Alternatives to the Classic MRI: High Tesla Imaging

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American Society of Neuroimaging

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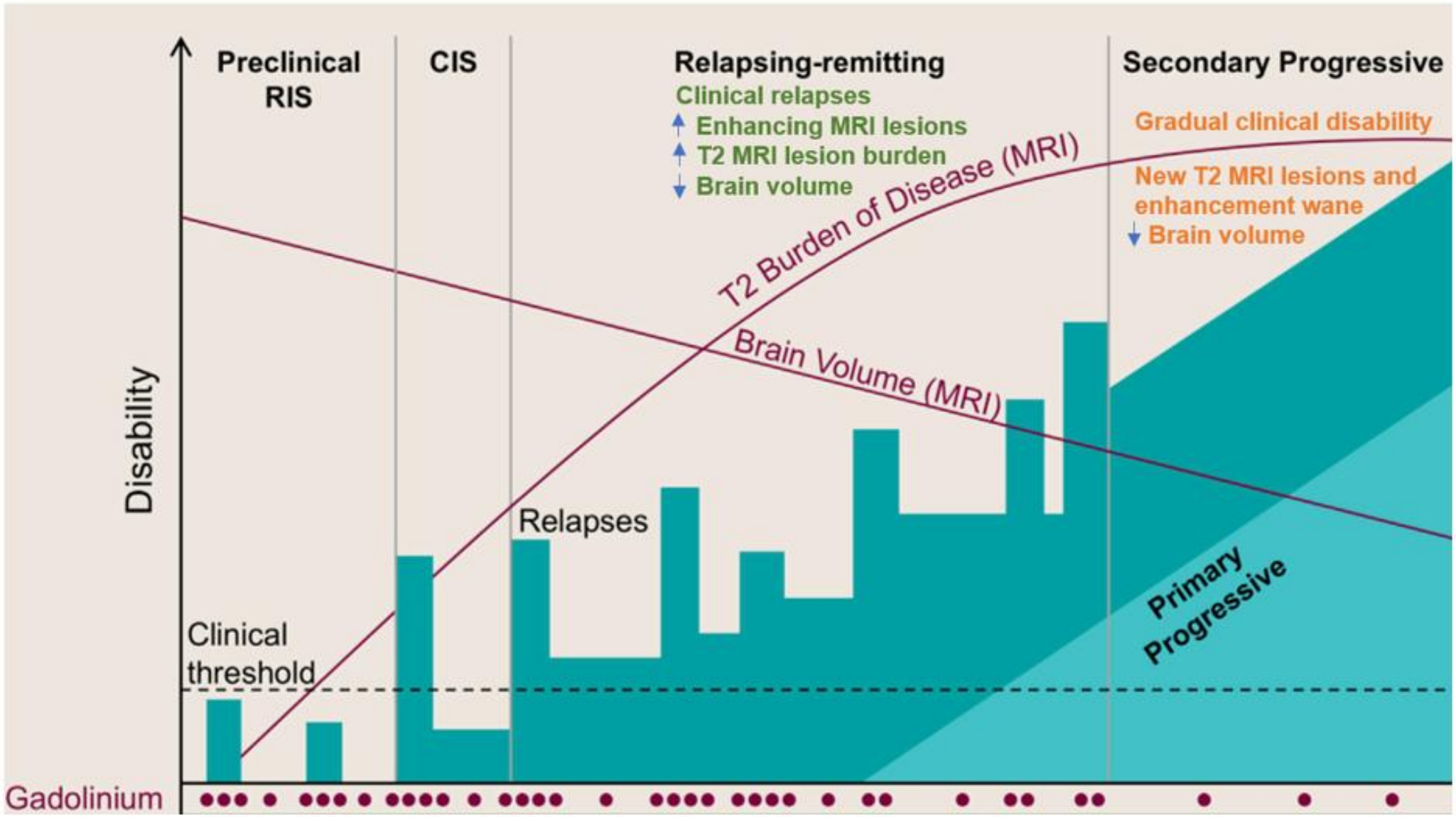
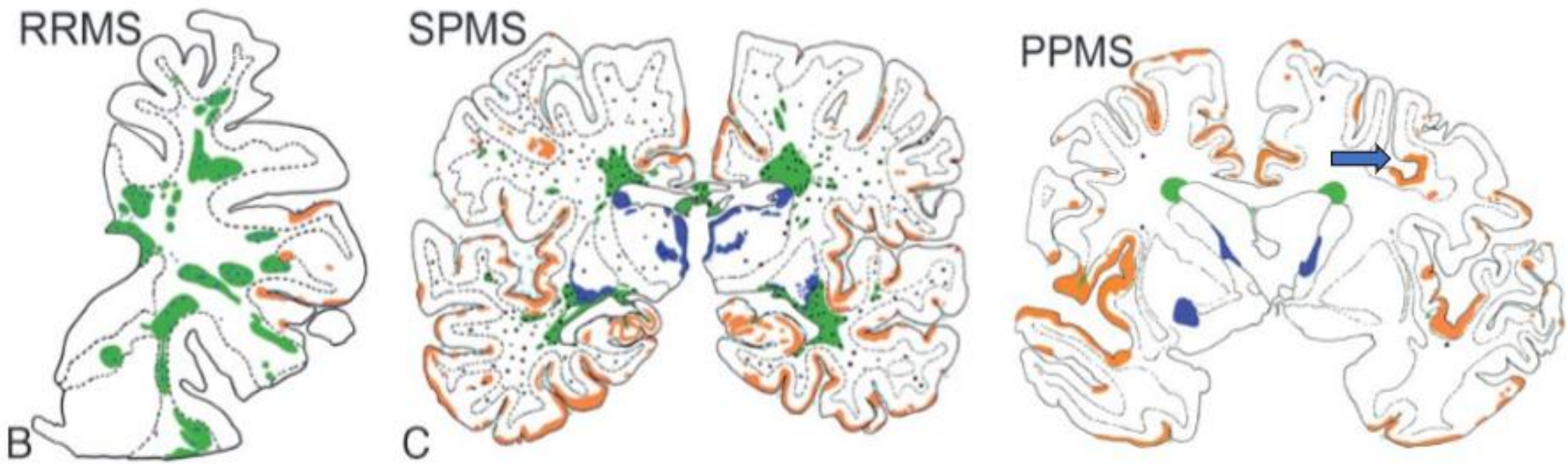
The Natural History of MS



A. Kutzelnigg et al *Brain* (2005), **128,** 2705–2712

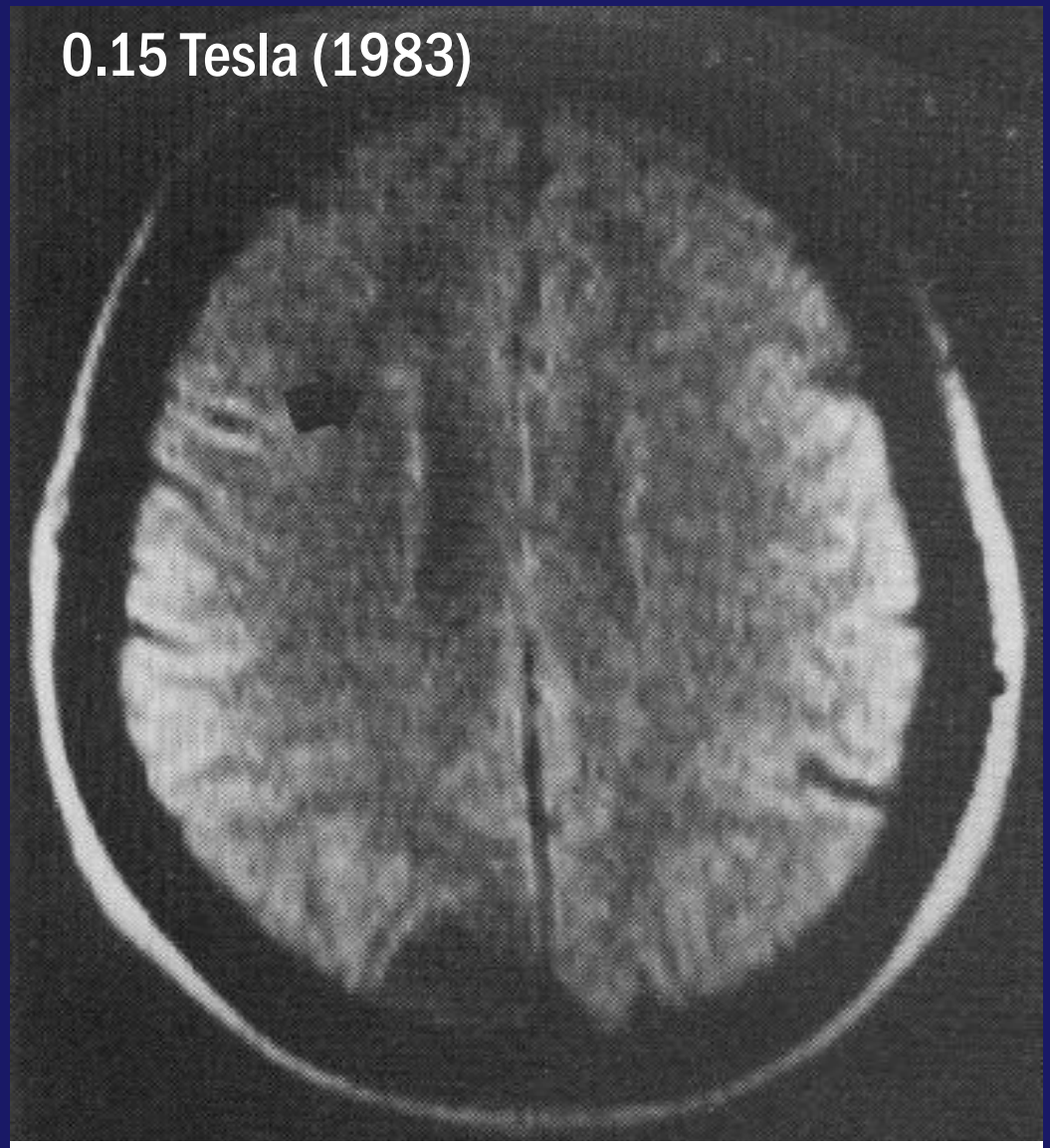


Periventricular white matter demyelination

Subpial cortical and thalamic gray matter demyelination and atrophy

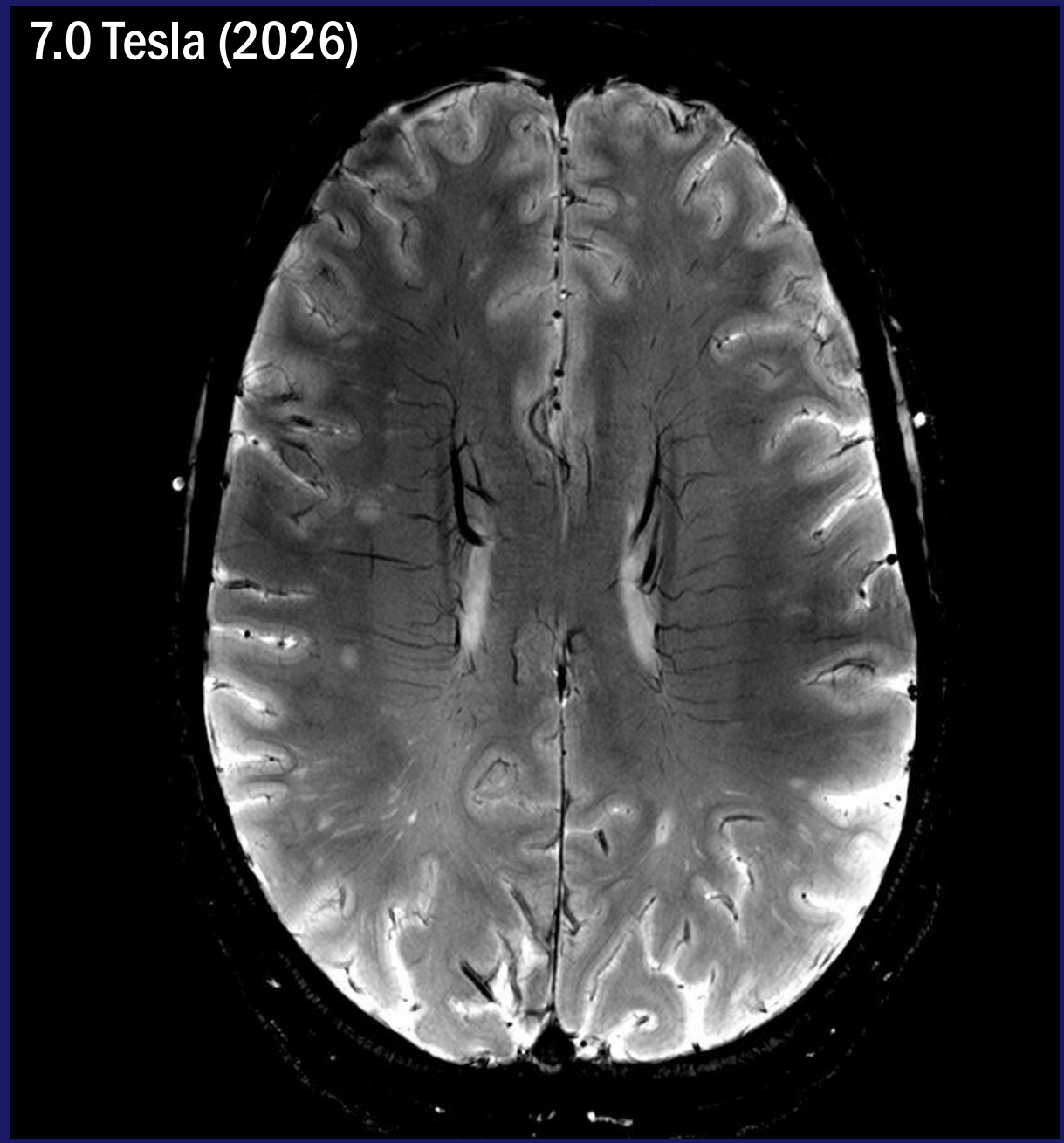
RR= relapsing-remitting; SP= secondary progressive; PP= primary progressive

0.15 Tesla (1983)



Young IR, Hall AS, Pallis CA et al: Nuclear magnetic resonance imaging of the brain in multiple sclerosis. *Lancet* 1981; 2: 1063–1066

7.0 Tesla (2026)



BWH 7T Scanner

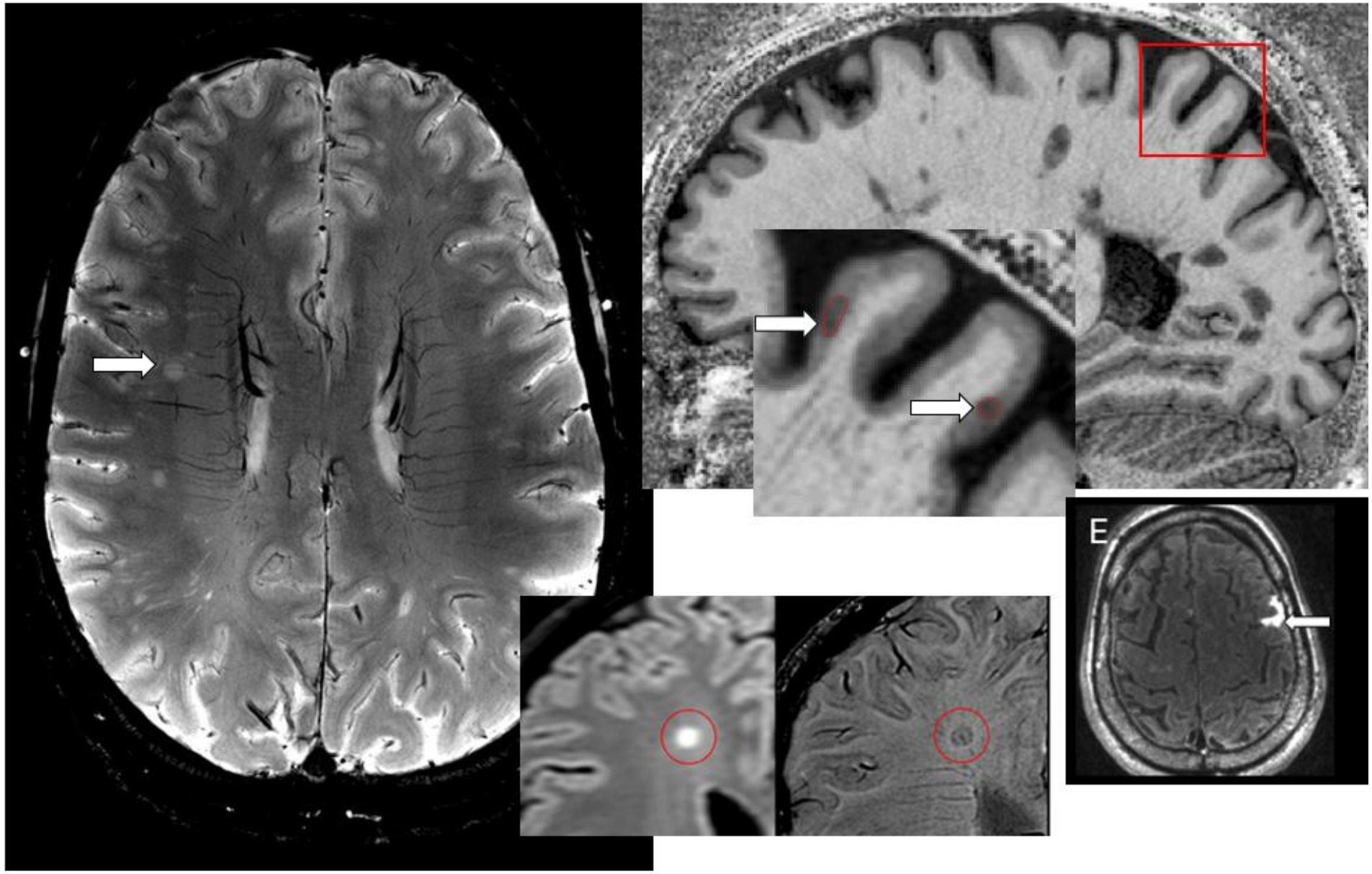
- Magnet: 7T Siemens Magnetom Terra Unit, 32-channel Nova Coil – single coil transmit/32 receiving coils
- Cost: $6 million
- 50% lighter than older 7T model
- FDA-approved for clinical use in MA in 2018
- MRI Protocol: 0.7 mm^3 voxels.
- Contrast: Images obtained pre-and 10-mins post-0.1 mmol/kg IV gadoterate meglumine (Dotarem©)

Outcomes in MS:

- ✓ Central vein sign
- ✓ Cortical lesions
- ✓ Thalamic lesions
- ✓ Leptomeningeal enhancement
- ✓ Paramagnetic rim lesions

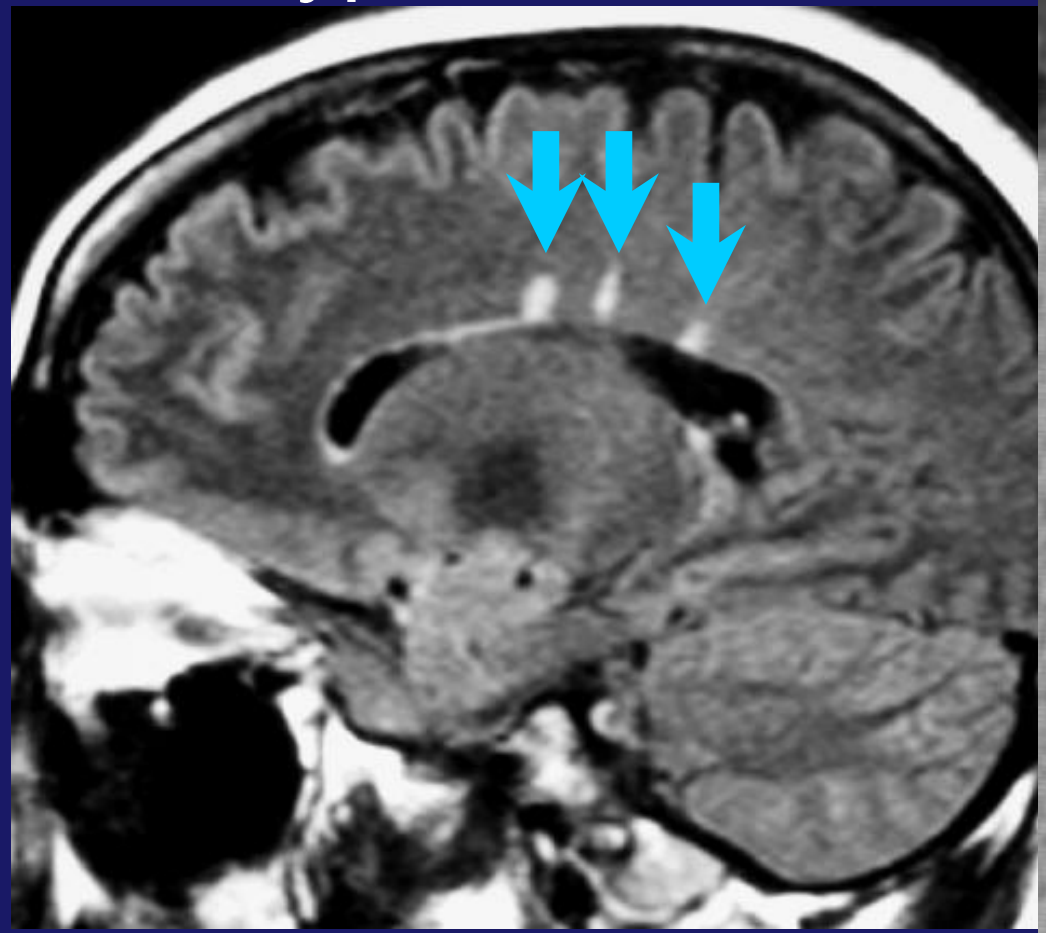
Sequence	Resolution (mm)	TR	TI	TE	Parallel Imaging	Flip Angle	Turbo Factor	Time (m:sec)
3D-T1 MP2RAGE	0.7 x 0.7 x 0.7	4540 ms	TI_1= 1040 ms TI_2= 3200 ms	3.43 ms	GRAPPA iPAT Factor (PE) = 4 iPAT Factor (3D) = 1	FI_1= 4.0 deg FI_2= 4.0 deg	240	8:07
3D-T2 FLAIR	0.7 x 0.7 x 0.7	9000 ms	2500 ms	301 ms	GRAPPA iPAT Factor (PE) = 3 iPAT Factor (3D) = 2	90 deg	225	8:08

7.0 T MRI at BWH - 2025

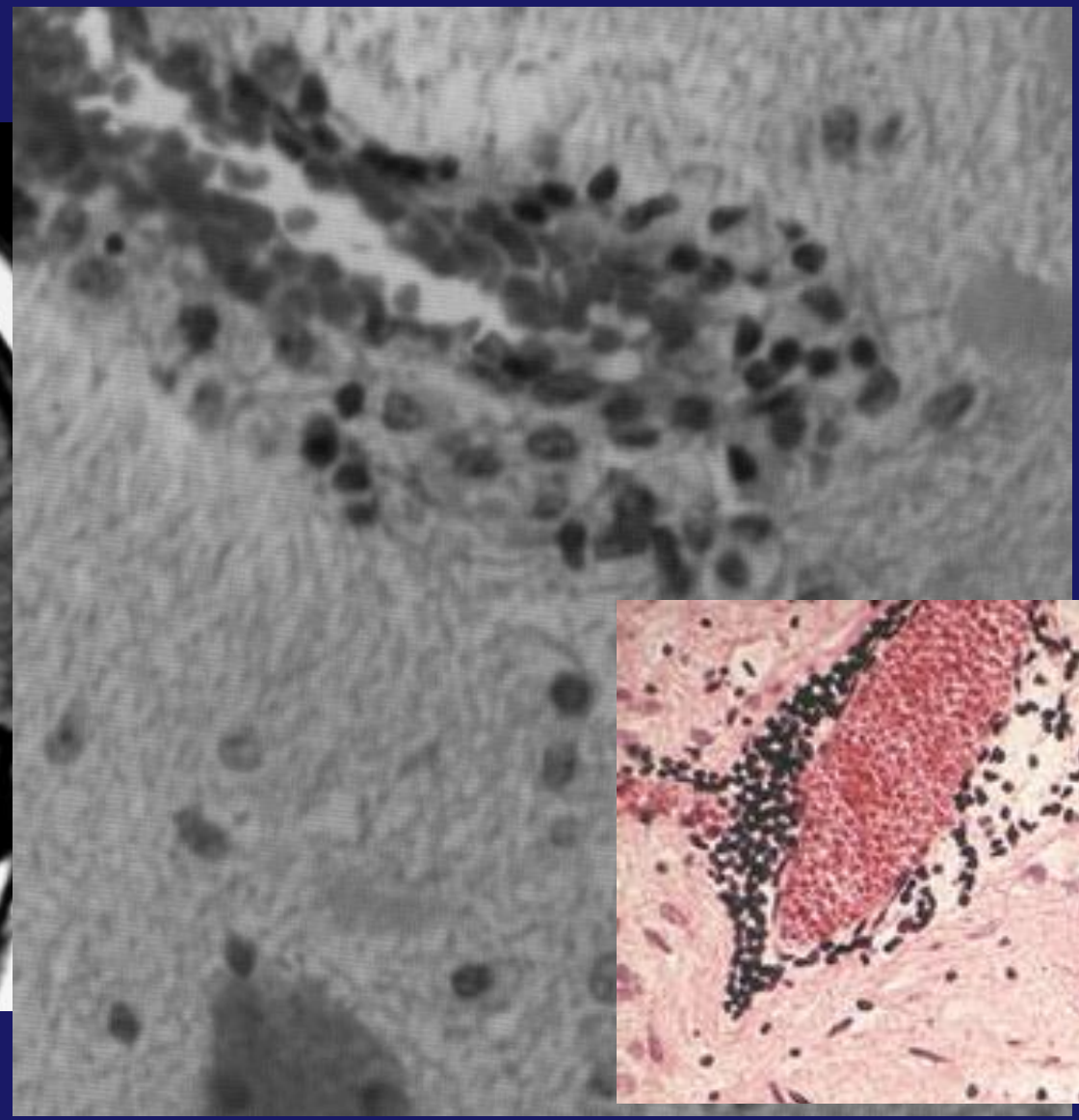


Classic MS Lesion Morphology

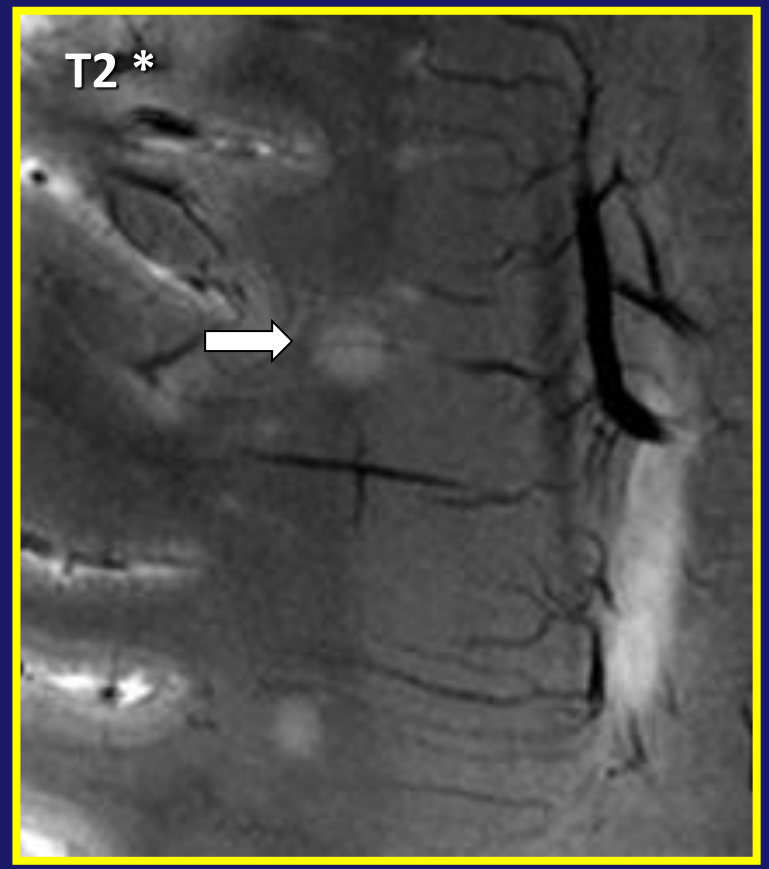
Typical of MS



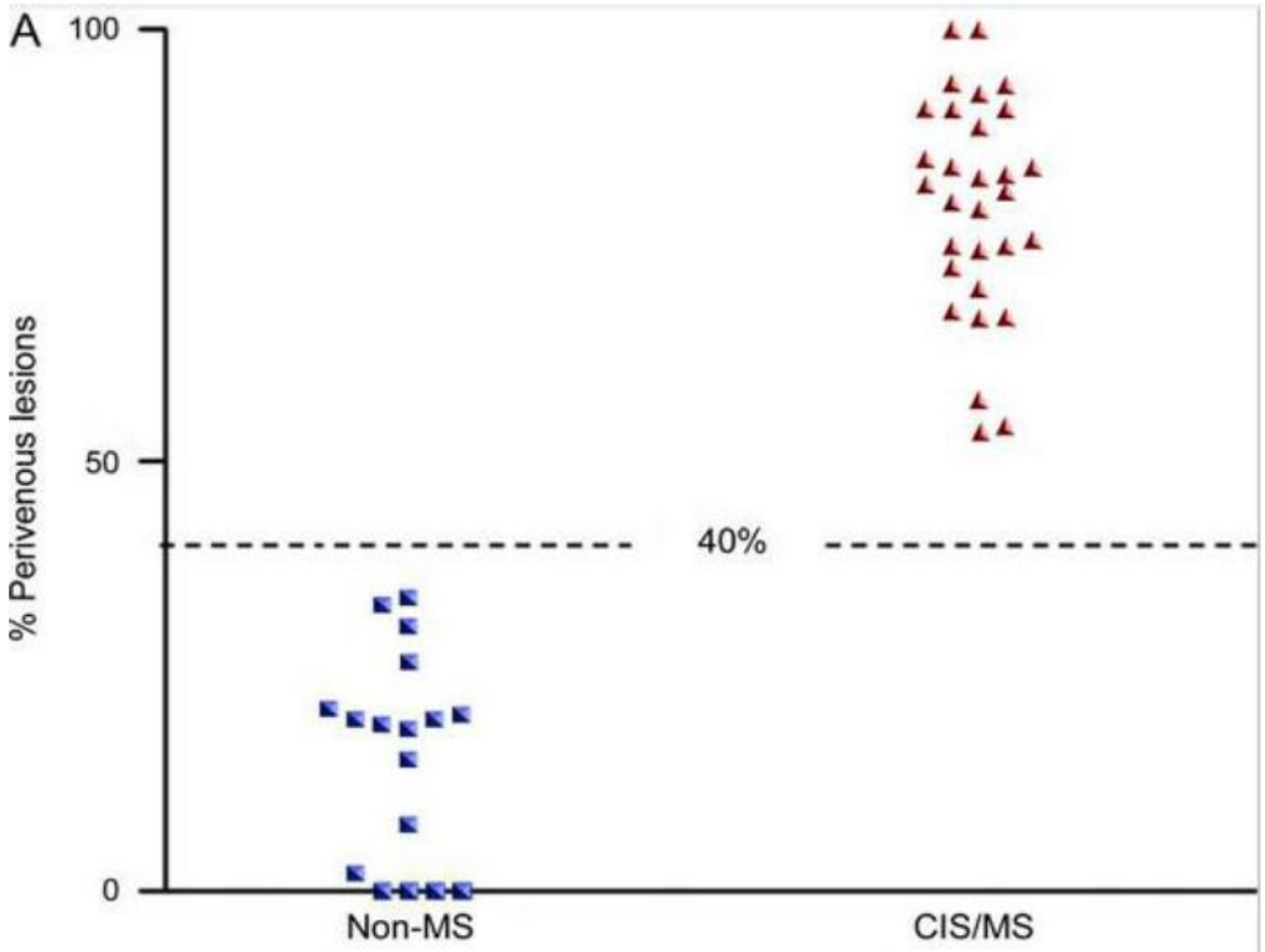
Perivenular



Central Vein Sign



MS Central Veins at 7T



Tallantyre et al. Neurology 2011;76:534–39

CONSENSUS STATEMENT

OPEN

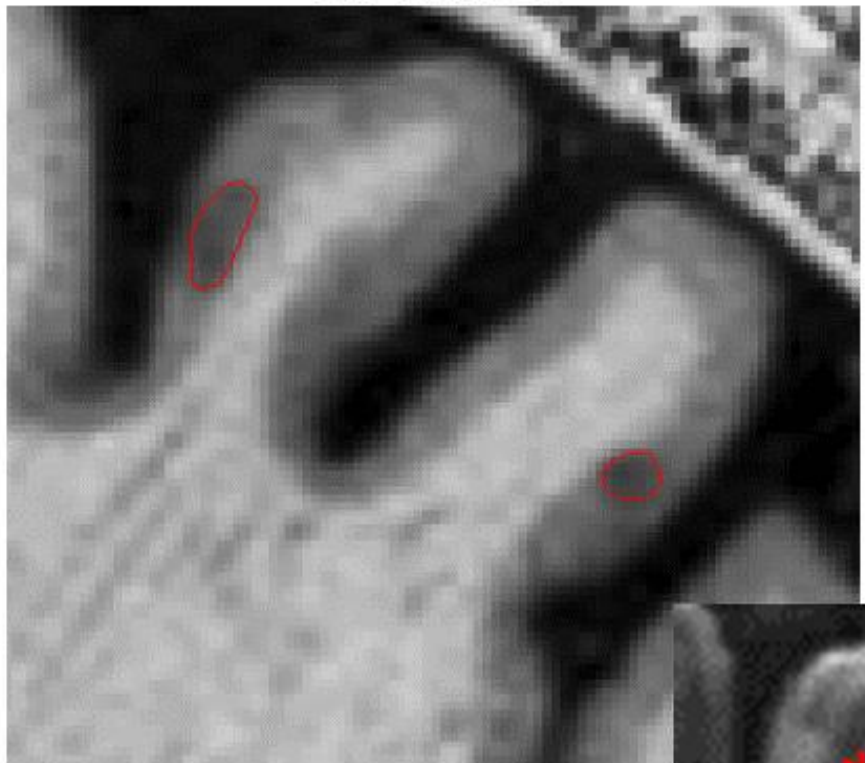
EXPERT CONSENSUS DOCUMENT

The central vein sign and its clinical evaluation for the diagnosis of multiple sclerosis: a consensus statement from the North American Imaging in Multiple Sclerosis Cooperative

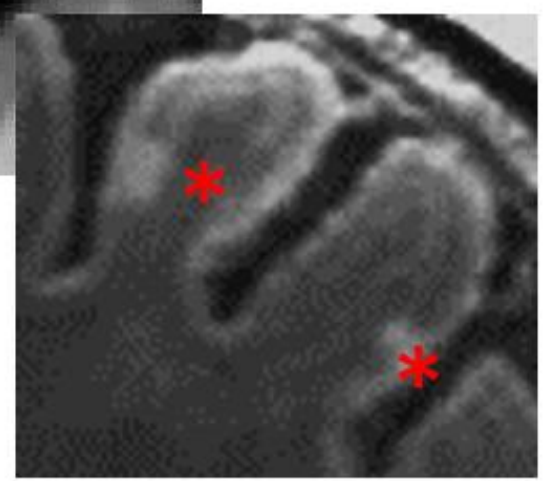
Pascal Sati[1], Jiwon Oh[2,3], R. Todd Constable[4], Nikos Evangelou[5], Charles R. G. Guttmann[6], Roland G. Henry[7], Eric C. Klawiter[8], Caterina Mainero[9], Luca Massacesi[10], Henry McFarland[1], Flavia Nelson[11], Daniel Ontaneda[12], Alexander Rauscher[13], William D. Rooney[14], Amal P. R. Samaraweera[5], Russell T. Shinohara[15], Raymond A. Sobel[16], Andrew J. Solomon[17], Constantina A. Treaba[9], Jens Wuerfel[18], Robert Zivadinov[19], Nancy L. Sicotte[20], Daniel Pelletier[21] and Daniel S. Reich[1] on behalf of the NAIMS Cooperative

Cortical Lesions: 7T MRI and Neuropathology

MP2RAGE



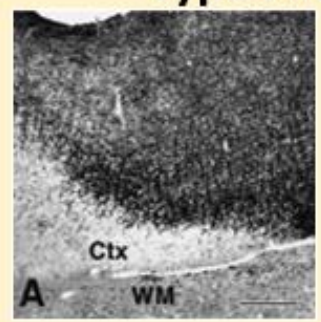
FLAIR

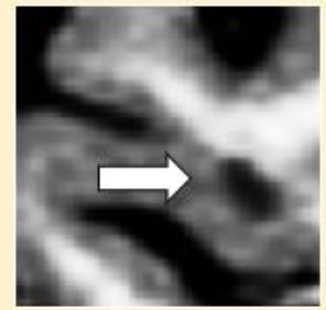


HARVARD MEDICAL SCHOOL

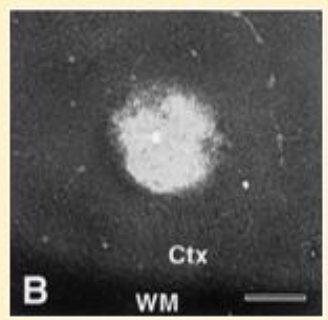
Myelin Histology BWH 7T MRI

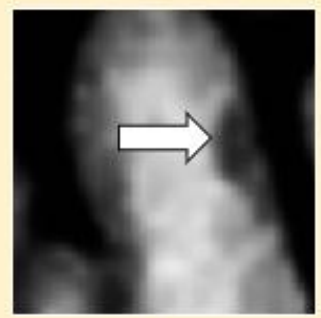
Type I - Leukocortical



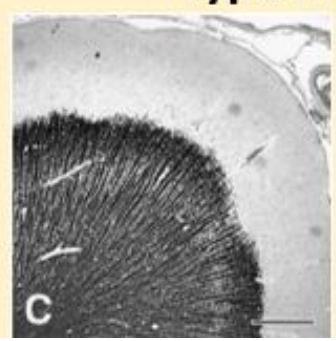


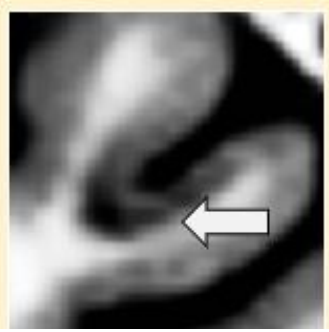
Type II - Intracortical





Type III - Subpial



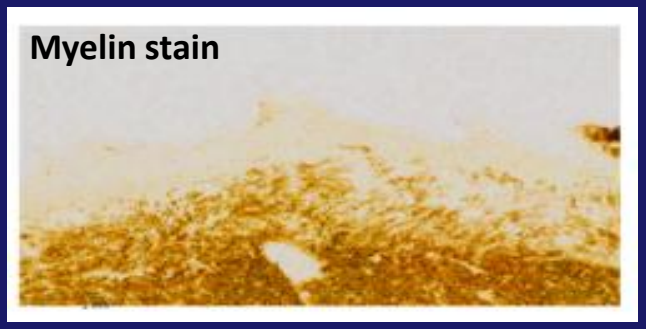


Thalamic Gray Matter Lesions

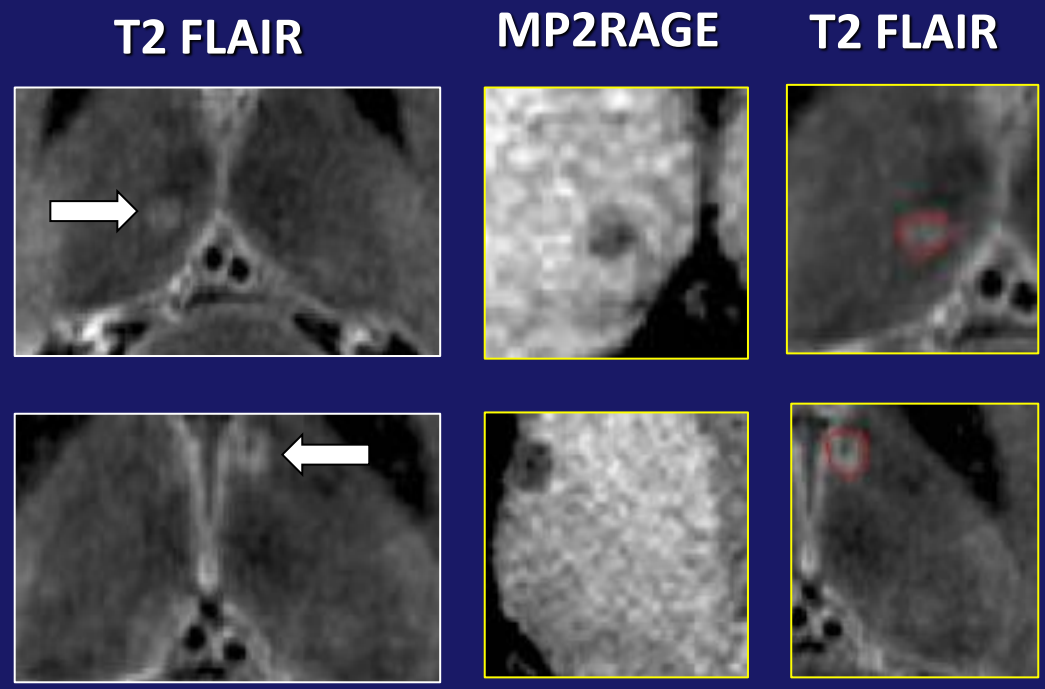
Mahajan et al. Ann. Neurol. 2020

Ovoid

Subependymal

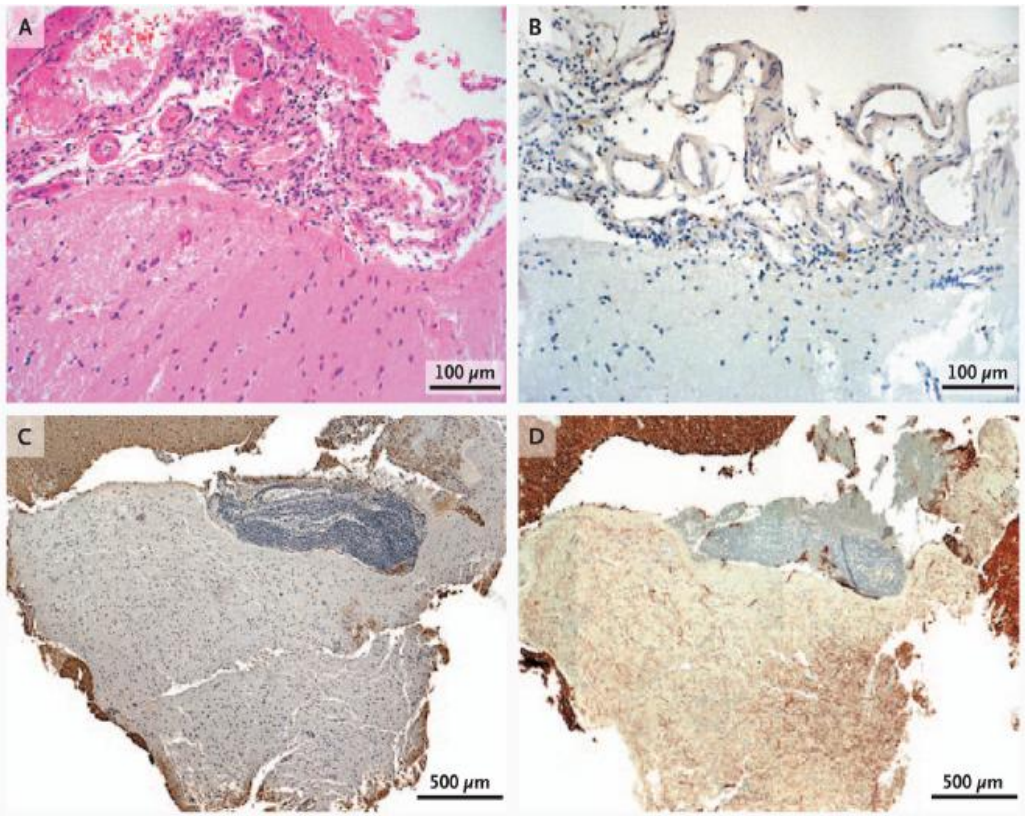


7T MRI Lesions - BWH



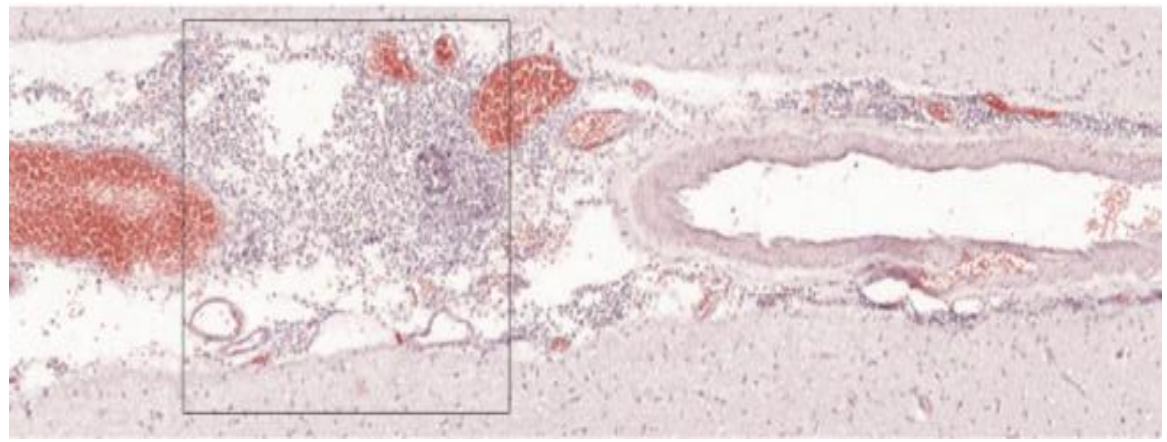
Leptomeningeal Inflammation and Gray Matter Demyelination in MS

Early MS (n=77) 58 RR, 19 CIS

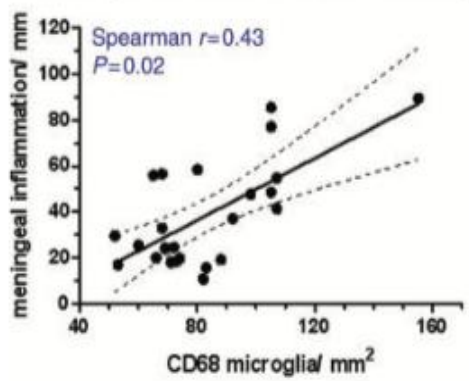


Lucchinetti et al. *NEJM* 2011

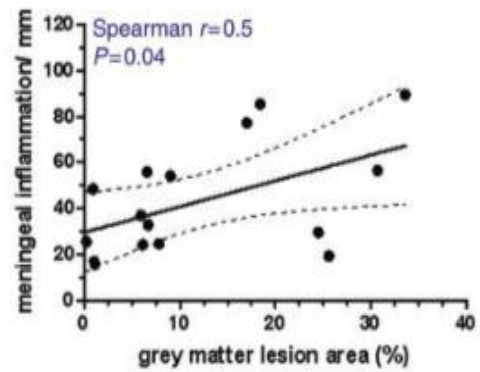
SPMS (n=123)



Meningeal infiltrates & cortical microglia

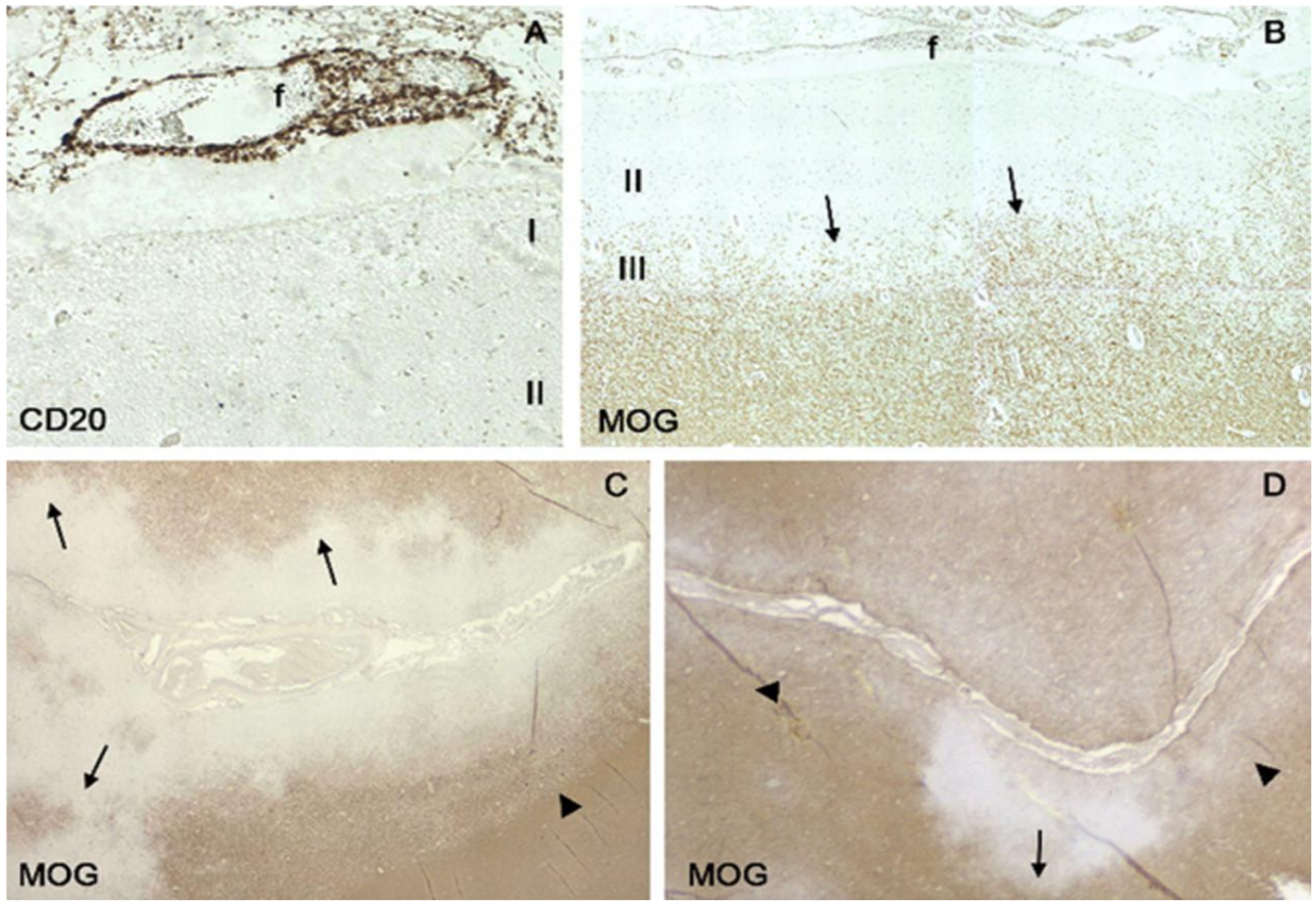


Meningeal infiltrates and grey matter lesions



Howell et al. *Brain* 2011

Meningeal B-Cell Follicles in MS



Follicle (+) Demyelination

Follicle (-) Demyelination

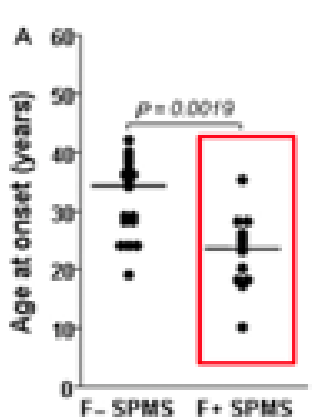
29 SPMS Patients

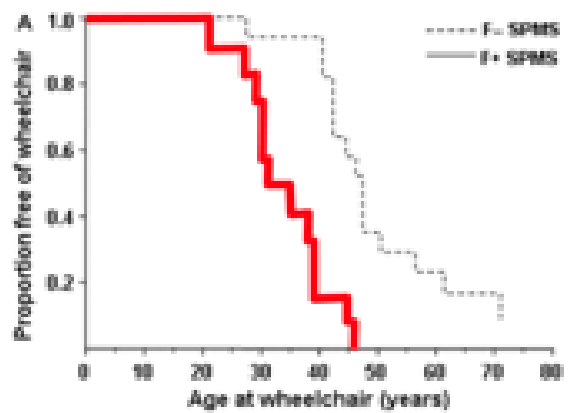
Postmortem Histology

1. **B-cell meningeal follicles are present in 40% of SPMS cases**

2. **Follicles are topographically associated with more extensive cortical demyelination.**

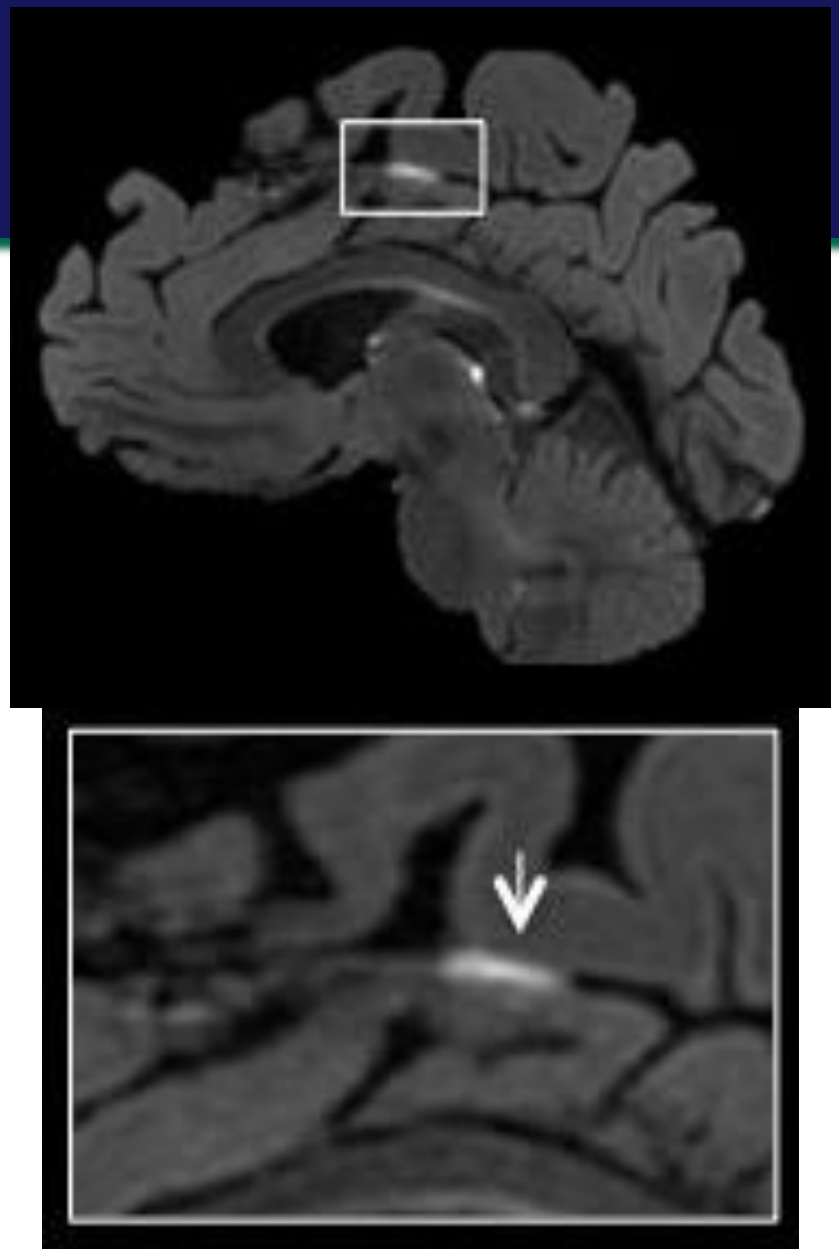
3. **3. Follicle-positive patients have more severe clinical course**





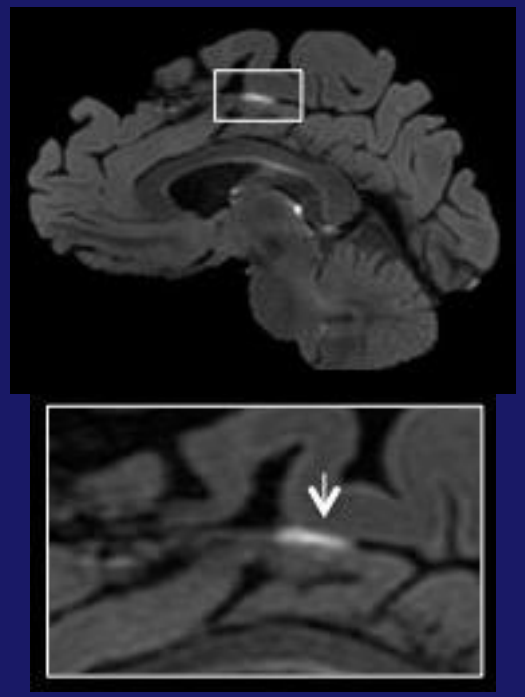
Magliozzi et al. *Brain* 2007;130:1089–1104.

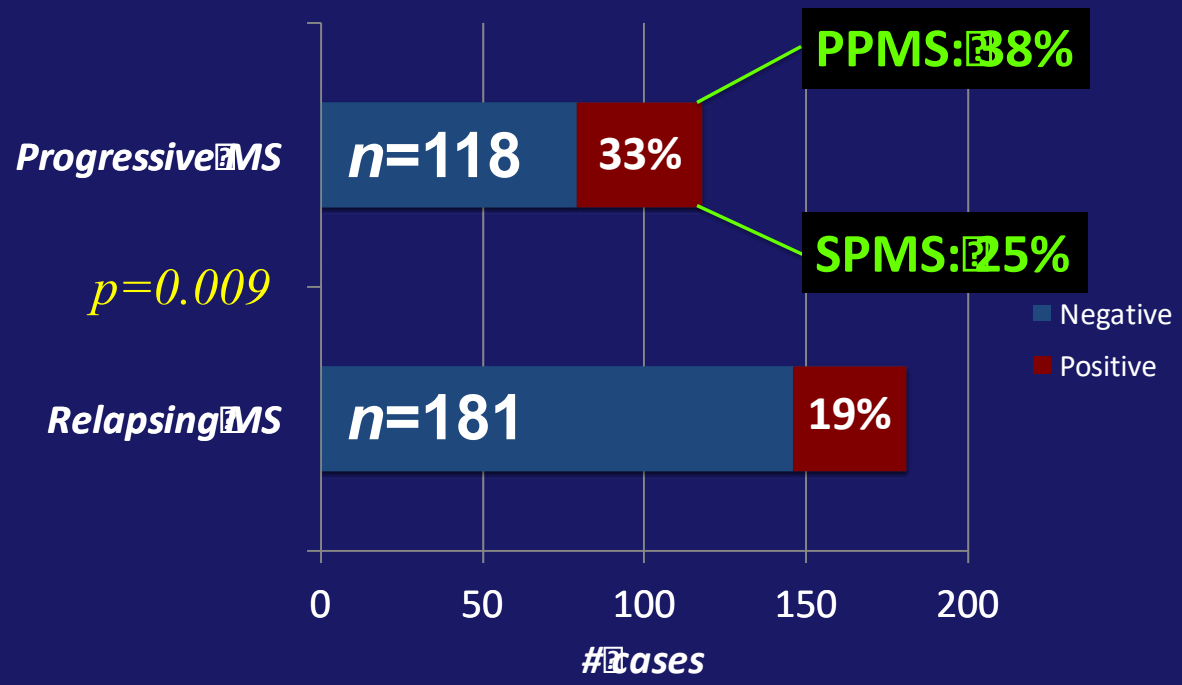
MRI Detection of Meningeal Inflammation In Vivo?

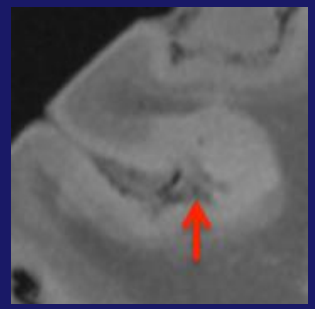


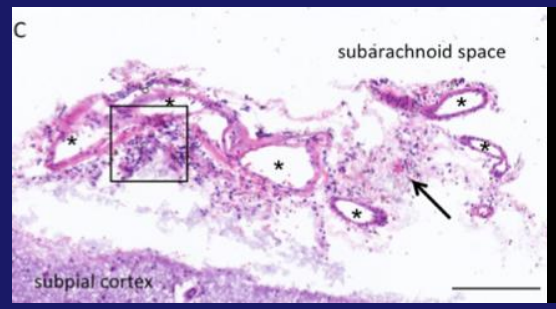
- ✓ **Hypothesis:** Localized meningeal fibrosis near meningeal follicles leads to trapping of small amounts of intravenous contrast within the subarachnoid space.
- ✓ **Post-contrast T2 FLAIR with delayed image acquisition (10 min post-Gad) has >10-fold increased sensitivity** for detection of contrast enhancement compared to routine T1 Gad at 3T.
- ✓ Comparison of pre- and post-contrast images demonstrates subtle foci of **leptomeningeal enhancement (LME)**

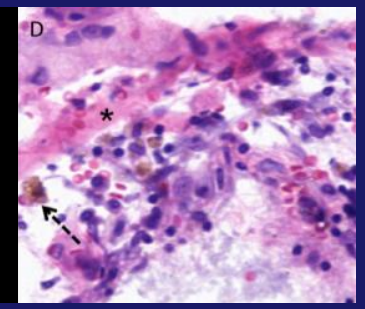
Leptomeningeal Enhancement in MS (3T)











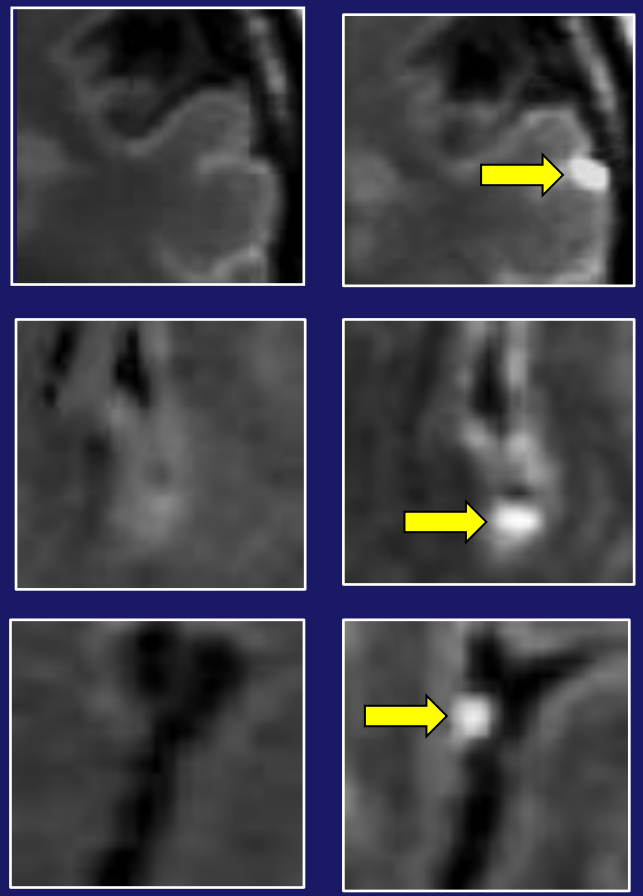
Absinta et al. Neurology 2015;85:18-28

7T MRI Leptomeningeal Enhancement

6 case examples are shown

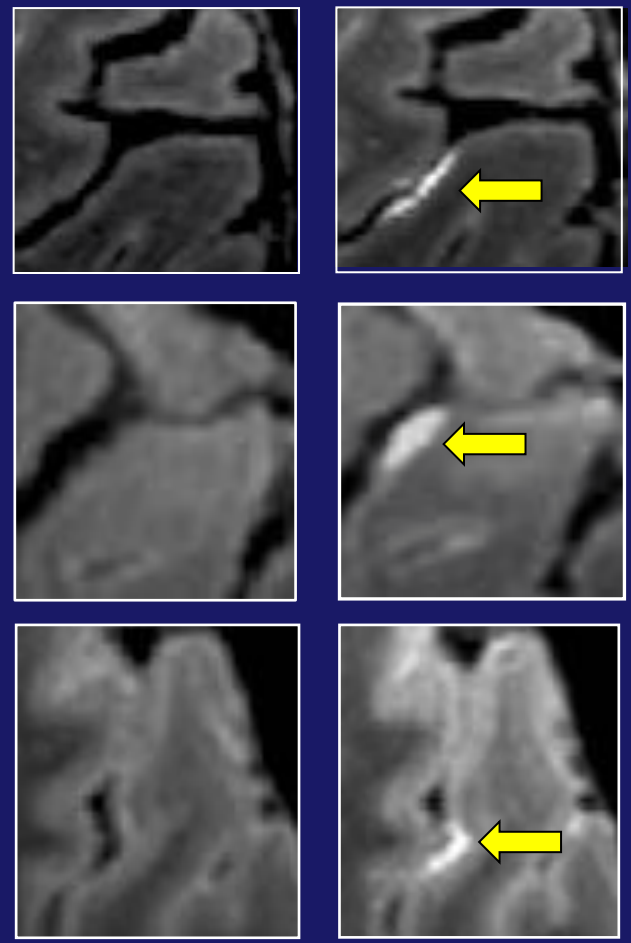
Nodular

Sag FLAIR Pre-Gad | Sag FLAIR Post-Gad



Spread

Sag FLAIR Pre-Gad | Sag FLAIR Post-Gad



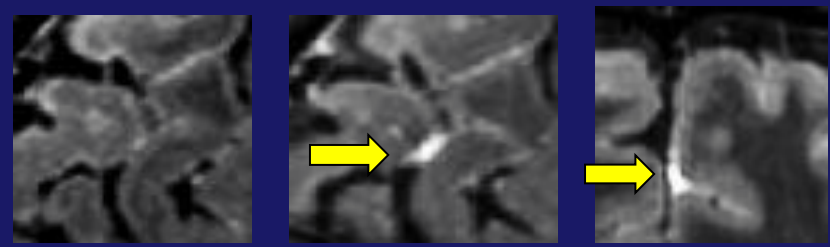
RRMS LME+ = 20/30 (67%)

Mean 2.8 ± 1.5 foci [range 1-5]

Normal Controls

1 of 15 (6.7%) had single LME focus

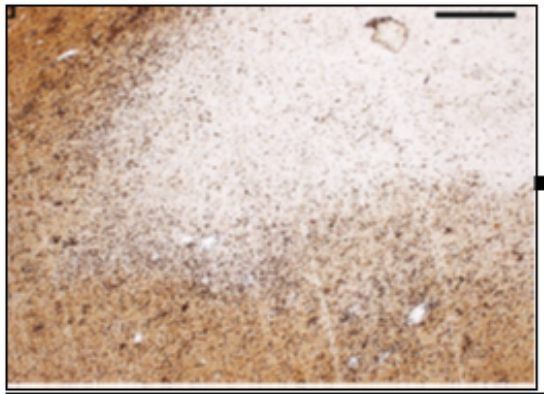
Sag Pre-Gad | Sag Post-Gad | Ax Post-Gad

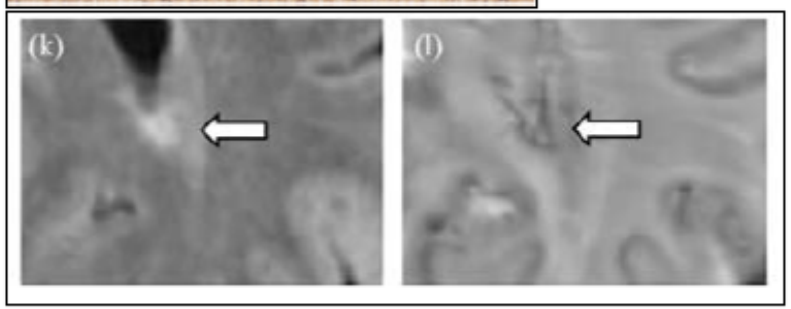


T2 FLAIR

Zurawski et al. *MSJ* 2020

Chronic Active Lesions (CALs) and Paramagnetic Rim Lesions (PRLs)

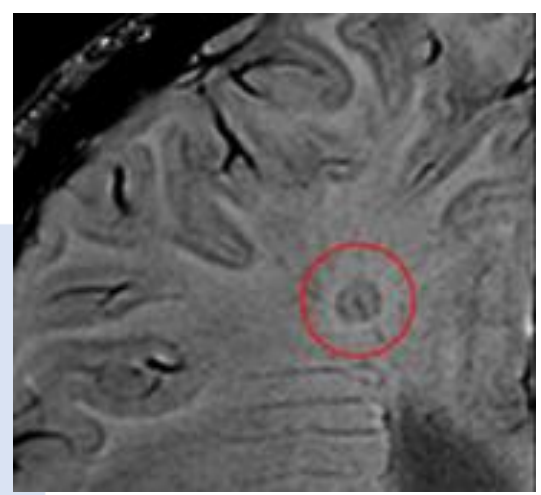




CALs are *chronic MS white matter lesions* characterized by a **rim of activated microglia** with ongoing myelin degradation products

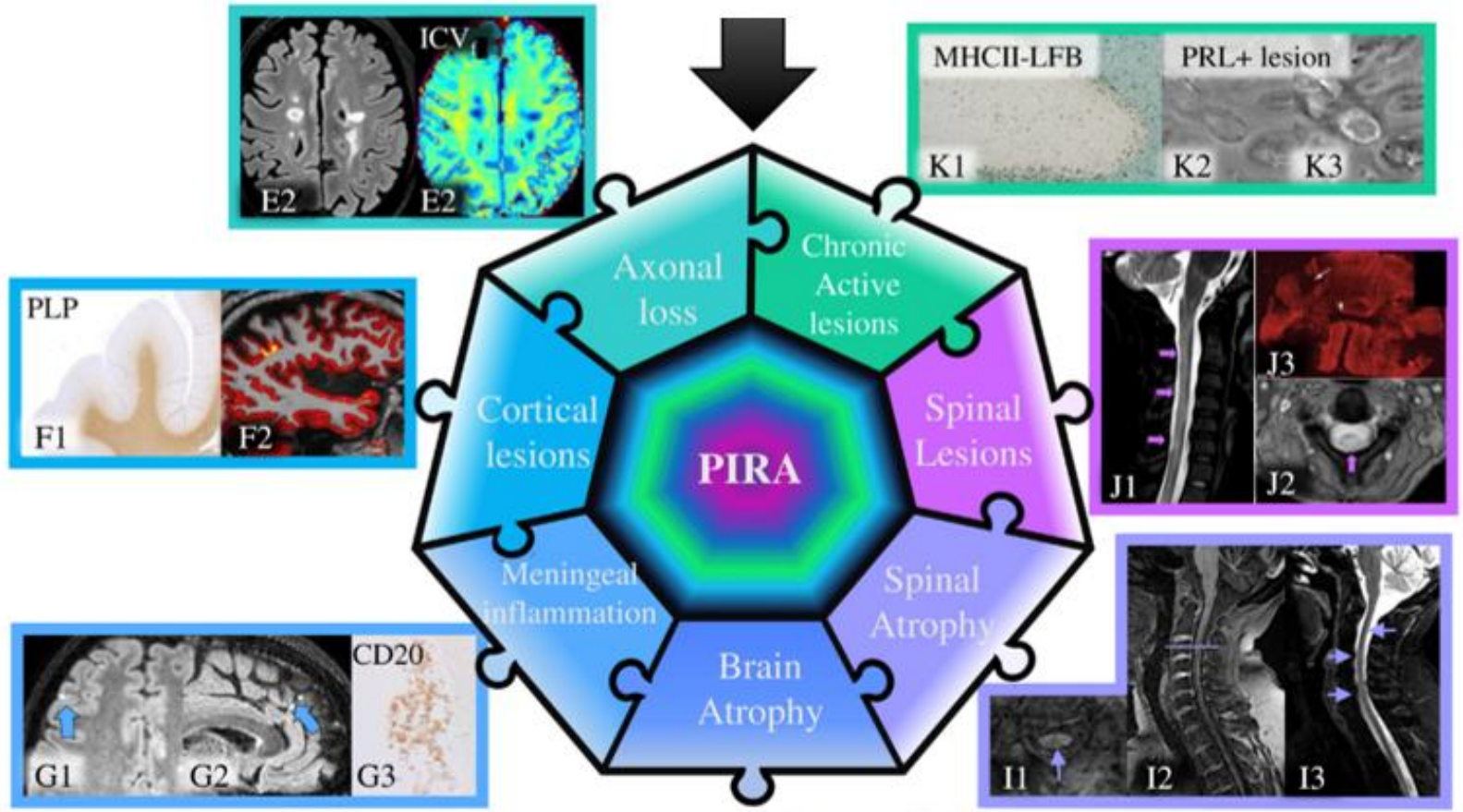
Evident in 78% of SP/PPMS cases in a large histopathologic validation study, and have **strong correlation with disease severity**

- **PRLs:** A subset of CALs are visualized using specialized MRI sequences, (T2*, phase contrast, R2*, QSM). MRI-neuropathological studies show the **paramagnetic rim correlates with iron accumulation in microglia**
- Pooled analysis of 31 MRI studies showed: **PRLs found in ~50% of RRMS and ~60% of progressive MS cases**.
- In a 4-year longitudinal study evaluating PRLs and PIRA: Patients on anti-CD20 therapy **with PIRA had higher baseline PRL counts**
- PRLs have now been adopted as supporting diagnostic criteria for MS



Luchetti, S. et al. *Acta Neuropath* (2018) 135: 511-528
Calabrese et al., *Annals Neurol* 2024;96:1-20.

Pathogenesis of Progression Independent of Relapse (PIRA)



Pathological changes

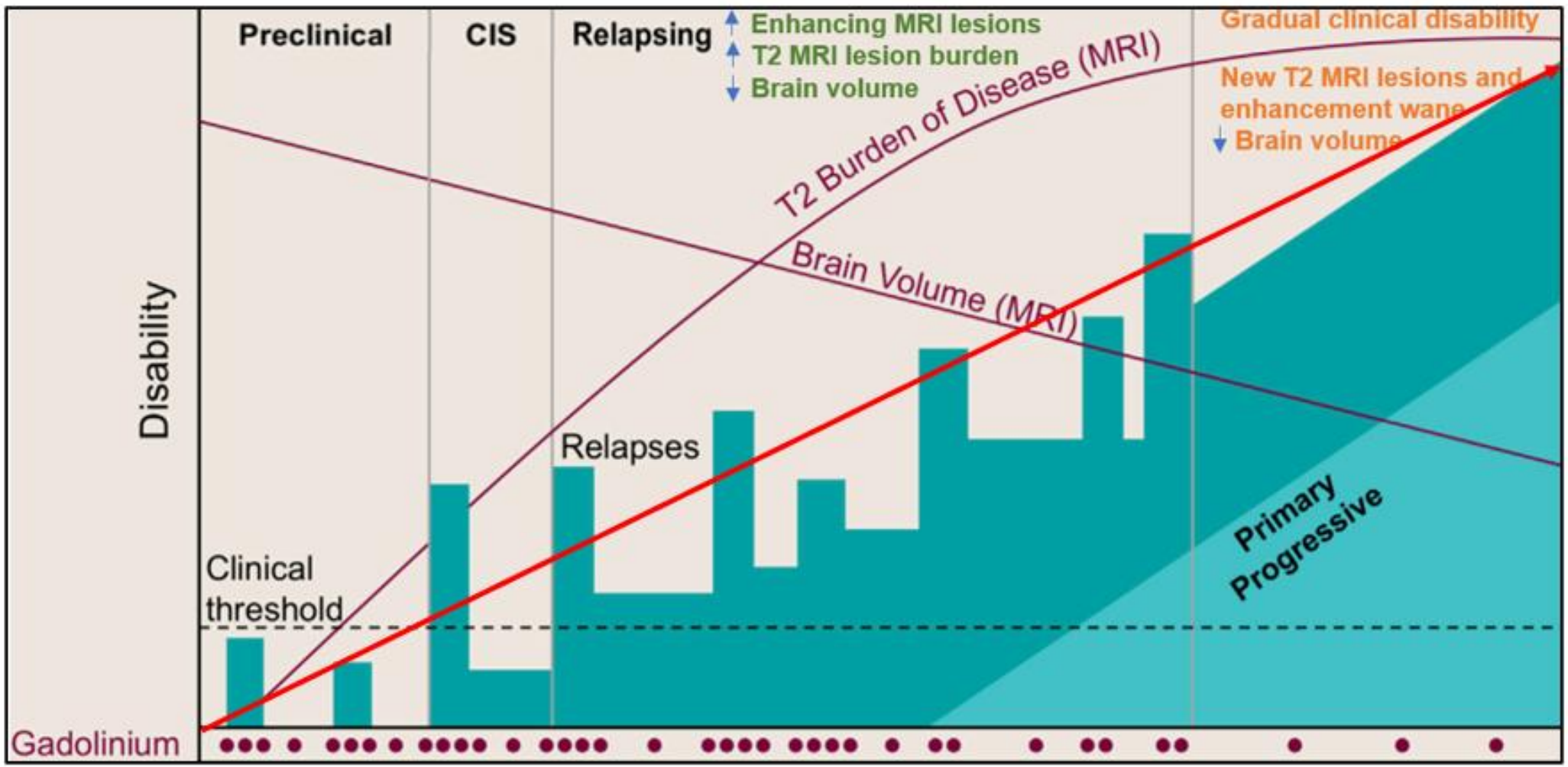
- Inflammation
- New waves of lymphocytes entering the CNS
- Blood–brain barrier disturbance
- New active CNS lesions
- Initial remyelination in active lesions

- Trapped inflammation
- Meningeal inflammatory aggregates
- Slow expansion of pre-existing lesions
- Subpial cortical demyelination
- Diffuse white matter injury
- Brain atrophy

Calabrese et al., *Annals Neurol 2024*

Reframing Progression?

Progression Independent of Relapse Activity (PIRA)



7T MRI and the Translational Research Program at BWH

LME is Related to Cortical and Thalamic Lesion Burden

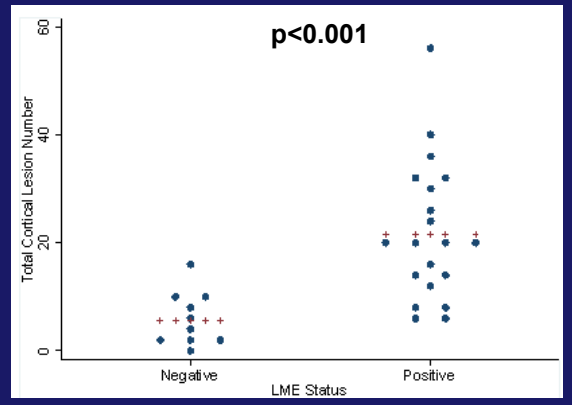
Cortical Lesions

	LME+	LME-	p-value
CL Number	**21.5 ± 12.6**	5.5 ± 5.0	<0.001
CL Volume (ml)	**0.80 ± 1.13**	0.13 ± 0.13	0.002

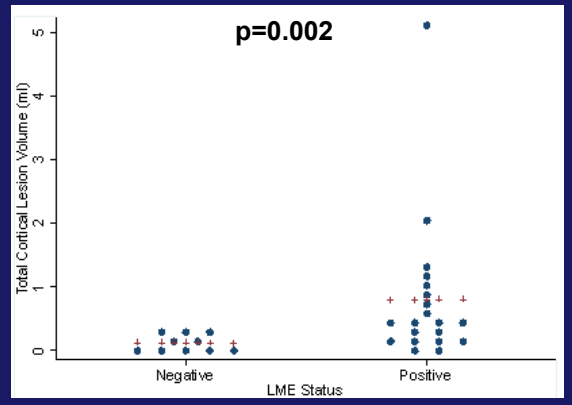
Thalamic Lesions

	LME+	LME-	p-value
TL Number	**3.95 ± 2.11**	0.70 ± 1.34	<0.001
TL Volume (ml)	**0.106 ± 0.09**	0.007 ± 0.01	<0.001

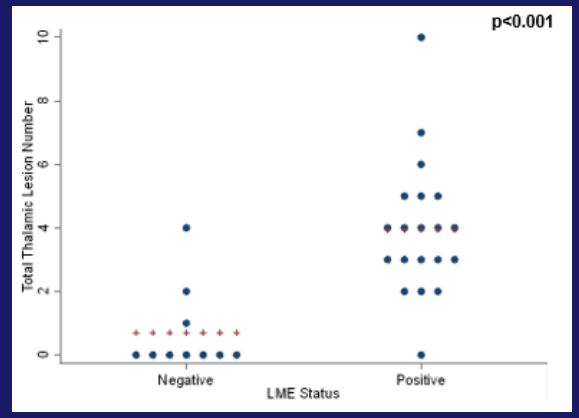
CL Number vs. LME



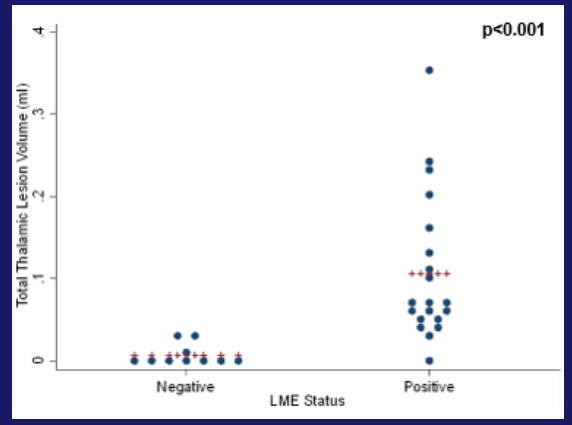
CL Volume vs. LME



Thalamic Lesion Number vs. LME



Thalamic Lesion Volume vs. LME



CL= cortical lesion; TL = thalamic lesion; LME = leptomeningeal enhancement

Zurawski et al. *MSJ 2020.*

Leptomeningeal Enhancement: 1-Year On-Study Change

LME Foci Number Correlation with On-Study Change

Variable	R_s	p-value
EDSS	0.10	0.63
Brain T2LV	0.50	0.01
BPV	0.28	0.17
Cortical Lesion Number	0.17	0.13
Cortical Lesion Volume	0.36	0.08
Thalamic Lesion Number	0.13	0.54
Thalamic Lesion Volume	0.24	0.24

- Baseline LME foci number correlates with 1-year change in WMLV (r=0.50, p=0.01) and shows a trend for CL volume change (r=0.36, p=0.08)

LME+ Cohort

	Baseline	Follow-up	p-value
T2 WMLV (ml)	11.0 ± 14.4	12.6 ± 16.3	<0.0001
CL number	22.9 ± 12.9	24.6 ± 14.9	0.01
CL volume (ml)	0.9 ± 1.2	1.0 ± 1.4	0.002
TL number	4.1 ± 2.3	4.3 ± 2.5	0.34
TL volume (ml)	0.10 ± 0.09	0.12 ± 0.10	0.005

LME+ subjects had on-study increase in:

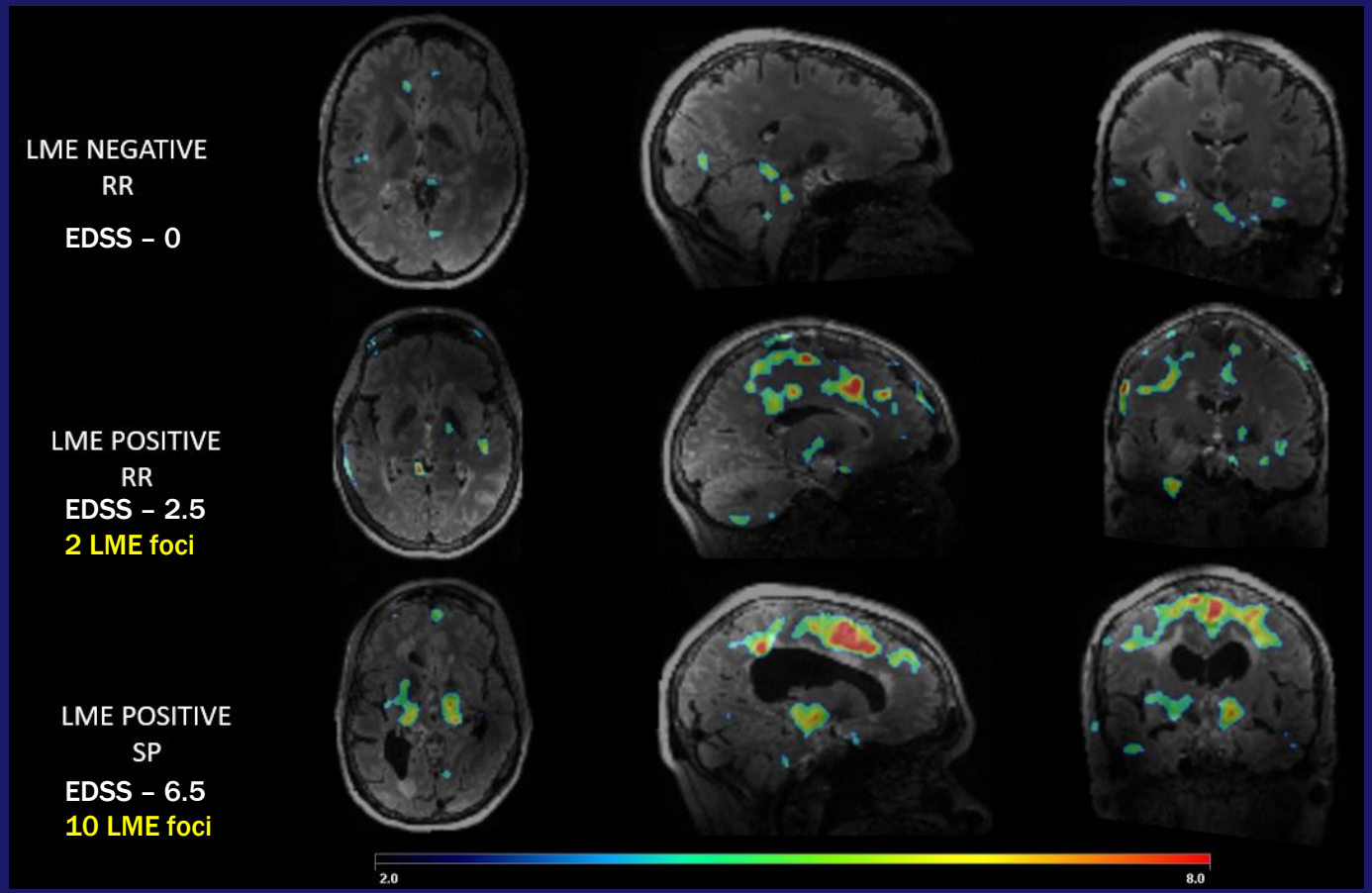
- WM lesion volume
- Cortical lesion number and volume
- Thalamic lesion volume

LME- Cohort

	Baseline	Follow-up	p-value
T2 WMLV (ml)	2.7 ± 2.3	3.3 ± 2.6	0.02
CL number	5.5 ± 5.2	5.9 ± 5.5	0.15
CL volume (ml)	0.1 ± 0.1	0.2 ± 0.2	0.27
TL number	0.9 ± 1.5	1.0 ± 1.4	1
TL volume (ml)	0.01 ± 0.01	0.01 ± 0.01	0.36

LME- subjects had on-study increase in WM lesion volume only.

LME Status and Brain ^{18}F-PBR06-PET Microglial Activity



Disease Category	LME Foci Number	Global SUV	Global GALP	Cortical GM GALP	Thalamus GALP	WM GALP
LME- RRMS	0	0.54	9664	6993	144	1990
LME+ RRMS	2	1.03	67251	34247	190	32145
LME+ SPMS	10	1	53554	16431	3045	33505

Singhal & Zurawski et al. unpublished

Nasal Foralumab in Non-active SPMS at BWH

'Non-active' SPMS:

- Ages 25-70
- EDSS score between 2.5 - 6.5
- SPMS clinical designation
- No relapses in the previous 2 years
- 6 months of disability accumulation while on DMT prior to enrollment

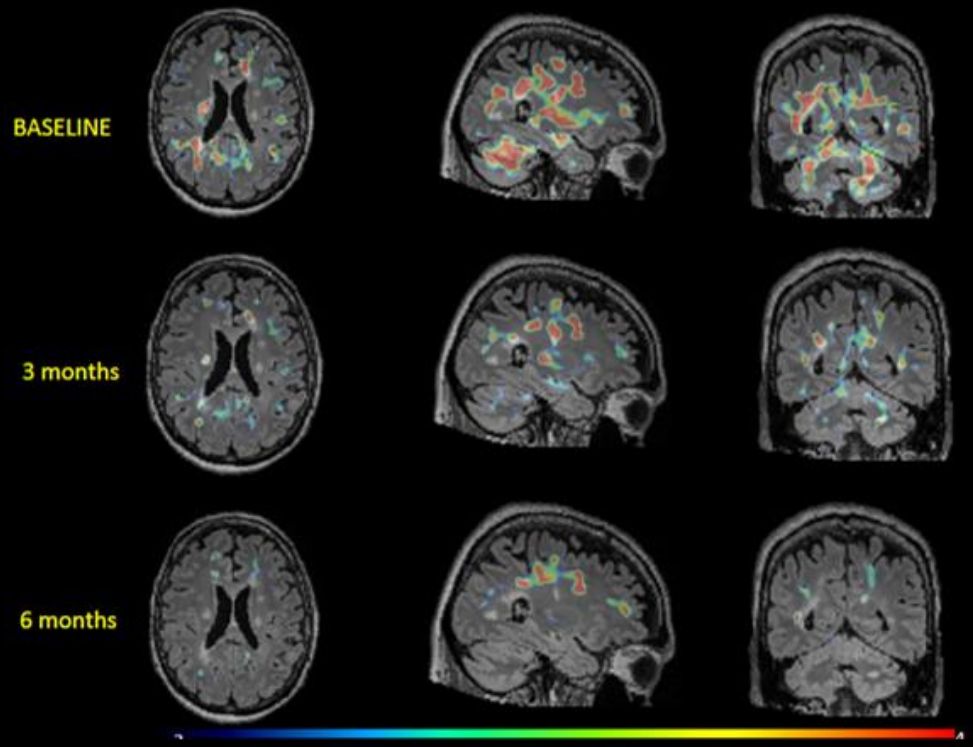
Treatment Regimen:

Nasal foralumab 50 µL per day, three times per week, for two weeks followed by 1 week off treatment.

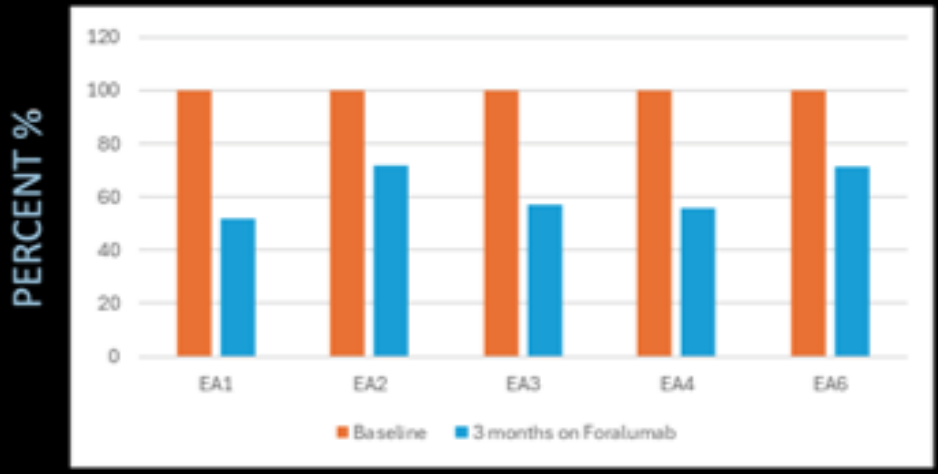
Outcomes:

- EDSS, 25-foot walk, Fatigue (MFIS)
- 3T, 7T MRI & PET scans at baseline and every three months.

Nasal foralumab stabilizes progression independent of relapse (PIRA) in MS



3-MONTH CHANGE IN WM Z-SCORES ON NASAL FORALUMAB



Stability of LME and Cortial Lesions

	7T Baseline				6-Month Follow-Up			
	LME Status	LME Foci Number	CL Number	CL Volume (mL)	LME Status	LME Foci Number	CL Number	CL Volume (mL)
EA1	+	3	31	0.80	+	2	31	0.77
EA2	+	7	32	1.60	+	7	32	1.55
EA3	+	7	47	1.92	+	6	47	1.85
EA4	+	2	18	0.44	+	2	18	0.43
EA5	+	4	13	0.35	+	4	13	0.33
EA6	+	7	17	0.50	+	9	17	0.50
Mean	100%	5	26.3	0.94	100%	5	26.3	0.90
St Dev		2.3	12.8	0.66		2.8	12.8	0.64

Improvement in Clinical Outcomes

	EDSS	Pyramidal score	T25FW	MFIS
EA1	–	↓	–	–
EA2	↓	–	↓	↓
EA3	–	–	↓	–
EA4	↓	–	–	↓
EA5	–	↓	↓	↓
EA6	–	–	–	↓

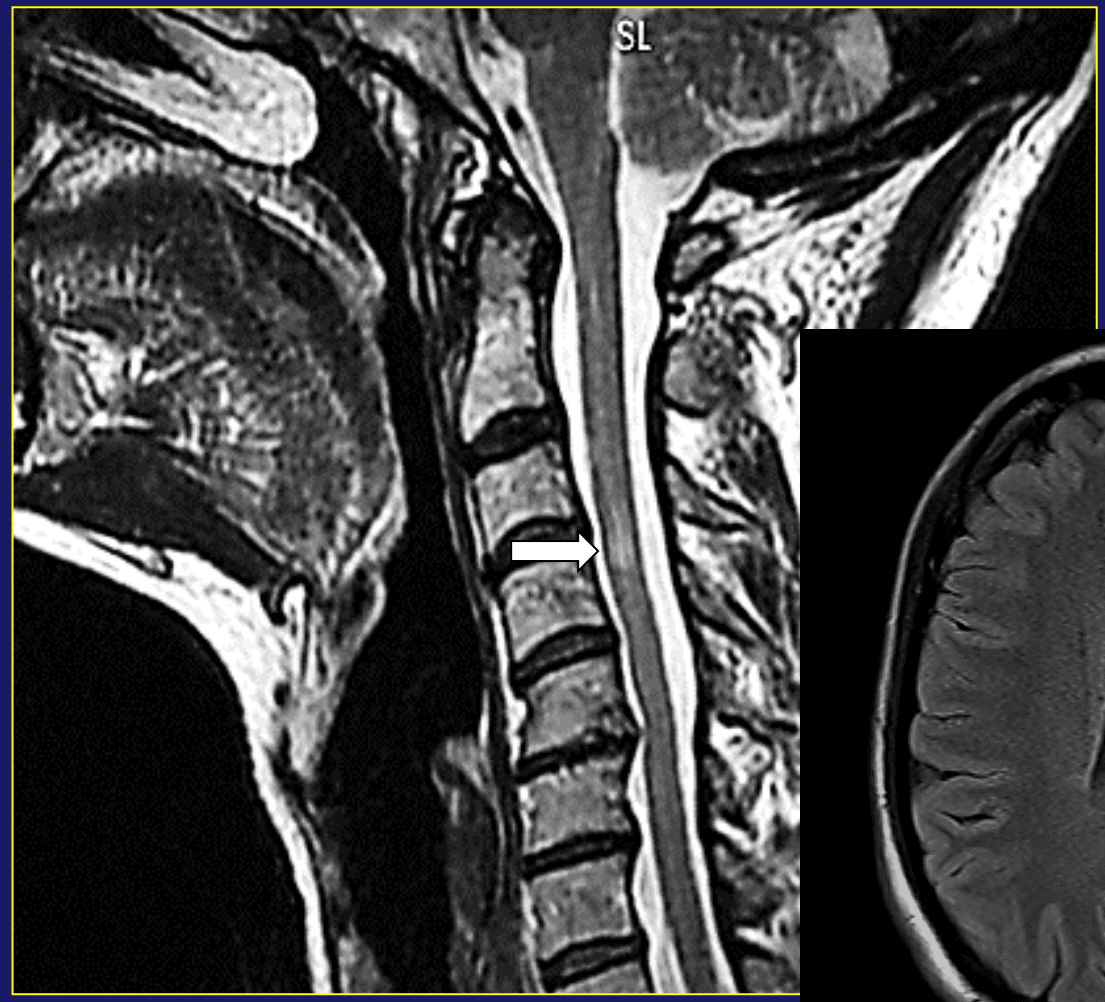
Singhal et al. AAN 2024, **Chitnis** et al. *Neurology & Neuronfl* 2025

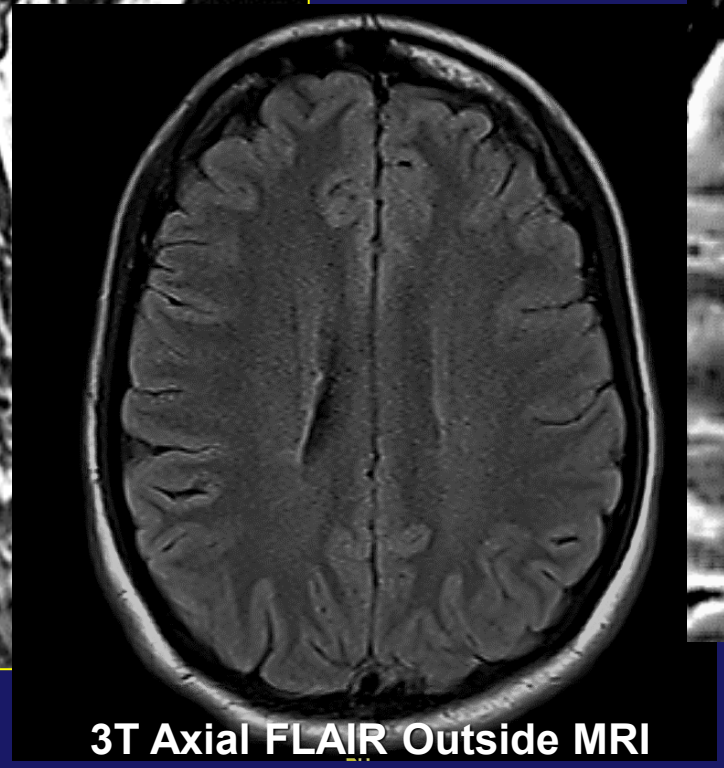
Applications of 7T MRI in the MS Clinic: Case Examples

Case 1: Making the MS Diagnosis

29-year-old F with an ‘isolated transverse myelitis’ has positive CSF oligoclonal bands

3T Sag STIR





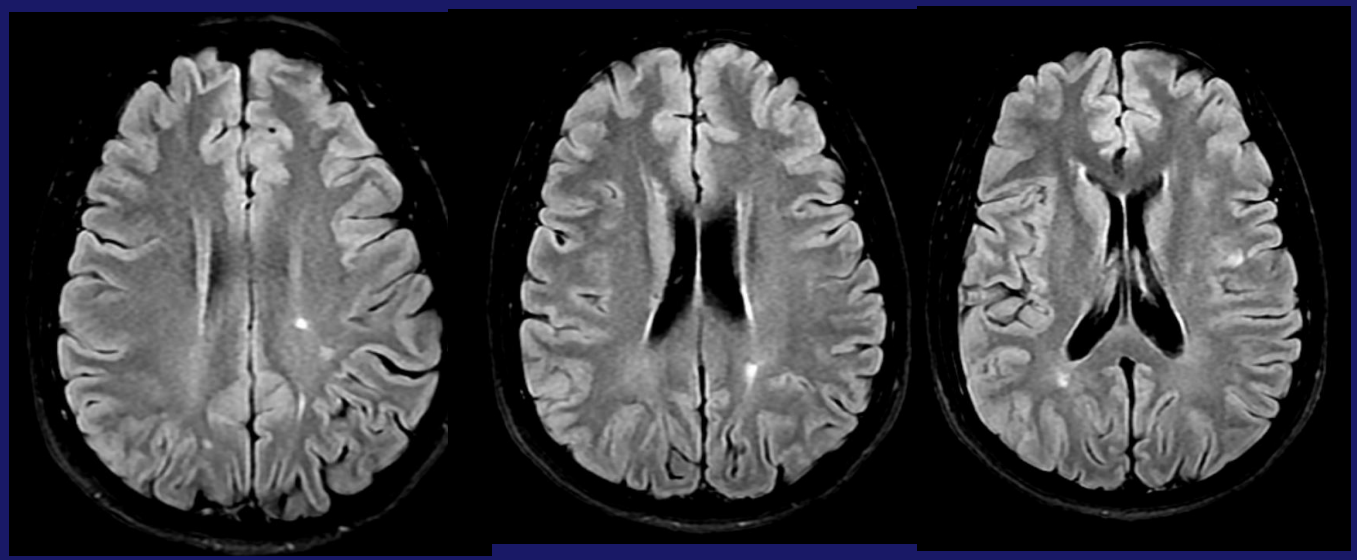
3T Axial FLAIR Outside MRI
‘No abnormality’

BWH 7T Axial FLAIR

T2* Central vein lesion

Case 2: Reassessing 'Possible MS'

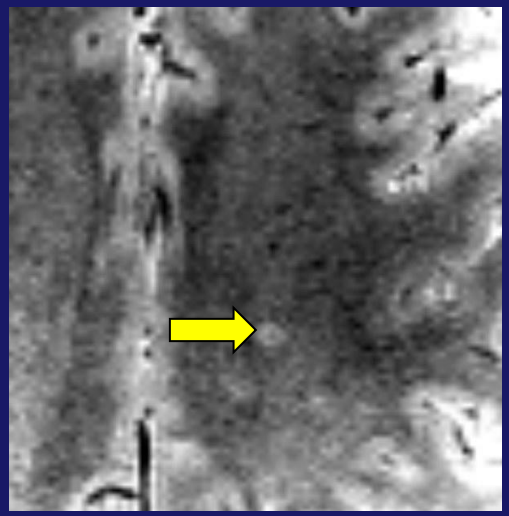
Outside 3T Ax FLAIR

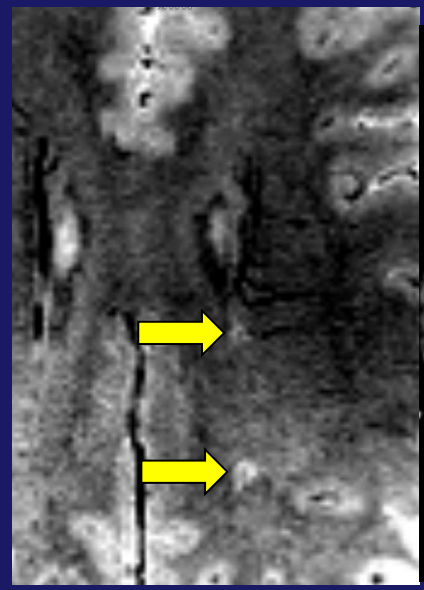


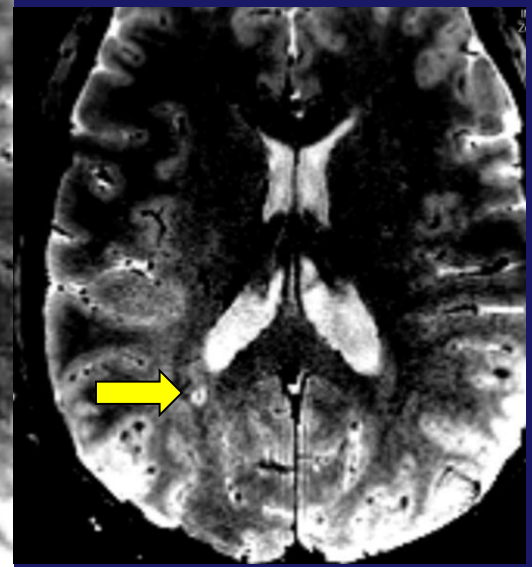
40-year-old woman with ocular migraines has an episodes of right eye vision loss different from her usual migraines. An eye exam and OCT are equivocal for neuritis.

MRI report: "Nonspecific FLAIR hyperintensities consistent with known history of migraine"

BWH 7T Axial T2*



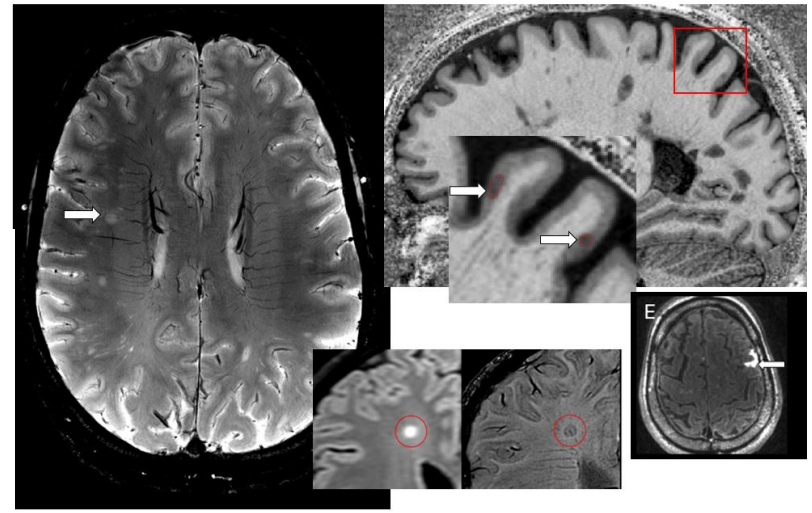




Case Outcome:

- 100% of evaluated lesions demonstrate central vein sign.
- Elevated risk of MS is suggested by 7T for MRI findings that were dismissed at 3T.
- Patient had LP, found with positive CSF OCBs, leading to MS diagnosis

Advantages of 7T MRI in the MS Clinic



1. Central vein sign: Aids in MS diagnosis (Revised 2024 McDonald Criteria), assessment of non-specific lesions for likely demyelinating etiology vs. diagnostic mimics
2. Paramagnetic rim lesions: Aids in MS diagnosis (Revised 2024 McDonald Criteria), prognostic value in assessing MS disease progression
3. Cortical lesions: 7T MRI doubles diagnostic yield for detection of CLs vs. 3T. CLs aid diagnosis (satisfy DIS criteria) and in prognosis related to disease progression
4. Leptomeningeal enhancement: Useful in assessing progression risk, used in tandem with CLs and PRLs

BRIGHAM HEALTH

BRIGHAM AND WOMEN'S HOSPITAL

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