement

- Biopsy is often required for final diagnosis, but possibility of MS should be considered to avoid aggressive surgery
Differentiation between tumefactive MS and GBM

- Less mass effect than GBM
- Open-ring sign
- Perfusion imaging
  (Cha, et al. *AJNR* 2001; 22:1109)
- Low density on noncontrast CT
  (Kim, et al. *Radiology* 2009; 251:467)
- No punctate hypointensity on SWI
  (Kim, et al, *AJNR* 2009; 30:1574)
Balo’s concentric sclerosis

- A rare variant of MS
- WM destroyed in concentric layers
- Formerly considered to be a monophasic rapidly progressive disease with a fatal outcome
- Increasing number of cases with better outcome (Karaarslan, et al. AJNR 2001;22:1362)
- Relatively more frequent in China and Phillippines
- Very rare in Europe, US and Japan

T2WI @ 3T
T1WI
DWI

Pathology (Myelin stain), Okazaki Fundamentals of Neuropathology
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Non-conventional MRI for MS

• Diffusion MRI
• High-field MRI, ultra high-field MRI
• Phase imaging
• SWI
• Double IR
• USPIO-enhanced MRI
Diffusion MRI in MS

• Active MS lesions may be partially hyperintense on DWI
  (Tsuchiya, et al. *EJR* 1997;31:165
    – T2-shine through effect
    – Cytotoxic edema

• Decreased FA on DTI
High-field ($\geq 3$T) MRI

- Higher SNR than 1.5 T
- More MS lesions detected
MS @ 3T
Cortical MS lesions at 7T

Iron depositions and venous dilatations shown on SWI in MS

Haacke, et al. JMRI 2009;29:537-44
Cortical MS lesions on Double inversion recovery (IR)

- 2 times than SE T2WI,
- 1.5 times than FLAIR

USPIO in MS

(Dousset et al. AJNR 2006;27:1000-5)

- **USPIO**: ultrasmall particles of iron oxide
- **Phagocytic activity**
  - High signal on T1WI, low on T2WI
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Why do we need surrogate tools to monitor MS evolution?

- Relapses are relatively infrequent and poorly related to disability accumulation
- Disability takes several years to accumulate
- Clinical scales are poorly reliable

Why MRI as a surrogate?

- Sensitive (5-10 times > relapses)
- Objective
- Continuous values/Linear scale
- Close to “actual” pathology
- Reproducible
- Easy to blind and standardize
- Retrievable data
Most widely used MR measurements for clinical trials

Loevblad, et al. *AJNR* 2010;31:983-9

- **T2WI**
  - T2 lesion load
  - New lesions
  - Enlarging lesions

- **Gd**
  - Total lesion number
  - New lesions
  - Enlarging lesions
T2-volume measurement by Fuzzy Connectedness

T2-lesion load in MS

- **Not so correlated with clinical symptoms**
  - Fisniku, et al. *Brain* 2008;131:807-17

- **Possible reasons**
  - T2 lesions correspond to various pathologies
  - Normal-appearing, dirty-appearing WM
  - Brain atrophy
Other MRI measurements used for clinical trials

Loevblad, et al. AJNR 2010;31:983-9

- T1 black hole
- Brain atrophy
- Spinal cord atrophy
- MTR (Whole brain MTR histogram)
- DTI
- MRS
- fMRI
Whole brain MTR histogram in MS

- Peak height of whole brain MTRH represents the amount of normal WM (myelin)
- Different MTRH between MS patients and controls (van Buchem et al. AJNR 1997; 18:1287)
- MTRH peak height correlates with neuropsychological tests (van Buchem et al. Neurology 1998; 50:1609)

van Buchem et al. AJNR 1997; 18:1287
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Neuromyelitis optica (NMO)

- Idiopathic, severe, demyelinating disease of the CNS that preferentially affects the optic nerve and spinal cord
- Formerly thought to be a variant of MS
- Specific antibody for NMO (NMO-IgG: aquaporin 4) -> distinct entity
- Pathologically, astrocytes are primally damaged (demyelination is secondary)
Diagnositic criteria for NMO


• Optic neuritis
• Acute myelitis
• ≥2 of the followings
  – Longitudinally extensive myelitis (≥ 3 vertebral segments seen on MRI)
  – Brain MRI not fulfilling MS criteria
  – Positive AQP4
## MS vs. NMO

<table>
<thead>
<tr>
<th></th>
<th>MS</th>
<th>NMO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age of</strong></td>
<td>29</td>
<td>39</td>
</tr>
<tr>
<td><strong>onset</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex (M:F)</strong></td>
<td>1 : 2</td>
<td>1 : 9</td>
</tr>
<tr>
<td><strong>MRI: brain</strong></td>
<td>Periventricular</td>
<td>• Normal or non-specific</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hypothalamic, brainstem</td>
</tr>
<tr>
<td><strong>MRI: spinal</strong></td>
<td>• Short-segment</td>
<td>• Longitudinally extensive (≥ 3 vertebral segments)</td>
</tr>
<tr>
<td><strong>cord</strong></td>
<td>• Peripheral</td>
<td>• Central</td>
</tr>
</tbody>
</table>

NMO

T2WI

Gd

T2WI
T2-hyperintense lesion density (MS vs. NMO)

- NMO: preferentially involves the central regions
- MS: preferentially involves the lateral and posterior regions

Brain lesions in NMO

Cloud-like enhancement in NMO

- Multiple patchy enhancing lesions with blurred margin
- 90% in NMO patients, 8% in MS patients
  - Specific to NMO
- Possibly caused by primary involvement of the BBB by the autoantibodies

Acute demyelinating encephalomyelitis; ADEM

- Severe inflammatory demyelinating disease, frequently secondary to infection or vaccinations
- Usually monophasic
- May recur (multiphasic disseminated encephalomyelitis; MDEM)
- May evolve to MS
- How different from MS?
- Is there any “diagnostic criteria?”
- Possible to differentiate from MS at the first attack?
Proposed criteria for differentiation between ADEM and MS (>15 yrs old) (Multi-centered study in France)

De Seze et al. Arch Neurol 2007;64:1426-32

• ≥2 of the followings -> ADEM
  – Atypical clinical symptoms for MS
    • Consciousness alteration, hypersomnia, aphasia, seizure, hemiplegia, etc.)
  – Absence of oligoclonal bands
  – Gray matter involvement on MRI

• No significant difference in infectious episodes or vaccinations between ADEM and MS
Role of MRI in the differentiation of ADEM from MS in children (<18 yrs old)


- ≥2 of the followings → MS
  - Absence of a diffuse bilateral lesion pattern
  - Presence of black holes
  - Presence of two or more periventricular lesions

- Sensitivity: 81%, Specificity: 95%

- Follow-up at least 3 years (6 years for <11 years old) is recommended when diagnosed as ADEM

- Most useful for differentiating a first attack of MS from ADEM (Ketelslegers, et al. *Neurology* 2010;74:1412-1415)
Summary

- MRI plays an important role in diagnosis of WM diseases (MS, NMO, ADEM).
- MRI is useful for biomarker in MS.
- There are differences in MRI of MS between Asian countries and western countries.
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