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de Neurorradiología



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NEURORRADIOLOGÍA

SAN SEBASTIÁN

7 - 9 de noviembre de 2024



“2024 McDonald diagnostic criteria”

Àlex Rovira

Secció de Neurorradiologia. Servei de Radiologia

Hospital Universitari Vall d'Hebron

Barcelona

alex.rovira.idi@gencat.cat



International Advisory
Committee on Clinical
Trials in MS

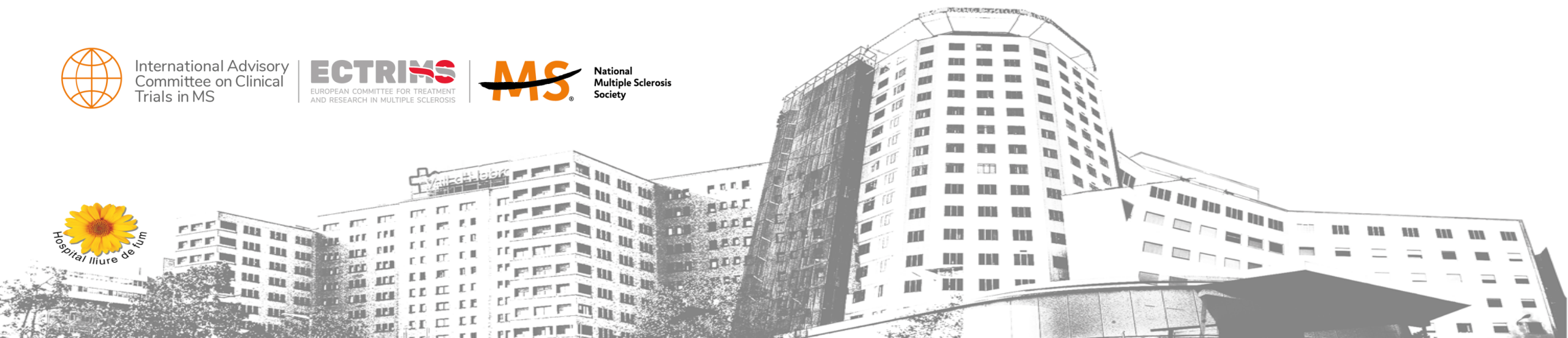
ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT
AND RESEARCH IN MULTIPLE SCLEROSIS

MS

National
Multiple Sclerosis
Society



Hospital lliure de fum

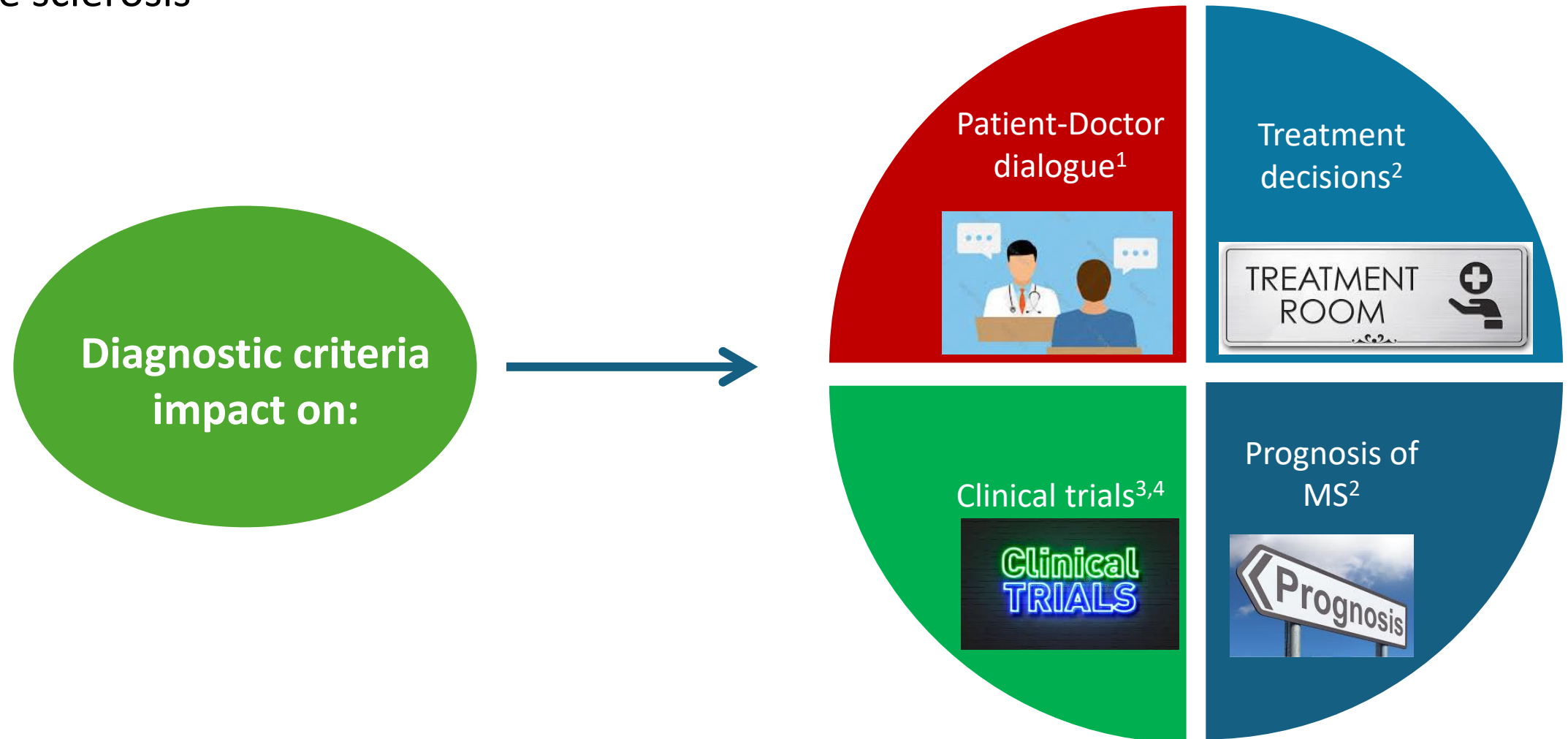


Disclosures

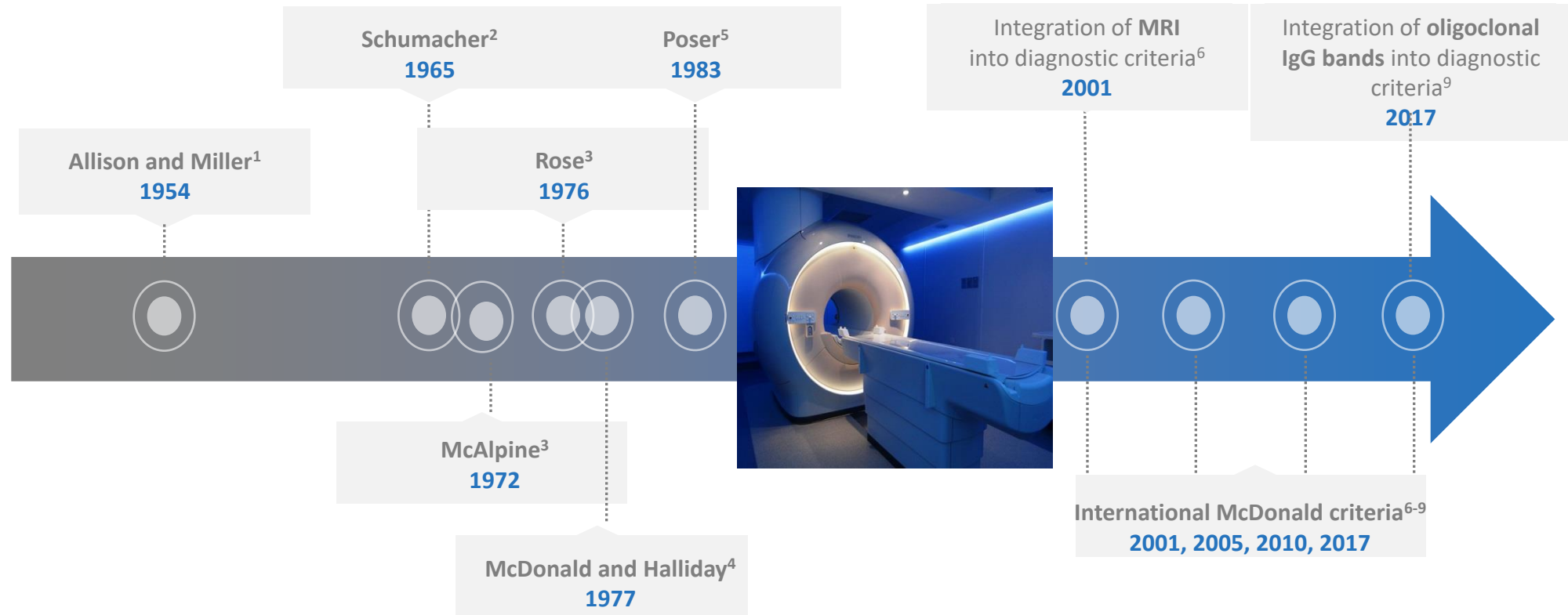
Àlex Rovira serves/ed on scientific advisory boards for Novartis, Sanofi-Genzyme, Synthetic MR, TensorMedical, Roche, and Biogen, and has received speaker honoraria from Bayer, Sanofi-Genzyme, Merck-Serono, Teva Pharmaceutical Industries Ltd, Novartis, Roche, Bristol-Myers and Biogen, is CMO and co-founder of TensorMedical

Diagnosis of Multiple Sclerosis

No single biomarker or clinical finding provides enough diagnostic accuracy for diagnosing multiple sclerosis



Diagnosis of Multiple Sclerosis through the ages

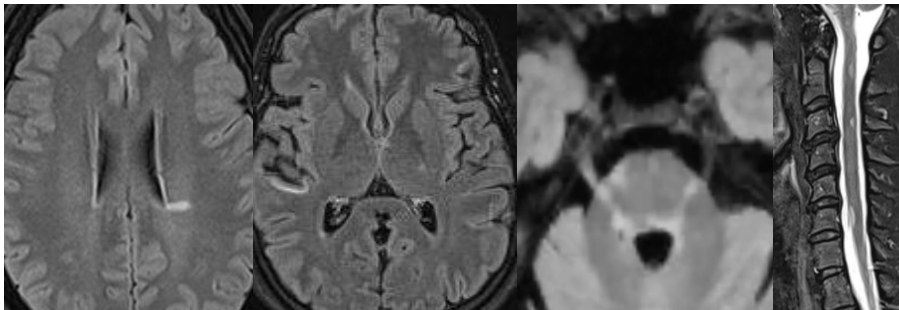


1. Allison and Millar. Ulster Med J. 1954;23(Suppl 2):1-27. 2. Schumacher et al. Ann N Y Acad Sci. 1965;122:552-568. 3. Gafson et al. Mult Scler Relat Disord. 2012;1:9-14. 4. McDonald and Halliday. Br Med Bull. 1977;33:4-9. 5. Poser et al. Ann Neurol. 1983;13:227-231. 6. McDonald et al. Ann Neurol. 2001;50:121-127. 7. Polman et al. Ann Neurol. 2005;58:840-846. 8. Polman et al. Ann Neurol. 2011;69:292-302. 9. Thompson et al. Lancet Neurol. 2018;17:162-173.

MS diagnosis: McDonald 2017 criteria

Dissemination in space (DIS)

- **≥1 T2 lesion* in 2 out of 4 regions of the CNS**
 - Periventricular
 - Cortical-Juxtacortical
 - Infratentorial
 - spinal cord



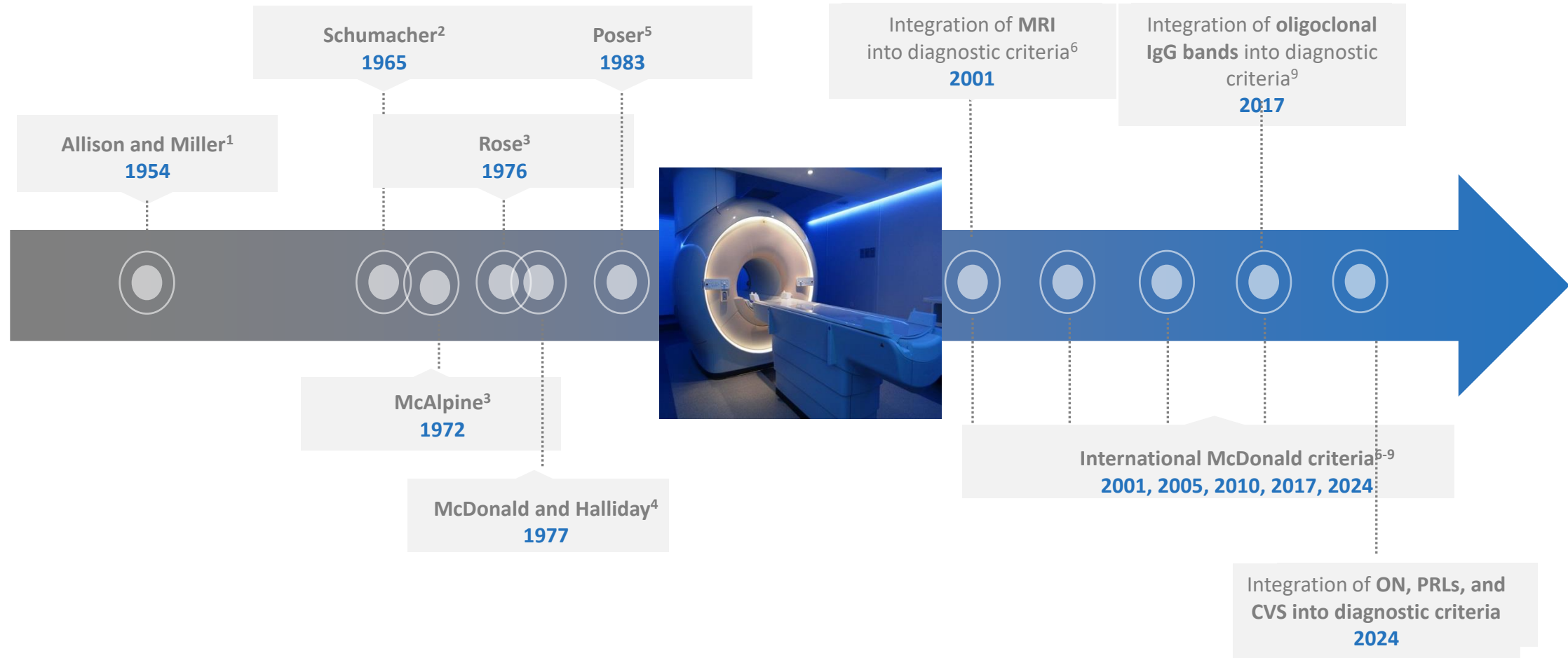
Dissemination in time (DIT)

- Simultaneous presence of Gd+ and non-enhancing lesions at any time
- New T2 and/or Gd+ lesion on follow-up MRI
 - Compared to reference (baseline) MRI
- Demonstration of DIS and presence of CSF specific oligoclonal bands

CNS= central nervous system; Gd=gadolinium, CSF=cerebrospinal fluid

*Gd not needed for demonstration of DIS

Diagnosis of Multiple Sclerosis through the ages



1. Allison and Millar. Ulster Med J. 1954;23(Suppl 2):1-27. 2. Schumacher et al. Ann N Y Acad Sci. 1965;122:552-568. 3. Gafson et al. Mult Scler Relat Disord. 2012;1:9-14. 4. McDonald and Halliday. Br Med Bull. 1977;33:4-9. 5. Poser et al. Ann Neurol. 1983;13:227-231. 6. McDonald et al. Ann Neurol. 2001;50:121-127. 7. Polman et al. Ann Neurol. 2005;58:840-846. 8. Polman et al. Ann Neurol. 2011;69:292-302. 9. Thompson et al. Lancet Neurol. 2018;17:162-173.

MS Diagnostic Criteria 2024

Proposed revisions

- **RIS is MS in specific situations (biological diagnosis)**
- **DIT** is not longer needed for diagnosis
- Need for paraclinical evidence to diagnose MS
- **Optic nerve may serve as a fifth topography**
- Updated DIS criteria
- **Addition of CVS and PRLs as optional paraclinical tools for diagnosis in certain situations**
- More strict features for confirming diagnosis in individuals over 50 years, or with headache disorders (including migraine), or with vascular disorders
- Laboratory tests (anti-MOG ab) for confirming diagnosis in children and adolescents
- Additional imaging features for PPMS diagnosis
- kFLCs as another tool to support diagnosis

2023 McDonald Criteria Review

29 Nov-2 Dec 2023

Barcelona, ES

*An Initiative of the International
Advisory Committee on Clinical Trials
in MS*



2023 McDonald Diagnostic Criteria Review Meeting
Barcelona, Spain

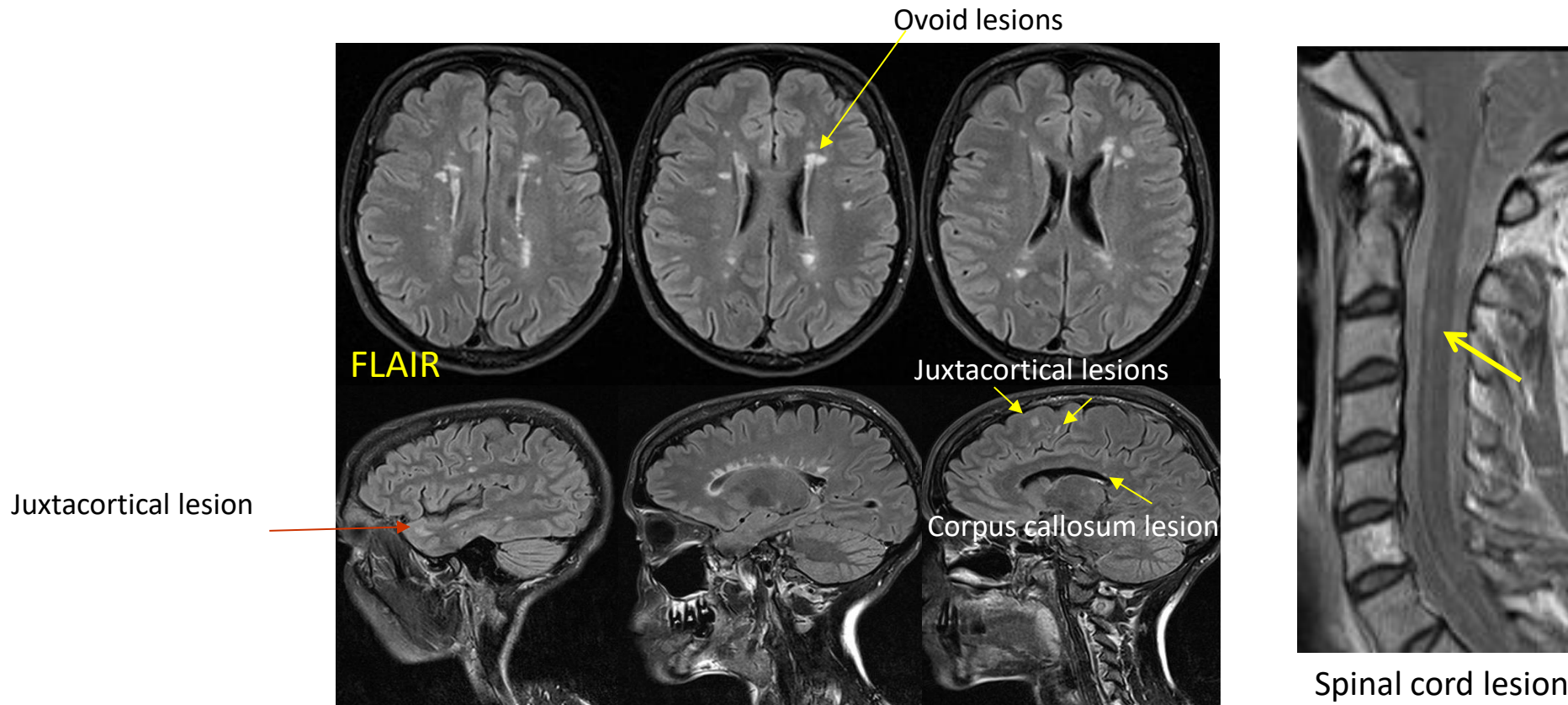


International Advisory
Committee on Clinical
Trials in MS

ECTRIMS
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AND RESEARCH IN MULTIPLE SCLEROSIS

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MS or incidental findings in a young male subject?



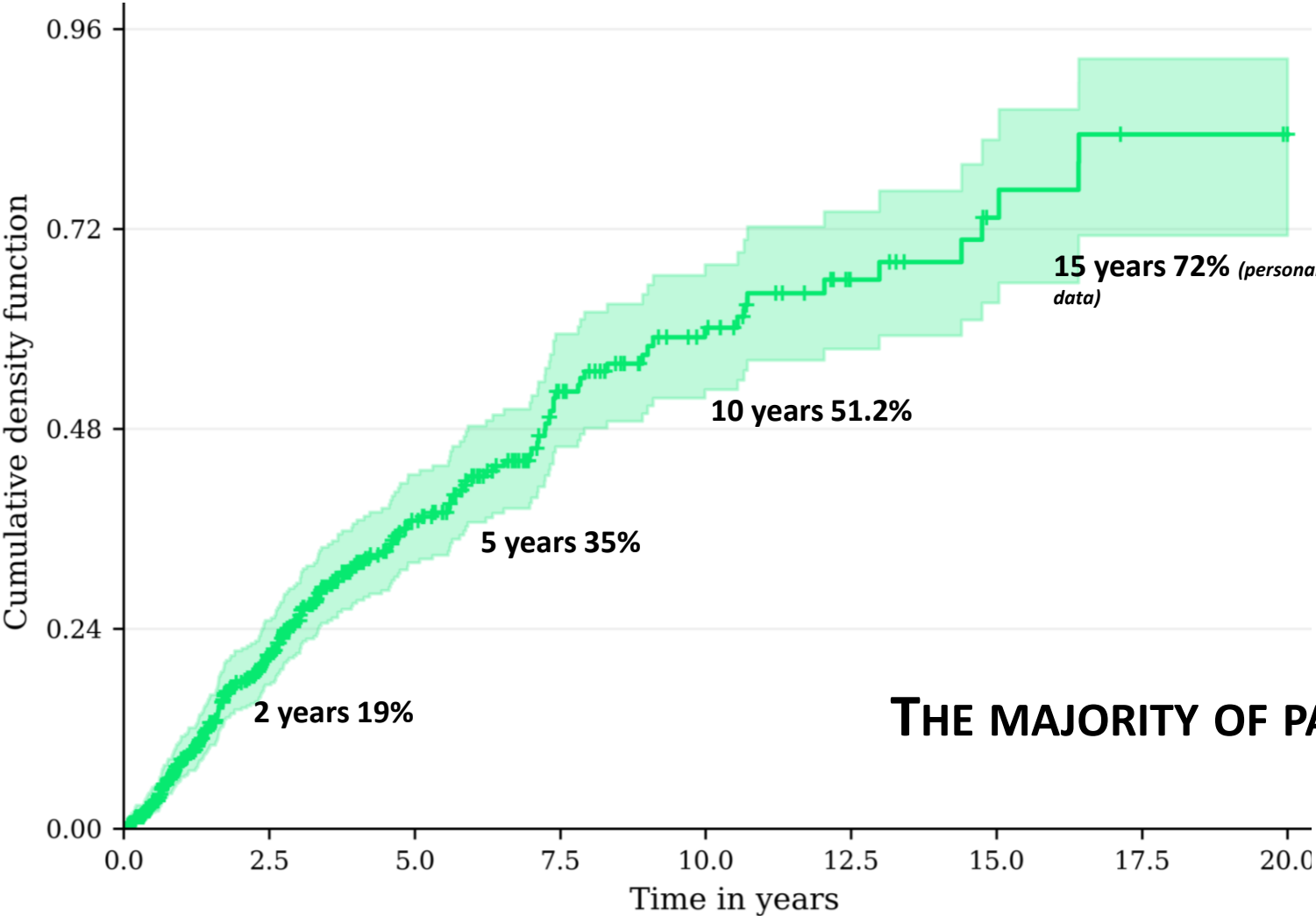
- Criteria for dissemination in space fulfilled
- Very high probability of a first clinical event

RIS / preclinical MS?



S C
Type 2

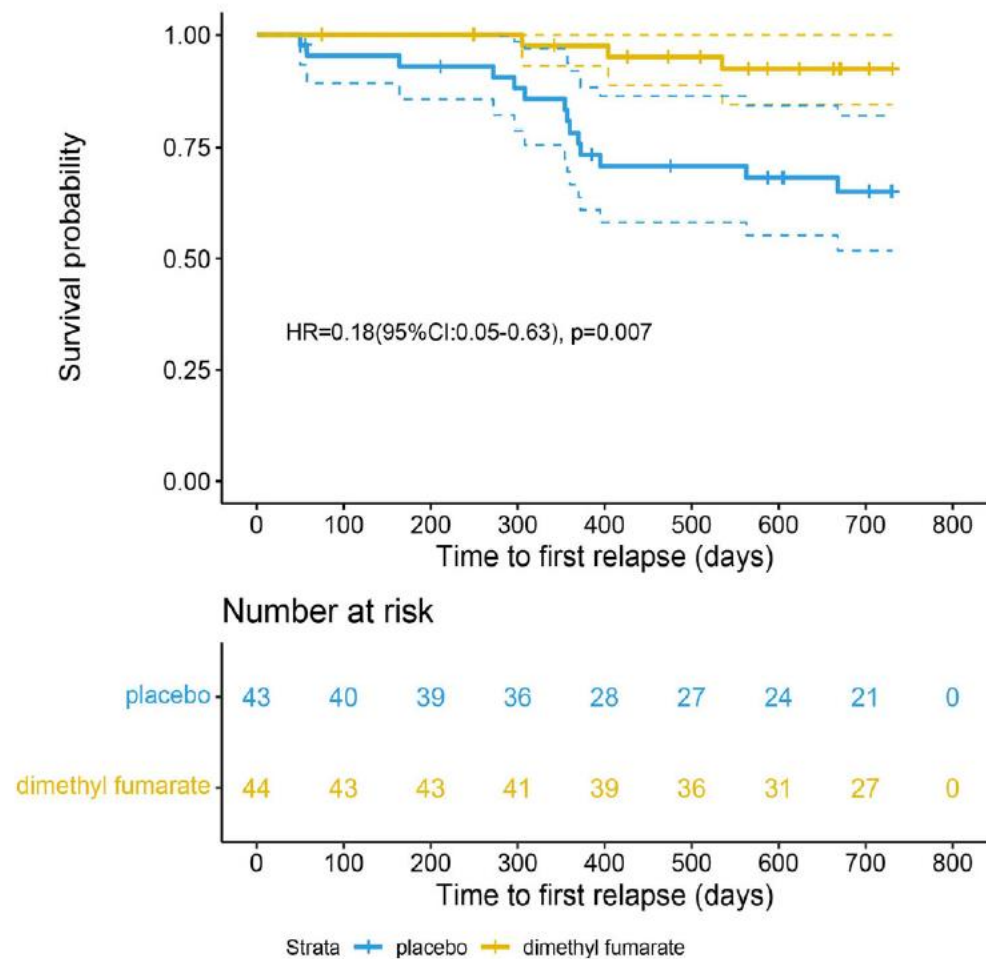
From RIS to clinical MS



THE MAJORITY OF PATIENTS WILL HAVE MS AT 10 YEARS

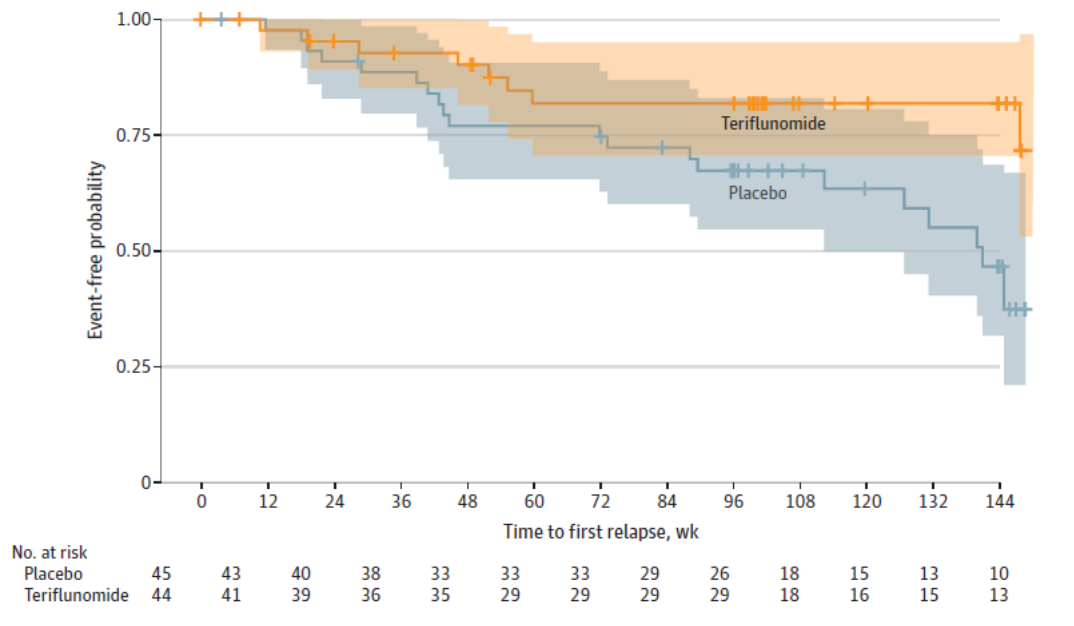
Radiologically Isolated Syndrome (RIS): Clinical trials

Dimethyl Fumarate Delays Multiple Sclerosis in Radiologically Isolated Syndrome The ARISE Randomized Clinical trial



Okuda et al. Ann Neurol 2023

Teriflunomide and Time to Clinical Multiple Sclerosis in Patients With Radiologically Isolated Syndrome The TERIS Randomized Clinical Trial



Lebrun-Fréney et al. JAMA Neurol 2023

2024 revisions of the McDonald criteria

Radiologically Isolated Syndrome

General Principle

- RIS is identified by the incidental discovery of CNS white matter T2-weighted hyperintense foci on MRI highly typical of MS but without clinical symptomatology related to inflammatory demyelination or findings on clinical examination.

Recommendations

- In patients with RIS, fulfilling DIS and DIT is sufficient for diagnosing MS.
- In patients with RIS, fulfilling DIS and OCB is sufficient for diagnosing MS.
- In patients with RIS fulfilling DIS, the presence of ≥ 6 CVS is sufficient for diagnosing MS.

DIS: at least 2 out of 5 topographies

Demonstration of optic nerve inflammation

- **Optic neuritis** represents the first manifestation of MS in **25-35% of CIS patients**
- Involvement of the optic nerve can be assessed by **MRI, VEP** and **OCT**
- **Different rates of optic nerve involvement** have been reported in established MS patients, **based on the sequence used**, and **MS disease duration** (ranging from **72.7% to 100%** in eyes with **prior history of ON**, and from **8.8% to 72%** in **asymptomatic eyes**)

Table 1. Optic nerve lesion detection by test.

Study population		Technique for optic nerve evaluation	Main results
Optic nerve MRI			
Acute/subacute ON			
Berg et al. ²⁹	First ON episode (CIS), n=104 (73% with abnormal brain MRI; median time since ON: 5 days)	Coronal fat-saturated T2 turbo and T1 post-Gd spin echo (1.5 T or 3.0 T)	T2 lesion: 79.8% T1 Gd+ lesion: 74% Both (T2 and T1-Gd+): 69.2%
Soelberg et al. ³⁰	First ON episode (CIS), n=31 (80.6% with abnormal brain MRI; median time since ON: 21 days)	3D FLAIR, or 2D FLAIR, or 2D STIR (1.5 T)	T2 lesion: 80.6% in first MRI
Cellina et al. ³¹	First ON episode (CIS), n=37 (51.4% with abnormal brain MRI; time since ON: 7 days; corticosteroids allowed)	3D transversal STIR, and transversal T1 spin echo fat-saturated post-Gd (1.5 T)	T2 lesions: 65.8% T1 Gd+ lesion: 34.1%
Bursztyn et al. ³²	First ON episode (CIS), n=92 (median time since ON: 11.5 days)	Coronal fat-saturated T2 turbo and coronal and axial fat-saturated T1 post-Gd (1.5 T or 3.0 T)	T2 lesion: 73.9% T1 Gd+ lesion: 78.3% Any (T2 and/or T1-Gd+): 83.7% Both (T2 and T1-Gd+): 69.6%
MS patients			
Hodel et al. ²³	ON confirmed clinically and with VEP, can include MS patients, n=31 (no clinical information provided)	2D coronal STIR FLAIR, 3D DIR sequence: 2D coronal and multi planar reconstruction, axial and coronal T1 post-Gd (3.0 T)	2D STIR FLAIR: 84% 2D DIR coronal: 88% 3D DIR multiplanar: 95%
Sartoretti et al. ²⁶	MS patients with no ON history, n=95 (disease duration : 8.9 years); control group with other diseases, n= 50	3D sagittal DIR with coronal reconstruction (3.0 T)	Asymptomatic ON lesion detection: 72% in MS patients; 0% in control group
Riederer et al. ²⁴	CIS/RRMS/SPMS patients, n=39 (53.8% with ON; might be acute); control group, n= 17	3D-DIR sequence	Whole cohort: 58.9% Patients with ON history: 100% Patients without ON history: 9.5%
London et al. ²⁵	CIS patients, n=66 (33.3% with ON; 92.4% DIS fulfilment)	Multiplanar 3D DIR reconstruction (3.0 T)	T2 lesion in ON-CIS: 100% T2 lesion in non-ON-CIS: 22.7%
Davion et al. ²⁷	MS patients, n=98 (median disease duration: 11.6 years); analysis conducted at an eye level	3D DIR and 3D FLAIR (3.0 T)	Whole cohort: 61.2% T2 lesion in ON eyes: 82.2% T2 lesion in non-ON eyes: 48.8%

Evidence supporting the addition of the optic nerve into DIS criteria

Optic nerve MRI, OCT and / or VEP

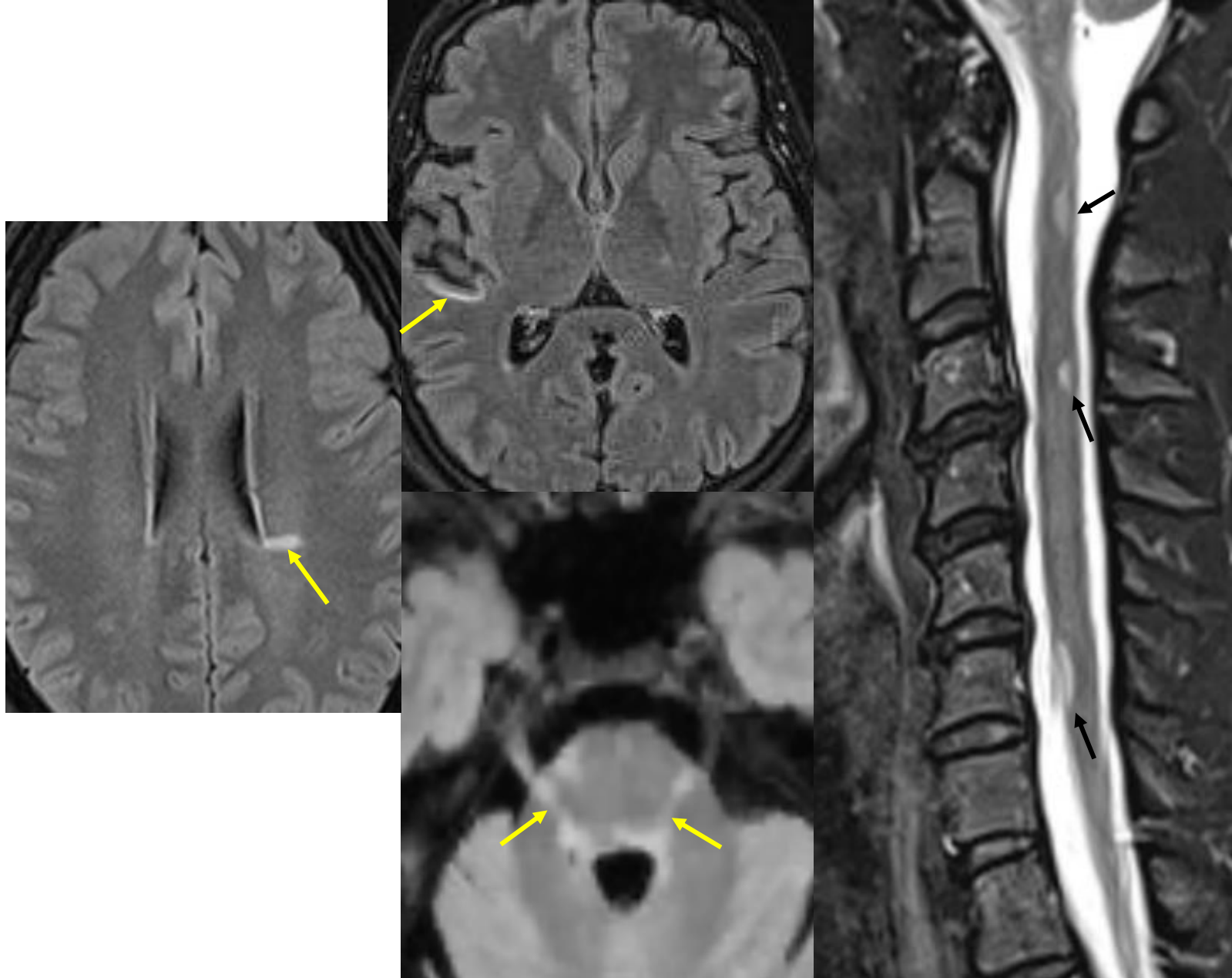
Table 2. Diagnostic performance of DIS criteria including the optic nerve.

Study design	Optic nerve assessment	2017 DIS	Modified DIS
Brownlee et al. ¹⁶	Retrospective, n=160 (81% ON) Outcome: CDMS Mean follow-up (years): 14.9	Clinical (26% VEP) Sensitivity: 0.83 Specificity: 0.68 Accuracy: 0.78	Sensitivity (in ON-CIS): 0.95 Specificity (in ON-CIS): 0.57 Accuracy (in ON-CIS): 0.81
Vidal-Jordana et al. ¹⁷	Retrospective, n=388 (35.6% ON) Outcome: CDMS Mean follow-up (years): 7.4	VEP Sensitivity: 0.79 Specificity: 0.52 Accuracy: 0.75	Sensitivity: 0.82 Specificity: 0.52 Accuracy: 0.78
Bsteh et al. ¹⁸	Retrospective, n=267 Outcome: CDMS Mean follow-up (years): 4.9	OCT Sensitivity: 0.78 Specificity: 0.84 Accuracy: 0.66	Sensitivity: 0.84 Specificity: 0.52 Accuracy: 0.81
Vidal-Jordana et al. ¹⁹	Prospective, n=157 (38.2%) Outcome: McDonald 2017 MS Mean follow-up (years): 2.3	Optic nerve MRI (71%), OCT (80%) and/or VEP (84%) Sensitivity: 0.88 Specificity: 0.82 Accuracy: 0.87	MRI Sensitivity: 0.92/Specificity: 0.72/ Accuracy: 0.87 OCT-pRNFL Sensitivity: 0.91/Specificity: 0.74/ Accuracy: 0.86 OCT-GCIPL Sensitivity: 0.91/Specificity: 0.80/ Accuracy: 0.88 VEP Sensitivity: 0.89/Specificity: 0.78/ Accuracy: 0.86

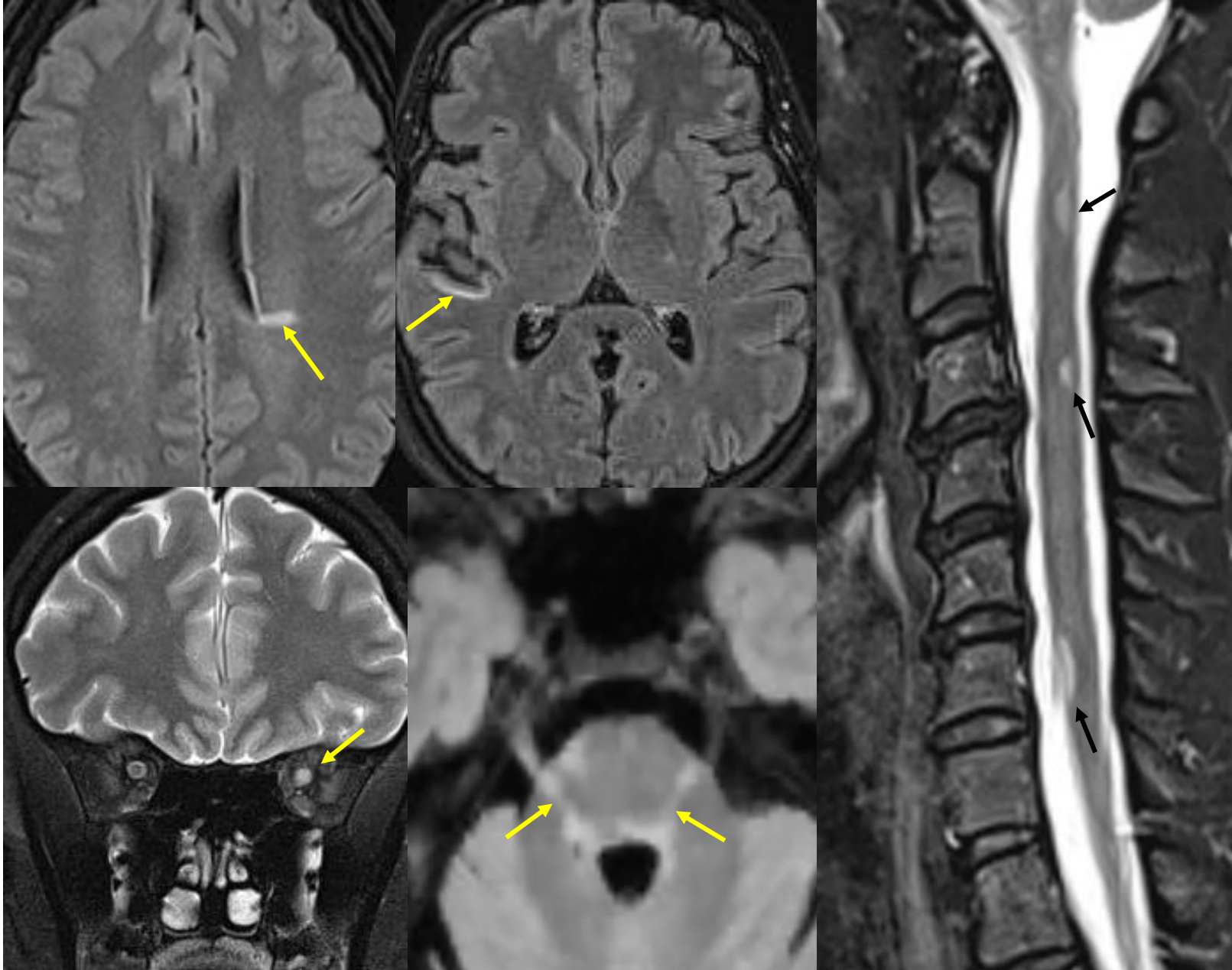
CDMS: clinical defined multiple sclerosis, referring usually to occurrence of second relapse during the follow-up; DIS: dissemination in space; GCIPL: ganglion cell and inner plexiform layer; MRI: magnetic resonance imaging; OCT: optical coherence tomography; ON: optic neuritis; pRNFL: peripapillary retinal nerve fibre layer; VEP: visual evoked potentials; CIS: clinically isolated syndrome.

All four studies evaluating the incorporation of the optic nerve to current (2017 McDonald) DIS criteria demonstrated an improvement in diagnostic performance with an increase in sensitivity and different impact on specificity, mainly due to study design and population, outcomes used, and time of follow-up.

4 topographies model (McDonald 2017)

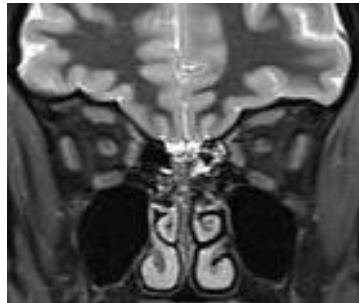
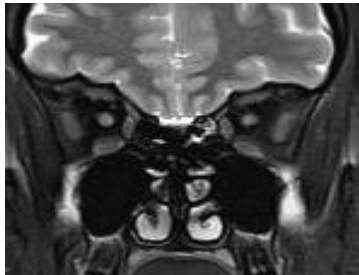


5 topographies model (McDonald 2024)



MRI optic nerve: Technical considerations

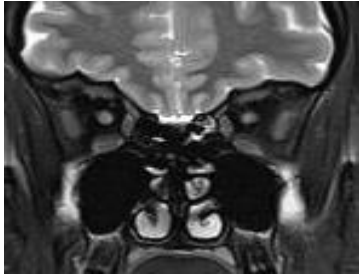
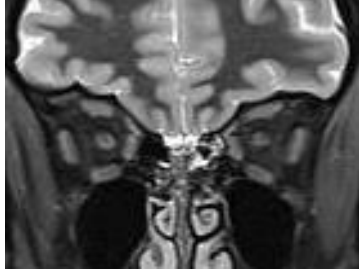
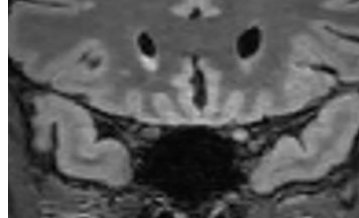
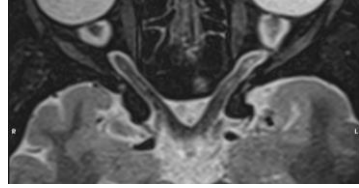
Rovira et al, Neuroimag Clin N Am 2024



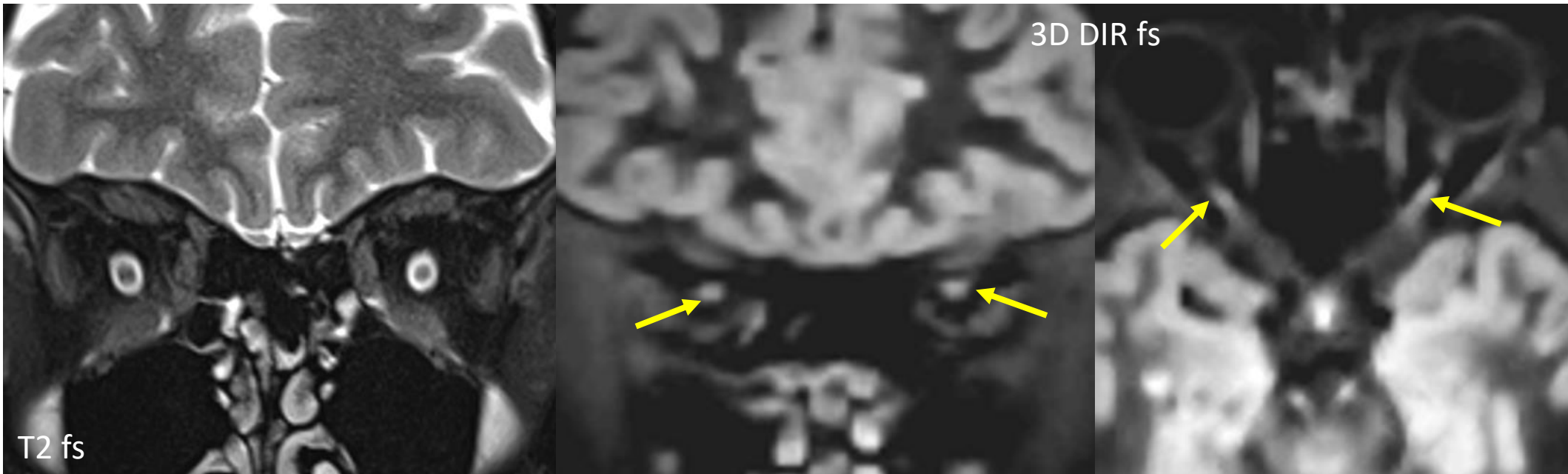
Sequence	Coverage	Advantages	Disadvantages
2D fat-suppressed T2-weighted fast/turbo SE	Anterior optic pathway	• Good effective fat suppression • High signal to noise ratio	• Impossible to perform multiplanar and curvilinear reformats (low in-plane resolution) • Poor fat suppression if field inhomogeneities are present • Difficult to achieve in low field strength magnets • Susceptibility artifacts • Limited sensitivity for detecting asymptomatic lesions and bilateral involvement
2D STIR	Anterior optic pathway	• Insensitive to field inhomogeneities • No susceptibility artifacts • Can be used in low field magnets	• Impossible to perform multiplanar and curvilinear reformats (low in-plane resolution) • Suboptimal effective fat suppression • Low signal to noise ratio • Poor contrast of abnormal high signal of the affected optic nerve and the normal perineural CSF • Limited sensitivity for detecting asymptomatic lesions and bilateral involvement

MRI optic nerve: Technical considerations

Rovira et al, Neuroimag Clin N Am 2024

	Sequence	Coverage	Advantages	Disadvantages
	2D fat-suppressed T2-weighted fast/turbo SE	Anterior optic pathway	• Good effective fat suppression • High signal to noise ratio	• Impossible to perform multiplanar and curvilinear reformats (low in-plane resolution) • Poor fat suppression if field inhomogeneities are present • Difficult to achieve in low field strength magnets • Susceptibility artifacts • Limited sensitivity for detecting asymptomatic lesions and bilateral involvement
	2D STIR	Anterior optic pathway	• Insensitive to field inhomogeneities • No susceptibility artifacts • Can be used in low field magnets	• Impossible to perform multiplanar and curvilinear reformats (low in-plane resolution) • Suboptimal effective fat suppression • Low signal to noise ratio • Poor contrast of abnormal high signal of the affected optic nerve and the normal perineural CSF • Limited sensitivity for detecting asymptomatic lesions and bilateral involvement
	3D T2-FLAIR with fat-suppression	Anterior optic pathway and whole brain	• Good effective fat suppression • High sensitivity • Simultaneous whole brain coverage • Multiplanar and curvilinear reformats	• Poor anatomical delineation • Only tested on 3.0 T magnets •
	3D DIR with fat suppression	Anterior optic pathway and whole brain	• Good effective fat suppression • High sensitivity (higher than 3D T2-FLAIR) • Simultaneous whole brain coverage • Multiplanar and curvilinear reformats	• Poor anatomical delineation • Low signal to noise ratio • Only tested on 3.0 T magnets
	3D-T2-STIR-ZOOMit	Anterior optic pathway	• High spatial resolution • High sensitivity • Optimal anatomical delineation • Multiplanar and curvilinear reformats • Combine qualitative (signal changes) and quantitative (volume) lesion assessment	• Long acquisition time • Field inhomogeneity artifacts (affecting assessment of the intracanalicular segment) • Truncation artefacts (central optic nerve linear hyperintensity) • Low signal to noise ratio • Limited availability of the sequence (vendor specific) • Only tested on 3.0 T magnets

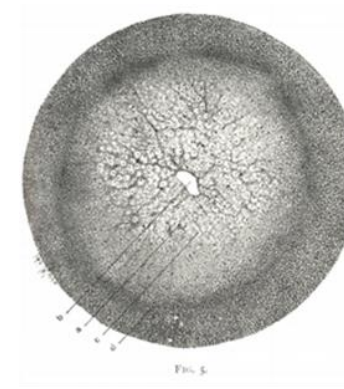
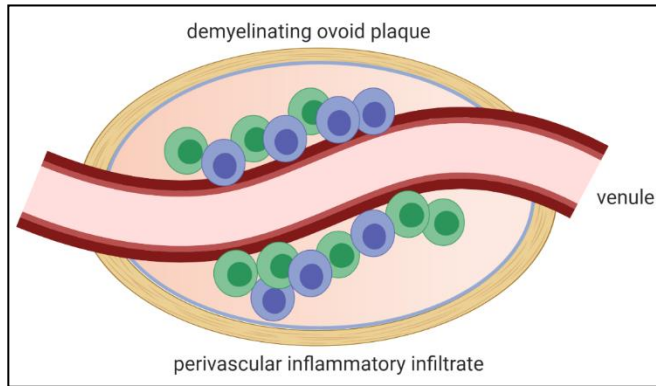
MRI in Optic Neuritis: 2D T2fs vs 3D DIR



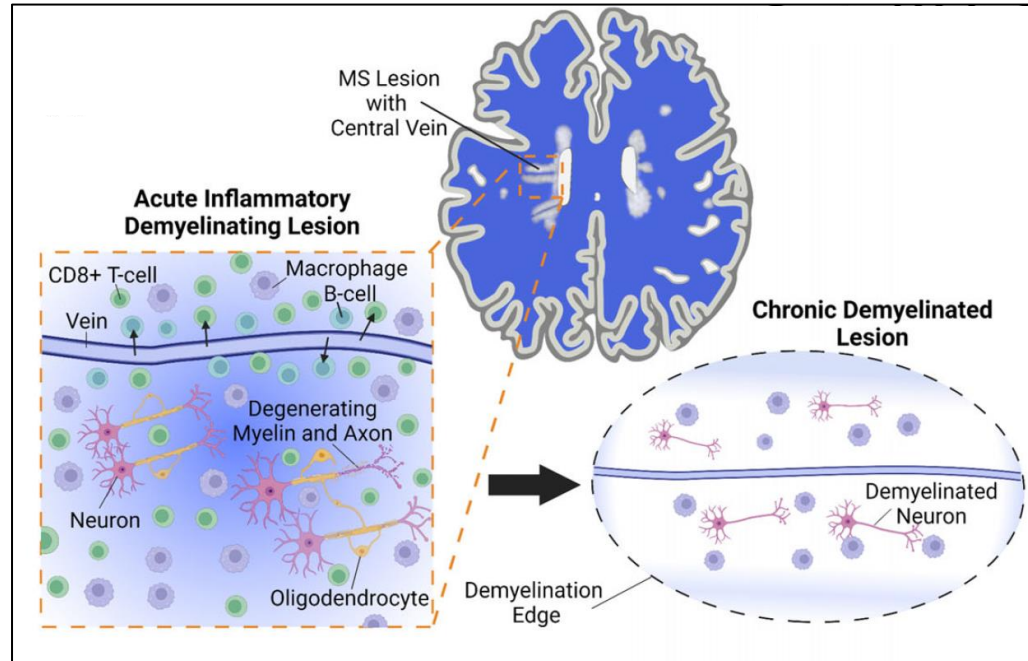
3D DIR

- outperforms 2D STIR for detecting optic nerve lesions
- detects signal changes in **38%** of asymptomatic nerves in CIS patients
- signal changes highly specific for optic nerve pathology (more sensitive than VEPs)

Ovoid shape: Dawson finger

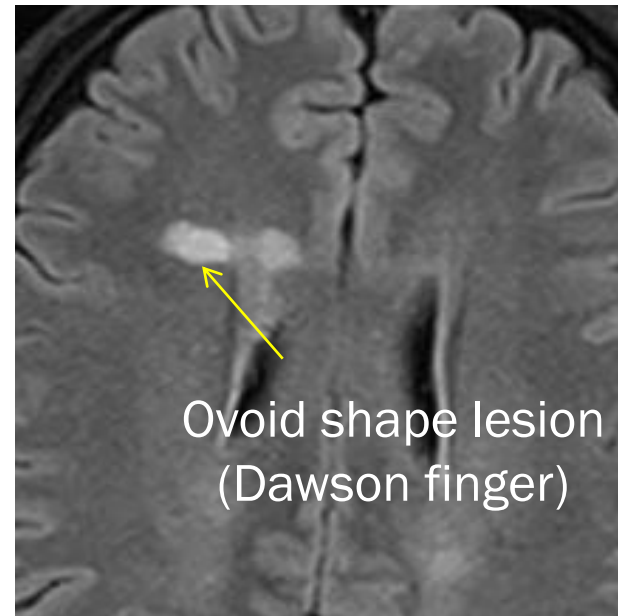


Dawson J. Trans Roy Soc Edinb 1916; 50:517-740
Horowitz et al. Am J Neuroradiol 1989;10:303-5

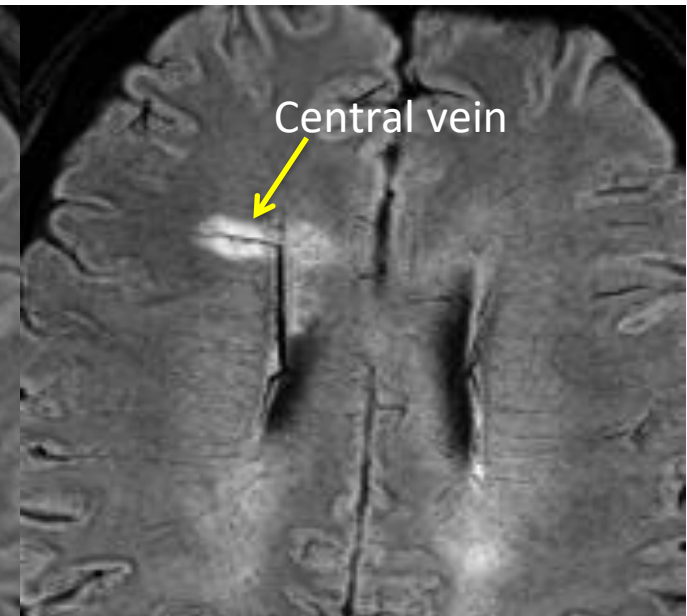


Gill et al., Eur J Immunol 2023

FLAIR

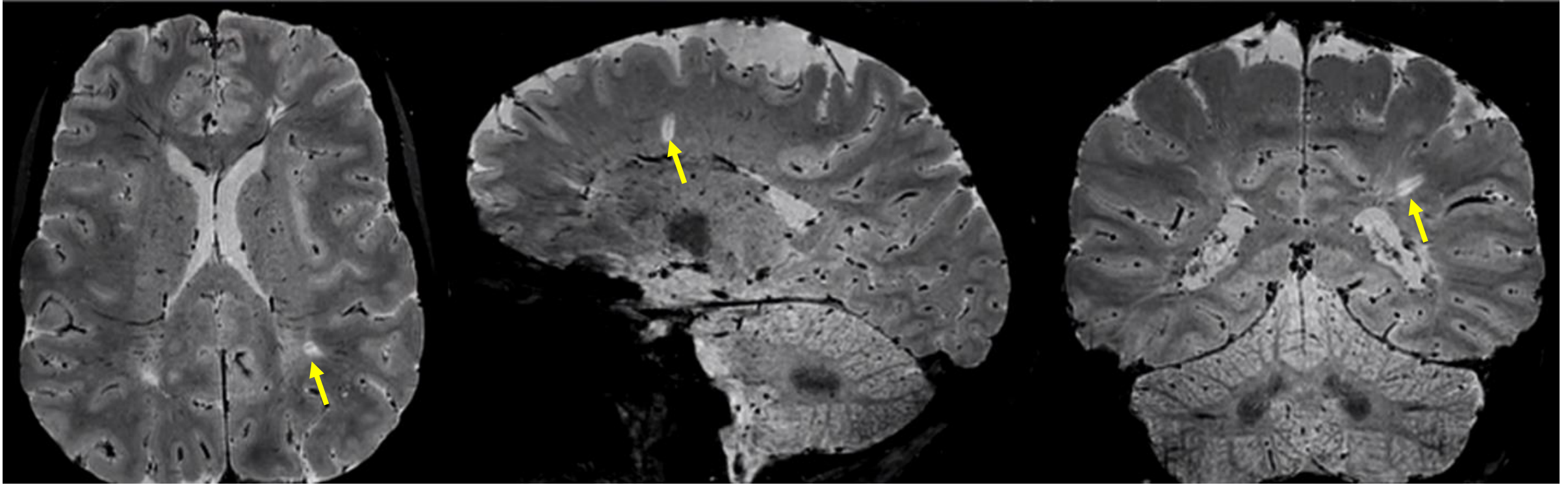


SWI (3T)



Central vein sign: 3D T2*w Segmented EPI GRE (T2*-EPI)

Sati et al. Mult Scler J 2014



- 3T Magnet
- 650 μm isotropic voxels
- Whole brain coverage in 6 minutes

NAIMS criteria

- Thin hypointense line or small dot
- Visualized in at least two perpendicular planes (and appears as a thin line in at least one plane)
- Small apparent vein diameter ($<2\text{mm}$)
- Runs partially/entirely through the lesion
- Positioned centrally in the lesion

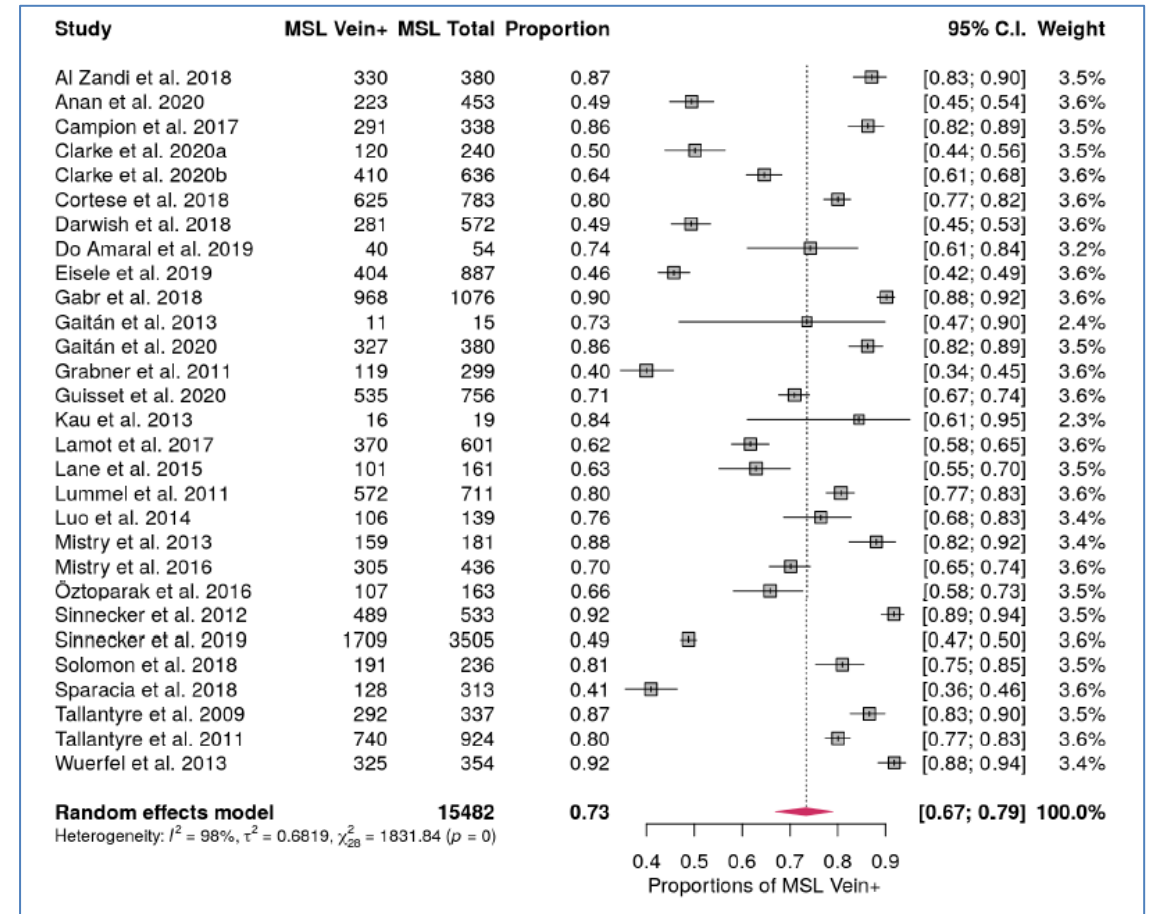
Sati et al. Nat Rev Neurol 2016

Central vein sign (CVS): Systematic review and meta-analysis

- CVS in the MS population was **73%**.
- Diagnostic performance in MS cases, providing a pooled **specificity of 92%** and a **sensitivity of 95%**.
- The optimal **cut-off value** was **40%** with excellent accuracy calculated by the area under the ROC (0.946).
- The 3D-EPI sequences showed both a higher pooled proportion compared to other sequences
- The 1.5 Tesla (T) scanners showed a lower (**58%**) proportion of MS lesions with a CVS compared to both 3T (**74%**) and 7T (**82%**).

Up to August 24, 2020

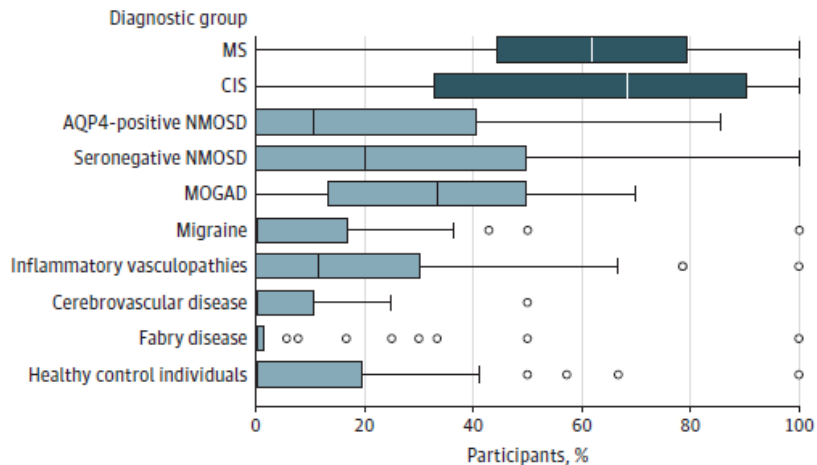
35 studies for quantitative analysis)



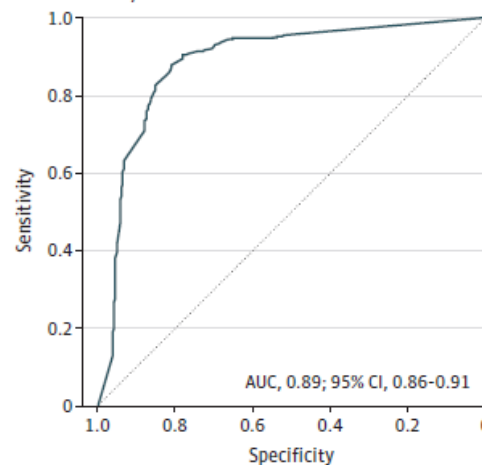
Central vein sign: diagnostic performance

Figure 3. Central Vein Sign (CVS) for Discrimination Between Multiple Sclerosis (MS)/Clinically Isolated Syndrome (CIS) and Other Diagnoses

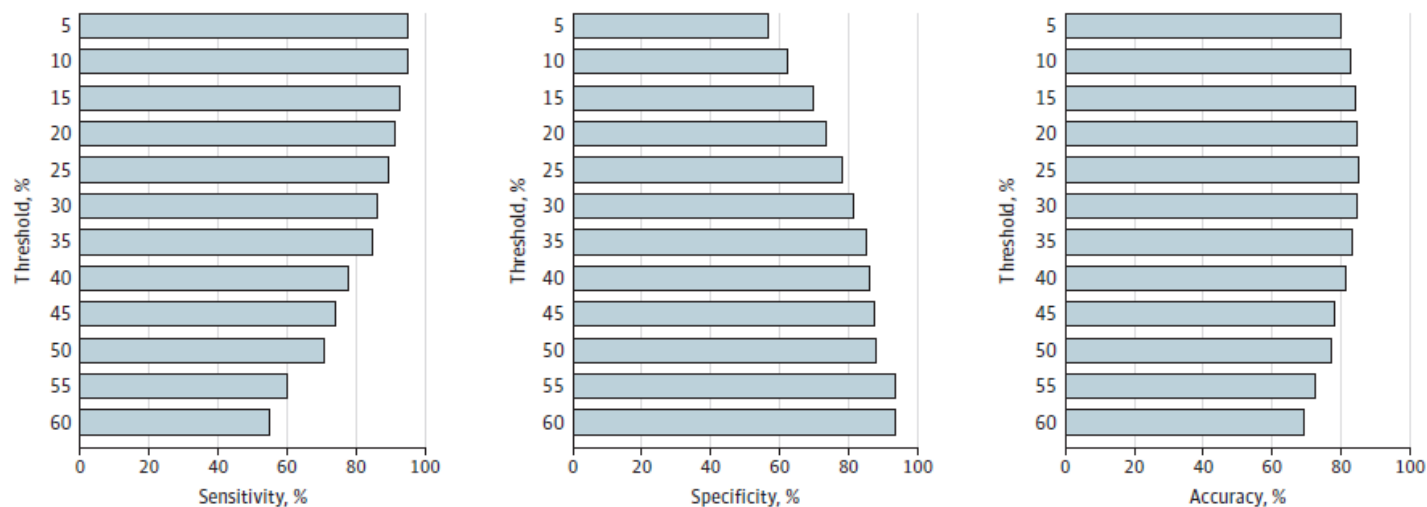
A Percentage of CVS-positive lesions per participant



B Performance of CVS in discriminating MS/CIS and other conditions



C Performance of CVS in discriminating MS/CIS and other conditions by CVS-positive proportion threshold



Central vein sign: assessment

Rating methods

> 40% WML CVS positive:

- Time consuming (assess all lesions)
- High variability
- Automated tools

Simplified methods

Select 3

- Patients with < 3 lesions excluded
- Positive if 3/3 are CVS+ OR 2/3 are CVS+

Select 3*

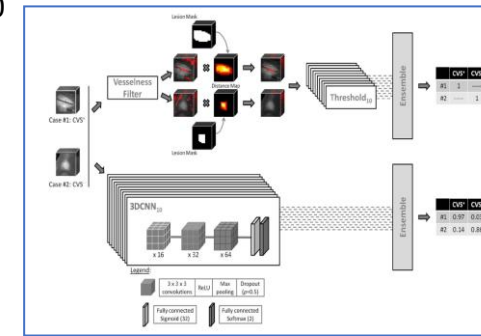
- Patients with < 3 lesions excluded
- Evaluate if at least 3 lesions are CVS+

Rule of 6 / Select 6*

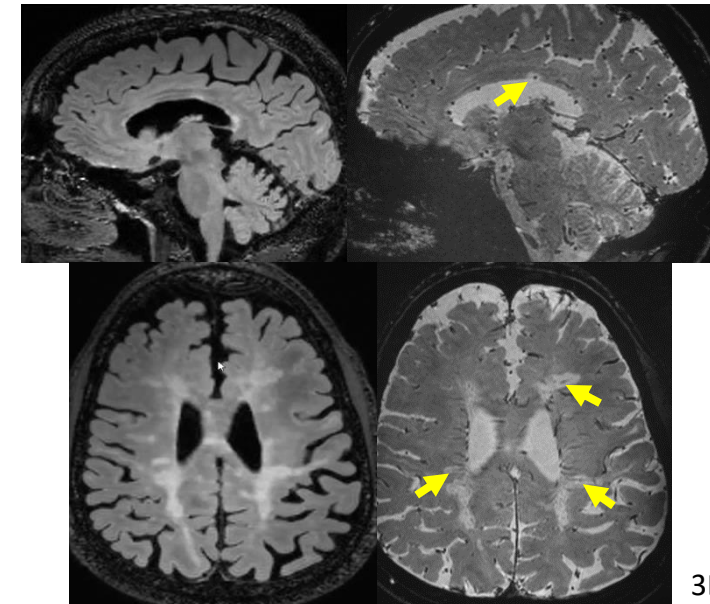
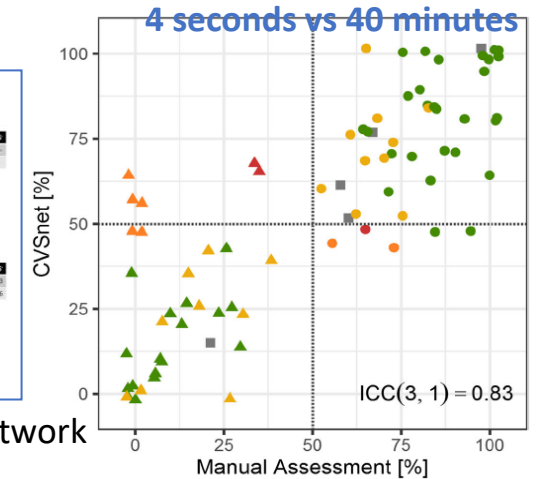
- Evaluate if at least 6 lesions are CVS+
- If <6 WM lesions, positive if CVS+ > CVS-
- Some studies: positive if 6/10 lesions are CVS+

Maggi et al. NMR Biomed 2020

Automatic assessment



3D Convolutional Neural Network



3D EPI GRE with Gad

2024 revisions of the McDonald criteria

Central Vein Sign

General Principles and Recommendations

- Demonstration of CVS by MRI may be used in the diagnosis of MS.
- Demonstration of CVS by MRI can increase specificity of diagnosis in MS.
- Demonstration of CVS is not mandatory for diagnosis of MS.
- In patients with typical symptoms and DIS the presence of **rule of 6 CVS** lesions is sufficient for diagnosis of MS.
- In patients with typical symptoms and typical lesions in one topography, the presence of **6 CVS plus DIT or CSF positive** is sufficient to diagnose MS

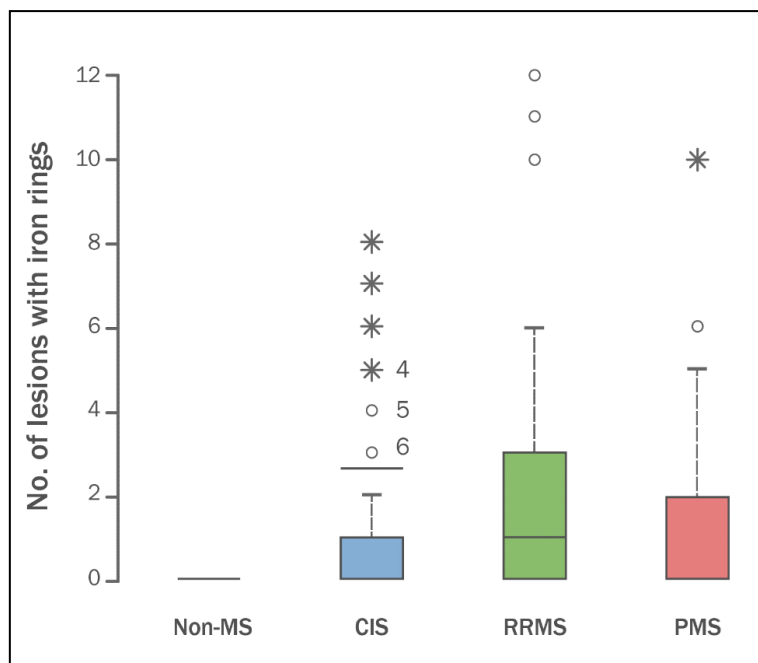
Paramagnetic rim lesions (PRLs): MS versus other CNS disorders



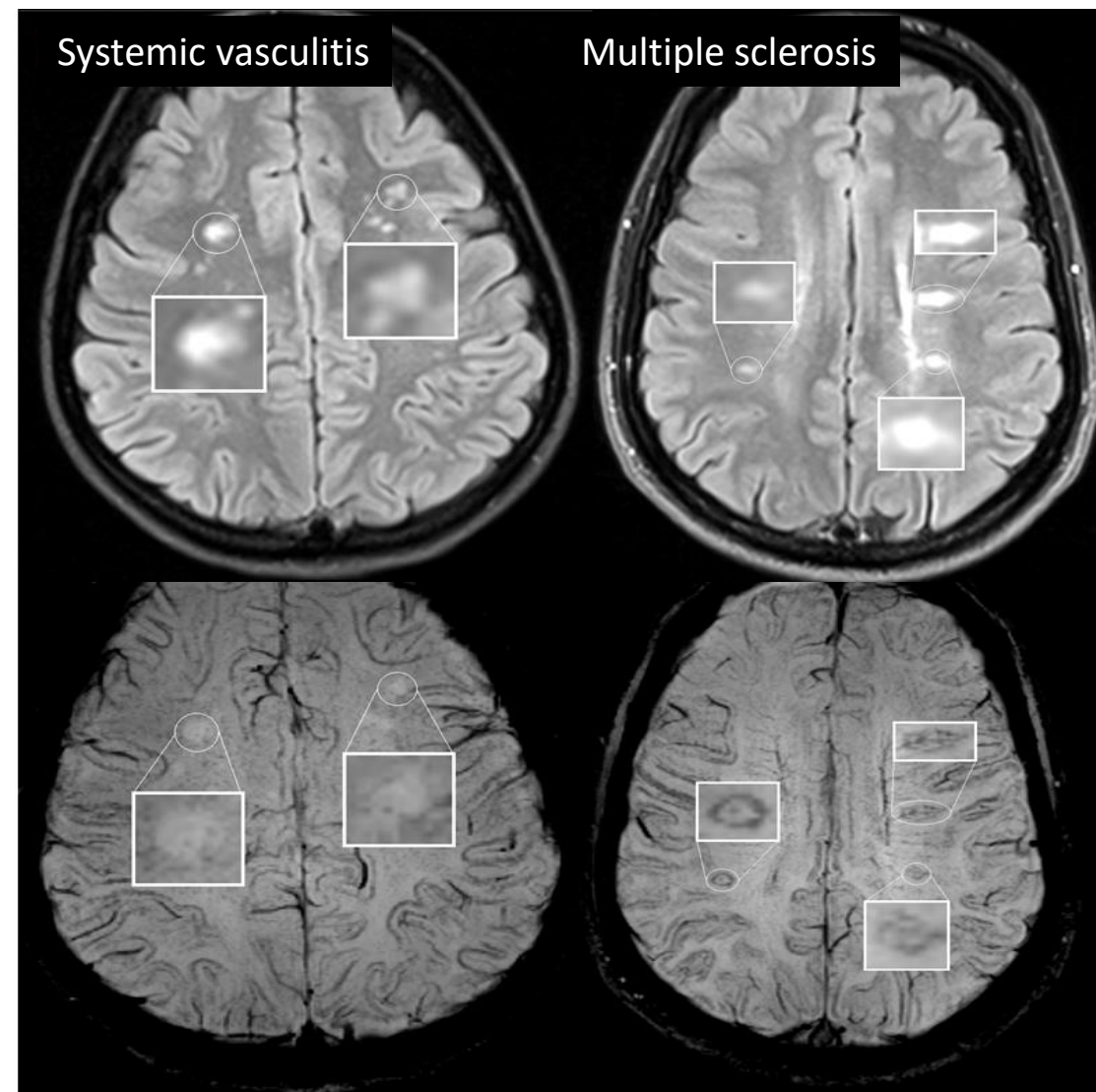
Calvi et al. Mult Scler J 2020

Iron

Microglia, Macrophages

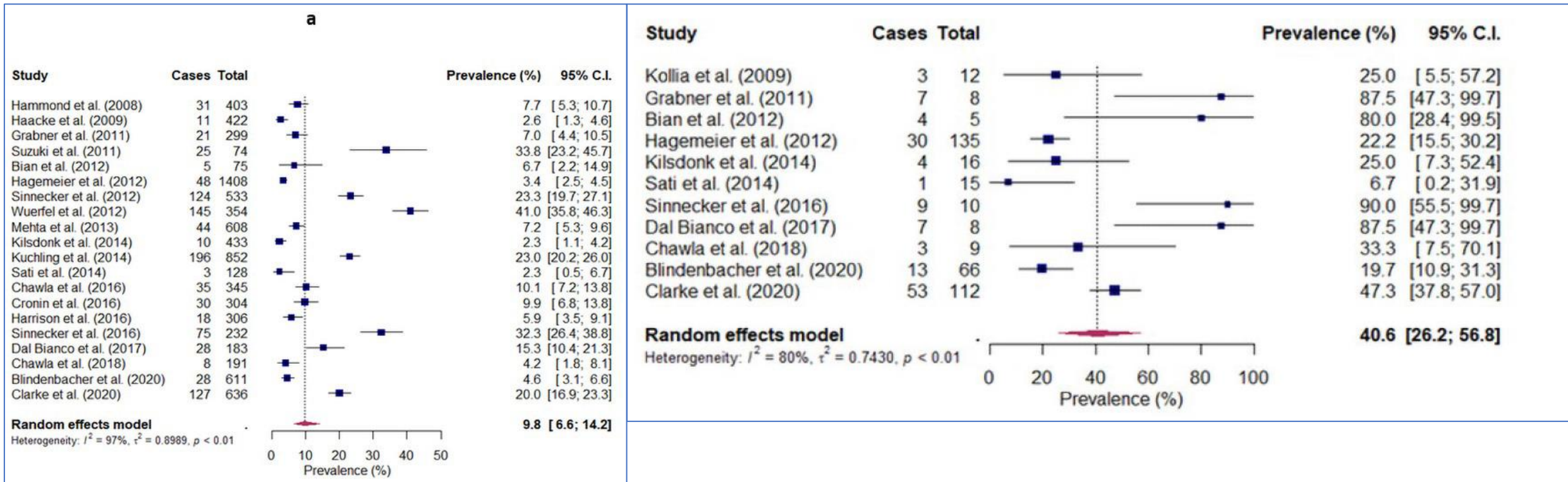


- 48% of CIS, 59% of RRMS and 39% of PMS patients had at least one lesion with an iron rim**



Paramagnetic rim lesions: Systematic review and Meta-analysis

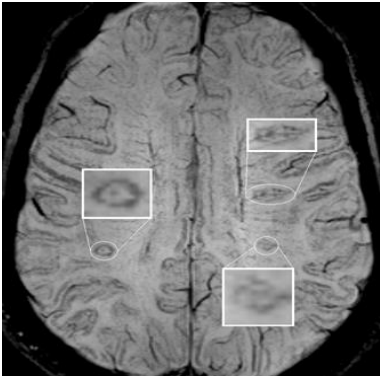
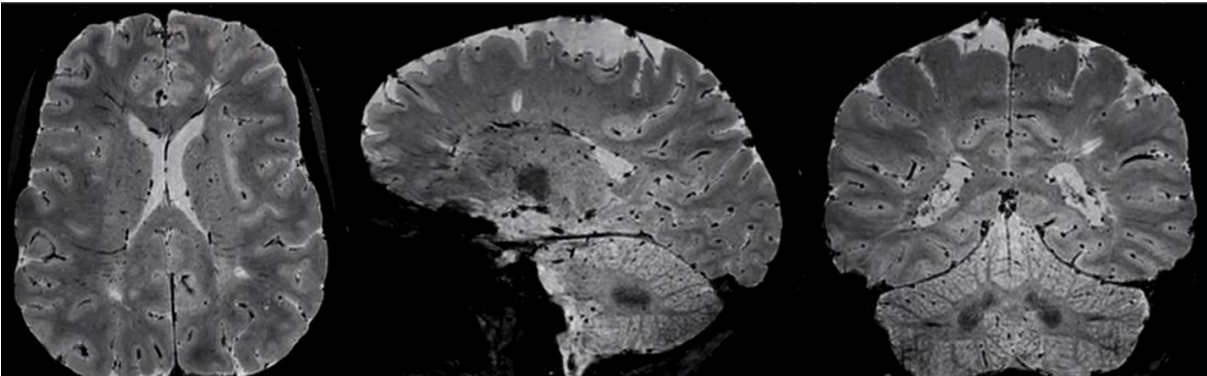
29 studies comprising 1230 patients



- Pooled prevalences of **9.8%** and **40.6%** for rim lesions at lesion-level and patient-level
- Significant variation across studies
- Clear guidelines should be introduced to standardize their assessment

MRI: Technical considerations

Recommended MRI protocol for CVS and PRL detection [†]							
Sequence name	TR	TE	FA	ETL	In-plane resolution	Slice thickness	Image Reconstruction [‡]
T2*-weighted 3D (multishot) echo-planar-imaging (3D-EPI ¹ or similar)	~60 ms	~35 ms	~10°	~15	0.5-0.8 mm	0.5-0.8 mm	(Enhanced) Magnitude Filtered Phase
OR							
Optimized ^{††} Susceptibility-Weighted-Imaging 3D Gradient-Echo (SWI ² , SWIp ³ , SWAN ⁴ , SWAN-venule ⁵ , or similar)	~30 ms	~20 ms	~5°	N/A	0.5-0.8 mm	1-3 mm	(Enhanced) Magnitude Filtered Phase



TR: Repetition time; **TE:** Echo time; **FA:** Flip angle; **ETL:** Echo train length, SWI: Susceptibility-weighted-imaging (Siemens Healthineers), SWIp: Susceptibility weighted imaging with phase enhancement (Philips), SWAN: T2 Star Weighted Angiography (GE Healthcare).

[†] Protocol applicable at 3T and 1.5T. Longer TR and TE [\[A2\]](#) are recommended at 1.5T if scan time allows. Acquisition during the 5-min delay after GBCA injection [\[A3\]](#) is also recommended, especially at 1.5T, to compensate for lower susceptibility effects.

^{††} **Optimized** SWI or similar using **low flip angle** is recommended for generating adequate T2*-weighted contrast on magnitude images necessary for CVS detection (e.g., hyperintense lesions and hypointense veins). See supplementary figure below for case-based example. If standard SWI or similar (with default flip angle) is used, then combination (or fusion) of SWI and T2-FLAIR is highly recommended for accurate CVS detection.^{6,7}

[‡] Enhanced Magnitude and Filtered Phase images can be obtained using vendor-provided image reconstruction methods (SWI, SWIp, SWAN, or similar). Enhanced Magnitude images are recommended for sensitive CVS detection. Filtered Phase images are recommended for sensitive PRL detection. Note that Quantitative Susceptibility Mapping (QSM) reconstruction⁸ can also be used when available.

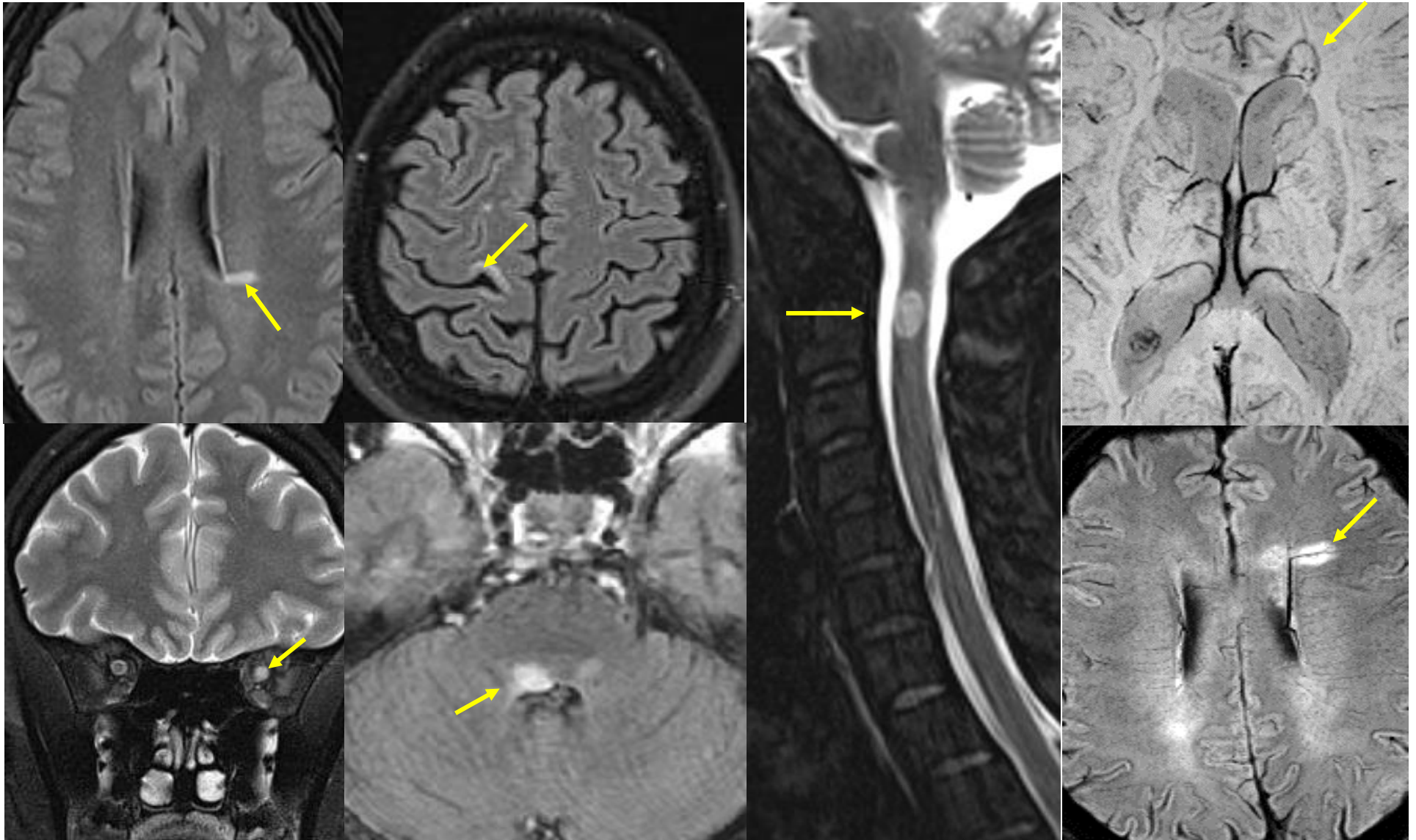
2024 revisions of the McDonald criteria

Paramagnetic Rim Lesions

General Principles and Recommendations

- Demonstration of PRLs by MRI may be used in the diagnosis of MS.
- Demonstration of PRLs by MRI can increase the specificity of diagnosis in MS.
- Demonstration of PRLs is not required for diagnosis of MS.
- In patients with typical symptoms and typical lesions in one topography, the presence of **≥1 PRL plus DIT or CSF positive** is sufficient to diagnose MS

5 topographies model plus new imaging features(McDonald 2024)



2024 revisions of the McDonald criteria

DIS Topographies	Additional criteria needed for relapse onset	Additional criteria needed for progression from onset (≥12 months)	Additional criteria needed for incidental imaging suggestive of demyelination (RIS)
4-5	None	None	Any of the following: • DIT • CSF • CVS
2-3	Any of the following: • DIT • CSF • CVS	Any of the following: • DIT • CSF • CVS	Any of the following: • DIT • CSF • CVS
1	Any of the following: • CSF and CVS • DIT and CVS • CSF and PRL • DIT and PRL	≥2 spinal cord lesions and any of the following • CSF and CVS • DIT and CVS • CSF and PRL • DIT and PRL	Not able to make diagnosis
0	Not able to make diagnosis	Not able to make diagnosis	Not able to make diagnosis

DIS: dissemination in space topographies on initial MRI Brain, MRI Spinal cord, MRI orbits (to be conducted in optic neuritis onset), and OCT/VEP (juxtacortical, periventricular, infratentorial, spinal cord, optic nerve)

DIT: dissemination in time, second clinical attack or simultaneous presence of gadolinium enhancing and non-enhancing lesions at any time, or by a new T2-hyperintense or gadolinium enhancing lesion on follow-up MRI

CVS: central vein sign, presence of ≥6 lesions or a majority of lesions with CVS when <6 lesions are present per NAIMS criteria

PRL: paramagnetic rim): presence of ≥1 lesions with a paramagnetic rim lesion per NAIMS criteria

CSF: cerebrospinal fluid, positive for oligoclonal bands or kappa free light chains

2024 Revision Contributors

29 Nov-2 Dec
2023
Barcelona

Xavier Montalban, MD^{1,*}, Christine Lebrun-Frenay, MD², Jiwon Oh, MD³, Georgina Arrambide, MD¹, Marcello Moccia, MD^{4,5}, Maria Pia Amato, MD⁶, Lilyana Amezcua, MD⁷, Brenda Banwell, MD⁸, Amit Bar-Or, MD⁸, Frederik Barkhof, MD⁹, Helmut Butzkueven, MD¹⁰, , MD, Olga Ciccarelli, MD⁵, Jeffrey A. Cohen, MD¹¹, Giancarlo Comi, MD¹², Jorge Correale, MD¹³, Florian Deisenhammer, MD¹⁴, Massimo Filippi, MD¹⁵, Julie Fiol¹⁶, Mark Freedman, MD¹⁷, Kazuo Fujihara, MD¹⁸, Cristina Granziera, MD¹⁹, Ari Green, MD²⁰, Hans-Peter Hartung, MD²¹, Kerstin Hellwig, MD²², Ludwig Kappos, MD¹⁹, Dorlan Kimbrough, MD²³, Joep Killestein²⁴, MD, Fred Lublin, MD²⁵, Romain Marignier, MD²⁶, Ruth Ann Marrie, MD²⁷, Aaron Miller²⁵, MD, Susanna Otero, MD¹, Daniel Ontaneda, MD¹¹, Sudarshini Ramanathan, MD²⁶, Daniel Reich, MD²⁷, Mara Rocca, MD¹⁵, Àlex Rovira, MD¹, Shiv Saidha, MD²⁸, Amber Salter, PhD²⁹, Jaume Sastre-Garriga, MD¹, Deanna Saylor, MD³⁰, Andy Solomon, MD³¹, Maria Pia Sormani, PhD³², Bruno Stankoff, MD³³, Mar Tintore, MD¹, Helen Tremlett, PhD³⁴, Anneke Van der Walt, MD⁹, Shanthi Viswanathan, MD³⁵, Heinz Wiendl, MD³⁶, Brigitte Wildemann, MD³⁷, Bassem Yamout, MD³⁸, Paola Zarin, PhD³⁹, **Peter Calabresi, MD²⁸, Timothy Coetzee, PhD¹⁶, Alan J. Thompson, MD⁵**



International Advisory
Committee on Clinical
Trials in MS

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EUROPEAN COMMITTEE FOR TREATMENT
AND RESEARCH IN MULTIPLE SCLEROSIS

MS
National
Multiple Sclerosis
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**XXXV Congreso de la Sociedad
Iberolatinoamericana de
Neurorradiología Diagnóstica y
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**LIII Reunión Anual de la Sociedad
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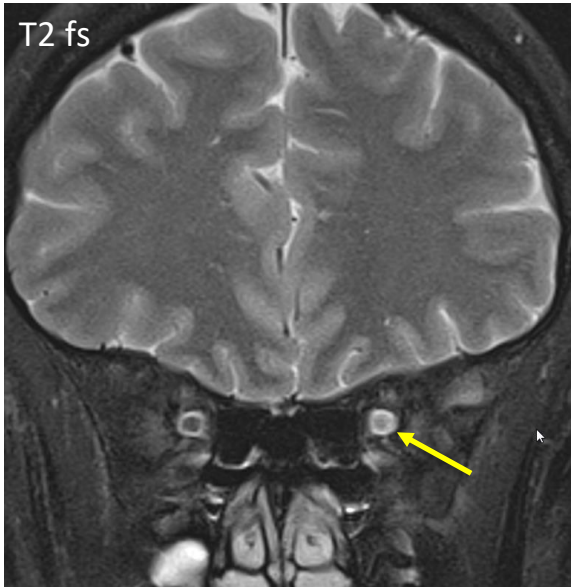
**Sociedad Ibero Latino Americana
de Neurorradiología Diagnóstica
y Terapéutica**



Optic nerve assessment with paraclinical tools

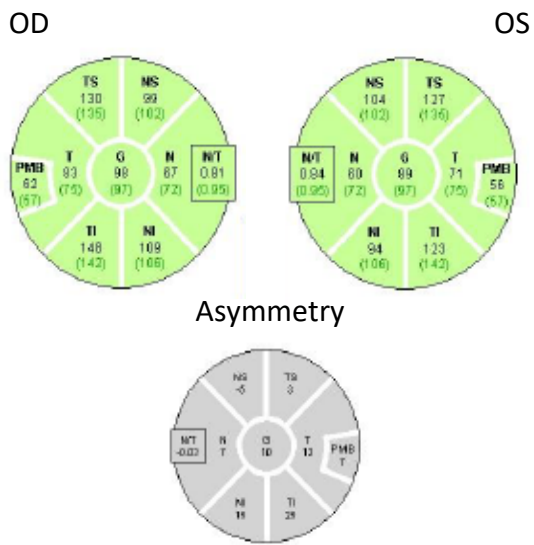
Importance of **interpreting test results**

Optic nerve MRI



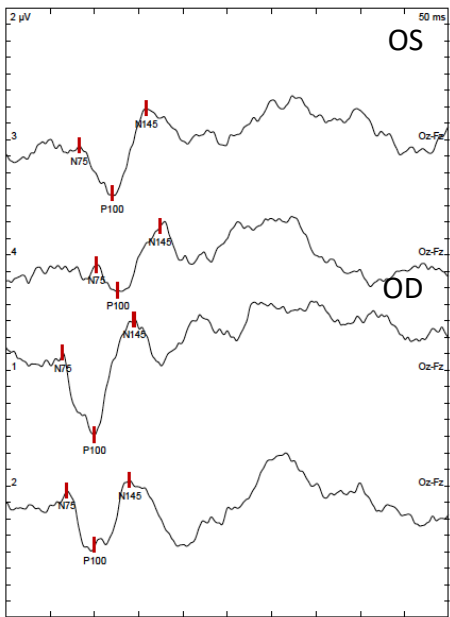
Presence of a T2 hypersignal in the optic nerve

OCT



Inter-eye asymmetry (IEA) $\geq 5 \mu\text{m}$ for pRNFL and/or $\geq 4 \mu\text{m}$ for GCIPL

VEP



Delayed P100 latency based on the normative data for each neurophysiology lab

Structural

Functional

Open questions for future Revision

- Demonstration of DIT using VEP and/or OCT
- Refinement of the use of PRLs and CVS
- Solitary sclerosis, and other atypical presentations
- Performance of the criteria in diverse populations (e.g. Asia, LATAM region, etc.)
- Use of other biomarkers as tools for diagnosis



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**Signs or Symptoms
suggestive of MS**

Initial workup suggestive of MS?

- Medical history and clinical examination
- Imaging and laboratory tests
- Differential diagnosis

No

MS diagnosis should only be
considered after ruling out
better explanations

Yes

Lesions present in ≥ 2 CNS topographies
or
Patients with ≥ 12 months progression and
 ≥ 2 spinal cord lesions¹

**Multiple Sclerosis may be diagnosed if one or more
of the following are also demonstrated:**

- CSF+²
- CVS+³
- Dissemination in Time⁴
- Lesions are present in 4 or 5 CNS topographies

Lesions present in 1 CNS topography
(including patients with ≥ 12 months
progression)

**Multiple Sclerosis may be diagnosed if one or more
of the following are also demonstrated:**

- CSF+ and CVS+
- CSF+ and PRL+⁵
- Dissemination in Time and CVS+
- Dissemination in Time and PRL+

