MRI of Multiple Sclerosis and Differential Diagnosis

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• Normal Myelination & Normal Variants
• Classification of white matter disease
• Small vessel ischemic disease (leukoaraiosis)
• Developmental white matter disease (leukodystrophy)
• Multiple Sclerosis on MRI

Typical MRI features
Mag Transfer Imaging
Diffusion Tensor Imaging
Imaging DDx

• Other WM Diseases:

ADEM (Acute Disseminated Encephalomyelitis)
CPM (Central Pontine Myelinolysis)
PRES (Posterior Reversible Encephalopathy Synd)
PML (Progressive Multifocal Leukoencephalopathy)
Normal Myelination: Birth

Dorsal Brainstem  Int Cap Post Limb

Motor corticospinal tracts

Osborn 1994
Normal Myelination: 3 to 4 months

Corticospinal tracts

Int Cap Ant Limb

Osborn 1994
Normal Myelination:
6 to 8 months

Osborn 1994
Birth (T1)

4 months (T1)

Barkovich 1995
8 months (T1)

12 months (T2)

Barkovich 1995
Myelination in Development

- begins 5th fetal month (path)
- caudal to cephalad
  - brainstem > cerebellum, BG > cerebrum
- dorsal to ventral
  - occipital lobes > frontal lobes
- Rapid first 2 yrs, continues into 3rd/4th decades
  - T1 relaxation changes continue into teens
Delayed Myelination

Perivascular Spaces
Corticopontine Tracts
48 year old 1 year s/p severe head trauma

Wallerian Degeneration
<table>
<thead>
<tr>
<th>Location</th>
<th>Structure</th>
<th>DDx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritrigonal WM</td>
<td>Parietal Association tracts</td>
<td>PVL, MS PVWMSVD</td>
</tr>
<tr>
<td>Frontal Horns</td>
<td>Loose Myelin</td>
<td>MS</td>
</tr>
<tr>
<td>Posterior Limb Internal Capsule</td>
<td>Corticopontine tract</td>
<td>ALS, CPM, MS</td>
</tr>
</tbody>
</table>
WM: Classification by Mech

• **Primary** demyelinating disease
  - Multiple Sclerosis

• **Secondary** demyelinating disease
  - Allergic
  - Viral
  - Vascular
  - Metabolic
  - Toxic
WM: Classification by Mech

- **Allergic (immunologic)**
  - Acute disseminated encephalomyelitis - ADEM

- **Viral**
  - HIV-associated encephalitis
  - Prog multifocal leukoencephalopathy - PML
  - Subacute sclerosing Panencephalitis - SSPE

- **Vascular**
  - Binswanger’s disease
  - Postanoxic encephalopathy
  - Toxic
White Matter Standards for Visual Scoring
WM: Classification by Mech

- **Toxic**
  - Radiation
  - Marchiafava-Bignami Disease (Corpus Collosum)
  - Disseminated necrotizing leukoencephalopathy
  - Drugs (chemoRx, methamphetamine, cocaine)
  - Toxins (triethyl, tin, lead)

- **Metabolic**
  - Central pontine myelinolysis (osmotic) - CPM

- **Traumatic:** Diffuse axonal shear injury - DAI
WM: Classification by Mech

- Dysmyelinating Disease
  - Adrenoleukodystrophy – Males, posterior, Pons/Medulla, Gad+
  - Metachromatic Leukodystrophy (MLD) – cerebellum, spares subcortical U fibers and BG – tigroid WM
  - Krabbe’s Disease – Ca++ BG
  - Alexander Disease – Big head, Anterior
  - Canavan’s Disease – Big head, NAA, stem/BG
  - Pelizaeus-Merzbacher Disease (PMD) – tigroid WM
Multiple Sclerosis: Imaging

- Abnormal MRI scans are found in:
  - 90% of patients with definite diagnosis of MS
  - 70% of patients with diagnosis of probable MS
  - 30%-50% of patients with possible MS

- 3 criteria for the MRI diagnosis of MS (Fazekas et al.):
  - Lesions abutting the lateral ventricles
  - Lesions with diameter greater than 0.6 cm
  - Lesions present in the posterior fossa
Multiple Sclerosis

• 85% have **ovoid perivent** lesions (Dawson’s fingers)

• 50 to 90% w “definite” MS have **CC** lesions

• 10% of adults have PF lesions

• Temporal lobe lesions are relatively specific for MS

• MS lesions generally lack mass effect

• Tend be darker and “punched out” on T1
Multiple Sclerosis: McDonald Criteria for MRI

• Typical MS demyelinating lesions meeting at least 3 of the following 4 criteria:
  - At least 1 Gd lesion or at least 9 T2 lesions
  - At least one infratentorial lesion
  - At least one juxtacortical lesion
  - At least 3 periventricular lesions
44 year old numbness legs and feet

35 year old R body numbness R leg weakness

Dawson’s Fingers
Flame shaped periventricular
21 year old optic neuritis

29 year “trouble controlling R side” body

Target Sign
23 year old vagueparethesias

39 year old headaches

Which one is Multiple Sclerosis?
23 year old vague parethesias

39 year old headaches

MS

Mets
Corpus Collosum
Punched out lesions on T1W
DDx: Corpus Callosum Lesions

• Tumors: GBM, Lymphoma, Lipoma
• Demyelinating Dz: MS, Marchiafava-Bignami, PML
• Infarct ("rare", dual arterial supply)
Which one is Multiple Sclerosis?

24 year old lethargy and respiratory illness

24 year old scattered parethesias

[Images of brain scans]
24 year old lethargy 
respiratory illness

24 year old scattered 
parethesias

Histoplasmosis

MS
Tumefactive MS
Tumefactive MS
40 year old nausea & dizziness

21 year old blurred vision
40 year old nausea & dizziness

21 year old blurred vision

Mets

MS
Multiple Sclerosis: Advanced MRI

- Magnetization transfer imaging
  - Decreased MTR (Mag Transfer Ratio) in MS

- MR Spectroscopy
  - Decreased NAA in normal appearing WM

- Diffusion tensor imaging
  - Decreased FA and increased MD in normal appearing WM

- High resolution grey matter imaging (7T)
  - Tiny foci of GM on double inversion FLAIR at 7T in MS
Magnetization Transfer

- Frequency bound
- Frequency free
- MT pulse ~2000 kHz off-resonance
- Saturation effect
- Energy transfer
  - Bound
  - Free
Dirty-Appearing White Matter in Multiple Sclerosis: Volumetric MR Imaging and Magnetization Transfer Ratio Histogram Analysis

Yulin Ge, Robert I. Grossman, James S. Babb, Juan He, and Lois J. Mannon

BACKGROUND AND PURPOSE: In contrast to “normal-appearing” white matter (NAWM) in patients with multiple sclerosis (MS), there are subtle, abnormal and diffuse signal intensity changes often seen on T2-weighted MR images, which we have referred to as “dirty-appearing” white matter (DAWM). These areas of DAWM have slightly higher signal intensity than that of NAWM, but lower than that of lesion plaques. Our study was designed to determine the volumetric and magnetization transfer ratio (MTR) features of DAWM in patients with MS.

METHODS: Dual-echo fast spin-echo MR imaging and magnetization transfer imaging were performed in 22 patients with relapsing-remitting MS. Slightly hyperintense DAWM areas were manually outlined on the basis of T2-weighted imaging findings. The volume and MTR of DAWM were calculated and compared with the volume and MTR of NAWM and T2 lesion plaques.

RESULTS: The average volume of DAWM (18.3 mL) was greater than the average volume of T2 lesion plaques (11.0 mL, P = .04), and the mean MTR in DAWM (38.7%) differed significantly (P < .0001) from that in NAWM (40.7%) and plaques (33.3%). There was a modest negative correlation between either mean MTR (r = −0.60; P = .003) of DAWM or peak height (r = −0.50; P = .02) of DAWM with T2 lesion load. Neither DAWM volume nor total T2 abnormality (DAWM + plaques) volume correlates with the Expanded Disability Status Scale.

CONCLUSION: The results of this study indicate that MTR is able to differentiate DAWM from lesion plaques and NAWM and that DAWM might be a different pathologic process of the disease. The notion and quantification of these subtle imaging findings of DAWM areas may improve our understanding of certain stages of disease progression and disease burden in patients with relapsing-remitting MS.
Fig 2. The average MTR histograms were generated from NAWM, DAWM, and lesion plaques. Note that the histogram of DAWM was located between the histograms of NAWM and lesion plaques.
Cerebral $N$-Acetylaspartate Is Low in Patients with Multiple Sclerosis and Abnormal Visual Evoked Potentials


RESULTS: PEPSI NAA values (water-normalized, CSF-corrected) were significantly lower in MS subjects with abnormal VEPs than in subjects with normal VEPs. MR-detectable lesion fractions and EDSS scores were also significantly different between the two VEP groups, but NAA comparison had a $P$ value 100 times less than either of these measures.

CONCLUSION: In patients with MS, NAA measurements in the optic pathways of the brain were sensitive to VEP abnormalities. NAA was more sensitive to VEP changes than were choline, creatine, MR-detectable lesions, and EDSS score.

Heide AC, Kraft GH et al, AJNR, 1998
Heide AC, Kraft GH et al, AJNR, 1998
Normal VEP

Abnormal VEP

Heide AC, Kraft GH et al, AJNR, 1998
Interferon Therapy Monitored in Normal Appearing WM with MRS

Bellmann-Strobl et al, Eur Radiol 2009
Interferon Therapy Monitored in Normal Appearing WM with MTR

Bellmann-Strobl et al, Eur Radiol 2009
Diffusion Tensor Imaging (DTI): Mean Diffusivity and Fractional Anisotropy

Free diffusion

Restricted diffusion

Isotropic diffusion

Anisotropic diffusion
Axial and Radial Diffusion: L1, L2, L3

Axial Diffusivity: L1
Radial Diffusivity: \( \frac{L2 + L3}{2} \)
Mean Diffusivity: \( \frac{L1 + L2 + L3}{3} \)

\[
FA: \frac{\sqrt{(L1 - L2)^2 + (L2 - L3)^2 + (L1 - L3)^2}}{\sqrt{2L1^2 + L2^2 + L3^2}}
\]
Example L1, L2, L3 TBSS maps
Fractional Anisotropy (FA) change for patients on Tysabri
1.5 vs 7T Imaging of intracortical lesions

Kollia K, et al, AJNR, 2009
7T Imaging of intracortical lesions

FIG 2. Axial 3D-DIR, 3D-FLAIR, 3D-TIWI, and 2D-T2WI at 7T MR imaging of a 37-year-old female patient with secondary-progressive MS. Arrows indicate an intracortical lesion that was scored on 3D-FLAIR and 2D-T2WI but not on 3D-DIR and 3D-TIWI.

Table 2: Lesion-wise analysis in patients with MS: total lesion detection and mean lesion count per patient

<table>
<thead>
<tr>
<th></th>
<th>3D-DIR (mean)</th>
<th>3D-FLAIR (mean)</th>
<th>2D-T2WI (mean)</th>
<th>3D-TIWI (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td>692 (18.7 ± 16.5)</td>
<td>594 (16.1 ± 13.5)</td>
<td>584 (15.8 ± 16.8)</td>
<td>621 (16.8 ± 16.7)</td>
</tr>
<tr>
<td>DWM</td>
<td>1162 (31.4 ± 32.3)</td>
<td>1197 (32.4 ± 27.3)</td>
<td>1323 (35.8 ± 34.2)</td>
<td>1109 (30.0 ± 34.6)</td>
</tr>
<tr>
<td>JC</td>
<td>728 (19.7 ± 29.7)</td>
<td>814 (22.0 ± 29.4)</td>
<td>414 (11.2 ± 16.8)</td>
<td>853 (23.1 ± 30.1)</td>
</tr>
<tr>
<td>Total WM</td>
<td>2582 (69.8 ± 7.1)</td>
<td>2605 (70.4 ± 8.2)</td>
<td>2321 (62.7 ± 13.1)</td>
<td>2583 (69.8 ± 6.6)</td>
</tr>
<tr>
<td>Mixed</td>
<td>72 (1.9 ± 3.0)</td>
<td>178 (4.8 ± 7.9)</td>
<td>82 (2.2 ± 3.8)</td>
<td>52 (1.4 ± 1.9)</td>
</tr>
<tr>
<td>IC</td>
<td>43 (1.2 ± 2.4)</td>
<td>39 (1.1 ± 2.7)</td>
<td>34 (0.9 ± 1.9)</td>
<td>15 (0.4 ± 0.9)</td>
</tr>
<tr>
<td>Total cortical GM</td>
<td>115 (3.1 ± 0.6)</td>
<td>217 (5.9 ± 2.7)</td>
<td>116 (3.1 ± 0.9)</td>
<td>67 (1.8 ± 0.7)</td>
</tr>
<tr>
<td>Total WM+GM</td>
<td>2697 (72.9 ± 12.9)</td>
<td>2822 (76.3 ± 12.7)</td>
<td>2437 (65.9 ± 14.1)</td>
<td>2650 (71.6 ± 13.1)</td>
</tr>
</tbody>
</table>

Note:—DWM indicates deep white matter; IC, intracortical; JC, juxtacortical; PV, periventricular.

* Data represent numbers of detected lesions per anatomic region.

ADEM: Acute Disseminated Encephalomyelitis

- “Monophasic” but often variable enhancement
- Relatively little mass effect
- Deep grey (thalami) common
- May have hemorrhage
- Subcortical (ADEM) Vs calloseptal (MS)
11 year old lethargy hemiparesis

3 year old rapidly ↓ mental status

ADEM
6 year old bilateral arm and leg numbness

5 year old drowsiness and seizure

ADEM
3 year old ↓ level of consciousness

9 year old 9 days of L hemiparesis

ADEM
CPM: Central Pontine Myelinolysis

- Transverse pontine fibers most severely involved Vs corticospinal tract
- Extra PM in 50%
- >75% EtOH or hyponatremia correction
- DWI bright early, may enhance
- Variable resolution
- Spastic quadriplegia, pseudobulbar palsy
Posterior Reversible Encephalopathy Syndrome (PRES)

- Most often caused by abrupt changes in blood pressure, seizures, or certain immunosuppressive medications.
- Vasogenic edema predominates in WM related to loss of autoregulatory ability
- Overall prognosis is good.
- DWI negative (Vs acute infarct cytotoxic edema)
- Usually in occipital, parietal, and temporal areas
48 year old post seizure

2 months later

PRES
Hypertensive Encephalopathy
Hypertensive Encephalopathy
Which one is PRES?

58 year old cardiac Tx w Seizure

45 year old w impaired vision

Which one is PRES?

1

2
58 year old cardiac Tx w Seizure

PRES

45 year old impaired vision

PML
PML: Progressive Multifocal Leukoencephalopathy

- JC papovavirus
- Most commonly HIV or other Immunocompromised
- Classically: WM “geographic” lesions without enhancement or mass effect
- Formerly endstage HIV w poor prognosis