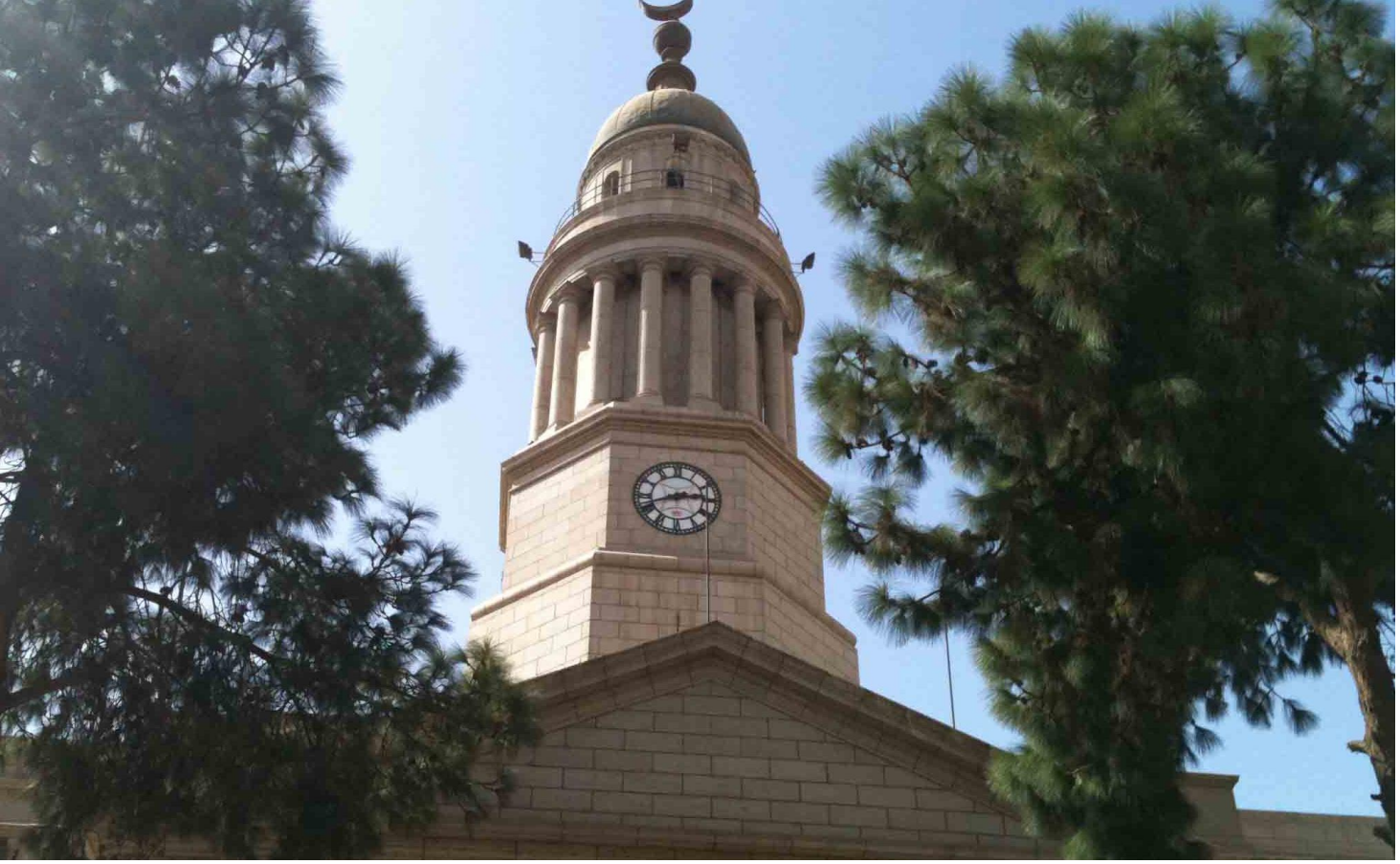
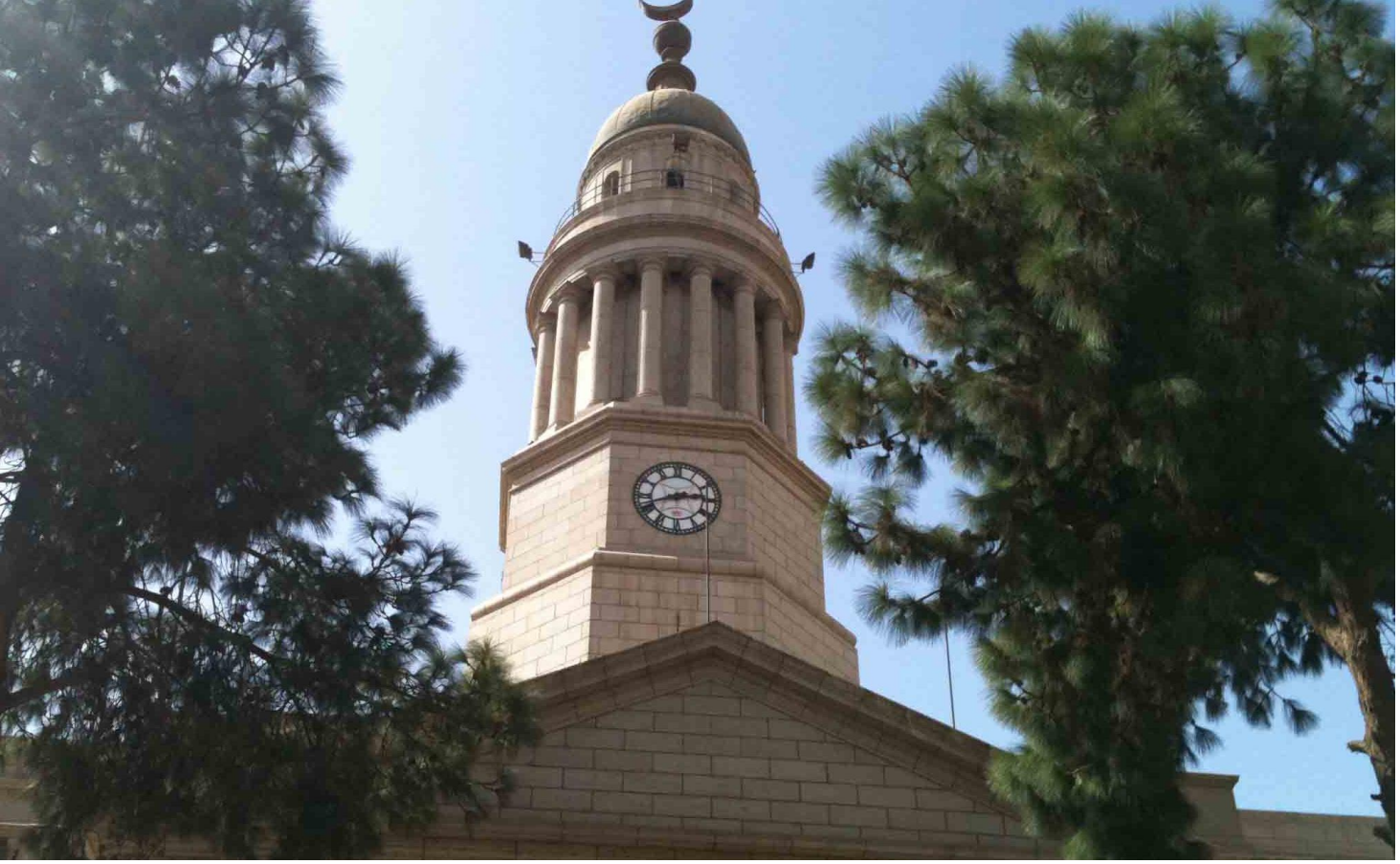


NeuroRadiology of Multiple Sclerosis



Amr Hasan, MD,FEBN

Associate Professor of Neurology - Cairo University

Famous Dictum

"The most common reason for falsely attributing a patient's symptoms to multiple sclerosis is faulty interpretation of the magnetic resonance imaging."

Loren A. Rolak
2007

Agenda

- MRI in diagnosis of MS
- MRI in D.D. of MS
- MRI in monitoring disease progression and response to DMT
- New imaging techniques

Agenda

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Magnetic Resonance Imaging (MRI)

- **The most important MRI biomarkers for MS are the following:**

i. **T1 lesions with contrast enhancement:** biomarkers of acute neuroinflammation (BBB disruption)

ii. **Hyperintense T2-weighted lesions:** reflecting a combination of mechanisms like inflammation, demyelination, axonal damage and edema. Their diagnostic value is high, but they correlate moderately with disability.

R. T. Shinohara, J. Goldsmith, F. J. Mateen, C. Crainiceanu, and D. S. Reich, "Predicting breakdown of the blood-brain barrier in multiple sclerosis without contrast agents," American Journal of Neuroradiology, vol. 33, no. 8, pp. 1586–1590, 2012.
P. A. Brex, O. Ciccarelli, J. I. O'Riordan, M. Sailer, A. J. Thompson, and D. H. Miller, "A longitudinal study of abnormalities on MRI and disability from multiple sclerosis," The New England Journal of Medicine, vol. 346, no. 3, pp. 158–164, 2002.

Magnetic Resonance Imaging (MRI)

iii. **Hypointense T1-weighted lesions (black holes):** considered as satisfactory biomarkers of axonal damage. Their correlation with disability remains debatable.

iv. **Whole brain atrophy biomarkers:** the most widely used measure is the brain parenchymal fraction. Brain atrophy worsening rates are higher in untreated MS patients (0.5%–1% annualized decrease) in comparison with healthy controls (0.1%–0.3%) . Brain atrophy worsening rate at initial diagnosis has been proposed as prognostic biomarker of disability eight years afterwards.

P. A. Brex, G. J. M. Parker, S. M. Leary et al., "Lesion heterogeneity in multiple sclerosis: a study of the relations between appearances on T1 weighted images, T1 relaxation times, and metabolite concentrations," Journal of Neurology Neurosurgery and Psychiatry, vol. 68, no. 5, pp. 627–632, 2000.
M. A. Sahraian, E. W. Radue, S. Haller, and L. Kappos, "Black holes in multiple sclerosis: definition, evolution, and clinical correlations," Acta Neurologica Scandinavica, vol. 122, no. 1, pp. 1–8, 2010.
N. De Stefano, A. Giorgio, M. Battaglini et al., "Assessing brain atrophy rates in a large population of untreated multiple sclerosis subtypes," Neurology, vol. 74, no. 23, pp. 1868–1876, 2010.
. Fisher, R. A. Rudick, J. H. Simon et al., "Eight-year follow-up study of brain atrophy in patients with MS," Neurology, vol. 59, no. 9, pp. 1412–1420, 2002.

Diagnostic Criteria

- Dawson criteria: 1916
- Schumacher criteria: 1965
- Poser criteria: 1983
- McDonald criteria: 2001
- McDonald criteria: 2005
- McDonald criteria: 2010

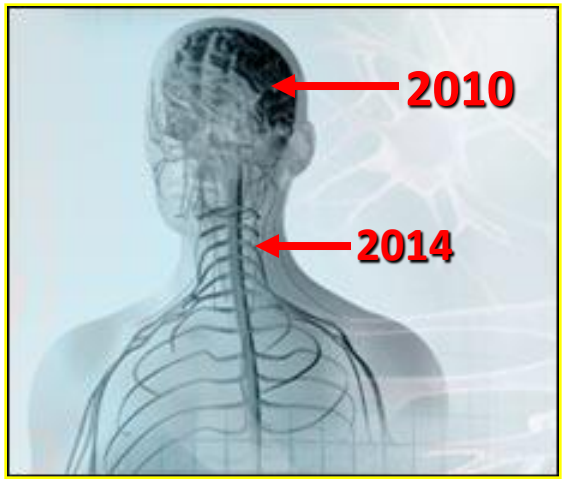
All criteria require dissemination in time and space

Summarized Diagnostic Criteria

1. Dissemination in space: Objective evidence of neurological deficits localized to two separate parts of the CNS

2. Dissemination in Time:

Onset of neurological deficits separated by at least one month



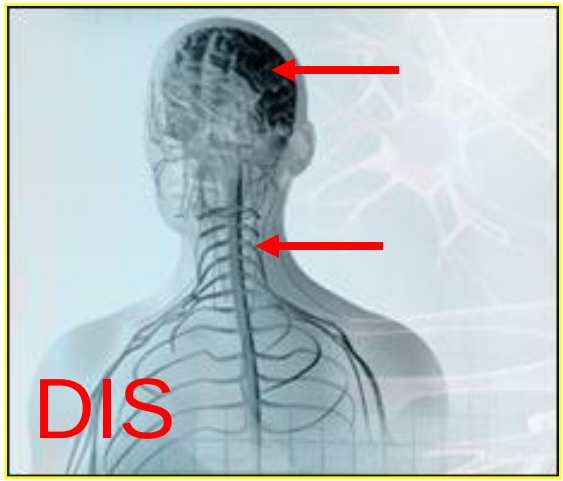
3. Rule out other explanations!

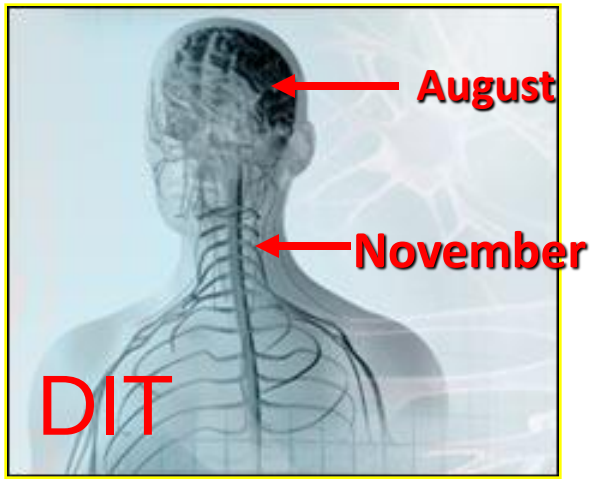
Diagnostic Criteria 2005

- Incorporate use of MRI

- Clinically Isolated Syndrom + MRI
  Dissemination in space + MRI
  Dissemination on time =

  Earlier MS Diagnosis



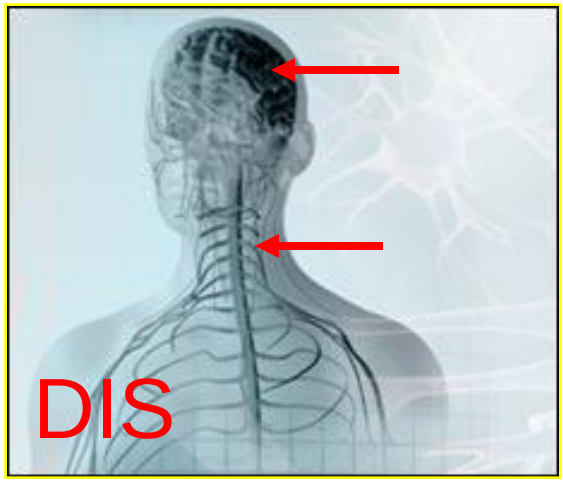


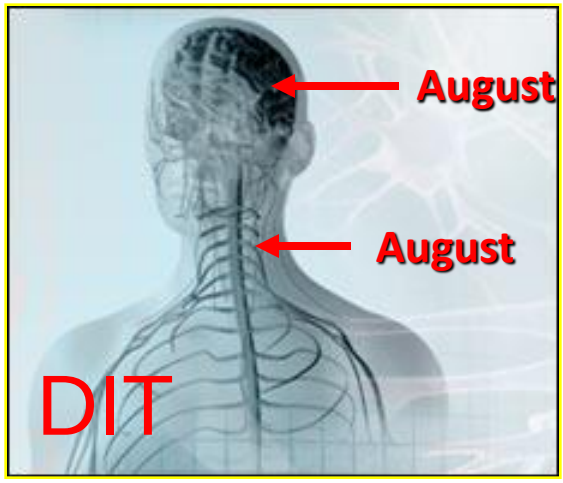
New Diagnostic Criteria 2010

- Incorporate use of MRI

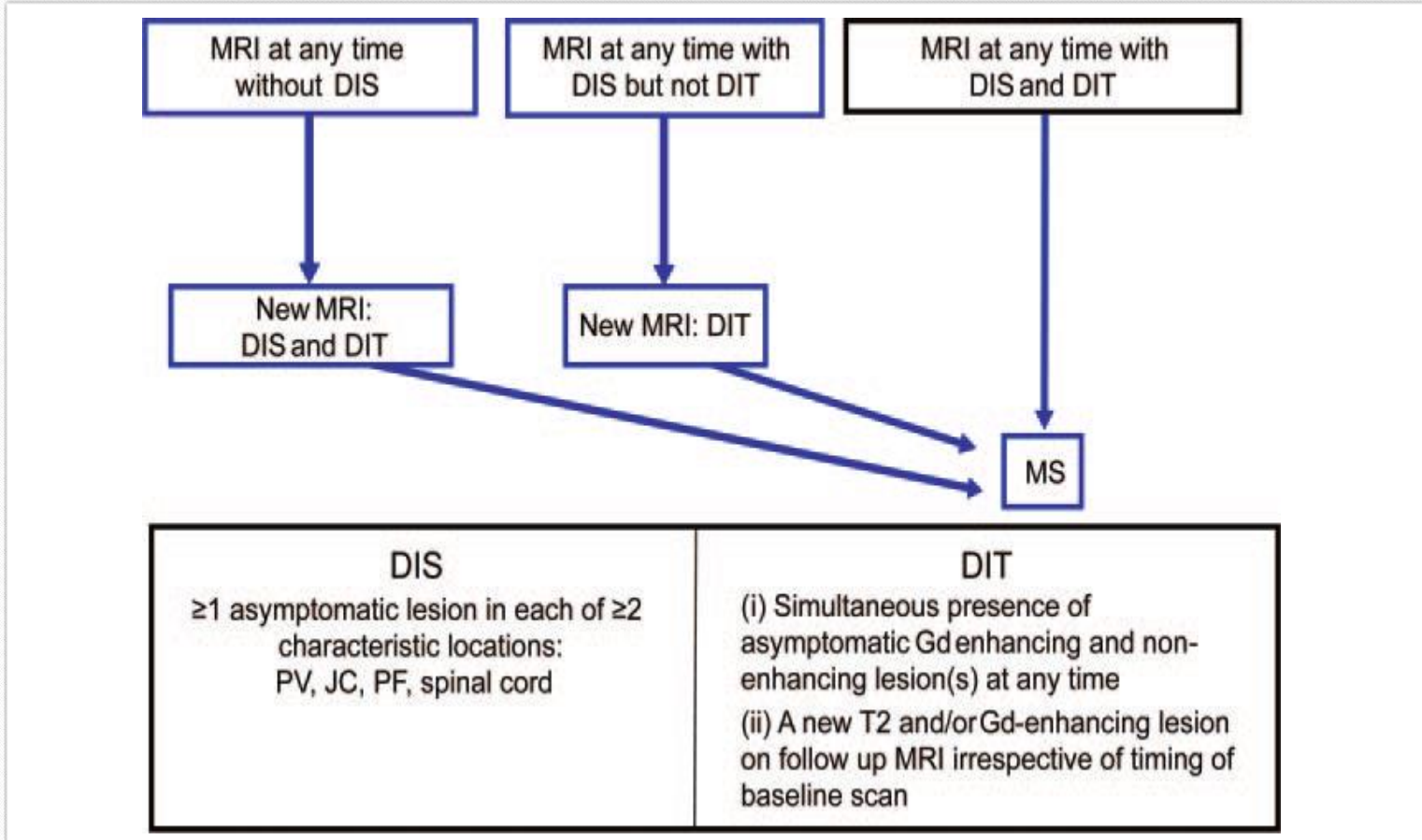
- Clinically Isolated Syndrom + MRI
  Dissemination in space + MRI
  Dissemination on time =

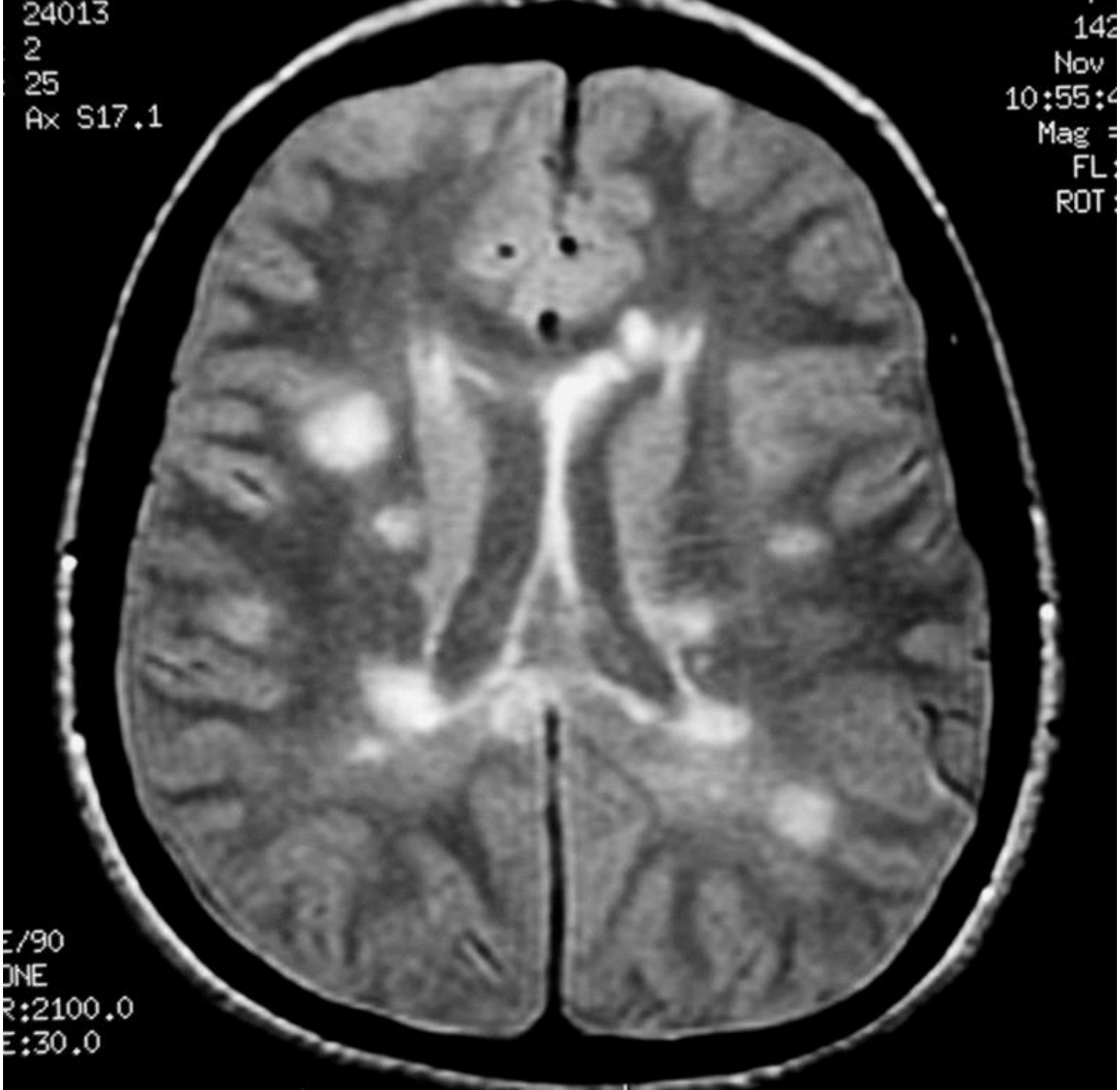
  Earlier MS Diagnosis





New Diagnostic Criteria 2010

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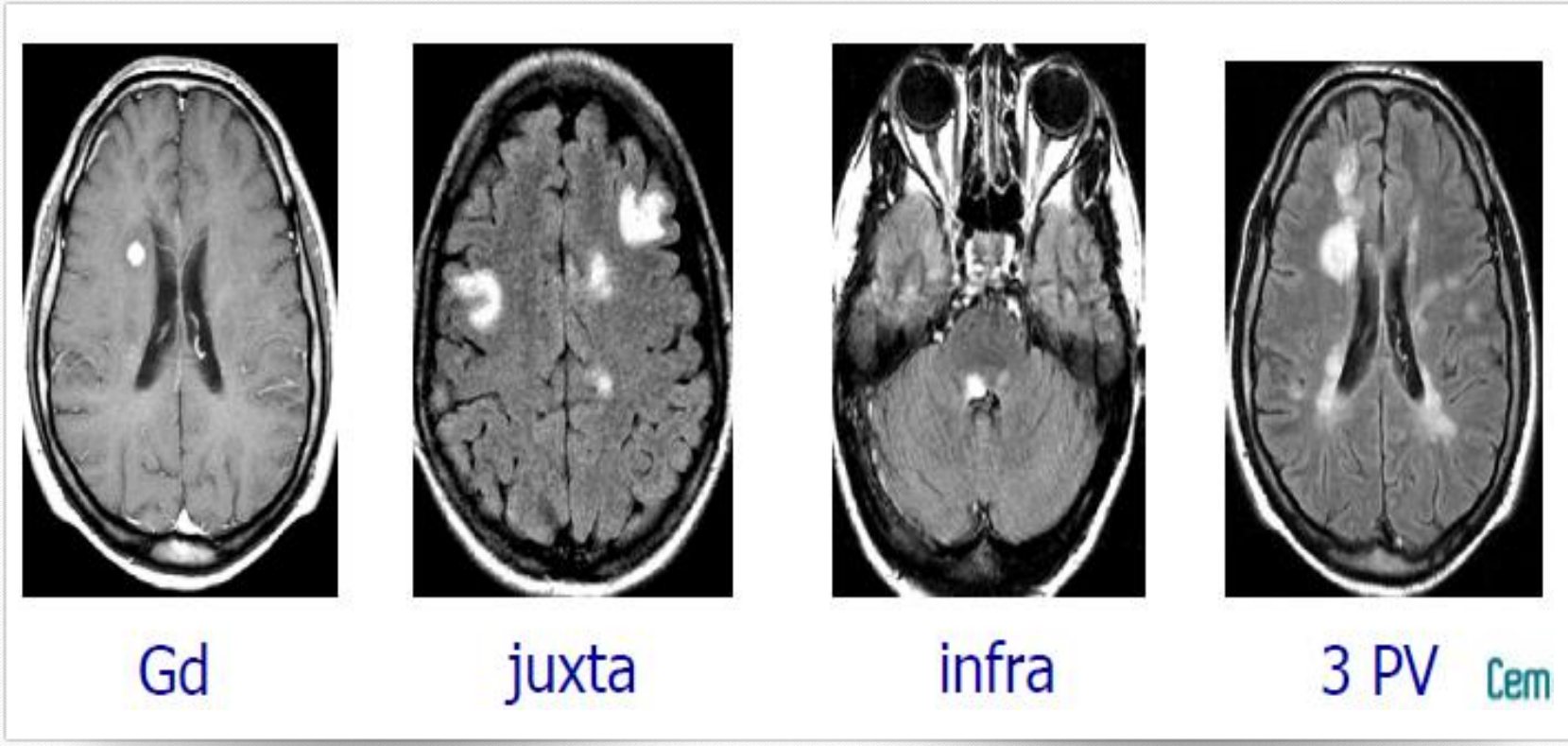
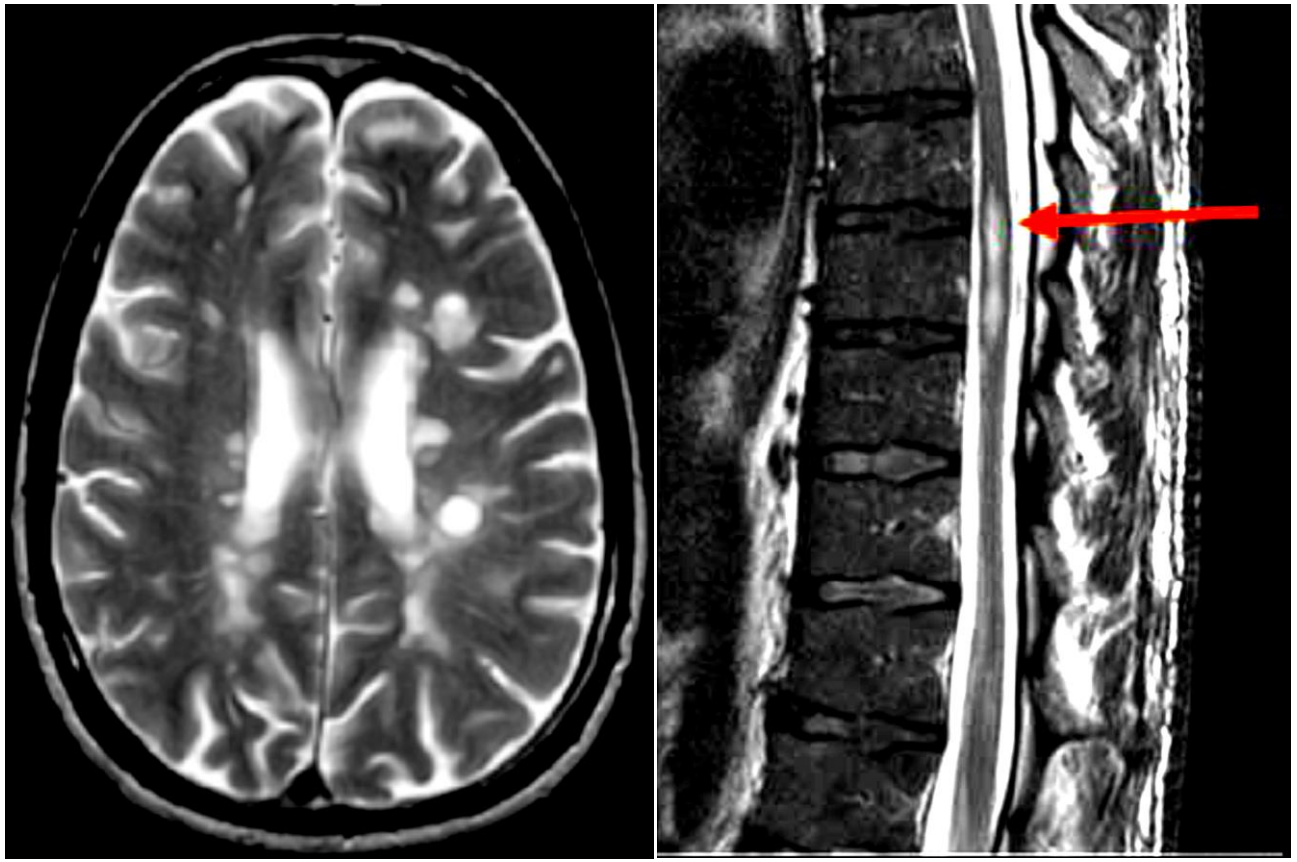
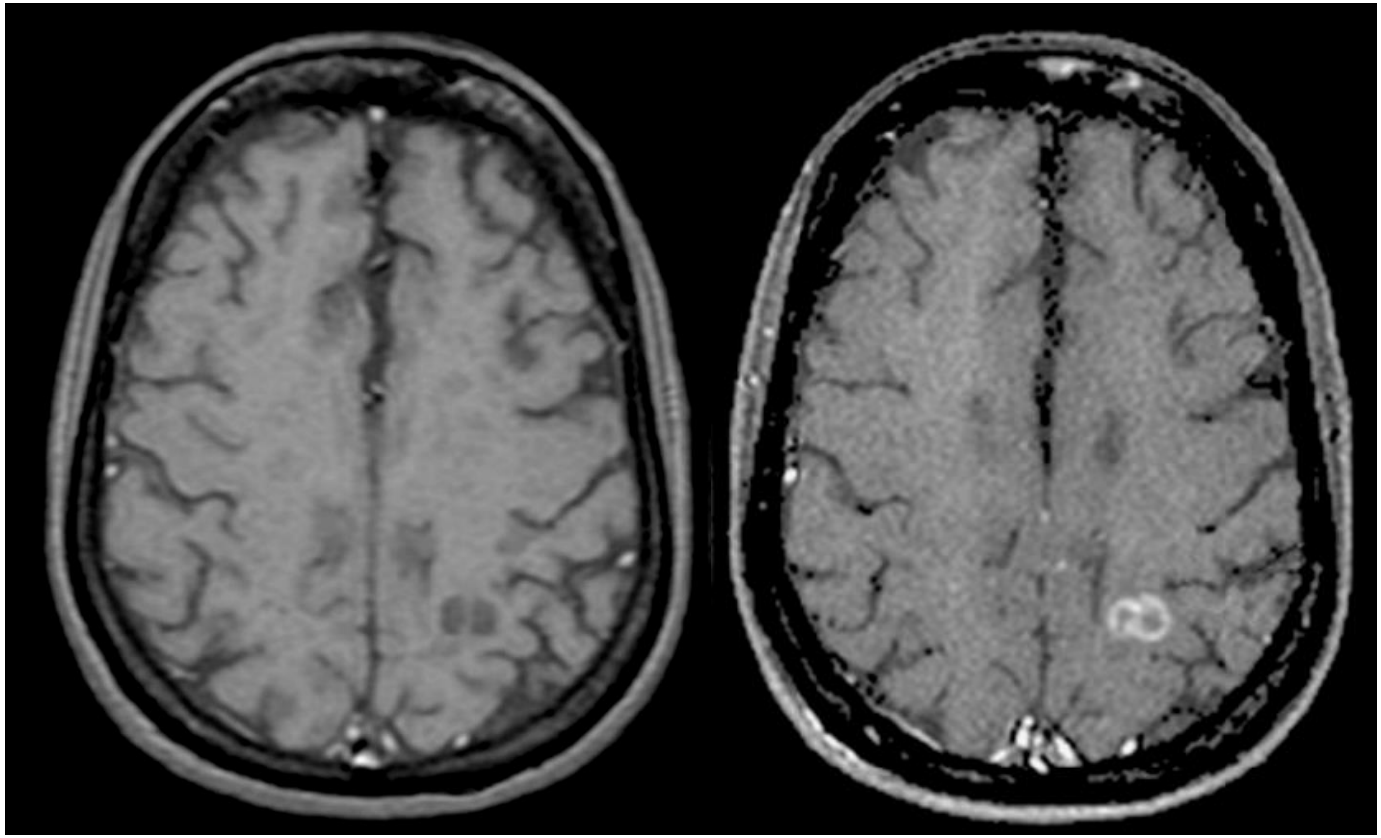
Magnetic resonance imaging



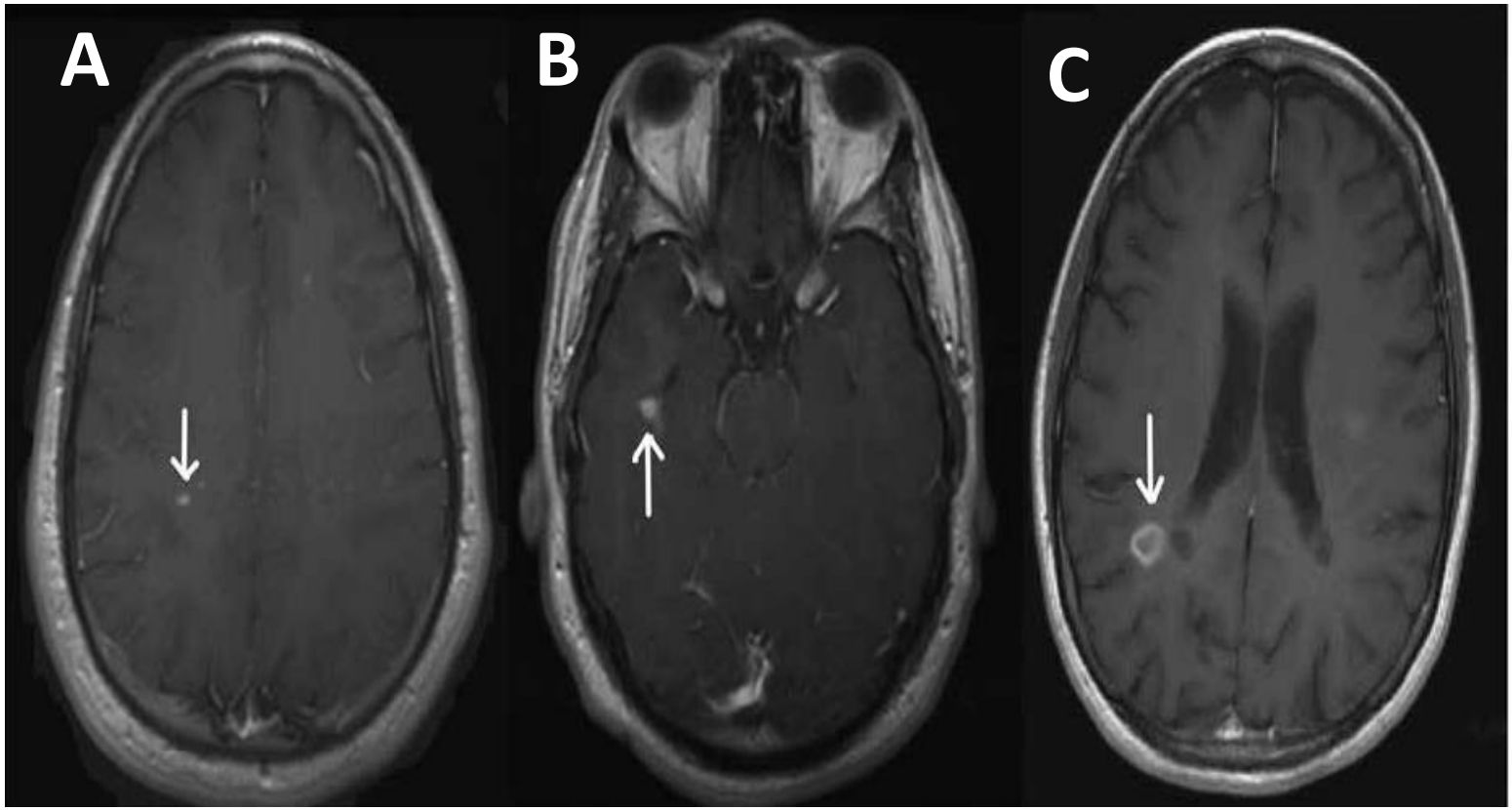
Magnetic resonance imaging
T2 weighted images showing plaques



Magnetic resonance imaging
T1 weighted Pre & Post Contrast



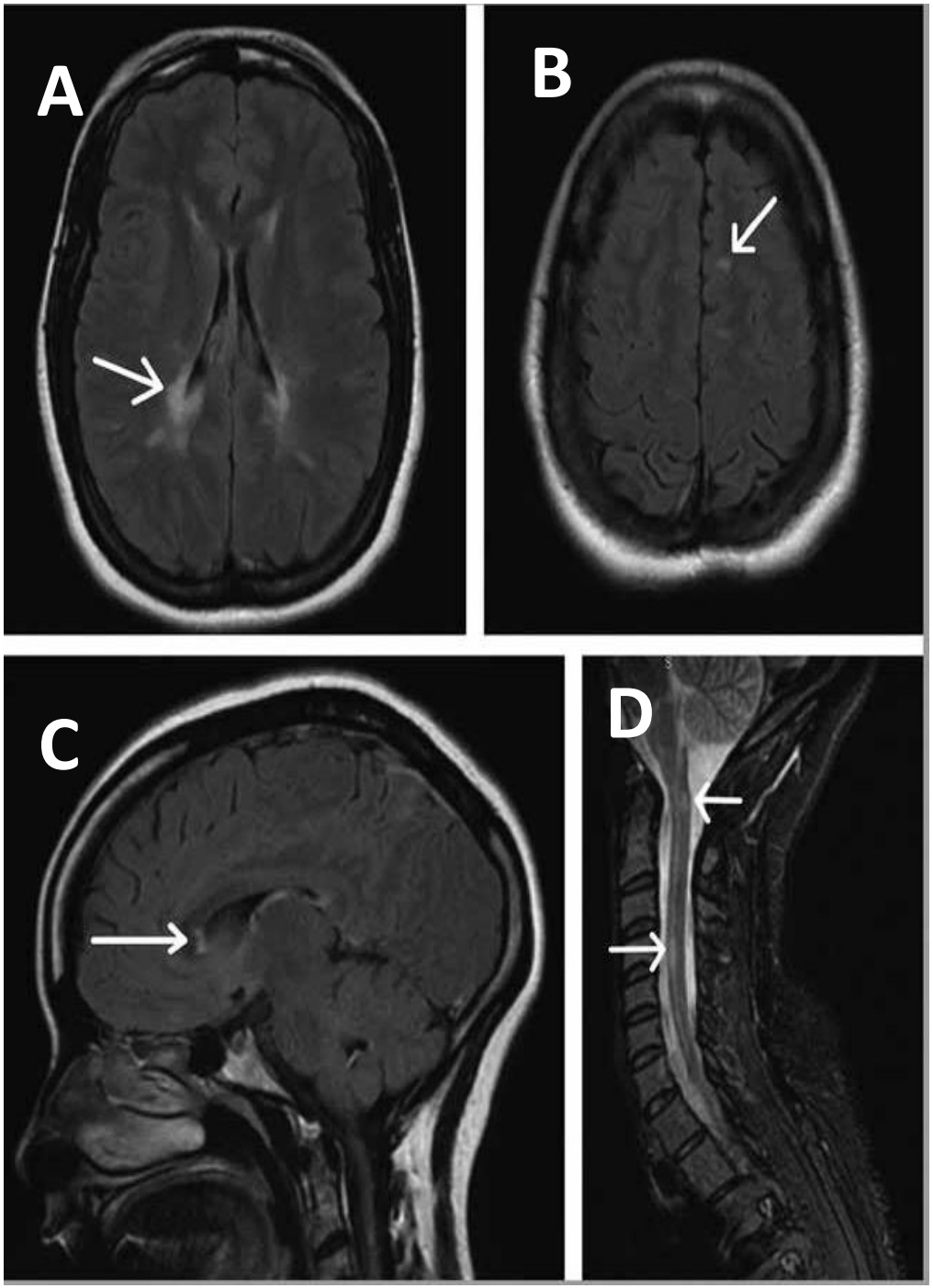
Magnetic resonance imaging
T1 weighted Pre & Post Contrast



(A)Punctate (b) Nodular (c) Ringlike

Case Study (1)

- A 28-year-old woman
- 4 months postpartum developed vertigo and diplopia that gradually improved over 4 days and eventually resolved.
- She had no history of other neurologic symptoms.
- Her neurologic examination was normal.
- Brain and spinal cord MRI showed multiple foci of T2 hyperintensity in the periventricular and juxtacortical white matter, cerebellum, brainstem, genu of the corpus callosum, and cervical spinal cord, including two contrast enhancing lesions



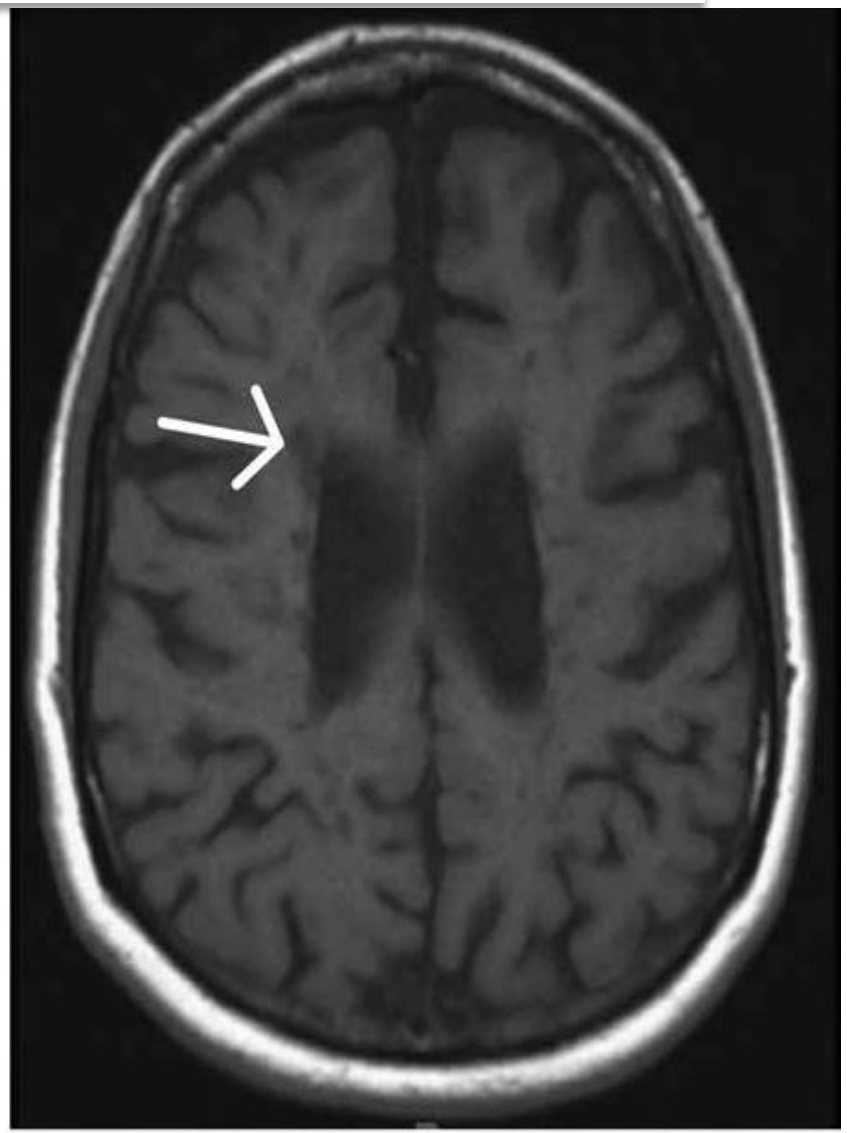
Brain and spinal cord MRI

Brain MRI at the time of diagnosis demonstrates
A: periventricular lesions (arrow)
B: Juxtacortical lesions (arrow)
C: corpus callosum lesions (arrow) on fluid
attenuated inversion recovery (FLAIR) sequences
D: Spinal cord short T1 inversion recovery (STIR)
image reveals lesions at C1 and C4 (arrows).

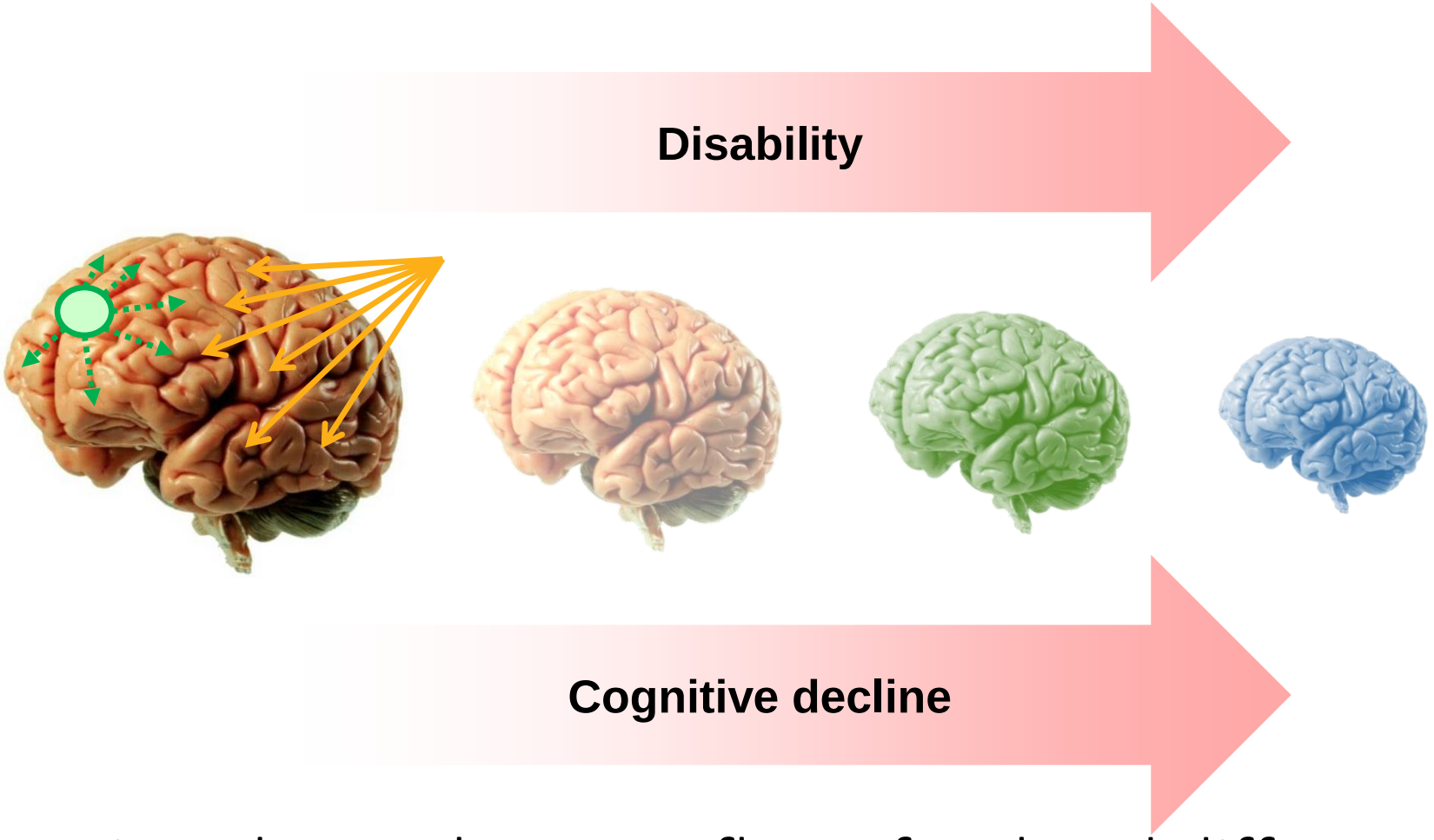
Brain Atrophy

- Atrophy progresses in MS at a rate (0.5- 1% per year) greater than that observed in typical aging.

T1-weighted imaging in a patient with MS exhibits significant atrophy with prominent sulci and numerous T1 hypointensities (arrow).



Brain Atrophy

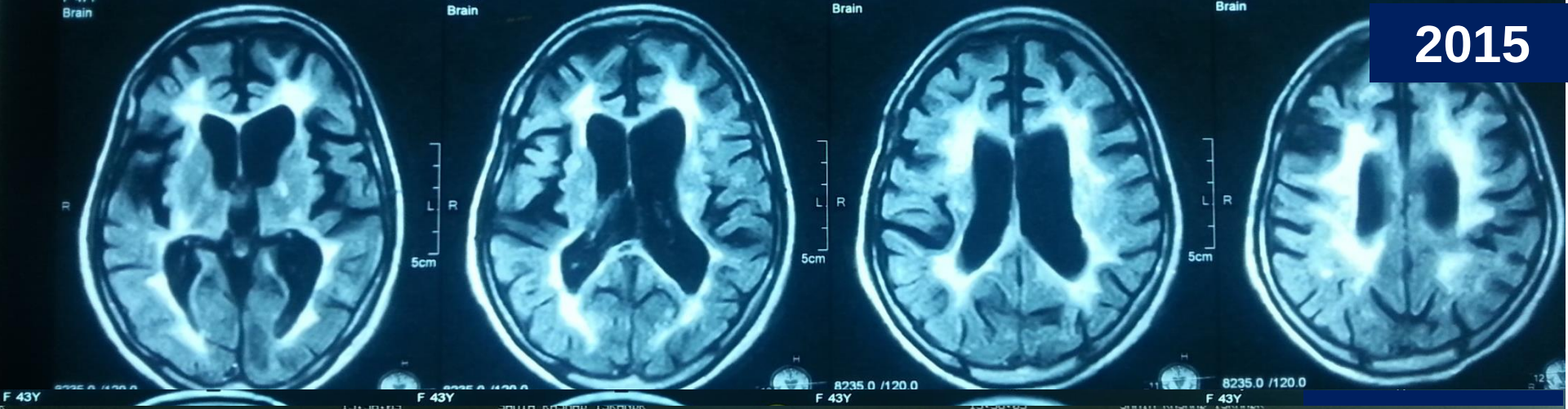


Brain volume change reflects focal and diffuse damage that impacts…

Case Study (2)

- 53 y old lady
- Presented with gradual progressive dementia, quadriparesis
- Was diagnosed at 2000 to have MS after 2 attacks of hemipresis and ataxia
- Infrequent seizures all through her illness

MS Unit
Cairo University
وحدة أبحاث و علاج التصلب المتعدد
MS Research Unit
قصر العيني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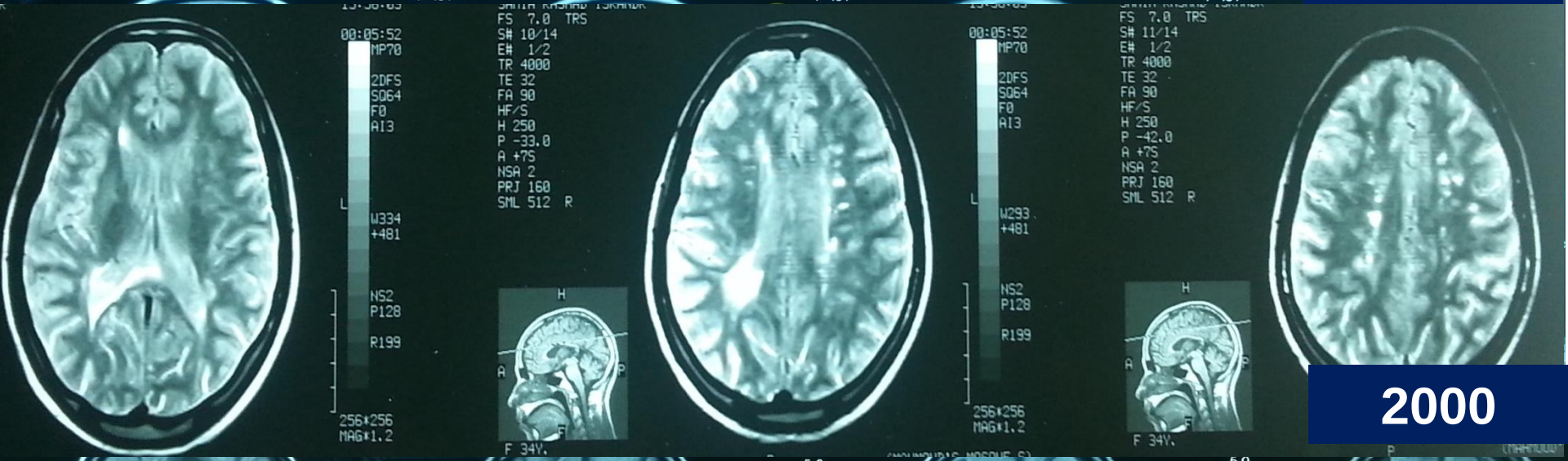
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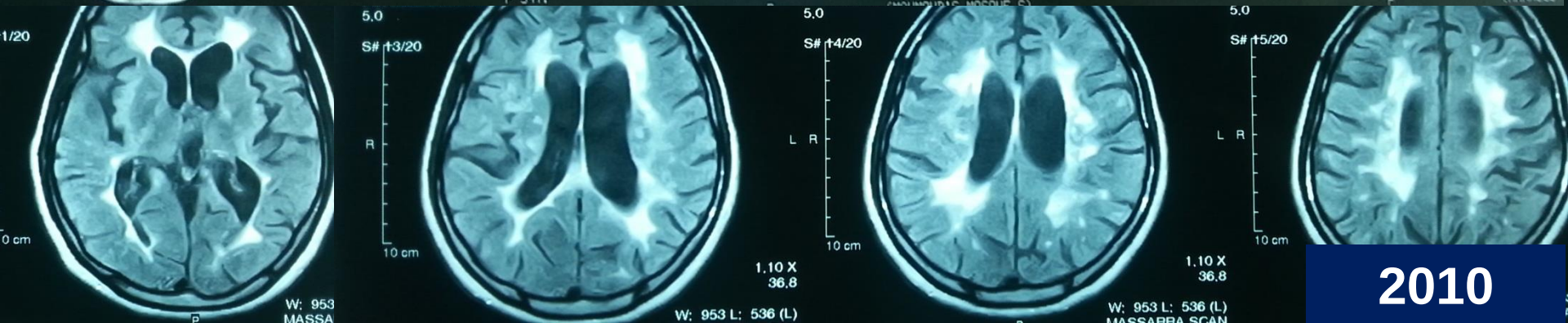
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2010

Spinal Cord Imaging

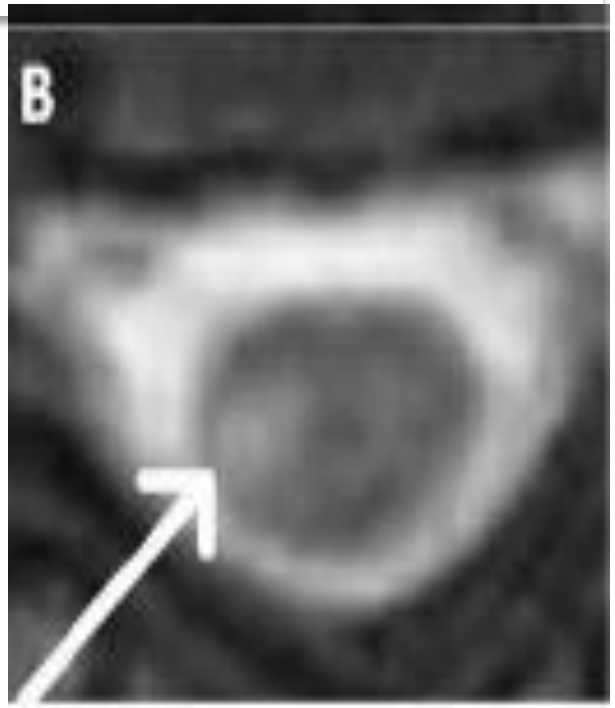
- Spinal cord imaging provides additional support for the diagnosis of MS in many instances.

- Spinal cord abnormalities are described in more than 80% of patients recently diagnosed with MS, with a proclivity for the cervical cord.

- Spinal cord lesions tend to span one vertebral segment or less.

Spinal Cord Imaging

- They tend to be located in an eccentric, dorsal, or lateral location in the axial plane of the cord and span less than half of the axial cord.



Spinal cord short T1 inversion recovery (STIR)
images in the sagittal (A) and axial (B) planes demonstrate eccentric lesions (arrows) that span less than one vertebral segment in a
patient with multiple sclerosis

Spinal Cord Imaging

In contrast, NMO spinal cord lesions are more likely to be longitudinally extensive, affect the spinal cord gray matter, and have associated T1 hypointensity.

Agenda

- MRI in diagnosis of MS
- MRI in D.D. of MS
- MRI in monitoring disease progression and response to DMT
- New imaging techniques

Agenda

- MRI in diagnosis of MS
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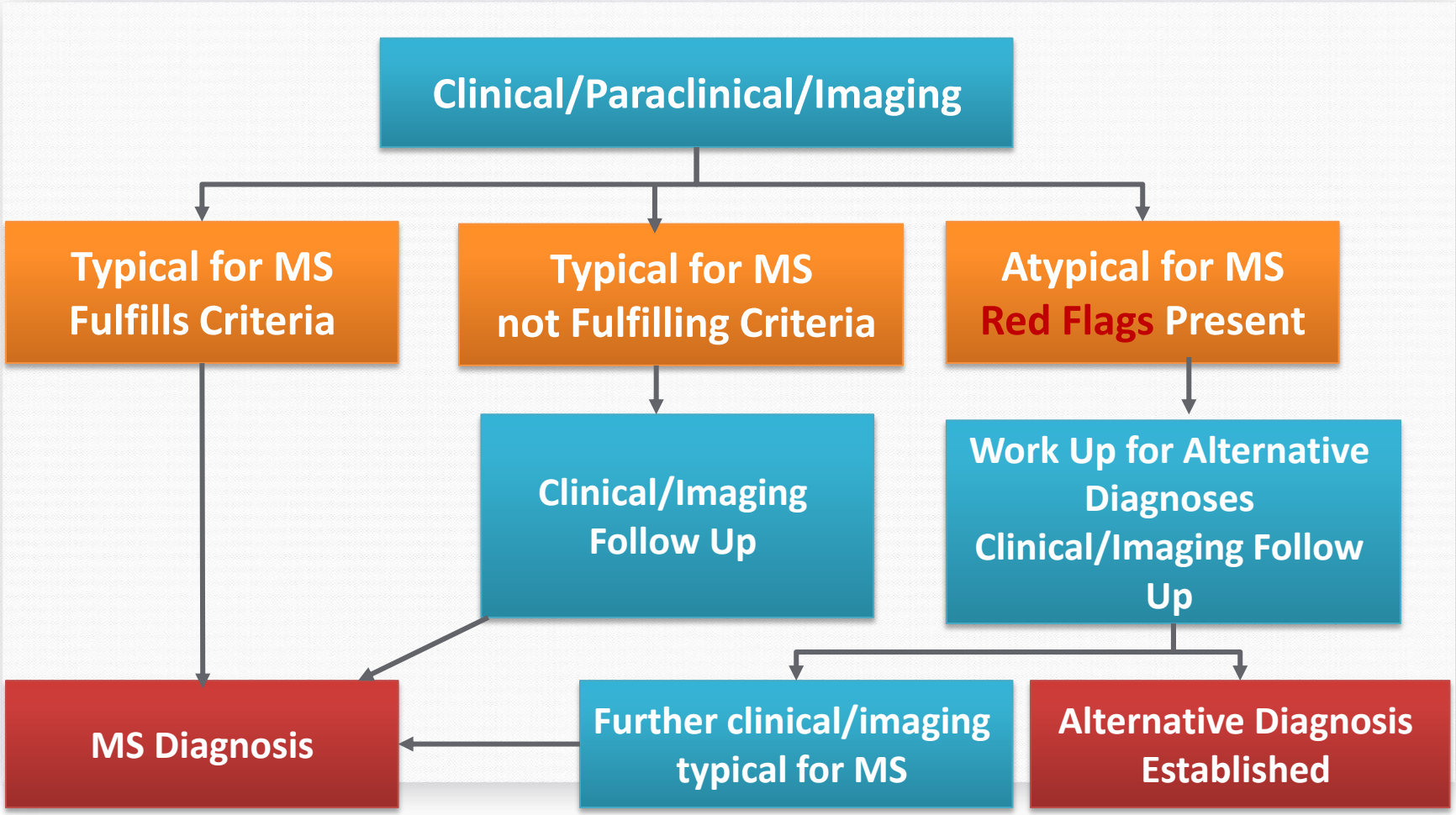
Mental map for diagnosis of MS



The Red Flags

Mult Scler. Nov 2008; 14(9): 1157–1174.
doi: 10.1177/1352458508096878
PMCID: PMC2850590

Differential diagnosis of suspected multiple sclerosis: a consensus approach

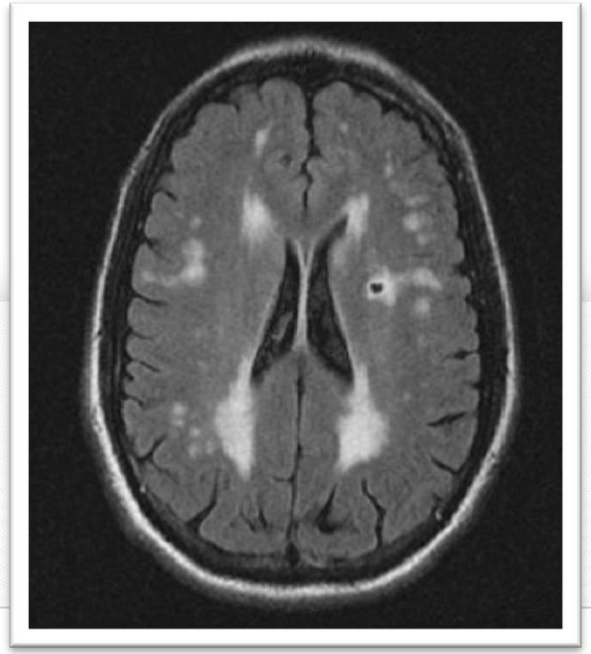
DH Miller,[1] BG Weinshenker,[2] M Filippi,[3] BL Banwell,[4] JA Cohen,[5] MS Freedman,[6] SL Galetta,[7] M Hutchinson,[8] RT Johnson,[9] L Kappos,[10] J Kira,[11] FD Lublin,[12] HF McFarland,[13] X Montalban,[14] H Panitch,[15] JR Richert,[16] SC Reingold,[16,17] and CH Polman[18]

Red flags

- **Major red flags** point fairly definitively to a non-MS diagnosis

- **Intermediate red flags** point to poor agreement and uncertainty among raters about the weighting of the flag for differential diagnosis in MS

- **Minor red flags** suggest that a disease other than MS should be considered and fully explored, but an MS diagnosis is not excluded.



Imaging Red Flags

MRI Red Flags (Major)

Cerebral venous sinus thrombosis	30	Behçet's disease; vasculitis; chronic meningitis, antiphospholipid or anticardiolipin antibody syndromes
Cortical infarcts	29	Embolic disease; thrombotic thrombocytopenic purpura; vasculitis
Hemorrhages/microhemorrhages	29	Amyloid angiopathy; Moya Moya disease; CADASIL; vasculitis
Meningeal enhancement	29	Chronic meningitis; sarcoidosis; lymphomatosis; CNS vasculitis

MRI Red Flags (Major)

Calcifications on CT scans	28	Cysticercosis; toxoplasmosis, mitochondrial disorders
Selective involvement of the anterior temporal and inferior frontal lobe	27	CADASIL
Lacunar infarcts	27	Hypertensive ischemic disease; CADASIL; Susac syndrome
Persistent Gd-enhancement and continued enlargement of lesions	27	Lymphoma; glioma; vasculitis; sarcoidosis

MRI Red Flags (Major)

Simultaneous enhancement of all lesions	26	Vasculitis; lymphoma; sarcoidosis
T2-hyperintensity in the dentate nuclei	26	Cerebrotendinous xanthomatosis
T1-hyperintensity of the pulvinar	25	Fabry disease; hepatic encephalopathy; manganese toxicity
Large and infiltrating brainstem lesions	24	Behçet's disease; pontine glioma
Predominance of lesions at the cortical/subcortical junction	23	Embolic infarction; vasculitis; progressive multifocal leukoencephalopathy

MRI Red Flags (Intermediate)

Hydrocephalus	23	Sarcoidosis or other chronic meningitis; lymphoma or other CNS neoplasm
Punctiform parenchymal enhancement	23	Sarcoidosis; vasculitis
T2-hyperintensities of U-fibers at the vertex, external capsule and insular regions	22	CADASIL
Regional atrophy of the brainstem	21	Behçet's disease; adult onset Alexander's disease
Diffuse lactate increase on brain MRS	21	Mitochondrial disease
Marked hippocampal and amygdala atrophy	21	Hyperhomocystinemia
Symmetrically distributed lesions	20	Leukodystrophy
T2-hyperintensities of the basal ganglia, thalamus and hypothalamus	20	Behçet's disease; mitochondrial encephalomyopathies; Susac's syndrome; acute disseminated encephalomyelitis

MRI Red Flags (Intermediate)

Diffuse abnormalities in the posterior columns of the cord	20	B12 deficiency; copper deficiency; paraneoplastic disorder
Lesions across GM/WM boundaries	19	Hypoxic-ischemic conditions; vasculitis; systemic lupus erythematosus
T2-hyperintensities of the temporal pole	19	CADASIL
Complete ring enhancement	18	Brain abscess; glioblastoma; metastatic cancer
Central brainstem lesions	17	Central pontine myelinolysis; hypoxicischemic conditions; infarct

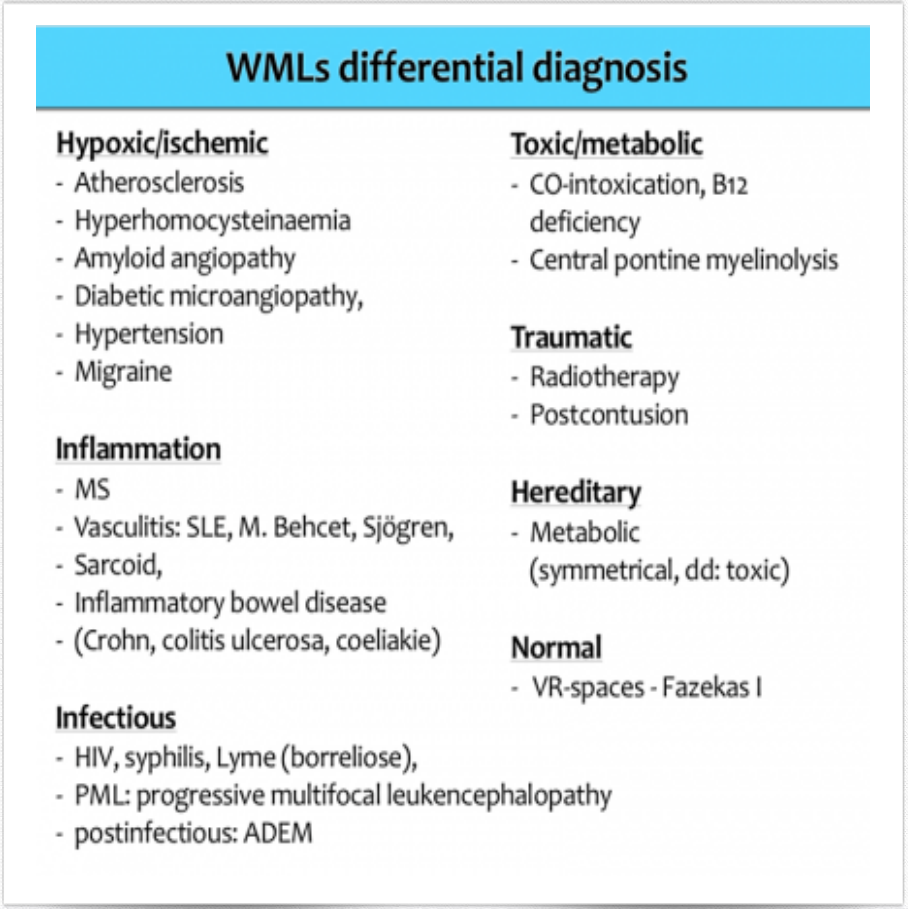
MRI Red Flags (Intermediate)

Predominant brainstem and cerebellar lesions	1 7	Behçet's disease; pontine glioma
Lesions in the center of CC, sparing the periphery	1 7	Susac's syndrome
Dilation of the Virchow-Robin spaces	15	Hyperhomocystinemia; primary CNS angiitis
Cortical/subcortical lesions crossing vascular territories	14	Ischemic leukoencephalopathy; CADASIL; vasculitis

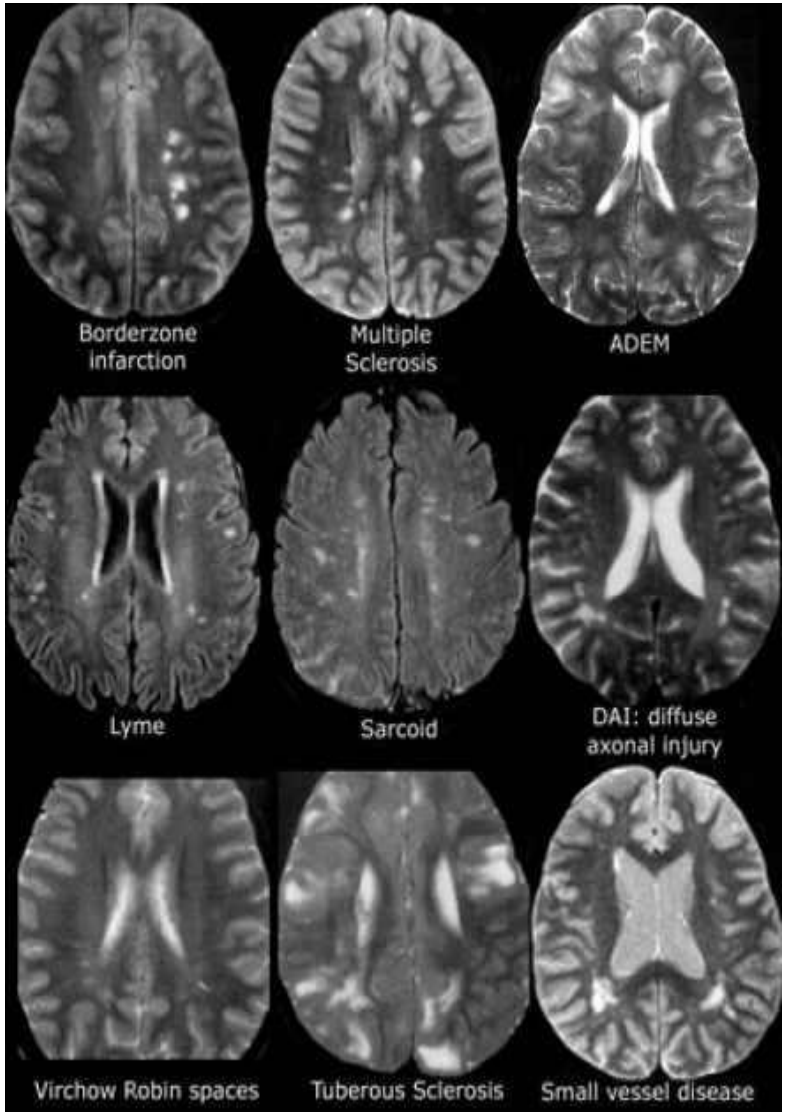
MRI Red Flags (Intermediate)

Large lesions with absent or rare mass effect and enhancement	1 3	Progressive multifocal leukoencephalopathy
No "occult" changes in the NAWM	1 3	Lyme disease, isolated myelitis, CADASIL
No enhancement	8	Progressive multifocal leukoencephalopathy; ischemic lesions; metachromatic leukodystrophy
No optic nerve lesions	9	Metastatic carcinoma; gliomatosis cerebri; toxoplasmosis
No spinal cord lesions	10	Multiple infarcts; vasculitis; progressive multifocal leukoencephalopathy
Large lesions	11	Glioblastoma; lymphoma; progressive multifocal leukoencephalopathy
No T1 hypointense lesions (black holes)	11	Ischemic degenerative leukoencephalopathy; progressive multifocal leukoencephalopathy
Marked asymmetry of WM lesions	12	Glioblastoma; lymphoma; cerebral infarction

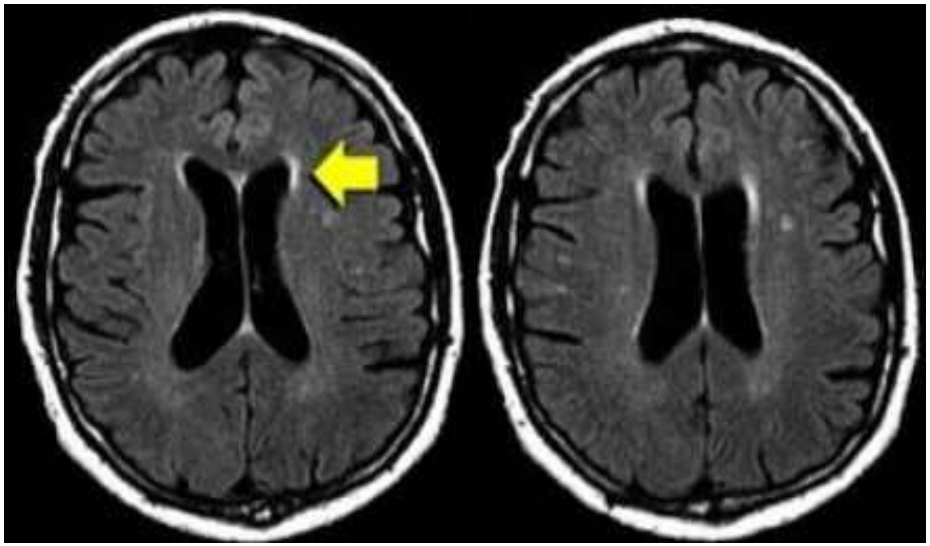
WMLs differential diagnosis



WMLs differential diagnosis

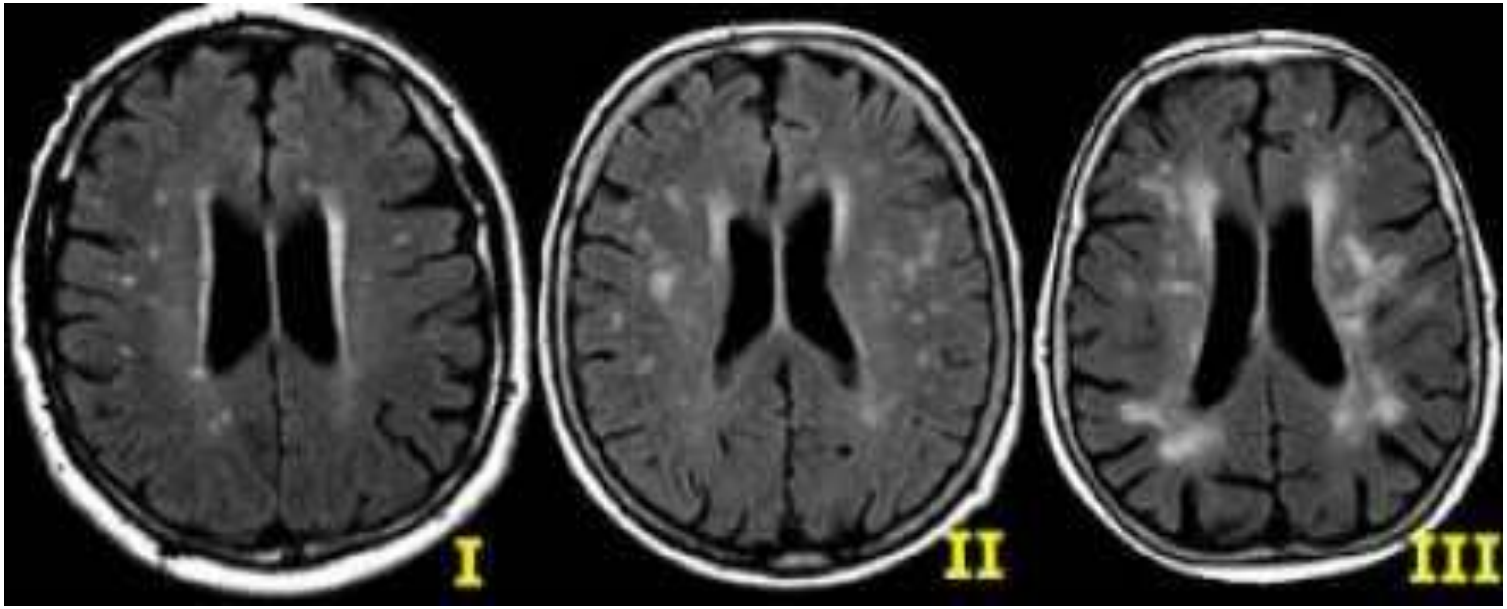


Normal Aging



- Periventricular caps and bands
- Mild atrophy with widening of sulci and ventricles
- Punctate and sometimes even confluent lesions in the deep white matter (Fazekas I and II).

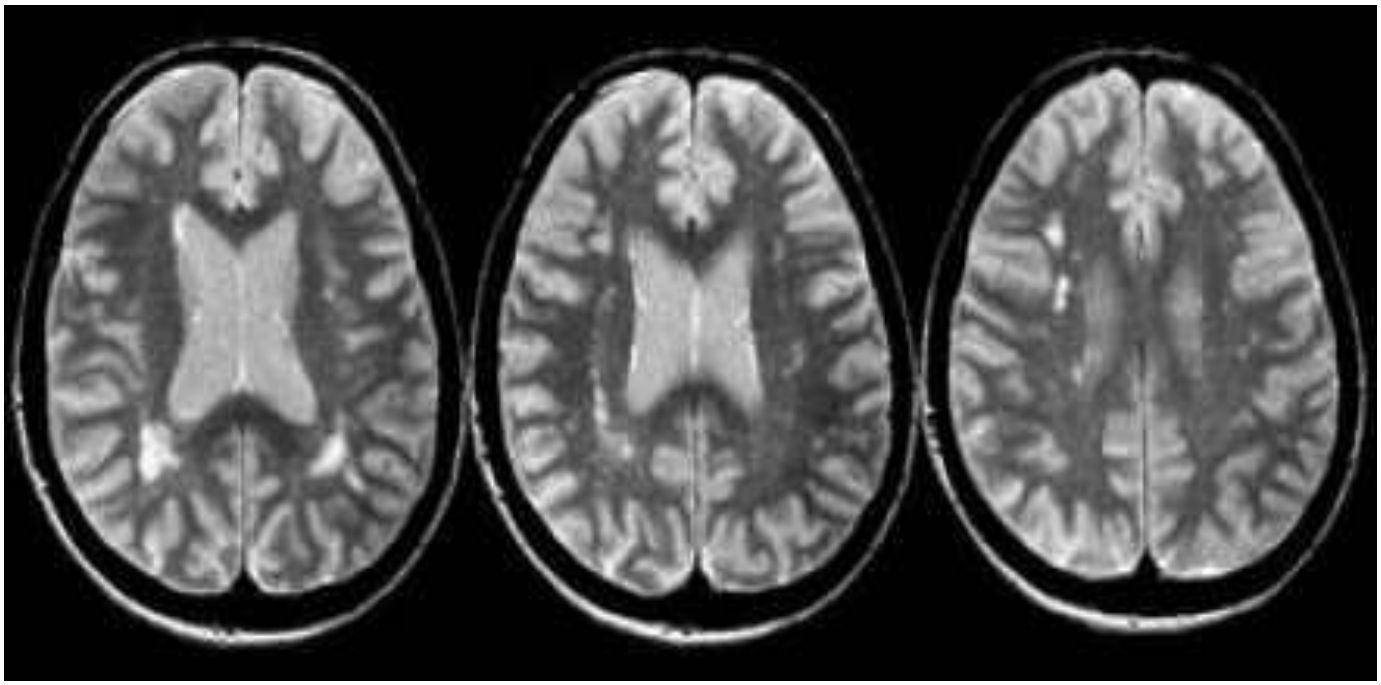
Normal Aging



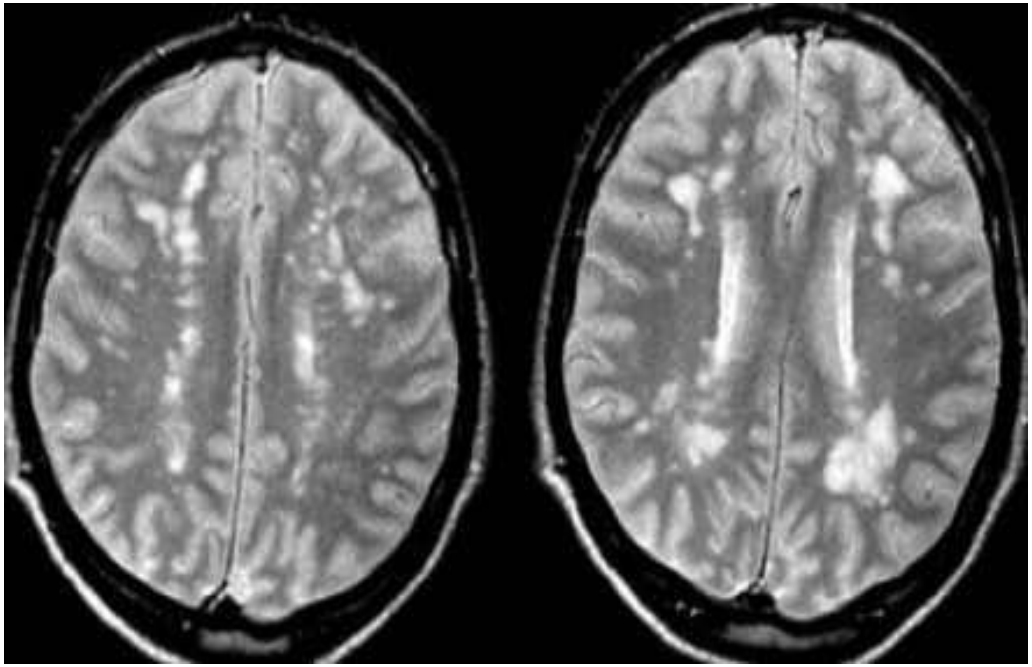
These white matter changes are classified according to Fazekas:

- **Mild -** punctate WMLs: Fazekas I)
- **Moderate -** confluent WMLs: Fazekas II - in the deep white matter can be considered normal in aging.
- **Severe** - extensive confluent WMLs: Fazekas III - always abnormal.

Infarctions



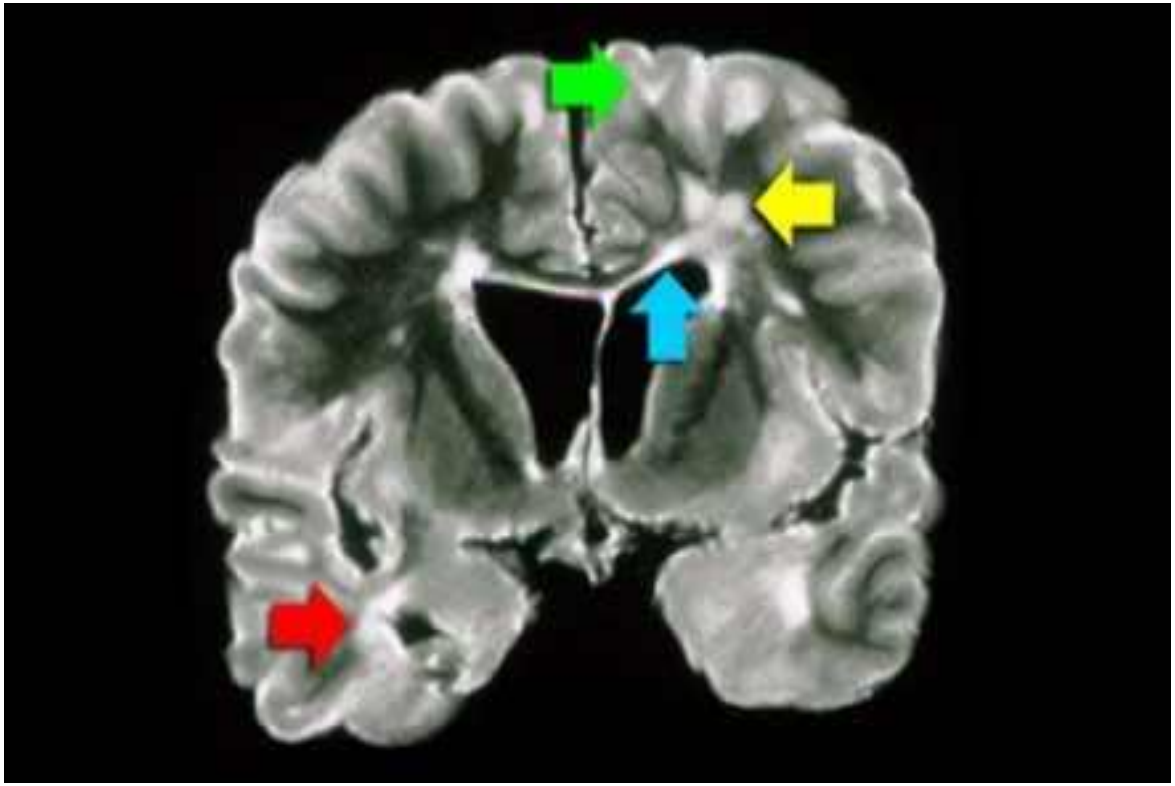
Infarctions



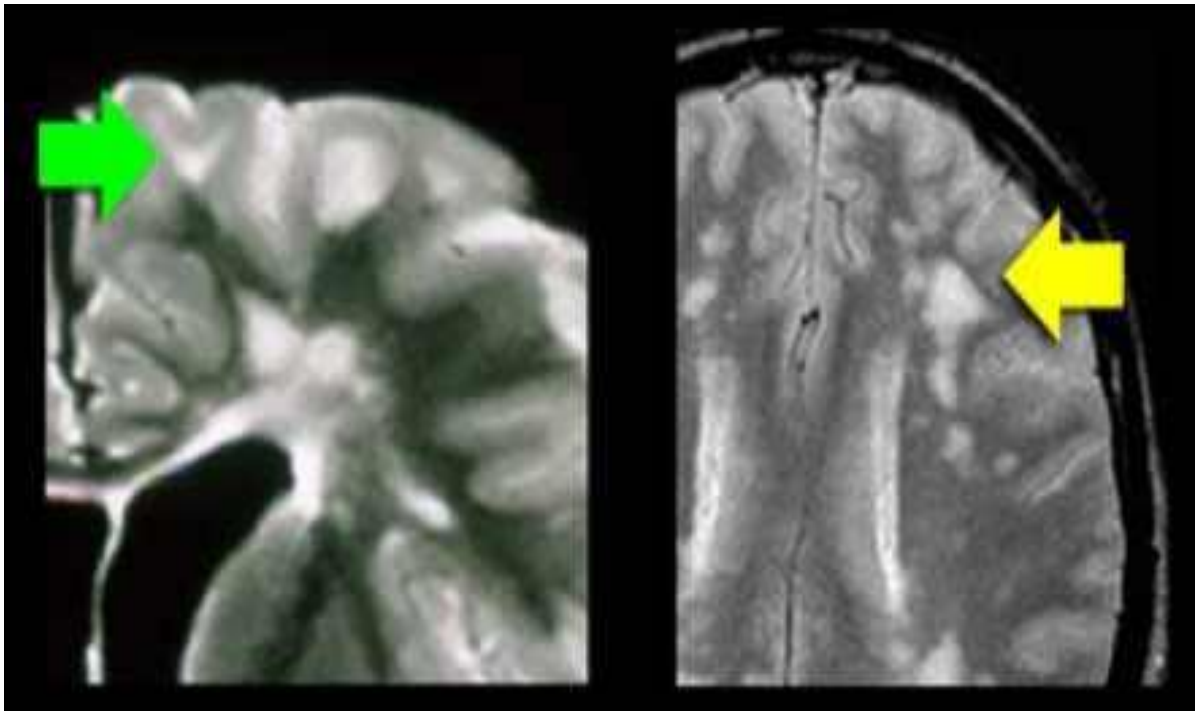
Distribution of white matter lesions

	Vascular	MS
Corpus callosum	- uncommon	- common
U-fibers	- uncommon	- common
Cortical lesions	- infarction	- sometimes
Basal nuclei	- typical	- uncommon
Infra tentorial	- uncommon	- typical
Temporal lobe	- uncommon	- early involvement
Periventricular	- uncommon	- typical
Spinal cord	- uncommon	- typical
Gd-enhancement	- no	- yes
Dawson fingers	- no	- typical
Distribution	- asymmetric	- symmetric/diffuse

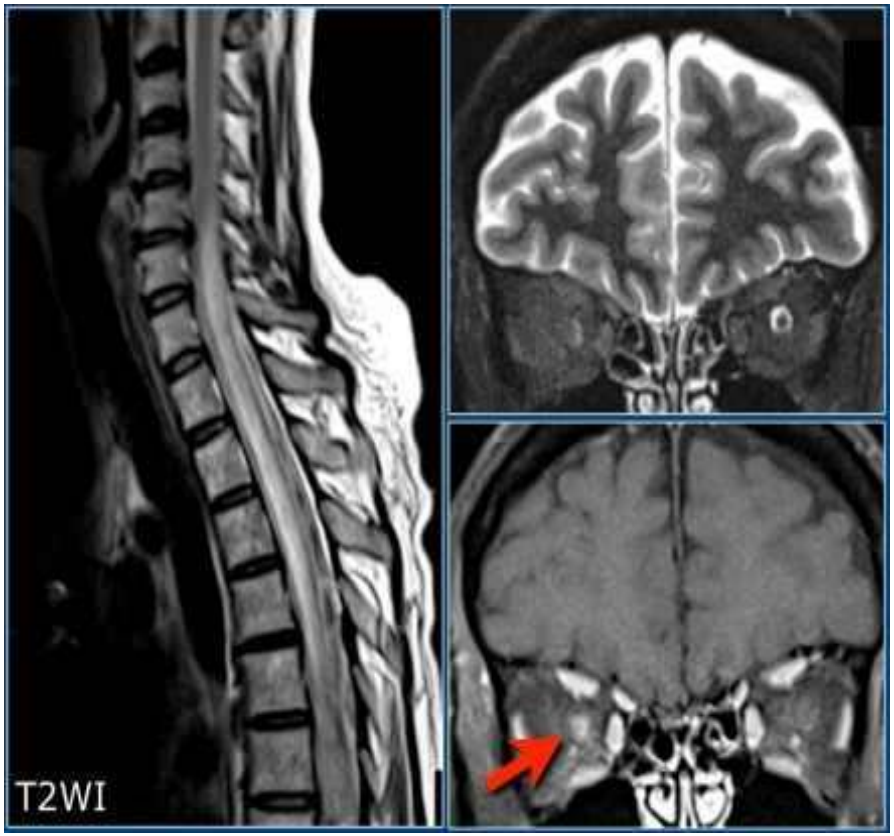
Distribution of white matter lesions



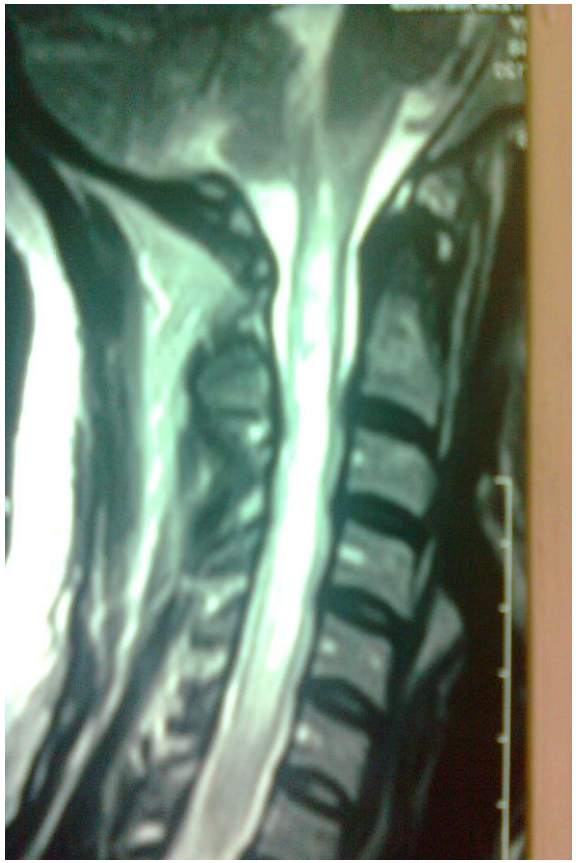
Distribution of white matter lesions



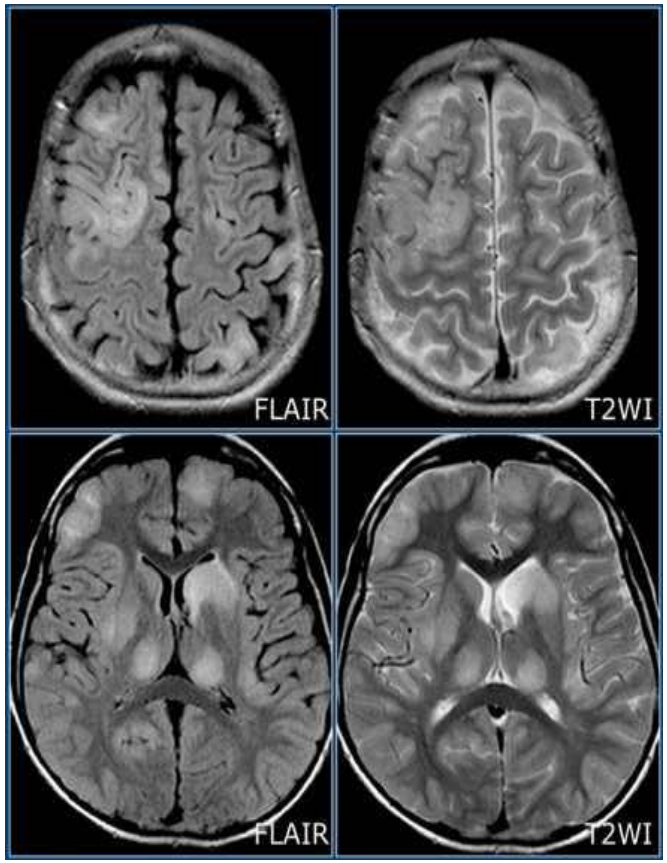
NMO



NMO



Distribution of white matter lesions

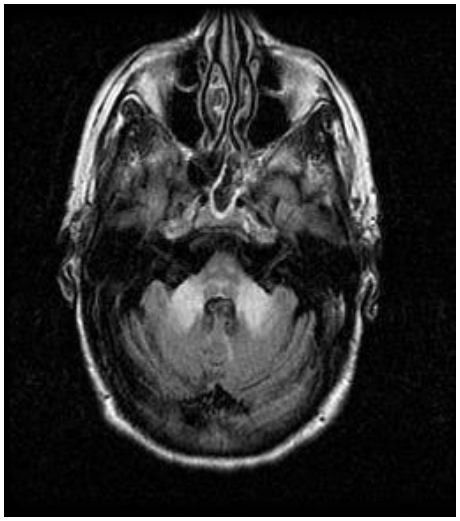


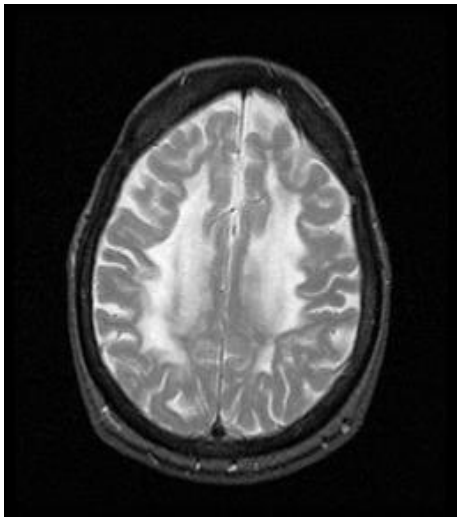
ADEM versus MS on MRI

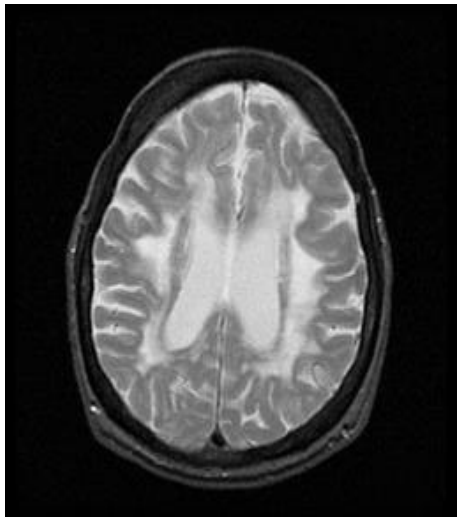
	ADEM	MS
Brian MRI	Fuzzy	Dawson fingers
GM involvement	Thalamus	Juxtacortical
Gadolinium	Patchy / absent	Focal
SC lesions	Long, swollen	Multiple, small
Follow-up	Resolution	New lesions

MRI Red Flags

Diffuse/Symmetric matter involvement



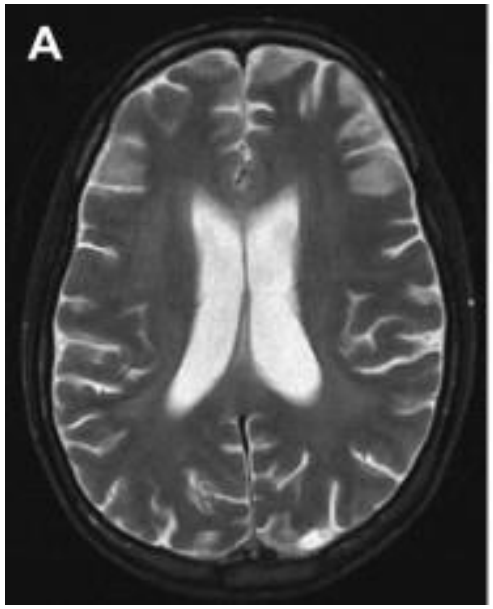


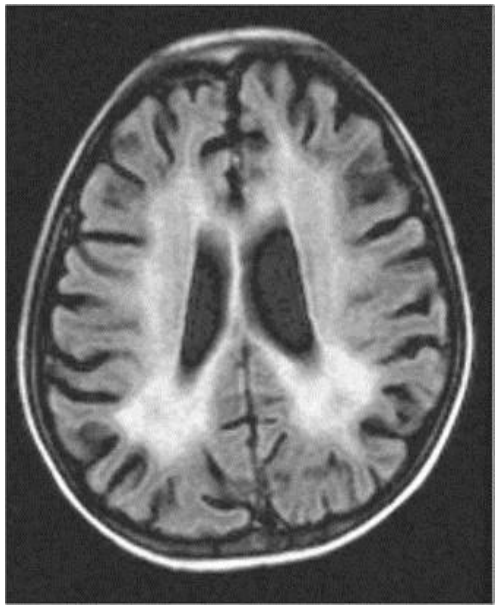


Adult Onset AD Leukodystrophy

MRI Red Flags

Diffuse/Symmetric white matter involvement

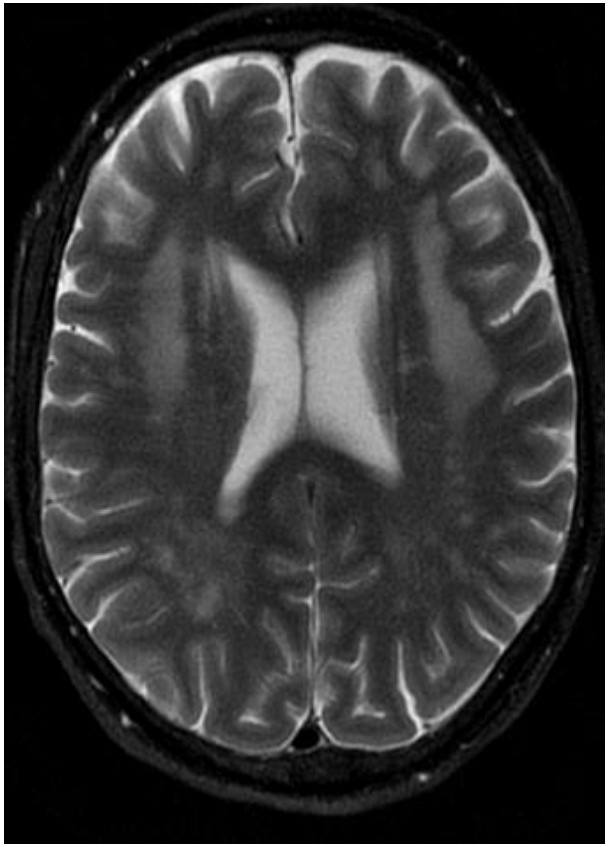




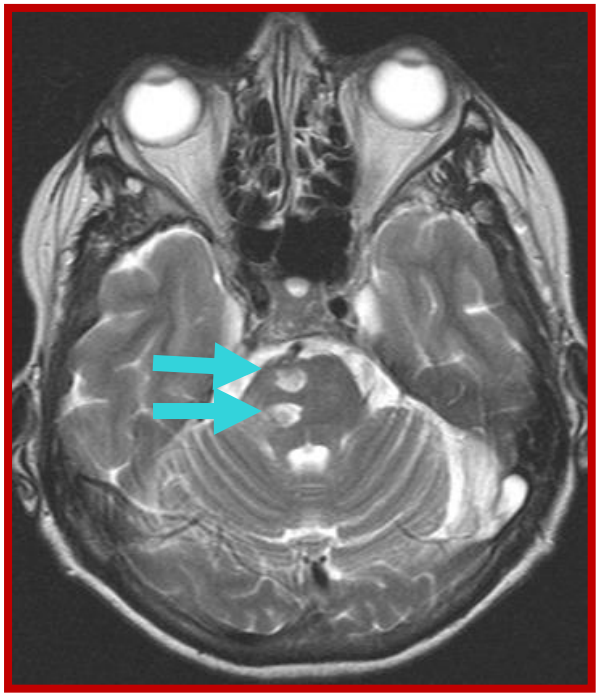
HIV Associated Neurocognitive Disorder

Nonspecific White Matter T2 lesions

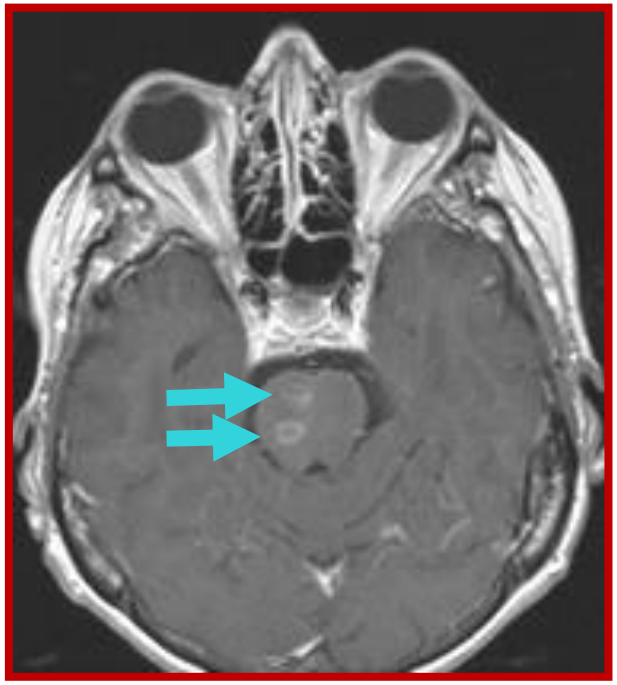
- Smoking
- Hypertension
- Diabetes
- Toxic
- Radiation
- Chemotherapy
- Congenital



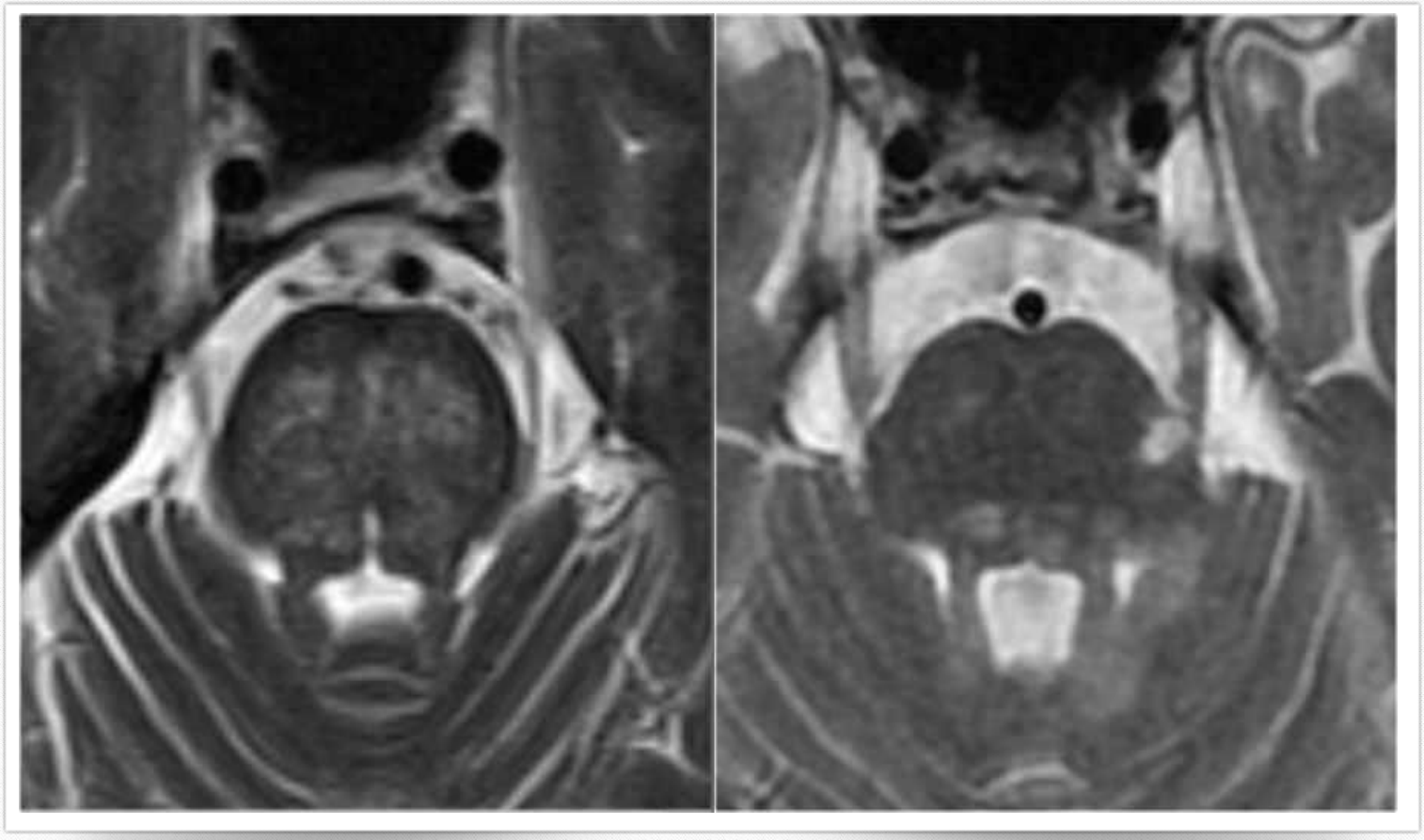
MRI Red Flags



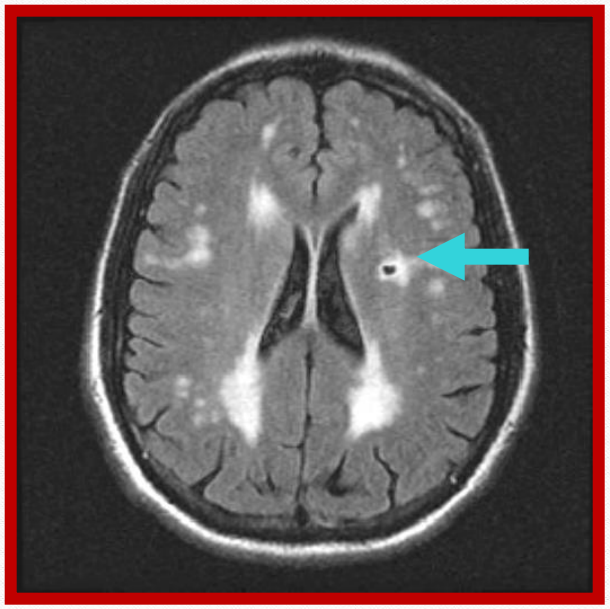
Neuro-Behçet

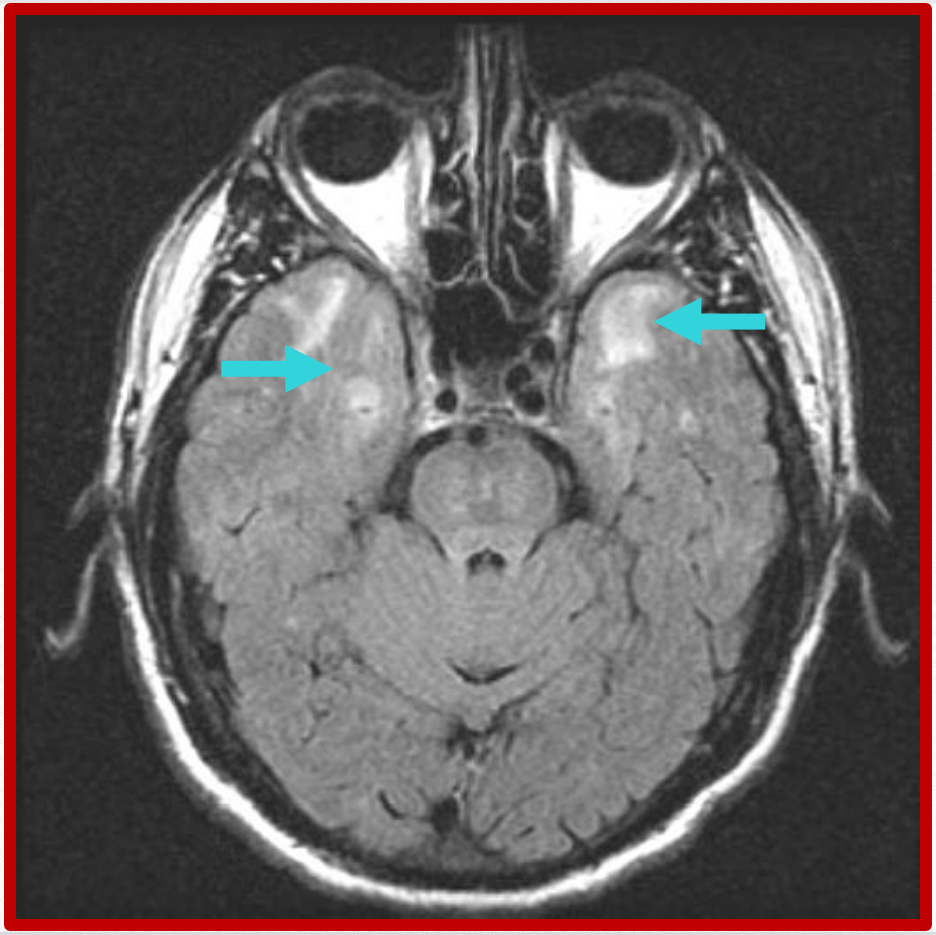


Atypical brainstem lesions



MRI Red Flags

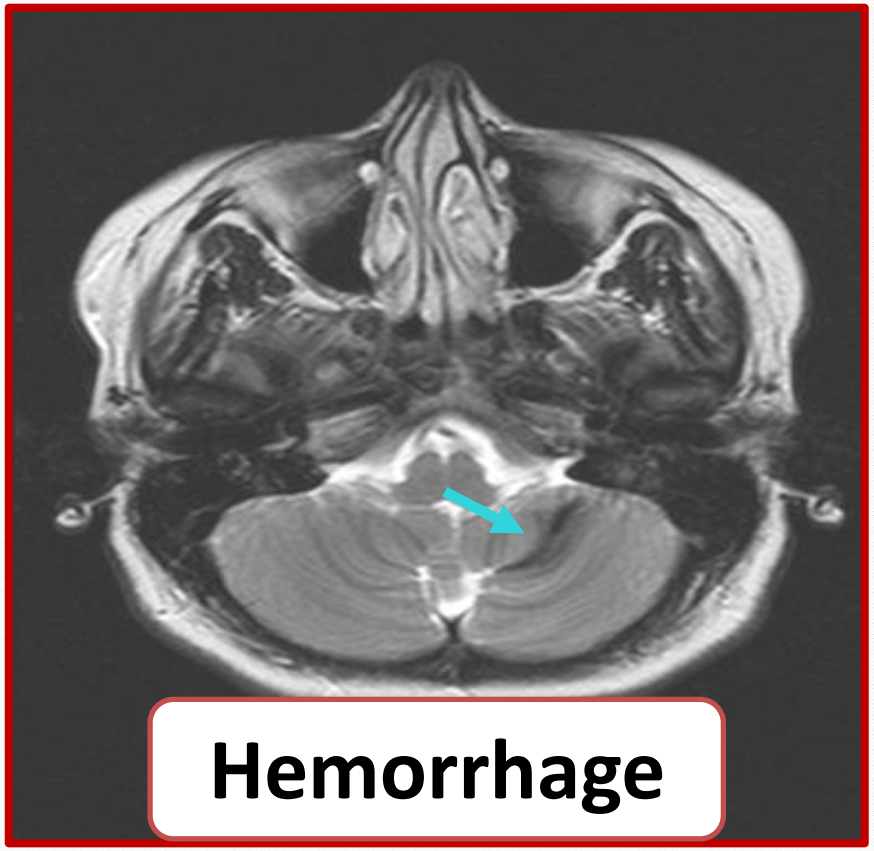




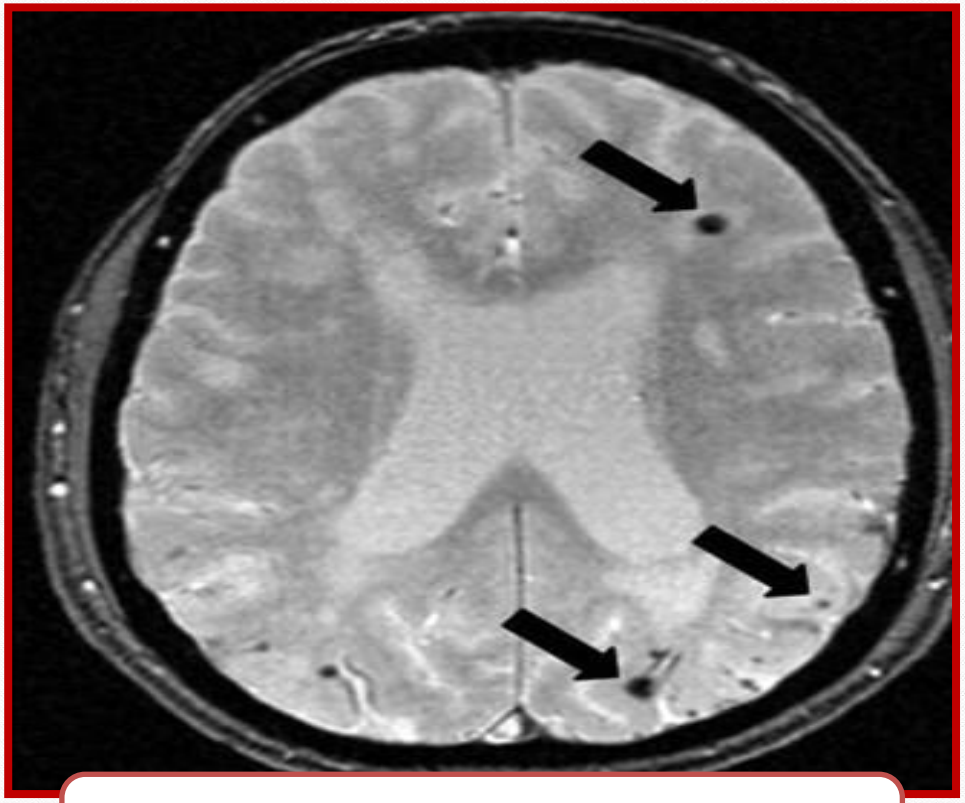
CADASIL

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

MRI Red Flags
Primary CNS Vasculitis

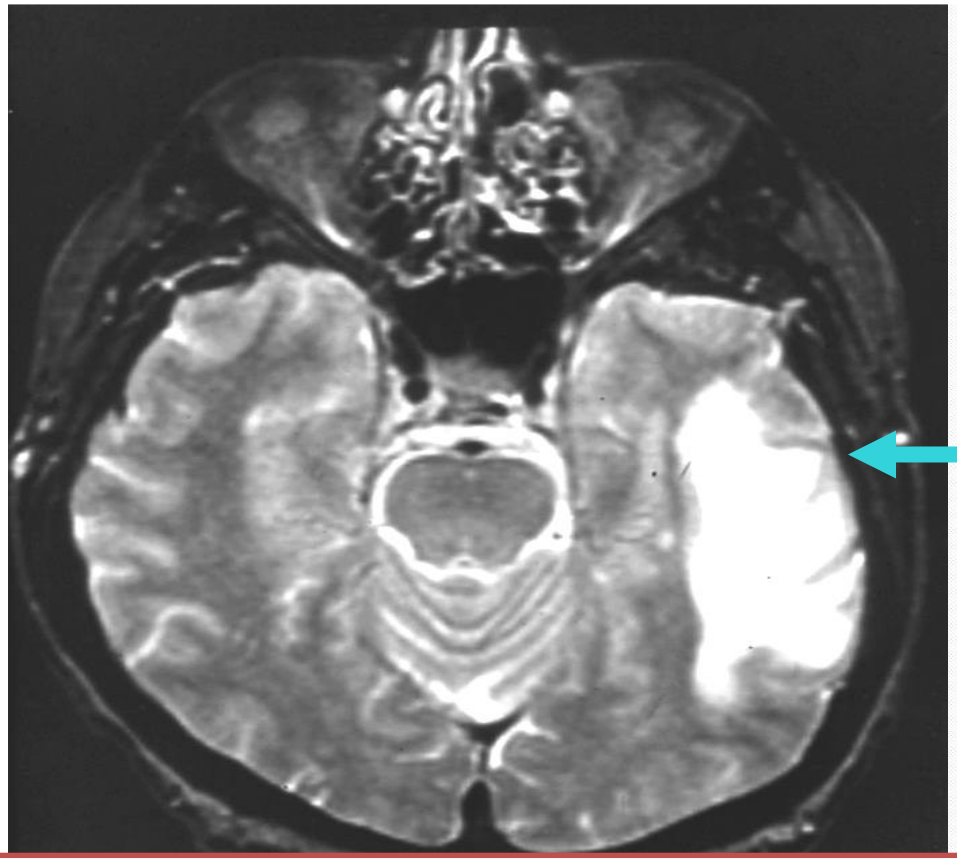


MRI Red Flags
Amyloid Angiopathy



Microhemorrhage

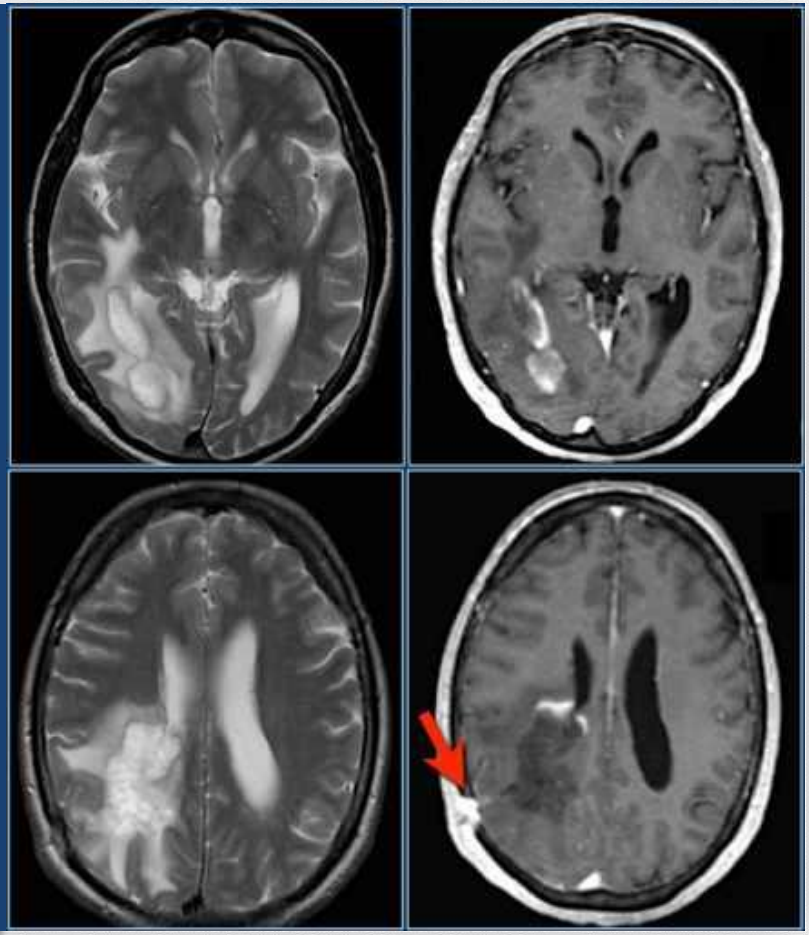
MRI Red Flags
Poorly defined lesion border



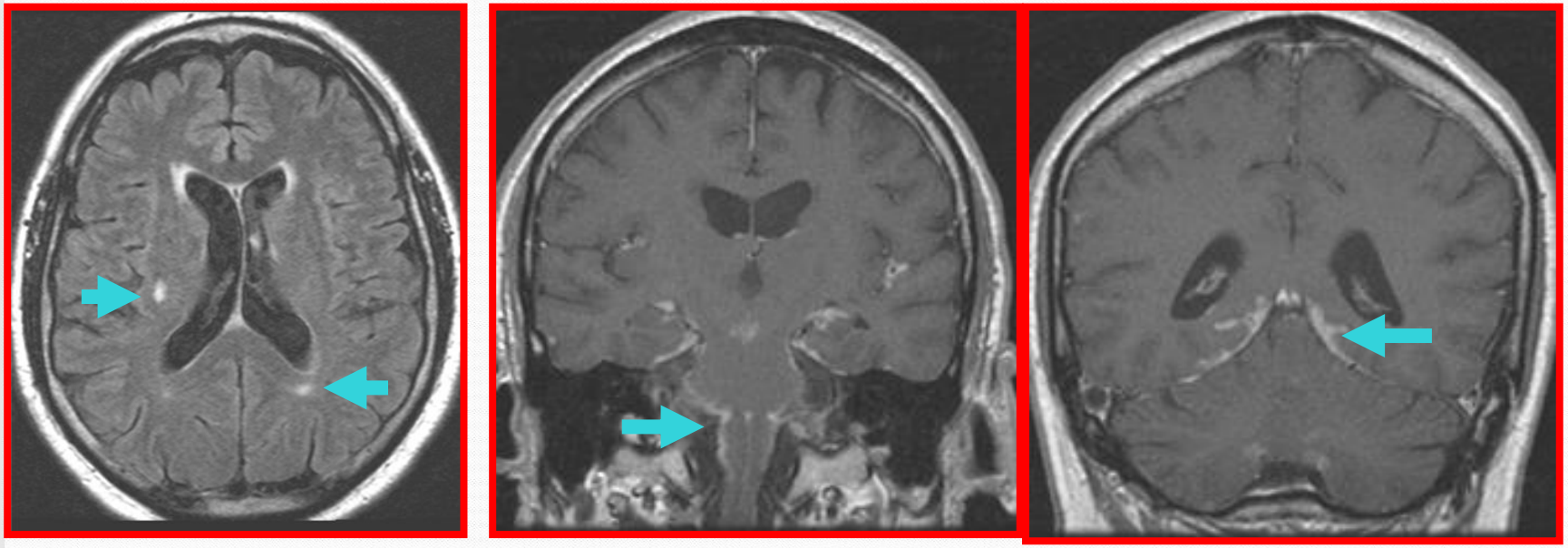
Progressive Multifocal Leukoencephalopathy

Tumefactive MS

- Post-gadolinium, there may be some peripheral enhancement, often with **an incomplete ring.**
- These lesions can be distinguished from gliomas or intraparenchymal abscesses, which typically have a **closed-ring enhancement.**

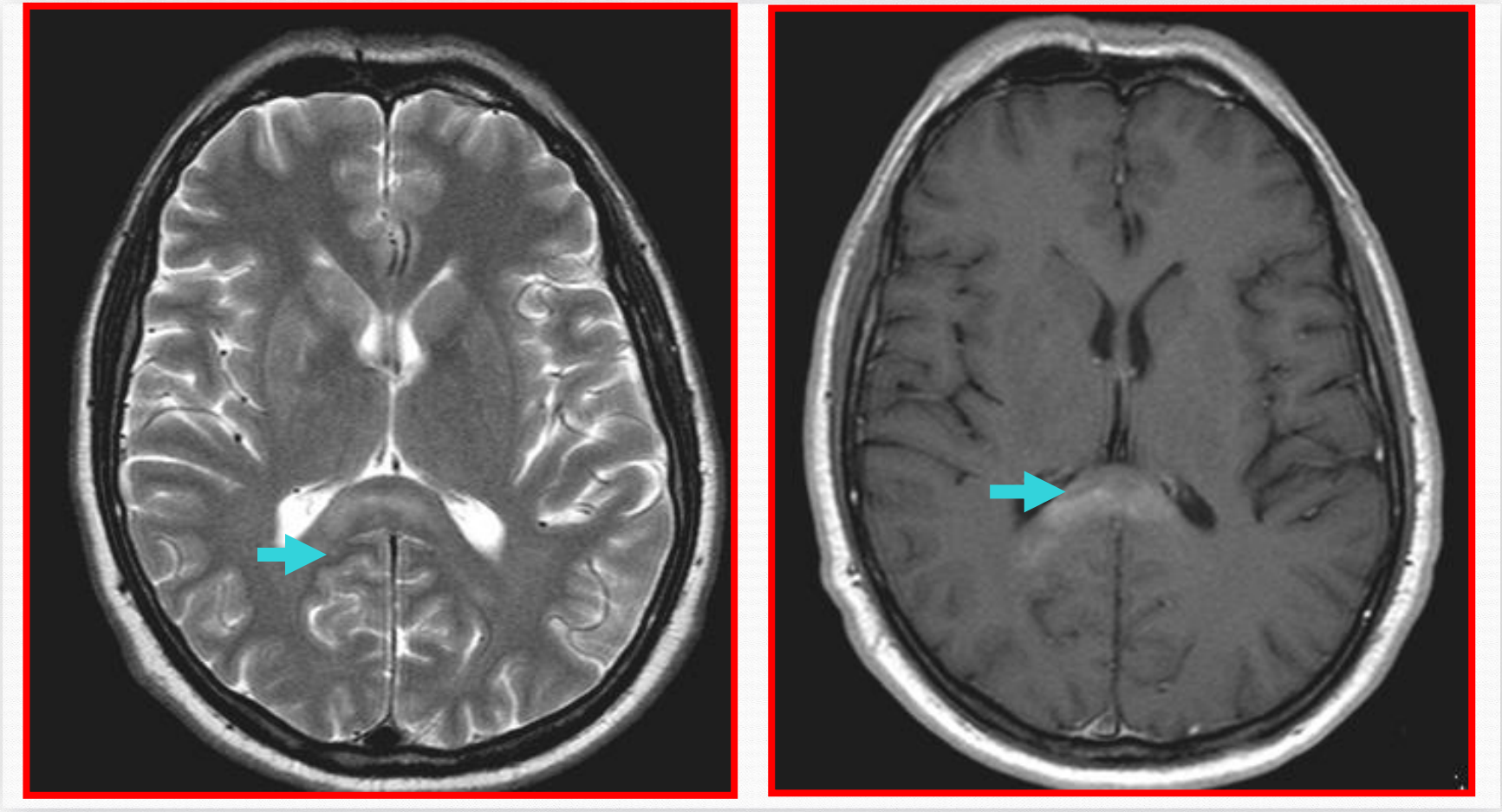


MRI Red Flags
Leptomeningeal enhancement



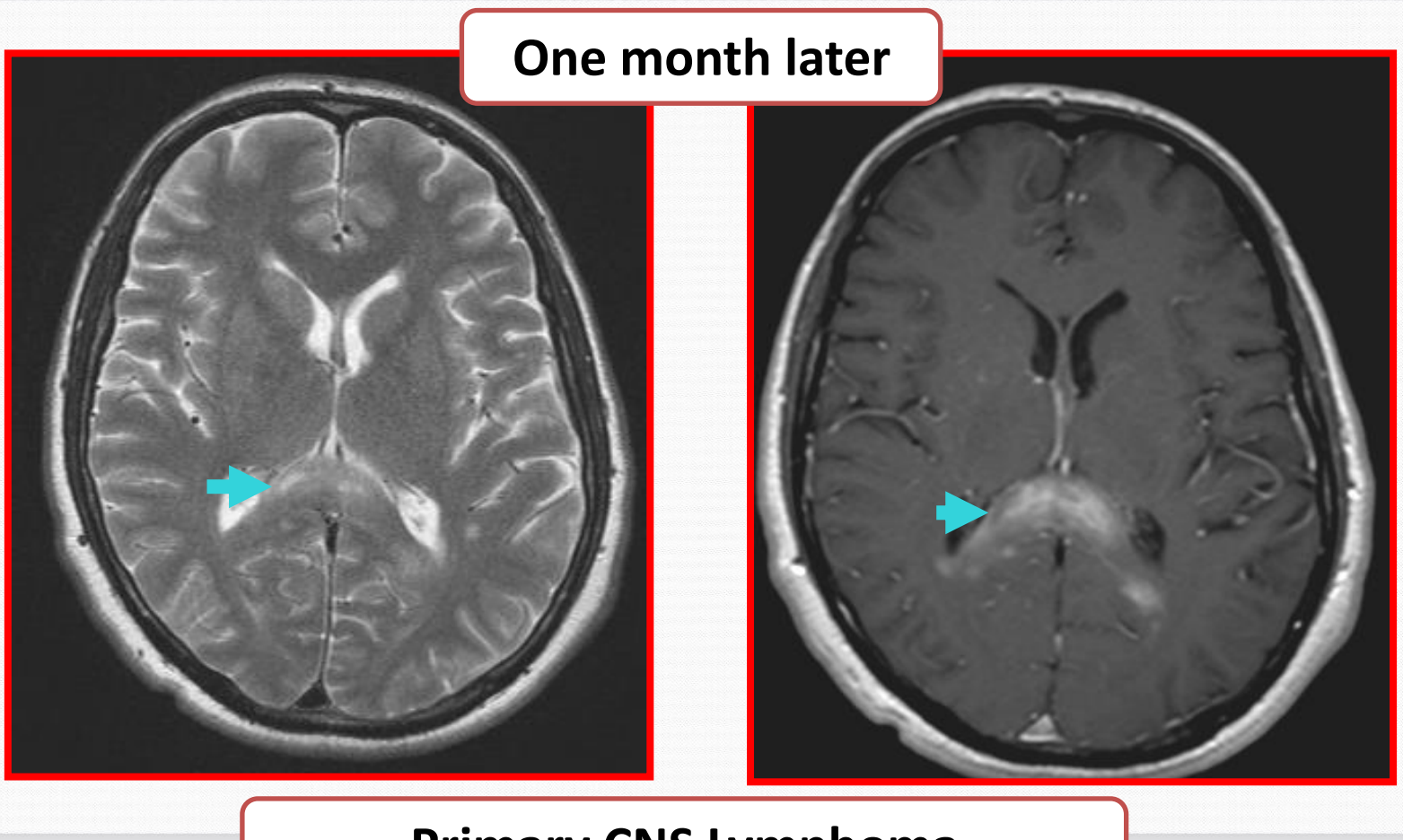
Neurosarcoidosis

MRI Red Flags

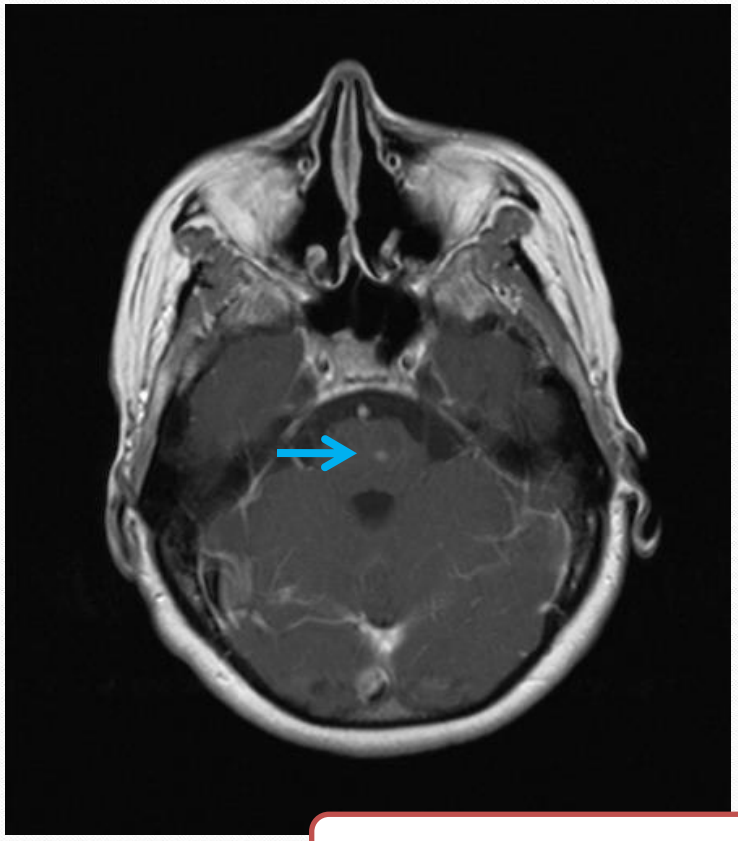


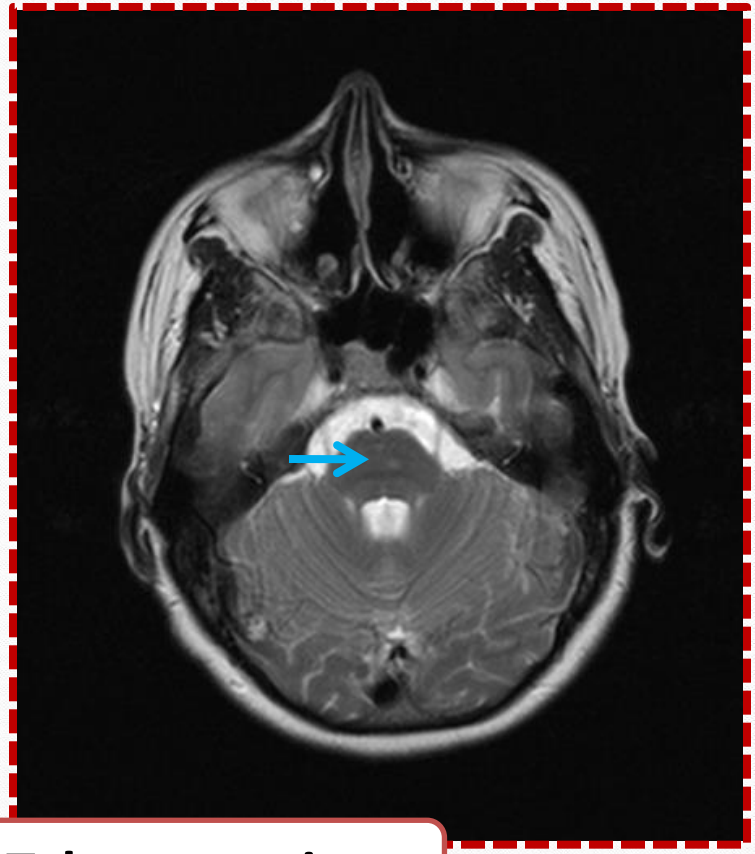
MRI Red Flags

Increasing lesion size/persistent enhancement



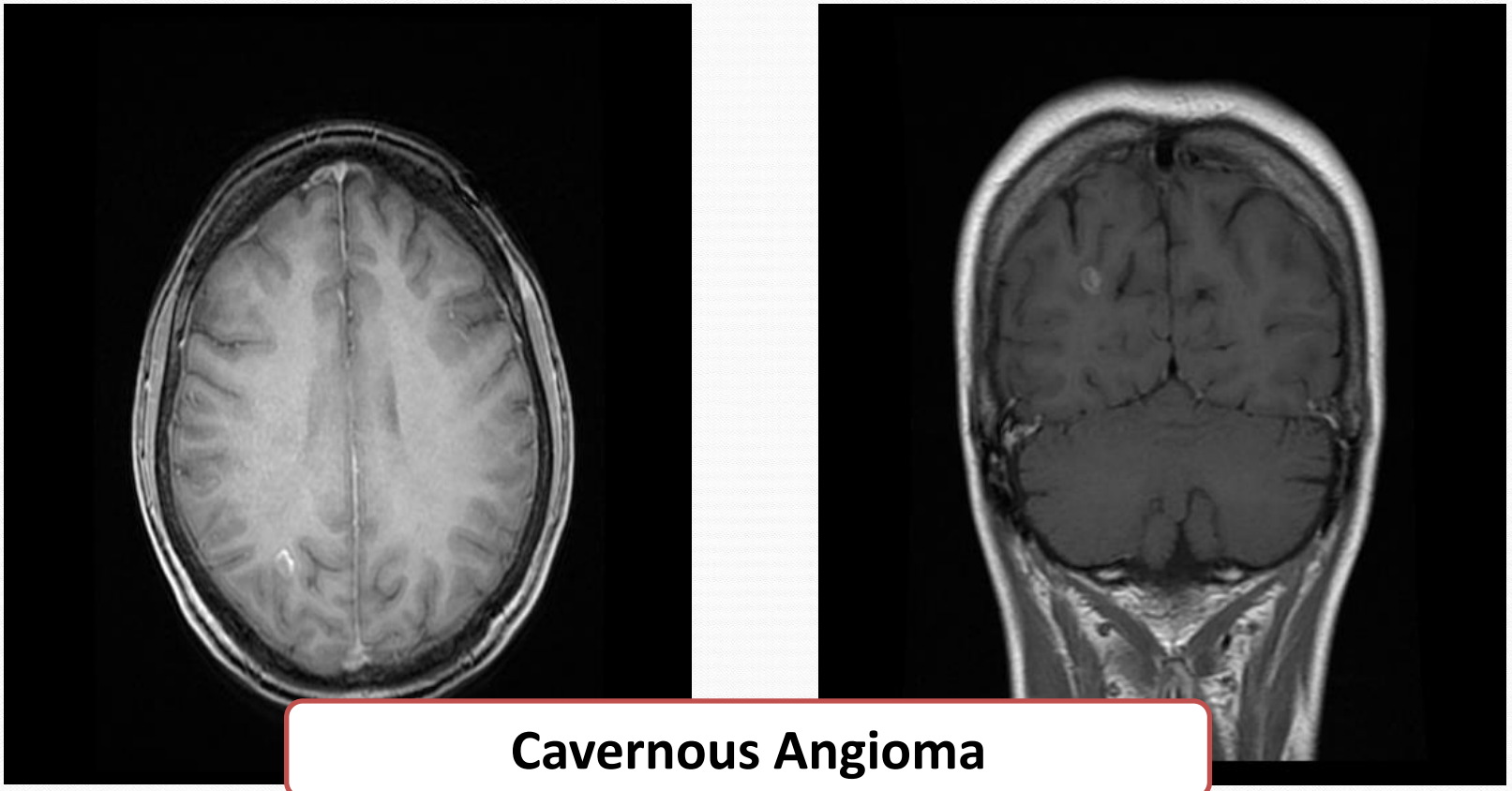
The Incidentals





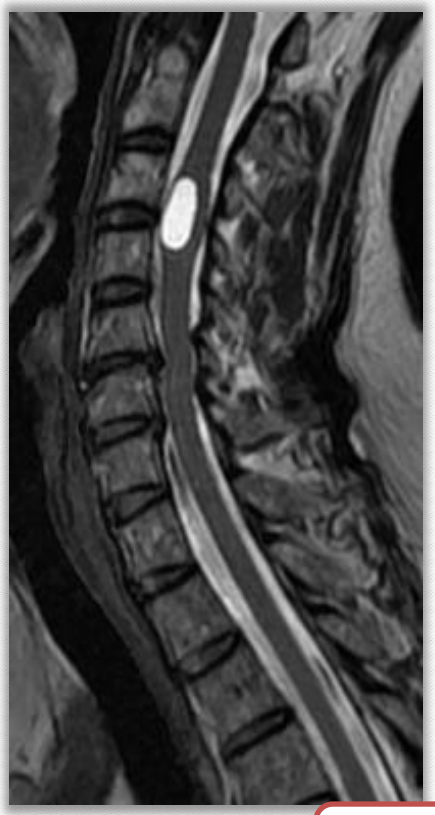
Capillary Pontine Telengectasia

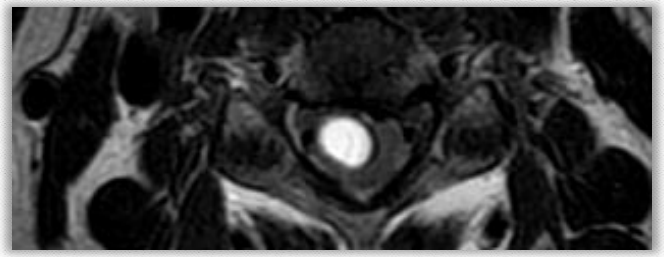
The Incidentals

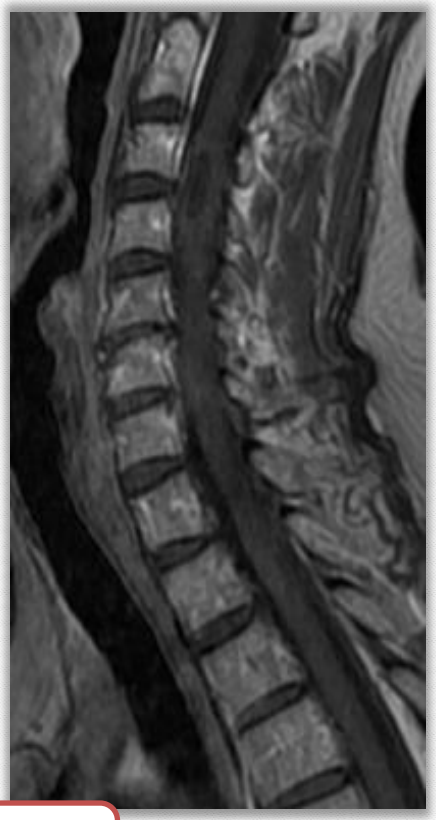


Cavernous Angioma

The Incidentals







Intraspinal Neurenteric Cyst

Neurologic symptoms + Incidental/Nonspecific brain MRI abnormality ≠ MS

Agenda

- MRI in diagnosis of MS
- MRI in D.D. of MS
- MRI in monitoring disease progression and response to DMT
- New imaging techniques

Agenda

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Using Neuroimaging to monitor patients with MS

- Subclinical inflammatory disease activity occurs commonly in MS and is captured to some extent by conventional MRI.

- Some patients with a first clinical demyelinating event (ie, CIS) will initially defer starting long-term MS disease modifying therapy.

- Radiologically isolated syndrome

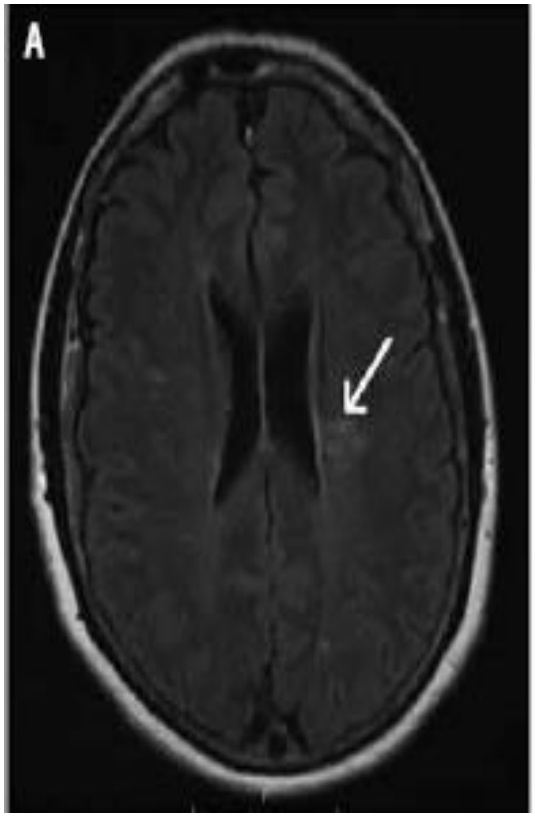
Case Study (3)

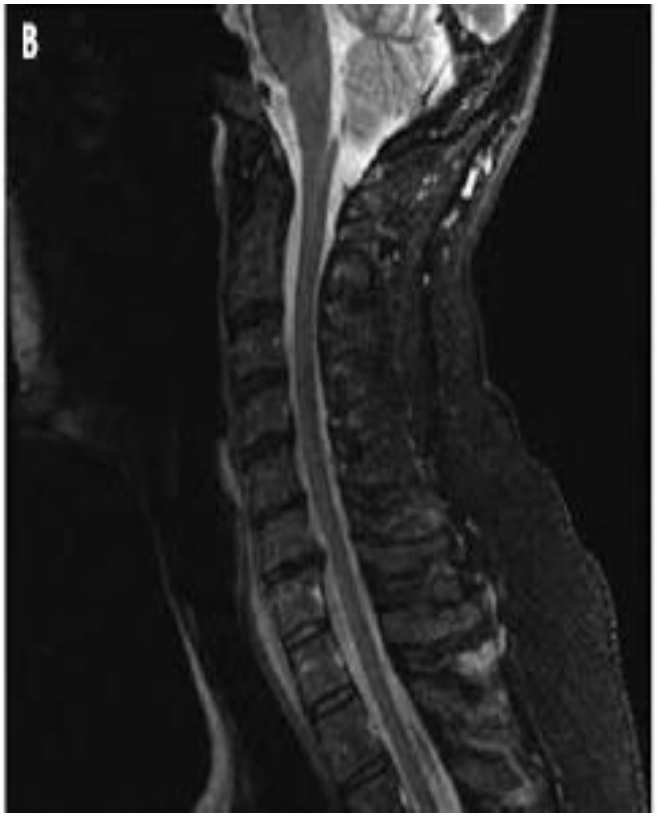
- A 55-year-old woman experienced an episode of difficulty reading the newspaper.
- Approximately 30 minutes later, she had trouble expressing herself when ordering coffee, lasting only seconds.
- Workup for these symptoms included imaging studies to evaluate for ischemia.
- Brain MRI was potentially consistent with demyelination with 10 T2 hyperintensities, some with the appearance of Dawson fingers. Spinal cord imaging was normal.

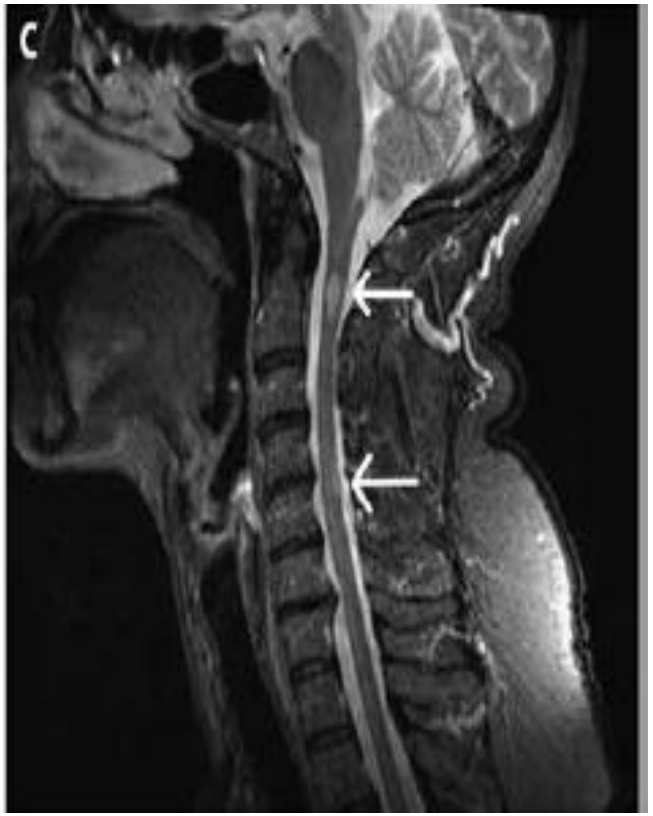
Case Study (3)

- Family history was notable for multiple sclerosis (MS) in her sister
- Without clinical events definitely attributable to demyelinating disease, the patient was diagnosed with a radiologically isolated syndrome.
- She did not start treatment for MS at that time.
- Serial imaging remained unchanged until 1 year later in the setting of left arm numbness.
- At that time, new cervical spinal T2 hyperintensities were discovered, including one at C1-2 .

Baseline and follow-up brain MRI







A: Brain MRI is remarkable for characteristic Dawson fingers (arrow).

B: Initial spinal cord MRI was normal.

C: Follow-up spinal cord imaging 1 year later shows interval development of lesions at C1-2 and C4-5 (arrows).

MRI in monitoring response to DMT

- A follow-up MRI should be performed 6 to 12 months after starting a new therapy.
- In a large retrospective study of MS patients on therapy, the presence of more than two enhancing lesions at 1 year was a predictor of poor clinical outcomes at 5 years.
- Annual to biannual monitoring of brain imaging during the relapsing stage of MS is commonly practiced despite the lack of clear consensus.

Kasr Alaini Protocol of Manangement of Multiple Sclerosis

Rio Score

Rio score is adopted to determine failure of ttt or non responding patient in order to escalate.

Rio Score	
Criterion	**Change over the first year**
MRI criterion = 0	≤2 active* T2 lesions
MRI criterion = 1	>2 active T2 lesions
Relapse criterion = 0	No relapses
Relapse criterion = 1	≥1 relapse
EDSS criterion = 0	Increase in EDSS score of <1 point
EDSS criterion = 1	Increase in EDSS score of ≥1 point, sustained over at least 6 months

Agenda

- MRI in diagnosis of MS
- MRI in D.D. of MS
- MRI in monitoring disease progression and response to DMT
- New imaging techniques

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- MRI in D.D. of MS
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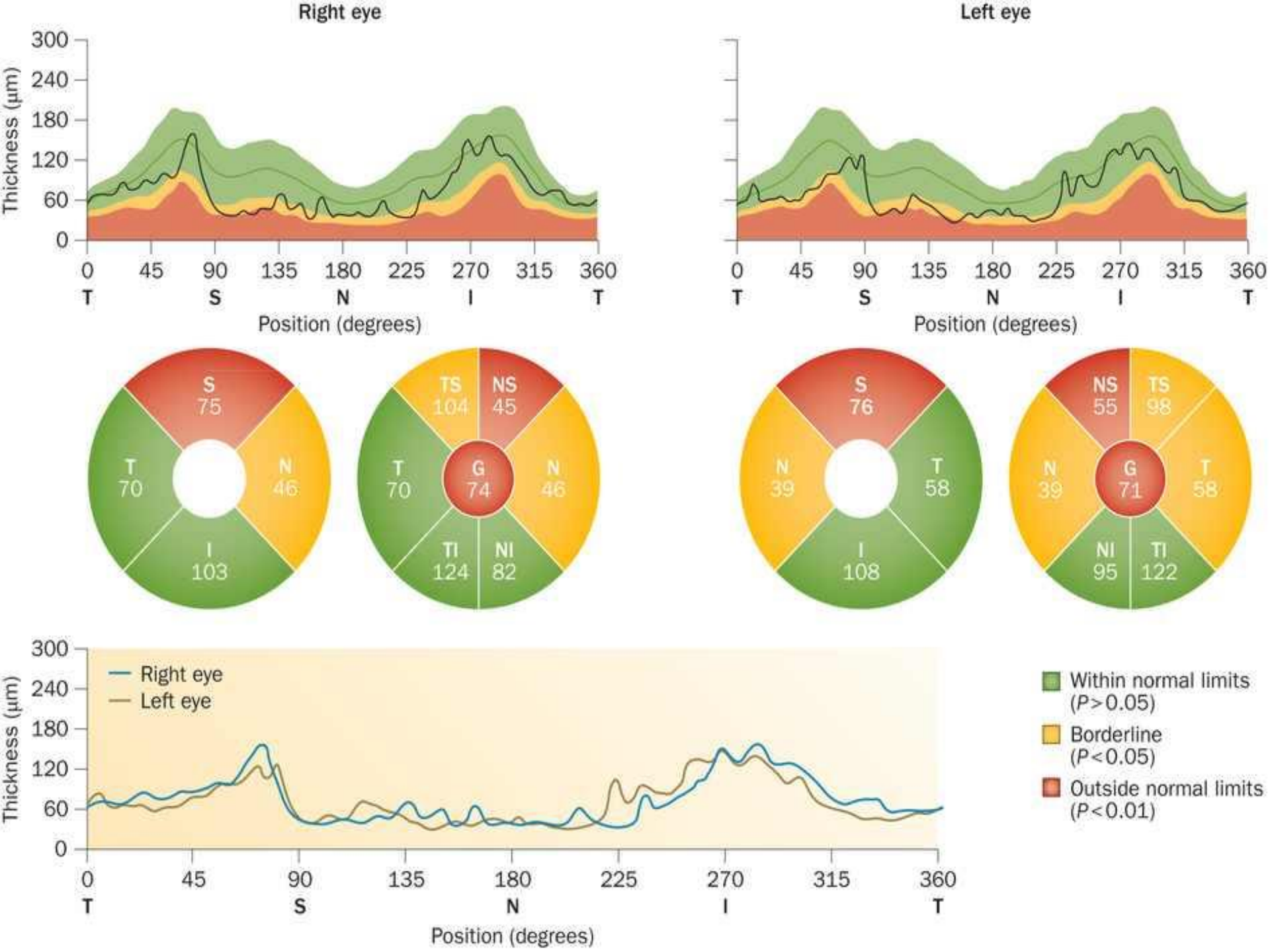
1. Optical Coherence Tomography (OCT)

- OCT is a noninvasive technique using emission of infrared light through the pupil and detection of its reflection from the retina.
- Retinal nerve fiber layer (RNFL) thickness can then be estimated. RNFL thinning can be used as a reliable biomarker of axonal loss, correlating adequately with brain atrophy measures.
- RNFL thickness can serve as biomarker of disease progression and neuroprotection by a certain therapeutical agent.

E. Grazioli, R. Zivadinov, B. Weinstock-Guttman et al., "Retinal nerve fiber layer thickness is associated with brain MRI outcomes in multiple sclerosis," Journal of the Neurological Sciences, vol. 268, no. 1-2, pp. 12–17, 2008.
R. Herrero, E. Garcia-Martin, C. Almarcegui, et al., "Progressive degeneration of the retinal nerve fiber layer in patients with multiple sclerosis," Investigative Ophthalmology & Visual Science, vol. 53, no. 13, pp. 8344–8349, 2012.

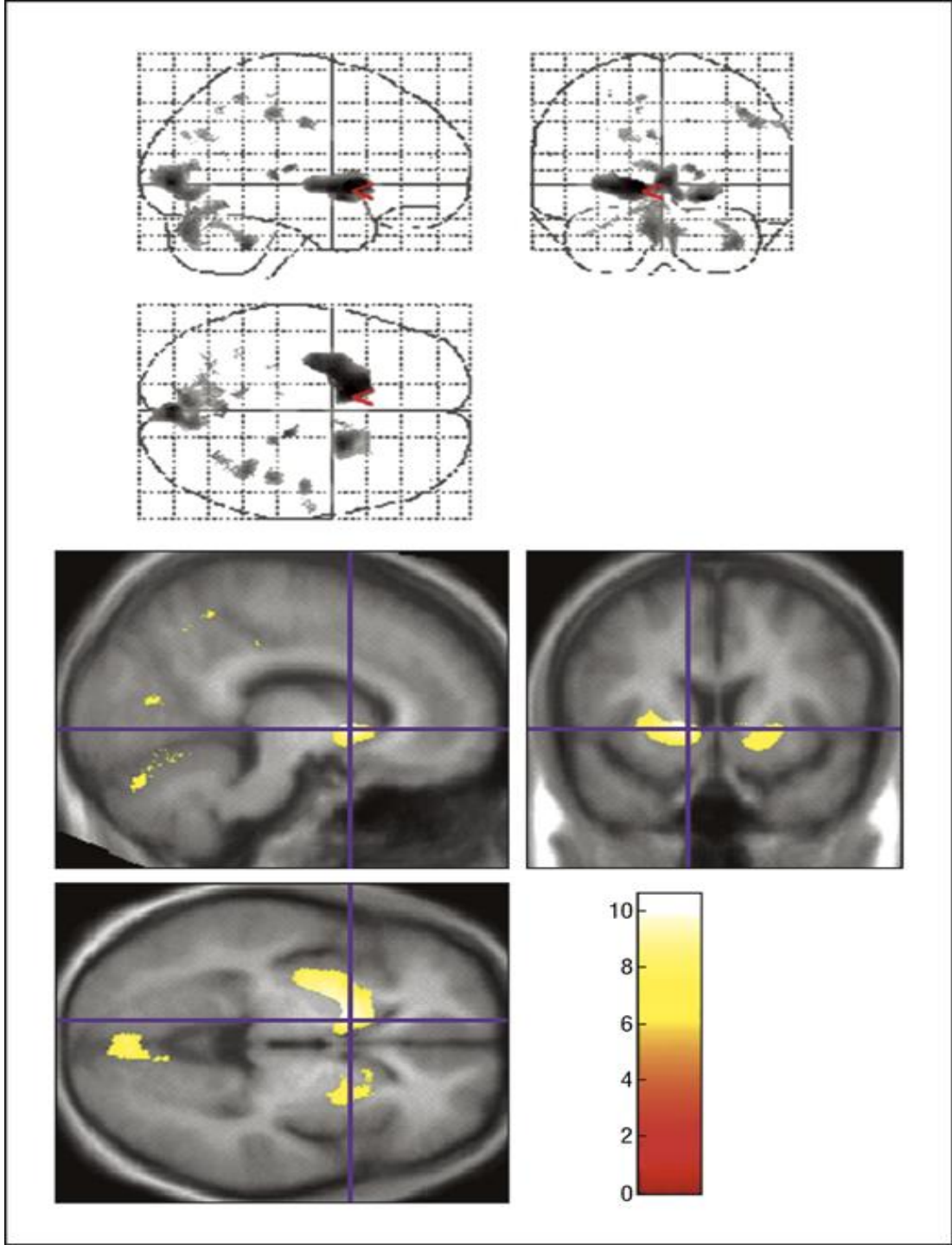

Right eye
Left eye
Thickness (µm)
300
240
180
120
60
0
0 45 90 135 180 225 270 315 360
T S N I T
Position (degrees)
S 75
T 70
N 46
I 103
TS 104
NS 45
T 70
G 74
N 46
TI 124
NI 82
S 76
N 39
T 58
I 108
NS 55
TS 98
N 39
G 71
T 58
NI 95
TI 122
Right eye
Left eye
Within normal limits (P>0.05)
Borderline (P<0.05)
Outside normal limits (P<0.01)

2. Voxel-based morphometry (VBM)

- Voxel-based morphometric (VBM) analysis is an accurate method that includes segmentation of brain volumes into GM, WM, and CSF, normalization to a standard space, and quantification of ***GM atrophy*** on a voxel-by-voxel basis.

Grossman MMcMillan CMoore P et al. What's in a name: voxel-based morphometric analyses of MRI and naming difficulty in Alzheimer's disease, frontotemporal dementia and corticobasal degeneration. *Brain* 2004;127628- 649

VBM



3. Contrast Magnetization Transfer Ratio (MTR)

- Magnetization transfer imaging is based on the transfer of magnetization between semisolid and water protons in different structural environments.
- In intact white matter myelin, protons are bound to macromolecules such as lipids, yielding a high magnetization transfer ratio (MTR). In contrast, in areas of demyelination, decreased binding of protons reduces MTR.

3. Contrast Magnetization Transfer Ratio (MTR)

- Longitudinal studies demonstrate decreases in MTR preceding contrast enhancement. There is marked reduction in MTR during contrast enhancement, followed by partial or complete resolution as inflammation reduces and remyelination occurs.
- Because of these features, this technique provides a promising primary outcome measure to evaluate remyelinating therapies in clinical trials.
- MTR may also provide insight into gray matter pathology which is not well visualized using conventional imaging.

4. Diffusion Tensor Imaging (DTI)

- DTI measures movement in several directions in space.
- In normal white matter, water diffusion is greater in the direction parallel to axons (ie, axial diffusivity [AD]) than perpendicular to axons (radial diffusivity [RD]).
- Mean diffusivity (MD) and fractional anisotropy (FA) are other descriptive diffusion characteristics.

M. Bozzali, M. Cercignani, M. P. Sormani, G. Comi, and M. Filippi, "Quantification of brain gray matter damage in different MS phenotypes by use of diffusion tensor MR imaging," American Journal of Neuroradiology, vol. 23, no. 6, pp. 985–988, 2002.

4. Diffusion Tensor Imaging (DTI)

- MD increases and FA decreases in hyperintense T2-weighted lesions. Similar alterations can be recorded in NAWM areas in conventional MRI, as well as in normal appearing gray matter (NAGM) areas, especially in progressive disease forms.

- A multicenter validation study indicated that FA is the most comparable DTI measure across centers and supports its use in multicenter clinical trials.

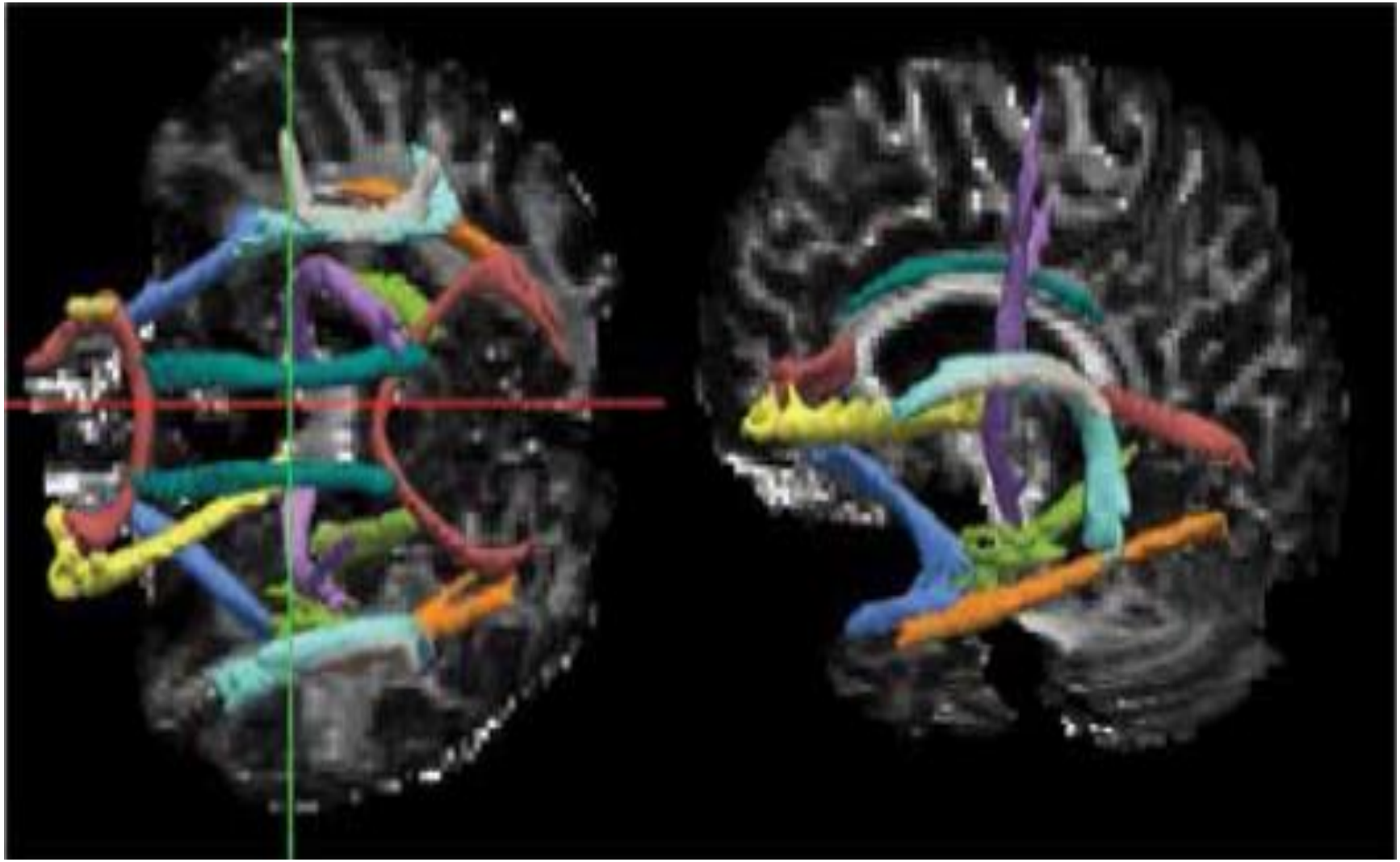
M. Wahl, A. Hübers, B. Lauterbach-Soon et al., "Motor callosal disconnection in early relapsing-remitting multiple sclerosis," Human Brain Mapping, vol. 32, no. 6, pp. 846–855, 2011.
Y. Liu, P. J. Mitchell, T. J. Kilpatrick, et al., "Diffusion tensor imaging of acute inflammatory lesion evolution in multiple sclerosis," Journal of Clinical Neuroscience, vol. 19, no. 12, pp. 1689–1694, 2012.
W. Tian, T. Zhu, J. Zhong et al., "Progressive decline in fractional anisotropy on serial DTI examinations of the corpus callosum: a putative marker of disease activity and progression in SPMS," Neuroradiology, vol. 54, no. 4, pp. 287–297, 2012.

4. Diffusion Tensor Imaging (DTI)

- Corpus callosum DTI abnormalities are present in early MS stages, even when lesions in conventional MRI are still absent .
- MD alterations precede visible in conventional MRI BBB injury by at least 5 months, being thus a reliable predictive biomarker for MS relapse.
- Corpus callosum DTI abnormalities in SPMS patients constitute a bad prognostic biomarker of future disability.

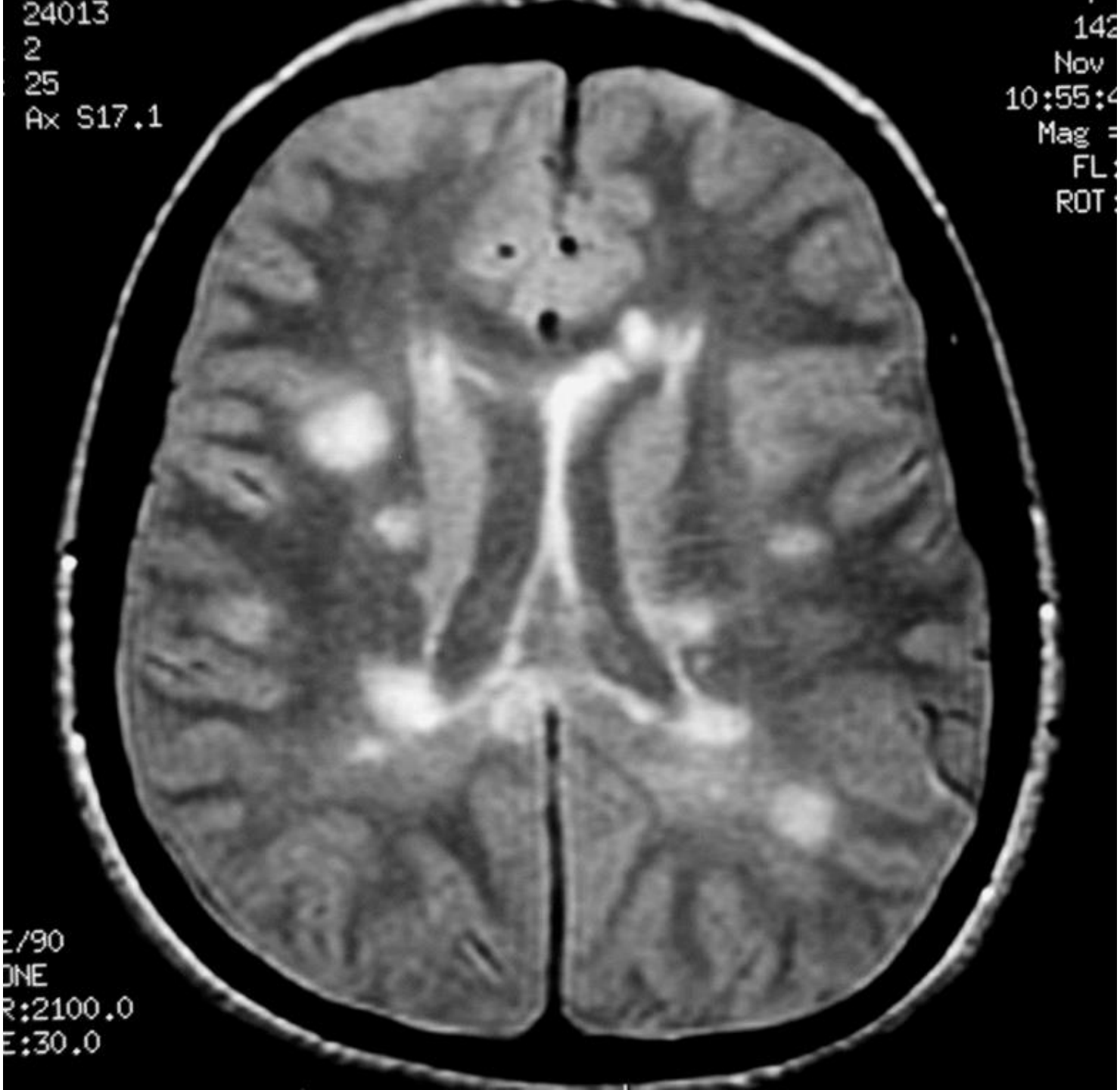
M. Wahl, A. Hübers, B. Lauterbach-Soon et al., "Motor callosal disconnection in early relapsing-remitting multiple sclerosis," Human Brain Mapping, vol. 32, no. 6, pp. 846–855, 2011.
Y. Liu, P. J. Mitchell, T. J. Kilpatrick, et al., "Diffusion tensor imaging of acute inflammatory lesion evolution in multiple sclerosis," Journal of Clinical Neuroscience, vol. 19, no. 12, pp. 1689–1694, 2012.
W. Tian, T. Zhu, J. Zhong et al., "Progressive decline in fractional anisotropy on serial DTI examinations of the corpus callosum: a putative marker of disease activity and progression in SPMS," Neuroradiology, vol. 54, no. 4, pp. 287–297, 2012.

4. Diffusion Tensor Imaging (DTI)

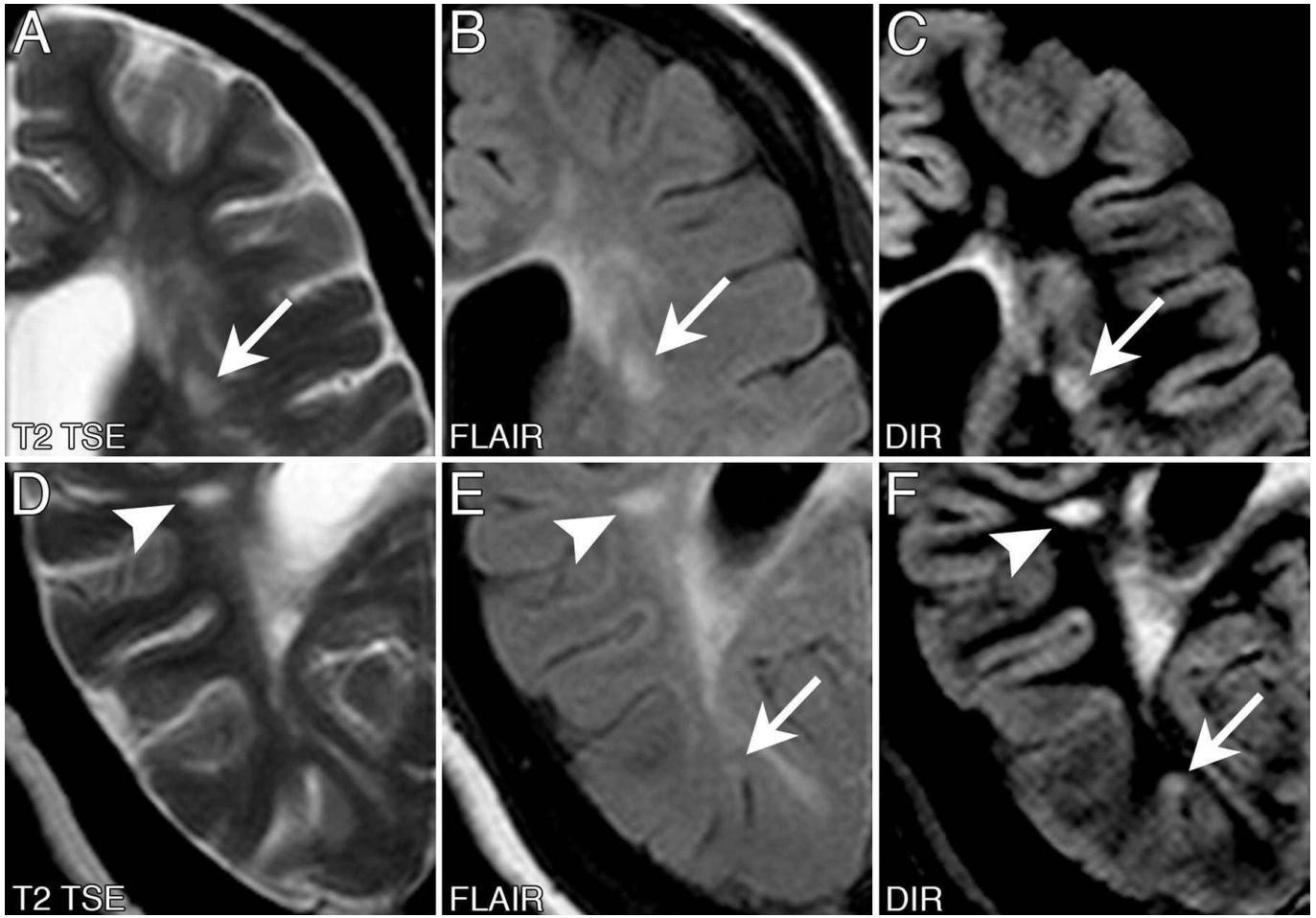


5. Double inversion recovery (DIR)

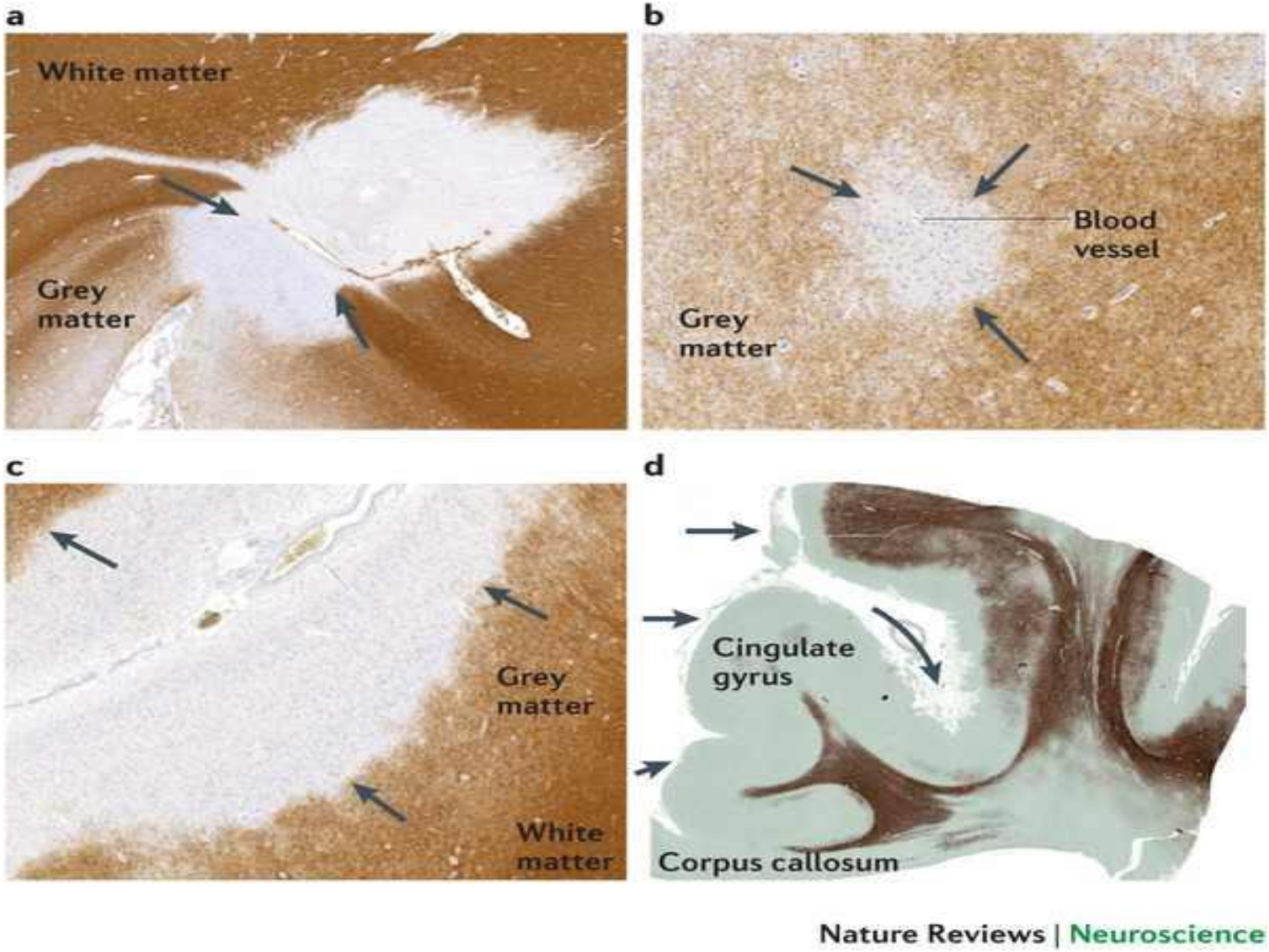
A sequence that suppresses both CSF and white matter signal for better delineation of the plaques.


24013
2
25
Ax S17.1
142
Nov
10:55:4
Mag
FL
ROT
E/90
ONE
R:2100.0
E:30.0

DIR



Types of grey matter lesions



Nature Reviews | Neuroscience

Pitfalls of DIR

- It does not always allow a correct identification of the two main CL subtypes recognized histologically, i.e., pure intracortical (IC) and leukocortical

- Differentiation of LC lesions from juxtacortical lesions is challenging and sometimes impossible.

- Missing the identification of small oval IC lesions

J Neurol Neurosurg Psychiatry. 2012 Sep;83(9):877-82. doi: 10.1136/jnnp-2012-303023. Epub 2012 Jul 17.

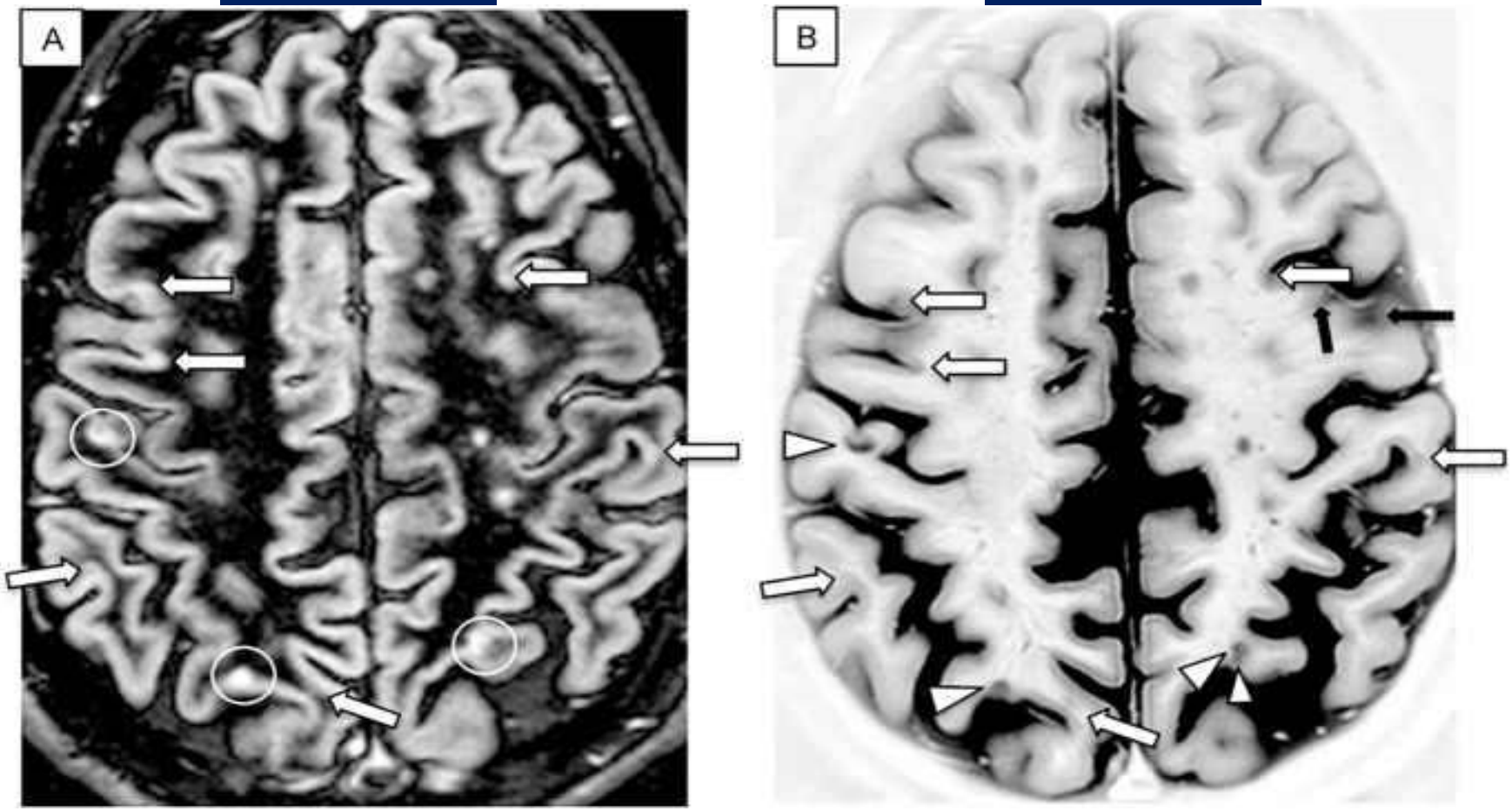
Improved detection of cortical MS lesions with phase-sensitive inversion recovery MRI.

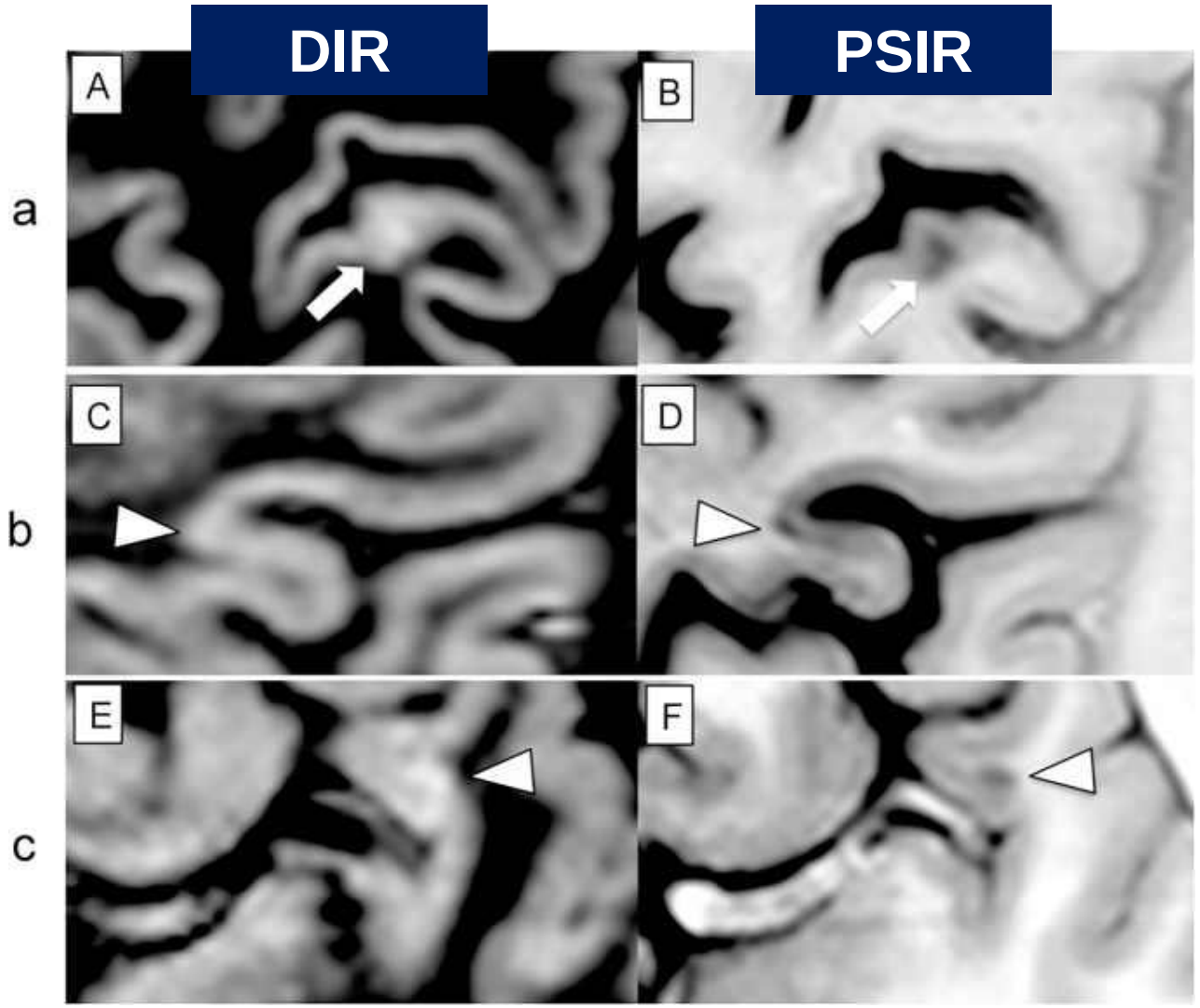
Sethi V[1], Yousry TA, Muhlert N, Ron M, Golay X, Wheeler-Kingshott C, Miller DH, Chard DT.

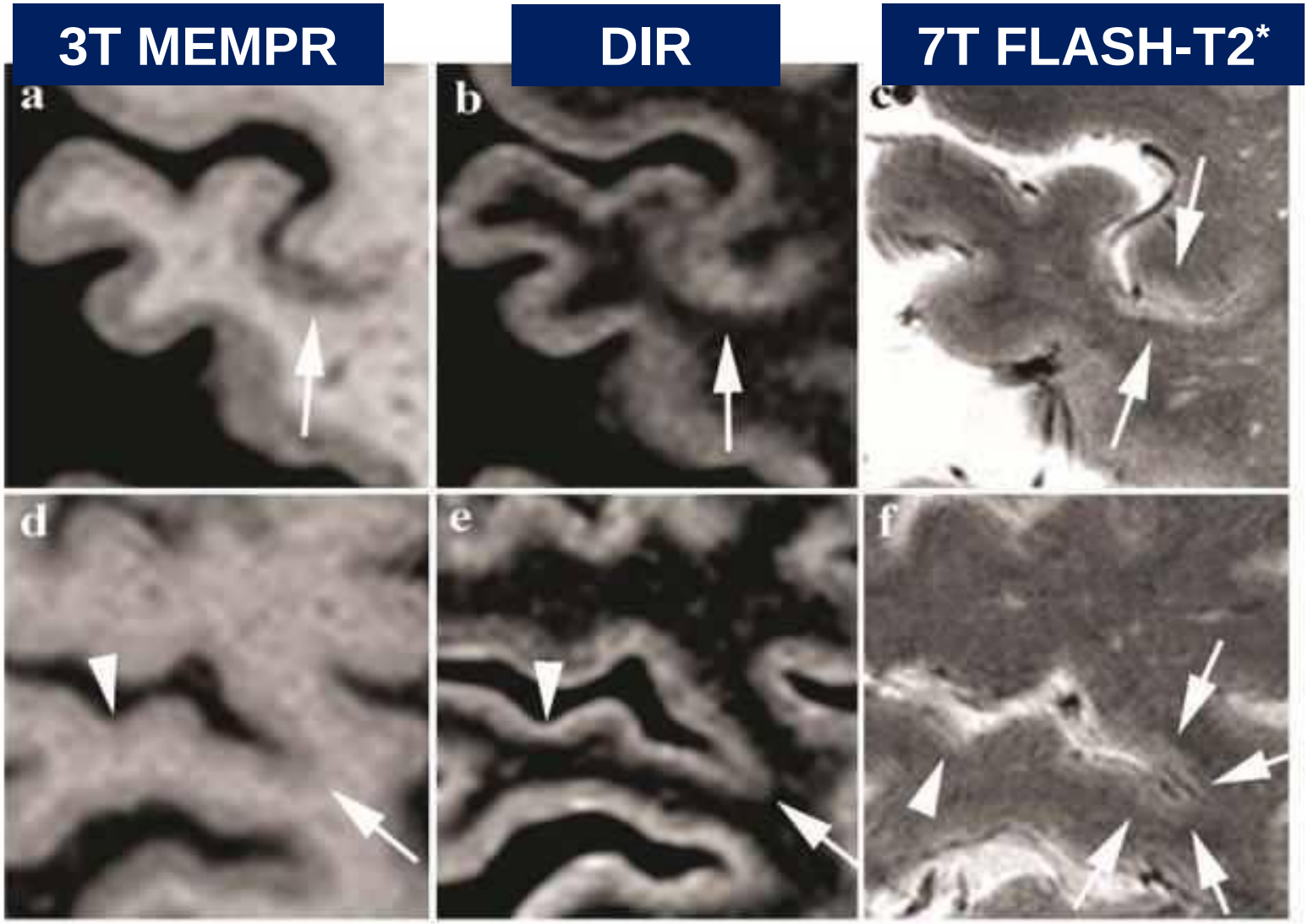
6. PSIR

DIR

PSIR




DIR
PSIR
A
B
C
D
E
F
a
b
c


3T MEMPR
DIR
7T FLASH-T2*
a
b
c
d
e
f

7. Magnetic Resonance Spectroscopy (MRS)

- **MRS is a novel imaging method for assessment of pathobiochemical disease processes. The following substances spectroscopic measurements are of particular value in MS:**

i. NAA: biomarker of neuronal and axonal integrity. NAA showed a progressive decline pattern in a two-year MRS followup of patients with RRMS .
ii. Choline: biomarker of myelin loss;
iii. Myoinositol and creatine: biomarkers of gliosis
iv. Glutamate: biomarker of acute inflammation.

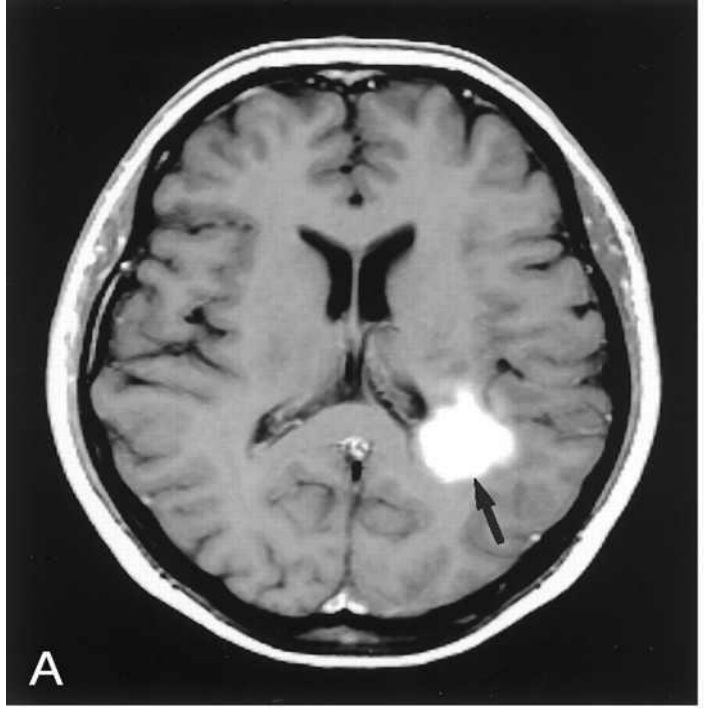
D. J. Rigotti, M. Inglese, I. I. Kirov, et al., "Two-year serial whole-brain N-acetyl-L-aspartate in patients with relapsing-remitting multiple sclerosis," Neurology, vol. 78, no. 18, pp. 1383–1389, 2012.

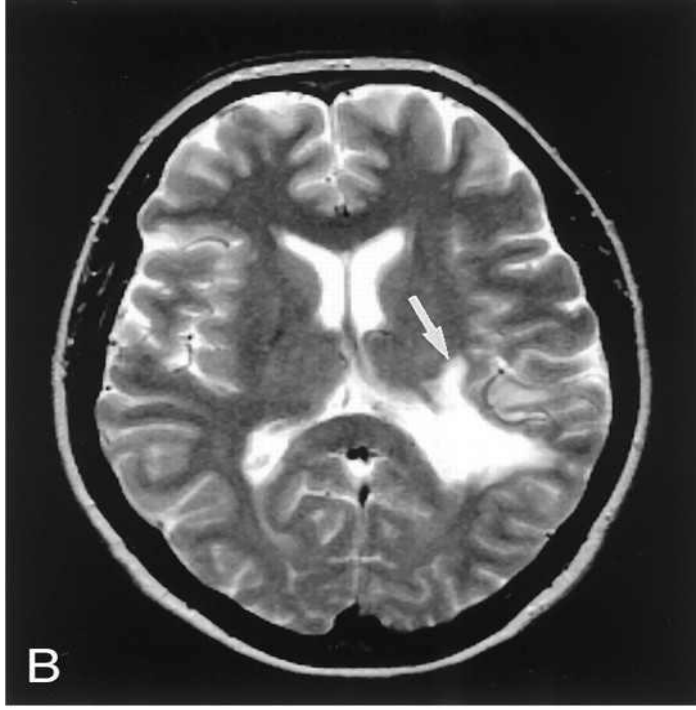
7. Magnetic Resonance Spectroscopy (MRS)

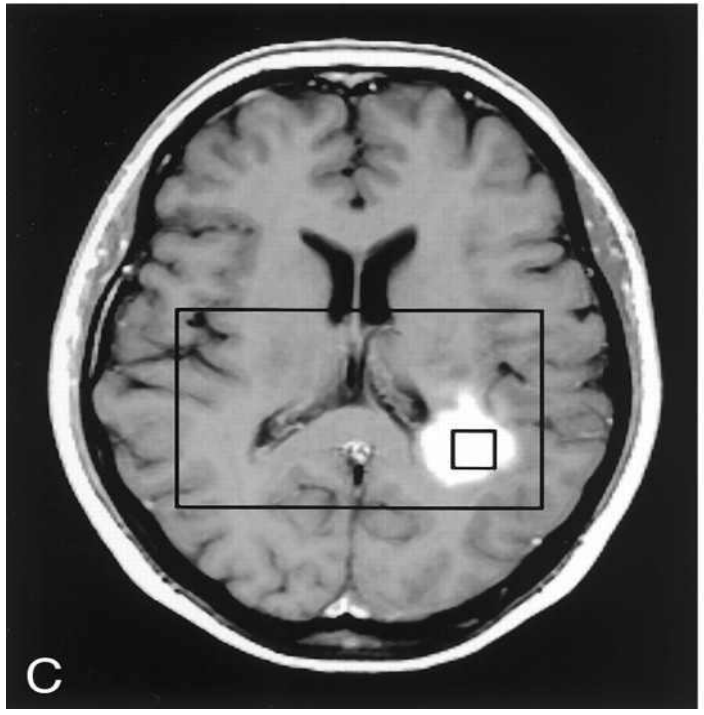
- Early spectroscopic changes represent a bad prognostic factor of future disability. Spectroscopic findings suggest that white matter abnormalities in RRMS are more prominent than grey matter abnormalities where the injury is less diffuse.
- The ratio of myo-inositol to NAA predicted future atrophy and disability progression

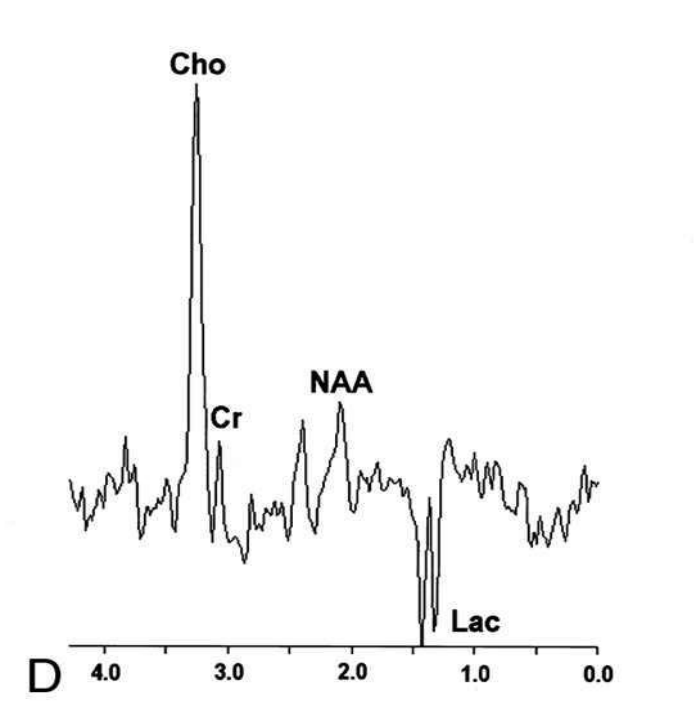
E. Hattingen, J. Magerkurth, U. Pilatus, A. Hubers, M. Wahl, and U. Ziemman, "Combined 1H and 31P spectroscopy provides new insights into the pathobiochemistry of brain damage in multiple sclerosis," NMR in Biomedicine, vol. 24, no. 5, pp. 536–546, 2011.
I. I. Kirov, A. Tal, J. S. Babb, J. Herbert, and O. Gonen, "Serial proton MR spectroscopy of gray and white matter in relapsing-remitting MS," Neurology, vol. 80, no. 1, pp. 39–46, 2012.

MRS









8. Positron Emission Tomography (PET)

- Modern PET tracers have the ability to bind in proteins that show upregulation in activated microglia, making possible an early visualization of NAWM and NAGM disorders, even before contrast enhancement in conventional MRI. At present, the use of PET in MS remains experimental.

U. Oh, M. Fujita, V. N. Ikonomidou et al., "Translocator protein PET imaging for glial activation in multiple sclerosis," Journal of Neuroimmune Pharmacology, vol. 6, no. 3, pp. 354–361, 2011.

9- Advanced Spinal Cord Imaging

CHALLENGING???

- Physiologic motion (ie, respiration, cardiac pulsation, CSF pulsation) and magnetic field inhomogeneity due to nearby vertebrae.

- Atrophy also occurs in the spinal cord in MS and correlates to a greater extent with disability than other brain measures of atrophy in patients with mild disability

10. Diffusion tensor spectroscopy (DTS)

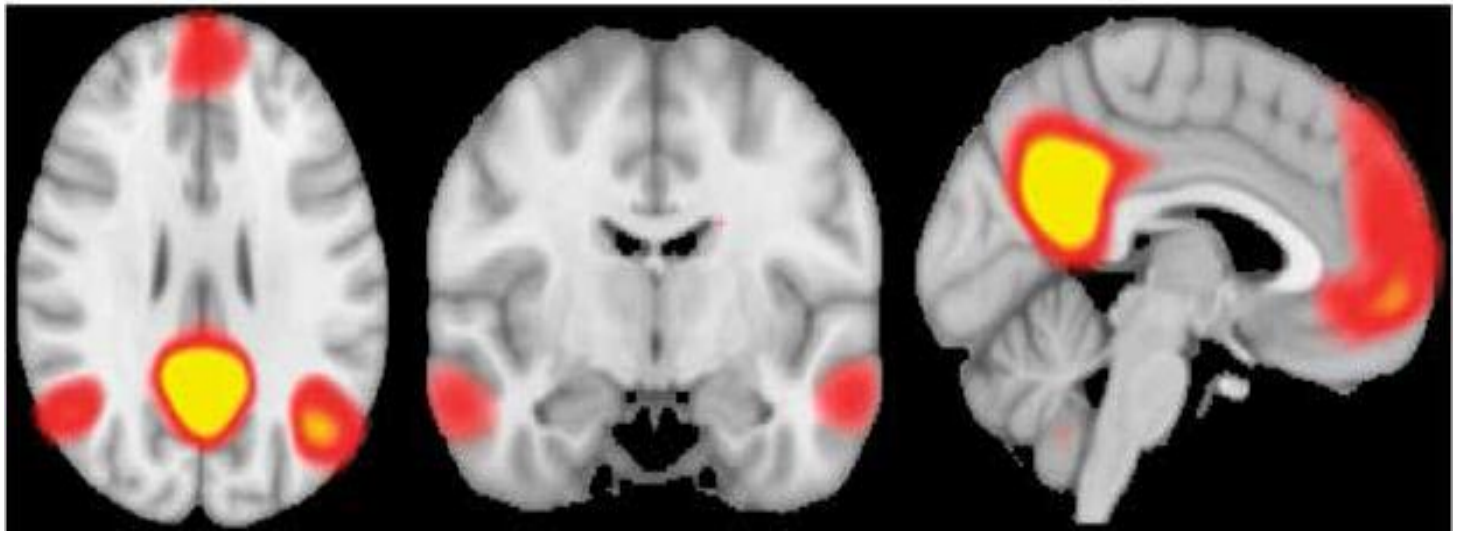
- Diffusion tensor spectroscopy (DTS), a technique combining properties of DTI and MRS, seems promising in better distinguishing axonopathy, demyelination, inflammation, edema, and gliosis.

- A new method of applying the technique of DTI to spectroscopy is termed “diffusion tensor spectroscopy.” Preliminary results indicate that reduced diffusion of NAA along axons may represent a marker of axonal damage.

E. T. Wood, I. Ronen, A. Techawiboonwong, et al., “Investigating axonal damage in multiple sclerosis by diffusion tensor spectroscopy,” Journal of Neuroscience, vol. 32, no. 19, pp. 6665–6669, 2012.

11- Functional MRI

- Functional MRI offers the advantage over other discussed imaging techniques by providing evidence for plasticity in MS.
- These results suggest an early adaptive mechanism in MS patients that is eventually overcome following increased disease burden.



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DEMYELINATING DISEASES: Edited by Hans-Peter Hartung

Magnetic resonance outcome measures in multiple sclerosis trials: time to rethink?

Filippi, Massimo; Preziosa, Paolo; Rocca, Maria A.

Measures		Pathological substrates	Clinical relevance	Sensitivity to changes	Application in clinical trials	Response to treatment
Active lesions (new T2 and Gd-enhancing)		Inflammation and demyelination	++	++	Yes	+++
Evolution of active lesions into permanent black holes		Axonal loss, demyelination, gliosis	+	++	Yes	++
Brain atrophy		Neuro-axonal loss, demyelination	+++	++	Yes	++
GM atrophy		Neuro-axonal loss, demyelination	+++	+++	Yes	++
Cervical cord atrophy		Neuro-axonal loss, demyelination	+++	++	Few, single-center, clinical trials	Undetermined
Cortical lesions		Inflammation, demyelination and axonal loss	++	++	Few, single-center, clinical trials	+
Quantitative MRI-based techniques	MT MRI	Demyelination	++	++	Yes	++
	^{1}H-MRS	Metabolic abnormalities (NAA/Cr ratio)	+	++	Yes	+
	DT MRI	Demyelination, axonal damage, gliosis	++	++	Not yet	Undetermined
Functional reorganization		Synaptic plasticity	++	++	Few, single-center studies, mainly on the	+

CONCLUSION

- MRI is integral to making the early and accurate diagnosis of MS.
- It provides valuable information for monitoring patients to identify the level of treatment response.
- The goal of emerging techniques is to provide markers more sensitive to changes in the disease and more specific to the underlying pathology.
- In doing so, improved correlation with current and future levels of disability can be achieved.

THANK YOU