Vall d'Hebron Hospital

Institut Català de la Salut

Generalitat de Catalunya
Departament de Salut

IDI
INSTITUT DE DIAGNÒSTIC PER LA IMATGE

XLVIII Reunión Anual
SOCIEDAD ESPAÑOLA DE NEURORRADIOLOGÍA

Caballerizas Reales · Palacio de la Magdalena | SANTANDER

24 - 26 de octubre de 2019

"Novedades en patología inflamatorio-desmielinizante"

Àlex Rovira
Secció de Neurorradiologia. Servei de Radiologia
Hospital Universitari Vall d'Hebron
Barcelona
alex.rovira@idi.gencat.cat

Disclosures

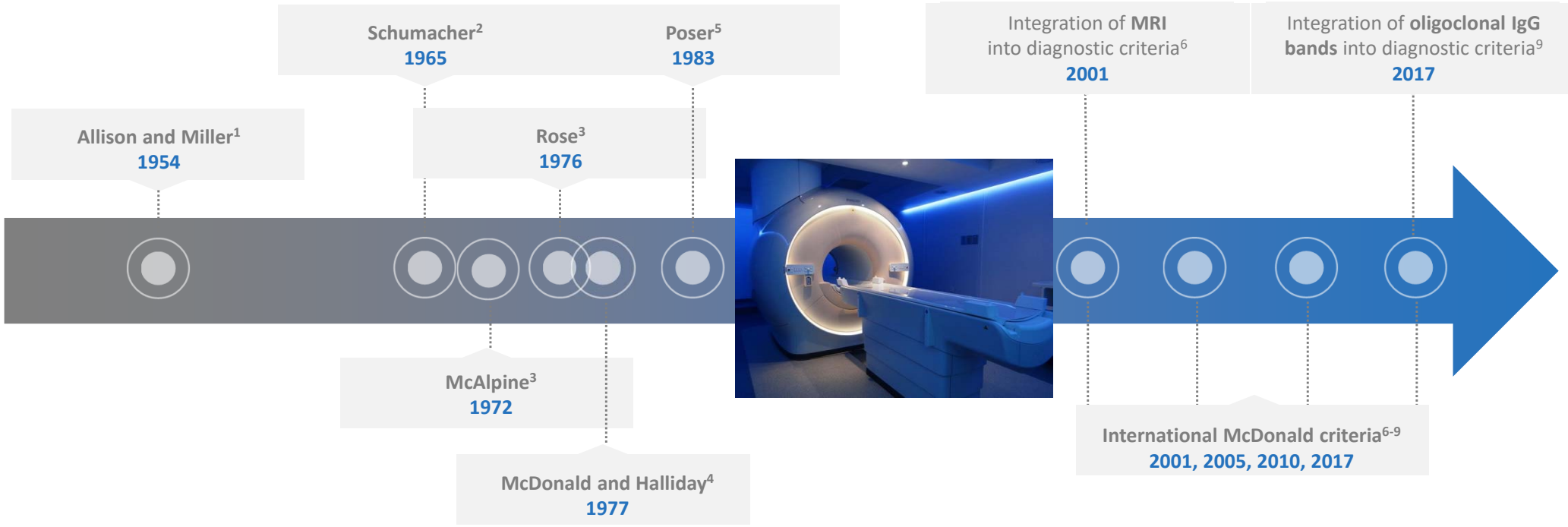
Alex Rovira
Section of Neuroradiology
University Hospital Vall d'Hebron
Barcelona, Spain

A. Rovira serves/ed on scientific advisory boards for Novartis, Sanofi-Genzyme, Biogen IDEC, OLEA Medical, Synthetic MR, Icometrix and Bayer, has received speaker honoraria from Bayer, Sanofi-Genzyme, Bracco, Merck-Serono, Teva Pharmaceutical Industries Ltd, Novartis, Roche and Biogen Idec, and has research agreements with Siemens AG.

Update in inflammatory-demyelinating diseases: Multiple Sclerosis

- MS diagnosis: McDonald 2017 criteria
- MAGNIMS guidelines 2020
- New MRI features
- MS prognosis
- MS treatment response
- Neurofilaments light chain (NfL)

Diagnosis of Multiple Sclerosis through the ages



- MRI = magnetic resonance imaging; MS = multiple sclerosis.

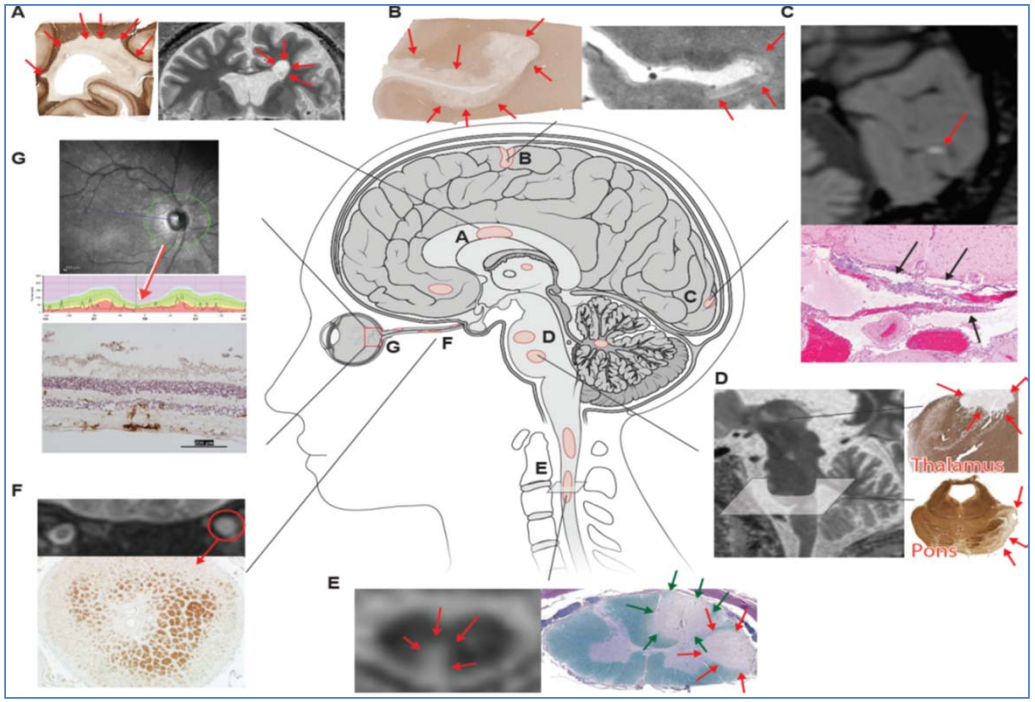
- 1. Allison and Millar. Ulster Med J. 1954;23(Suppl 2):1-27. 2. Schumacher et al. Ann N Y Acad Sci. 1965;122:552-568. 3. Gafson et al. Mult Scler Relat Disord. 2012;1:9-14. 4. McDonald and Halliday. Br Med Bull. 1977;33:4-9. 5. Poser et al. Ann Neurol. 1983;13:227-231. 6. McDonald et al. Ann Neurol. 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: 2017 McDonald criteria

Dissemination in space (DIS)

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

Thompson AJ et al. Lancet Neurol 2017

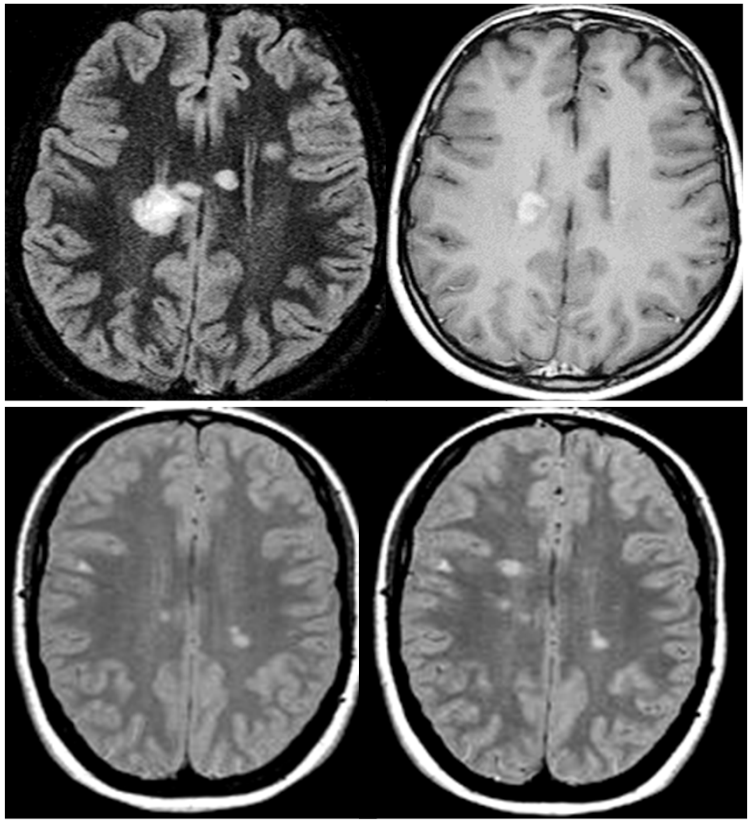


Reich DS et al. N Engl J Med 2018

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

***symptomatic or asymptomatic**

MS diagnosis: 2017 McDonald criteria



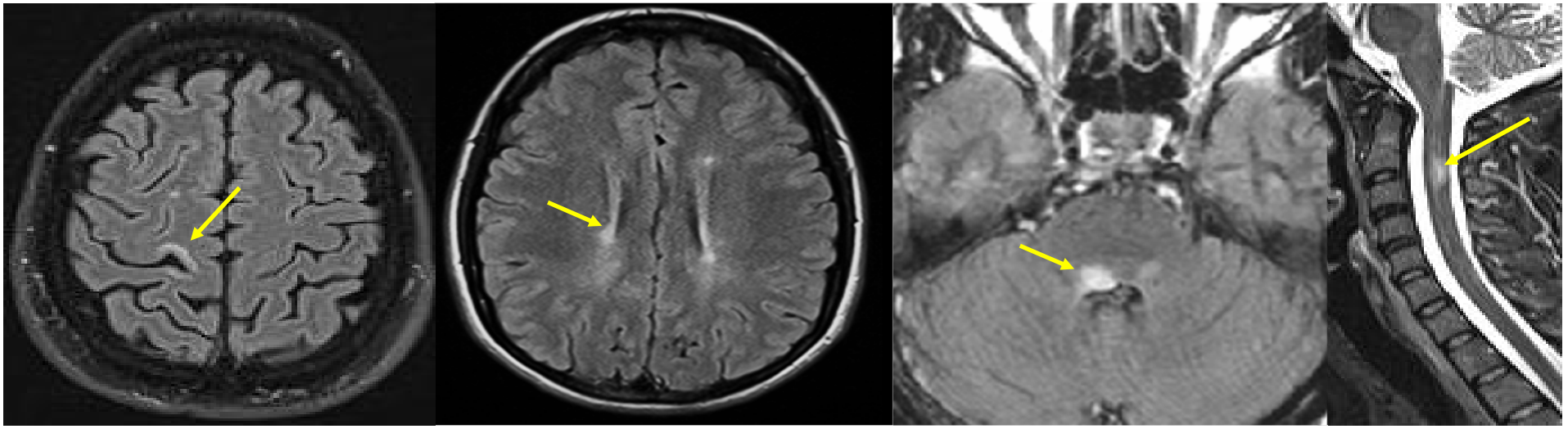
Dissemination in time (DIT)

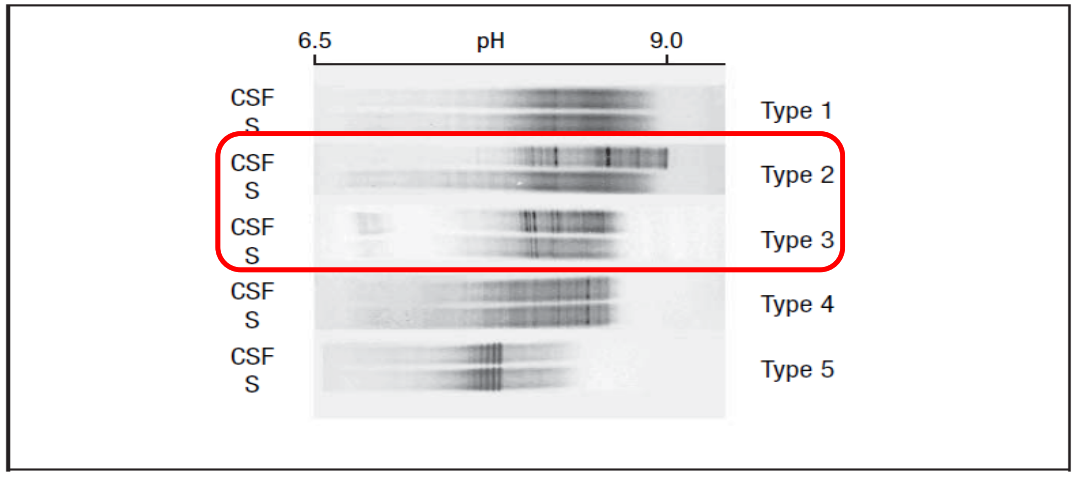
- Simultaneous presence of Gd+ and non-enhancing lesions at any time

- New T2 and/or Gd+ lesion on follow-up MRI
  - Compared to reference (baseline) MRI

Thompson AJ et al. Lancet Neurol 2017

MS diagnosis: McDonald 2017 criteria (DIS plus OB)





Presence of **OB in CSF** is accepted as an alternative to DIT

Thompson AJ et al. Lancet Neurol 2017

MS diagnosis: 2017 McDonald criteria

Dissemination in space (DIS)

- **≥1 T2 lesion* in 2 out of 4 regions of the CNS**
  - Periventricular
  - 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

or

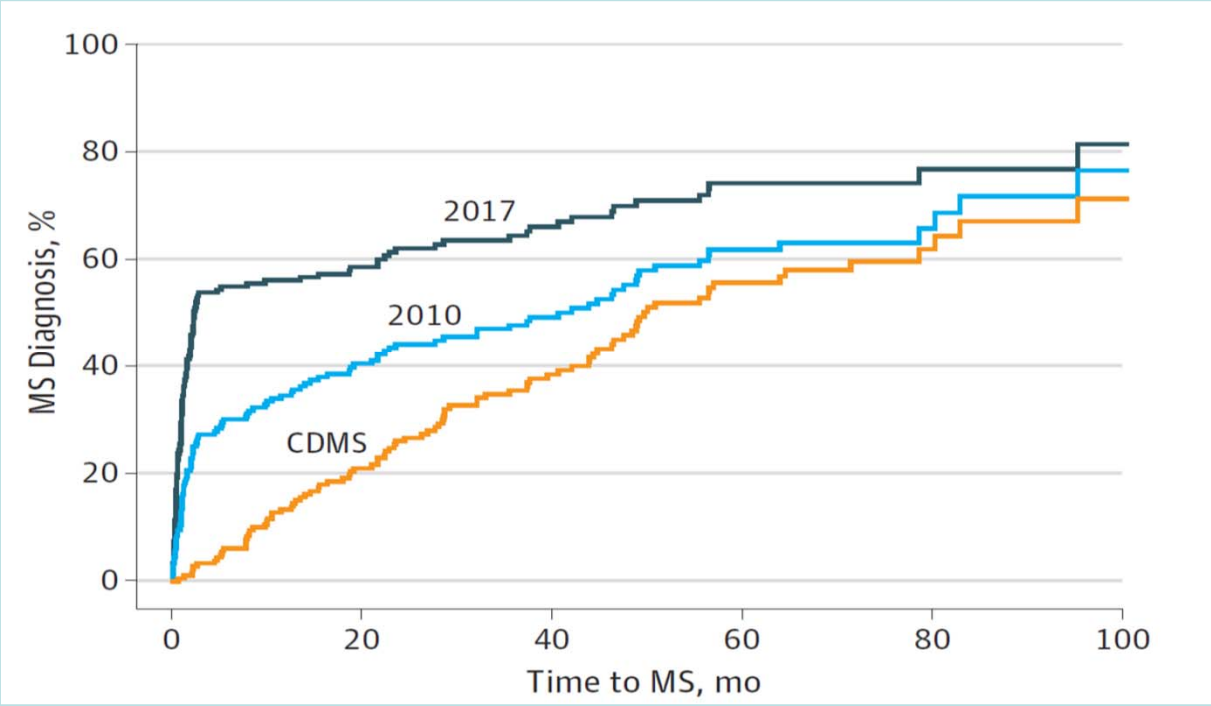
- Demonstration of DIS and presence of CSF specific oligoclonal bands

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

*Gd not needed for demonstration of DIS

Thompson AJ et al. Lancet Neurol 2017

Application of the 2017 Revised McDonald Criteria



van der Vuurst de Vries et al. JAMA Neurol 2018

The 2017 revised McDonald criteria associated with:

- greater sensitivity (earlier diagnosis)
- but less specificity

for a second attack than the previous 2010 criteria.

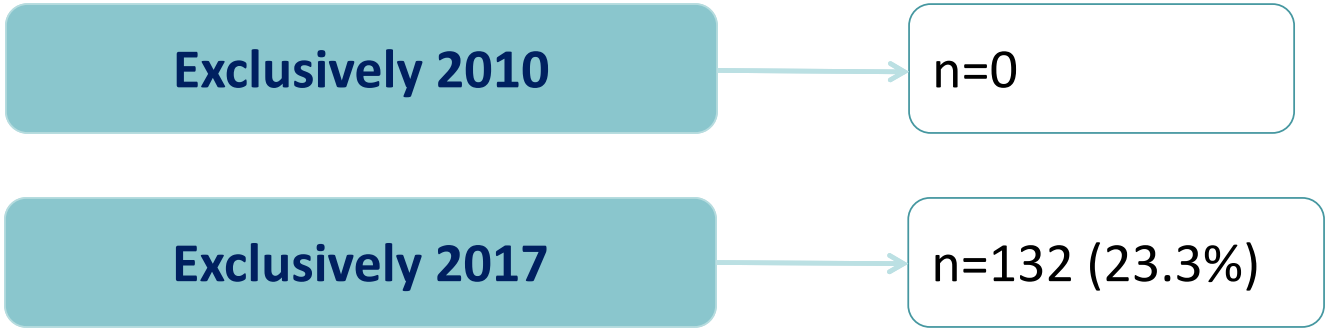
McDonald 2017 leads to a higher number of MS diagnoses in patients with a less active disease course.

Application of the 2017 Revised McDonald Criteria (Vall d'Hebron experience)

McDonald criteria

n=566	Criteria fulfillment n (%)
DIS and DIT 2010	**159 (28.1)**
DIS and DIT 2017	**168 (29.7)**
DIS and +OB 2017	**263 (46.5)**
Complete 2017 McDonald criteria	**291 (51.4)**

Patients fulfilling:



Standardisation and harmonisation of MRI acquisition

- High quality MRI scans
- Optimisation of MRI sensitivity (brain and spine)
- Facilitation of comparative analysis (visual, automated)
- Integration in multicentre studies
- Implementation of quantitative and automated MRI assessments
- Creation of big data repositories (MRI, clinical, OCT, fluid biomarkers...)
    - Prognostic models
    - Treatment response predictive models

MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis – clinical implementation in the diagnostic process

Rovira A et al. *Nat Rev Neurol*. 2015

MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis – establishing disease prognosis and monitoring patients

Wattjes M et al. *Nat Rev Neurol*. 2015

Revised recommendations of the consortium of MS Centers Task Force for a standardized MRI protocol and clinical guidelines for the diagnosis and follow-up of MS

Traboulsee A et al. *AJNR 2016*

OCT, *optical coherence tomography;* ***MRI,*** *magnetic resonance imaging.*

European Commission decision on use of GBCAs

- Use GBCAs only if essential
- Use GBCAs at lowest dose needed
- Only macrocyclic agents
    - Exceptions: Primovist/Multihance (liver-imaging), Magnevist joint-imaging

Despite lack of evidence of the clinical effects (in subjects with normal renal function) and limitations in the assessment of gadolinium deposition in CNS, special caution in patients at higher risk:

- Patients requiring multiple lifetime doses
- Pregnant and paediatric patients
- Patients with inflammatory conditions
- Patients receiving radiotherapy

Minimise repetitive GBCA imaging studies when possible

- No use of GBCAs
- Lower dose
- Alternatives to GBCAs

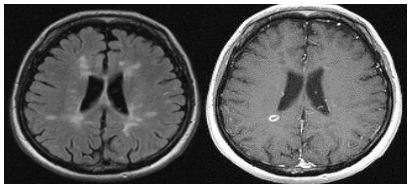
Multiple sclerosis
Inflammatory bowel disease
Paediatric oncologic patients

***CNS**, central nervous system; **GBCA**, gadolinium-based contrast agents.*

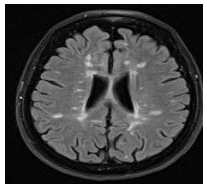
European Medicines Agency 23/11/2017 EMA/625317/2017.

MRI in monitoring MS

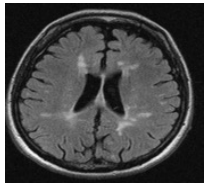
Initial	Re-Baseline	First follow up[a,b]	Second follow up[a, b]	Follow ups[a, b]
Diagnostic[c] Pre-treatment	3–6 months after treatment onset **Gad optional[e]**	12 months after Re-Baseline	24 months after Re-Baseline	Every year[d]
Gad highly recommended		**Gad optional[f]**	**Gad optional**	**Gad optional[e]**

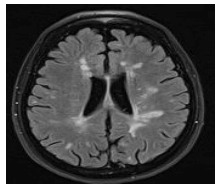


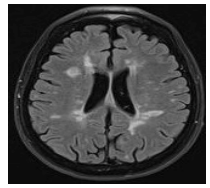
Assess markers of poor prognosis



Active lesions should be ignored (unless associated with clinical activity or unexpected high MRI activity)







Apply predictive response/prognostic scales/models

DMT, *disease-modifying treatment;* ***GA,*** *glatiramer acetate;* ***IFN,*** *interferon.*

[a] Shorter follow-up MRI (6 months) if isolated significantly MRI activity or isolated clinical activity; [b] Add spinal cord MRI to brain MRI if clinically indicated;

[c] Add spinal cord MRI to brain MRI for initial diagnosis or if never performed; [d] Less frequent MRIs in clinically stable patients treated with IFN or GA;

[e] Gad required if clinical activity/progression; [f] Particularly in patients receiving moderate efficacy DMTs.

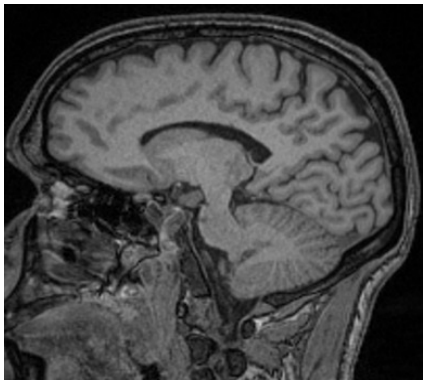
1. *Rovira A et al. Nat Rev Neurol. 2015;11:471-82;* ***2.*** *Wattjes M et al. Nat Rev Neurol. 2015;11:597-606;* ***3.*** *Traboulsee A et al. AJNR Am J Neuroradiol. 2016;37:394-401.*

Brain MRI protocol for monitoring: new

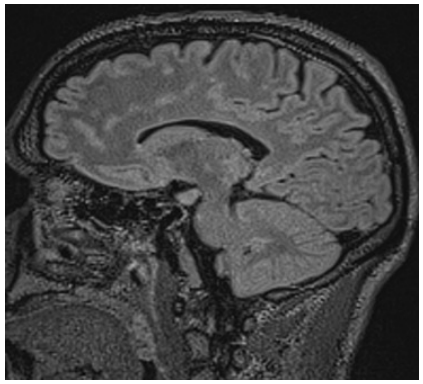
Vall d'Hebron Hospital

Delete: T2/PD
Add: DWI (safety)

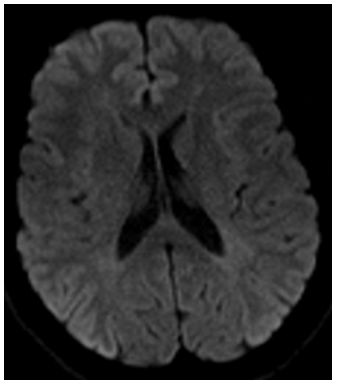
Optional



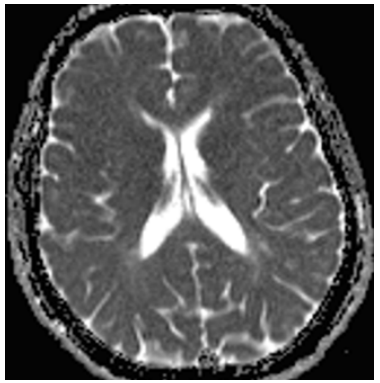
3D T1 MP-RAGE



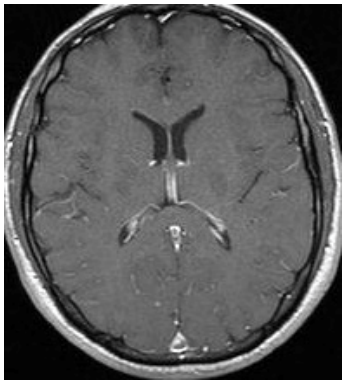
3D T2-FLAIR



DWI



ADC



CE-T1WI

0.1 mmol/kg BW (macrocyclic GBCA) only in selected cases

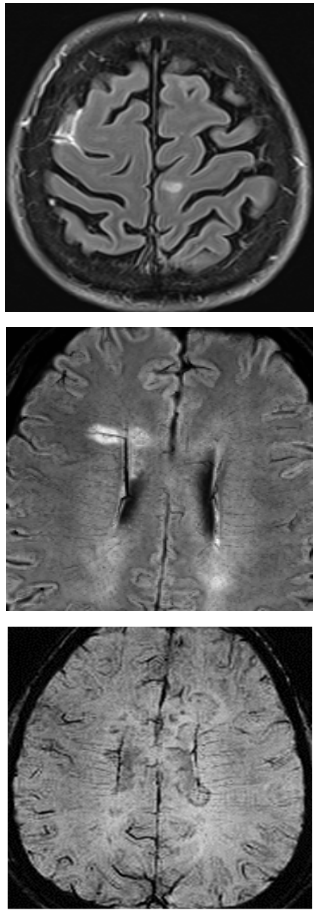
Minimum delay 5-10 minutes

ADC, apparent diffusion coefficient; BW, body weight; CE, contrast enhanced; DWI, diffusion-weighted imaging; FLAIR, fluid attenuated inversion recovery; GBCA, gadolinium-based contrast agents; MP-RAGE, Magnetisation Prepared - RApid Gradient Echo; PD, proton density.

1. Rovira A et al. Nat Rev Neurol. 2015;11:471-82; 2. Wattjes M et al. Nat Rev Neurol. 2015;11:597-606; 3. Traboulsee A et al. AJNR Am J Neuroradiol. 2016;37:394-401.

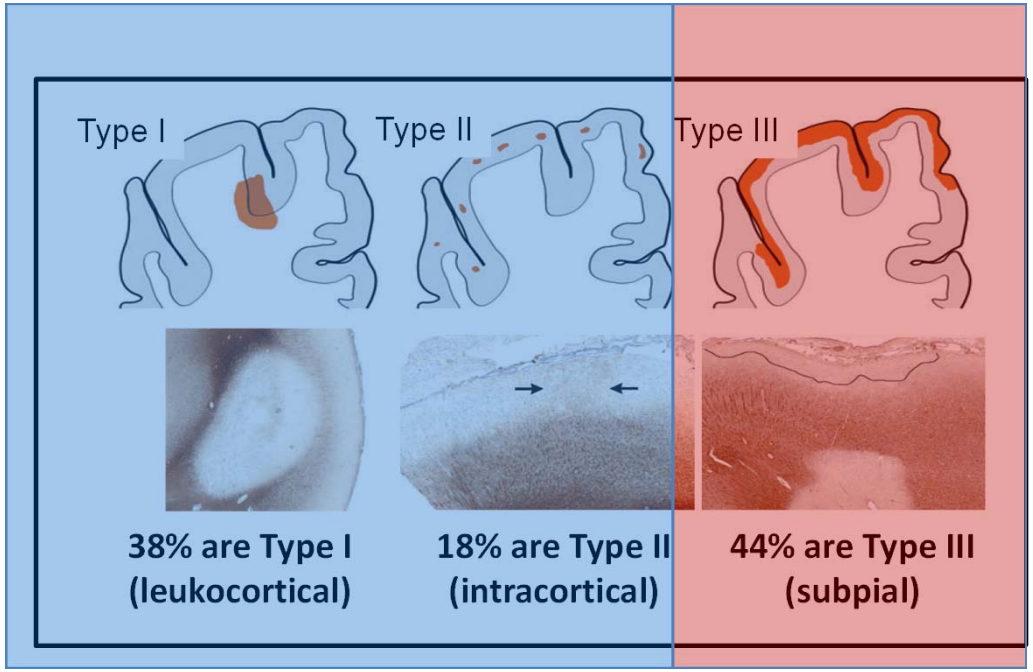
New MRI findings in Multiple Sclerosis

- ✓Leptomeningeal enhancement
- ✓Central vein sign
- ✓Hipointense rims/ dots



Focal lesions in grey matter: 90% of MS autopsy cases show cortical demyelination

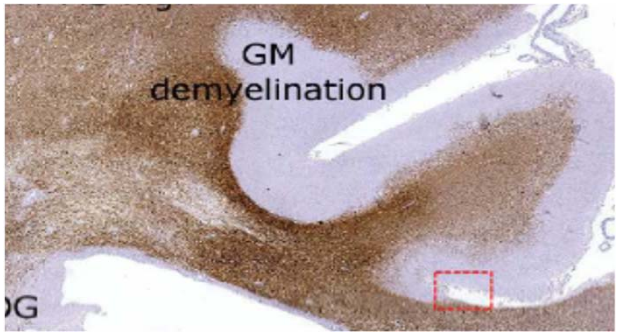
- Characterised by:
  - demyelination[1]
  - microglial activation[1]
  - often meningeal inflammation[2,3]
- Less often associated with[4]
  - immune cell influx
  - complement activation
  - BBB leakage
- Difficult to detect by MRI[5]
- Three types of cortical lesion*[6]



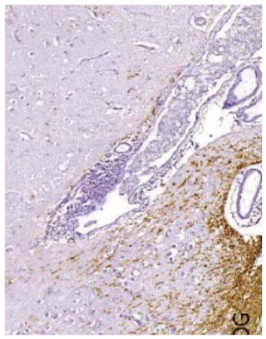
*Based on post-mortem tissue samples taken from 22 patients with MS. Leukocortical Type I lesions involve neocortex and subcortical white matter; intracortical Type II lesions are confined to the neocortex and often located around a vessel; subpial Type III lesions extend from the pial surface into the neocortex. 1. Peterson JW *et al. Ann Neurol* 2001; 2. Lucchinetti CF *et al. N Engl J Med* 2011; 3. Magliozzi R *et al. Ann Neurol* 2010; 4. Klaver R *et al. Prion* 2013; 5. Filippi M *et al. Neurology* 2010; 6. Wegner C *et al. Neurology* 2006

TMC Academy

Subpial demyelination: cortical lesiones type III



Subpial demyelination



Meningeal inflammation (B and T cells)

Lesion type	Number	Mean lesion size (mm^2)	Percentage of total demyelinated Area
1 (mixed WML/GML)	17	29.2	14.4
2	18	2.4	1.2
3	65	35.5	67.0
4	9	66.2	17.3
Intracortical lesions (2–4)	92	32.1	85.6

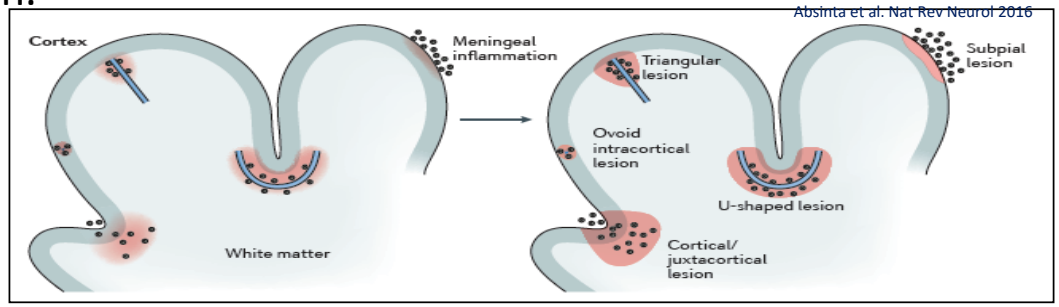
Bo et al. J Neuropathol Exp Neurol 2003

Most common cortical lesion

Affects the largest cortical area

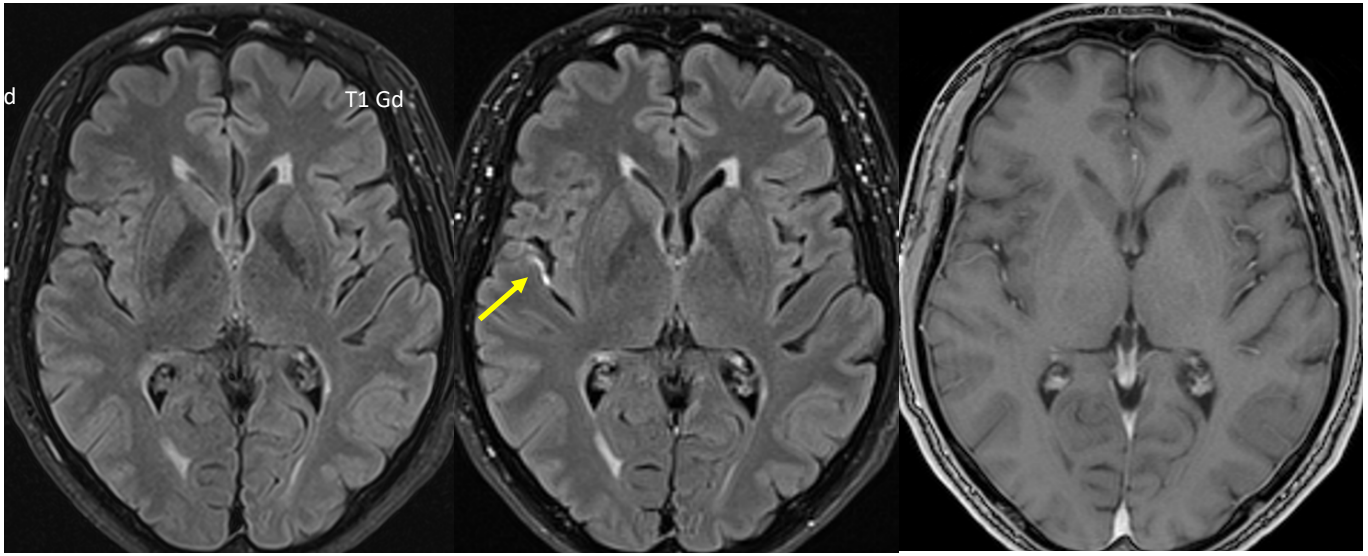
A common appearance:

- long ribbons of subpial demyelination, often affecting several adjacent gyri
- wedge-shaped, with the basis at the surface of the brain.



Absinta et al. Neurology 2017; Absinta et al. Neurology 2015; Howell et al. Brain 2013; Lucchinetti et al. 2011

Cortical lesiones: type III



- Meningeal inflammatory infiltrates are found in most patients with MS and 40%–50% of subjects with SPMS
- Meningeal infiltrates may play a contributory role in the underlying subpial grey matter pathology (subpial demyelination, atrophy)
- Presence of B cell folicle-like structures
- Associated with an agressive disease course
- Associated with leptomeningeal contrast enhancement (BBB dysfunction of leptomeningeal vessels)

Absinta et al. Neurology 2017; Absinta et al. Neurology 2015; Howell et al. Brain 2013; Lucchinetti et al. 2011

Leptomeningeal enhancement: dynamic changes

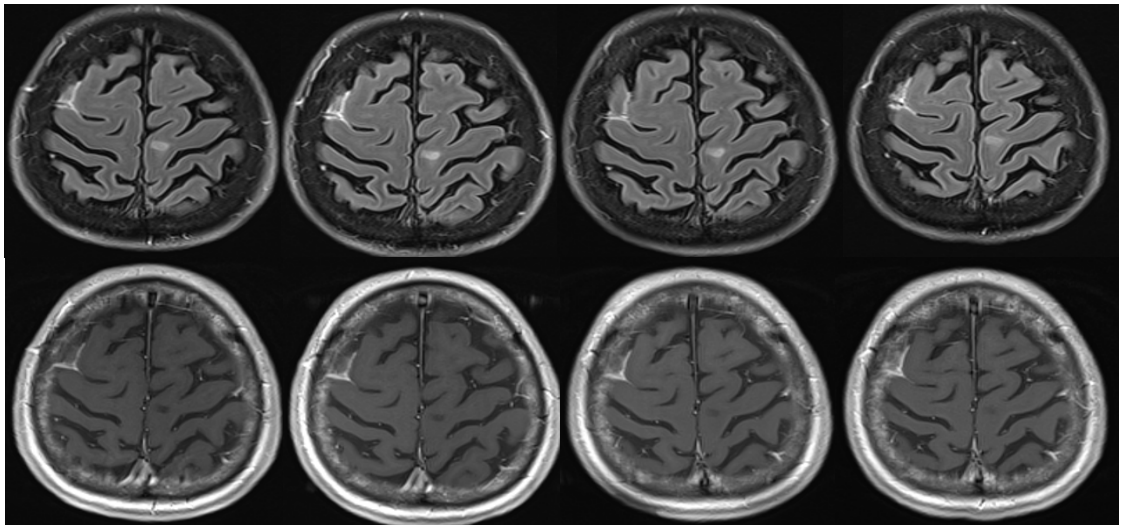


Table 3: Anatomic distribution within the brain of enhancing meningeal foci at baseline

Brain Region	No. of Foci at Baseline	Percentage of Foci at Baseline
Right frontal	60	21.1
Left frontal	64	22.5
Right parietal	44	15.5
Left parietal	44	15.5
Right occipital	20	7.0
Left occipital	24	8.4
Right temporal	16	5.6
Left temporal	8	2.8
Right cerebellum	2	0.7
Left cerebellum	2	0.7

- LME persistence range from 71% to 100% at 1 year and 73% to 100% at 2 years,
- Subarachnoid spread/fill and subarachnoid nodular subtypes persist less often than vessel wall and dural foci.
- Persistence is not significantly different between those on/off treatment and those with **progressive/non-progressive disease phenotypes**.
- The number of persisting foci was significantly **different in subjects with/without increasing EDSS scores** (median, 12 versus 7.5, *P* .04).

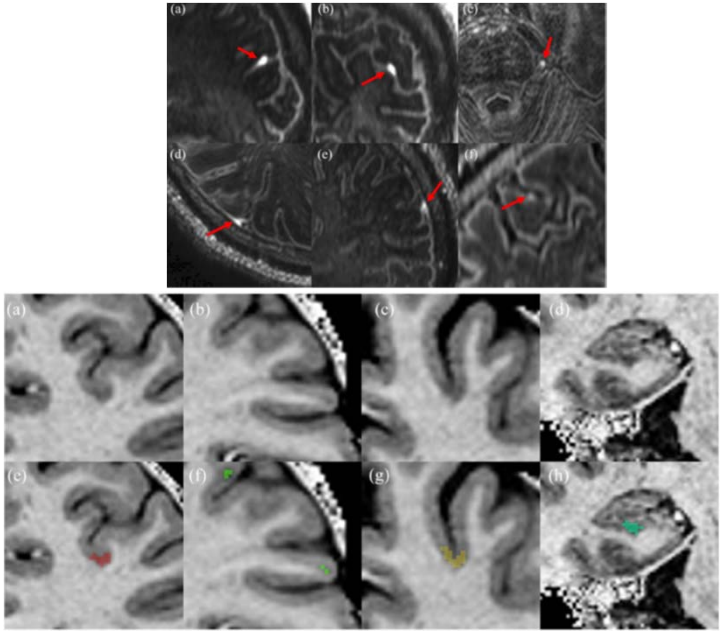
Jonas et al. Am J Neuroradiol 2018

Leptomeningeal enhancement and cortical damage (7T)

Autopsy data suggest that patients with leptomeningeal follicles are prone to increased cortical demyelination and neuronal los (Magliozzi et al. Brain 2007; Howell et al. Brain 2011)

Table 2. Correlation matrix for RRMS participants only.

	Nodular count	Spread/fill-sulcal	Spread/fill-gyral	Spread/fill-infratentorial	Spread/fill count	LME—any count
Leukocortical CL count	0.13	0.30	0.01	0.13	0.17	0.16
Leukocortical CL volume	0.33	0.04	0.15	0.06	0.12	0.18
Intracortical CL count	0.04	0.28	0.04	<–0.01	0.18	0.16
Intracortical CL volume	0.07	0.12	0.01	−0.09	0.06	0.05
Subpial CL count	0.07	0.14	−0.10	−0.13	0.03	0.07
Subpial CL volume	0.05	0.15	0.09	−0.12	0.14	0.17
Hippocampal CL count	−0.17	**0.53****	0.33	0.19	**0.46****	**0.39***
Hippocampal CL volume	−0.17	**0.43***	0.31	0.12	**0.38***	0.31
Total CL count	0.09	0.32	0.03	0.07	0.20	0.19
Total CL volume	0.17	0.20	0.23	−0.01	0.24	0.27
Cortical GM volume	−0.30	**–0.41***	−0.32	**–0.37***	**–0.44***	**–0.49****
Mean cortical thickness	0.07	**–0.45***	**–0.57****	**–0.42***	**–0.64****	**–0.59****
Cerebral WM volume	0.07	0.13	0.20	**0.38***	0.20	0.21
WM lesion volume	0.09	0.28	0.14	0.17	0.20	0.24

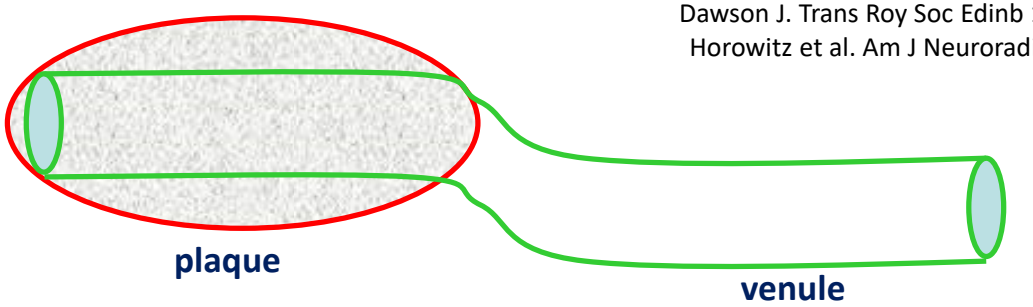


- Relationship between LME and cortical GM atrophy
- No association of LME and neocortical CLs.

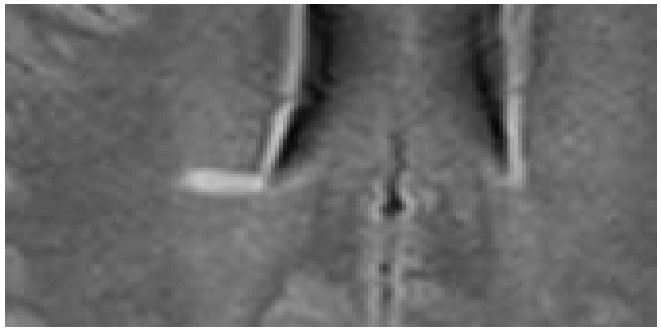
Meningeal inflammation is involved with neurodegenerative inflammatory processes, rather than focal lesion development.

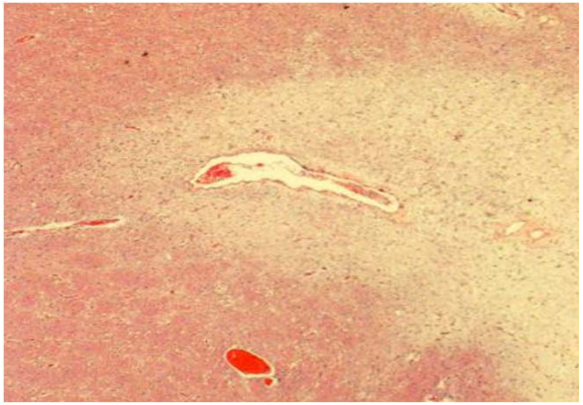
Ighani et al. Mult Scler J 2019

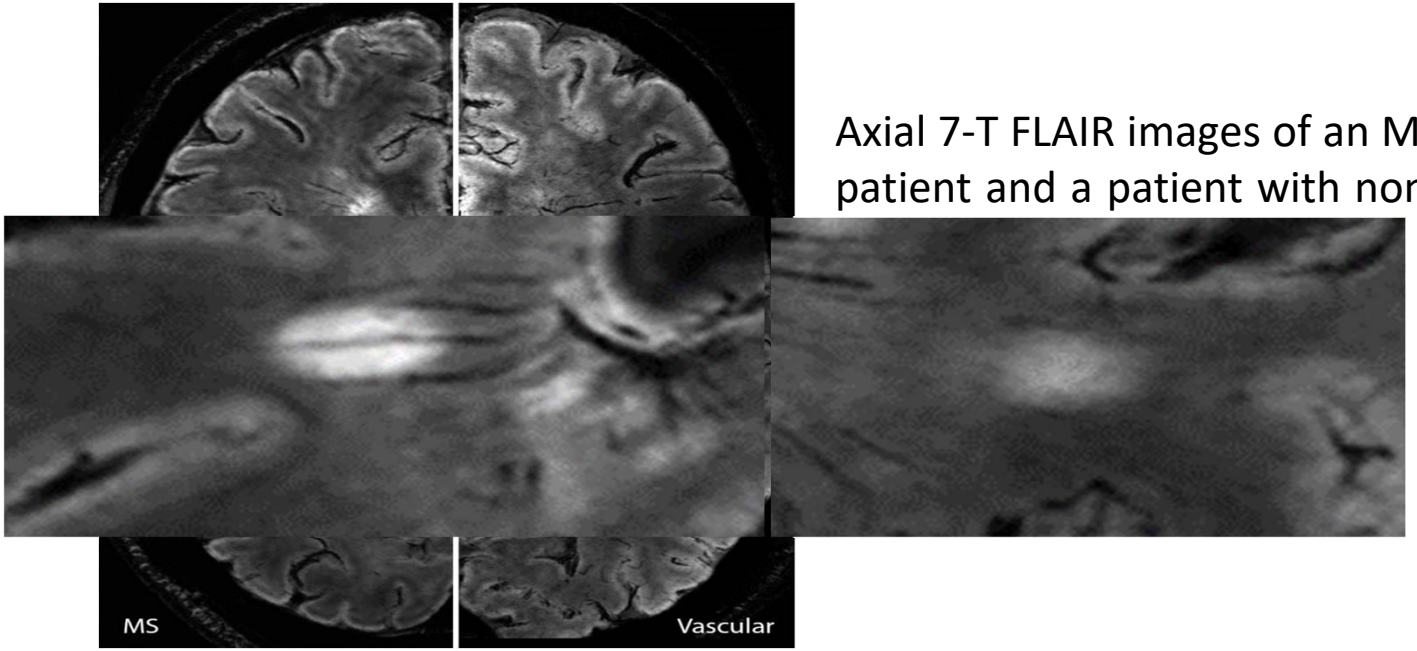
Susceptibility-weighted MR imaging in MS



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





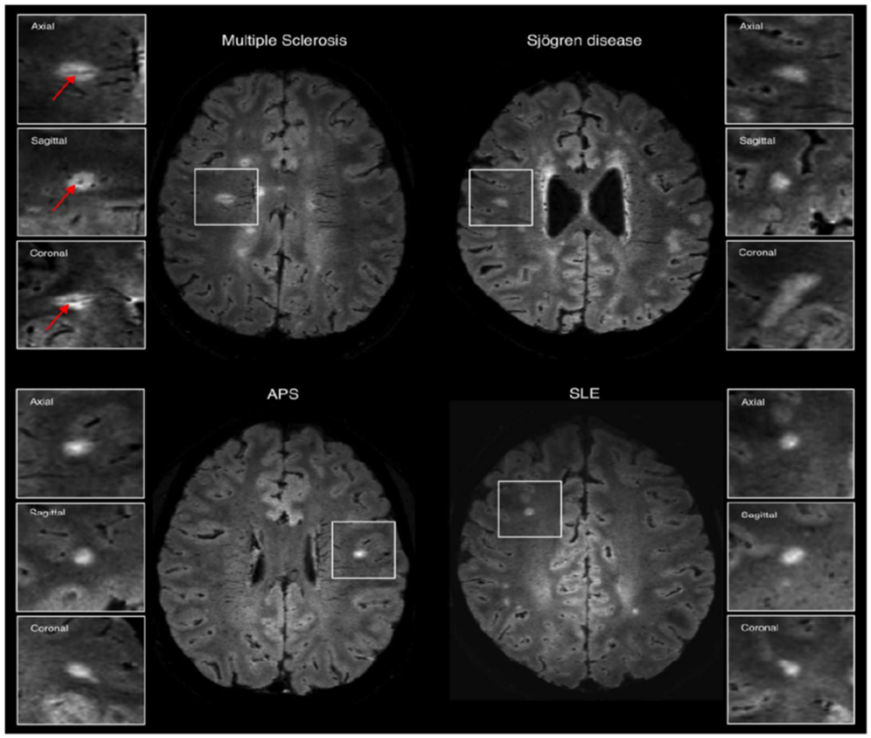


Axial 7-T FLAIR images of an MS patient and a patient with non-

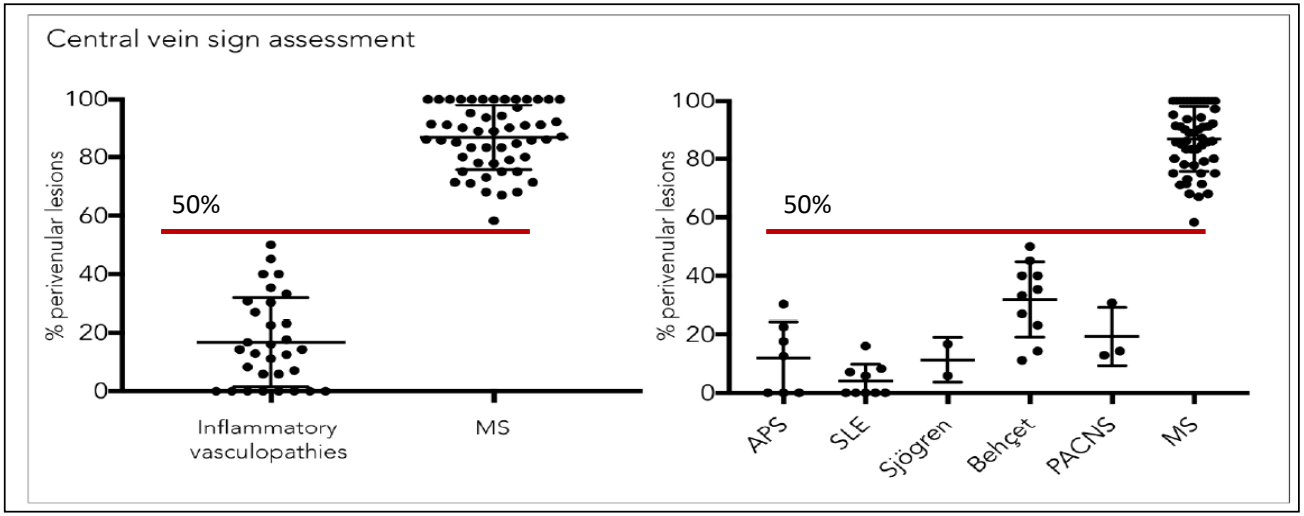
Kilsdonk ID et al. *Eur Radiol.* 2014;24:841–849

Central vein sign (3.0 - 1.5T)

31 patients with inflammatory CNS vasculopathies and 52 with RRMS
3D T2*-w EPI acquired during or after iv injection of a single dose (0.1 mmol/kg) of GBCA



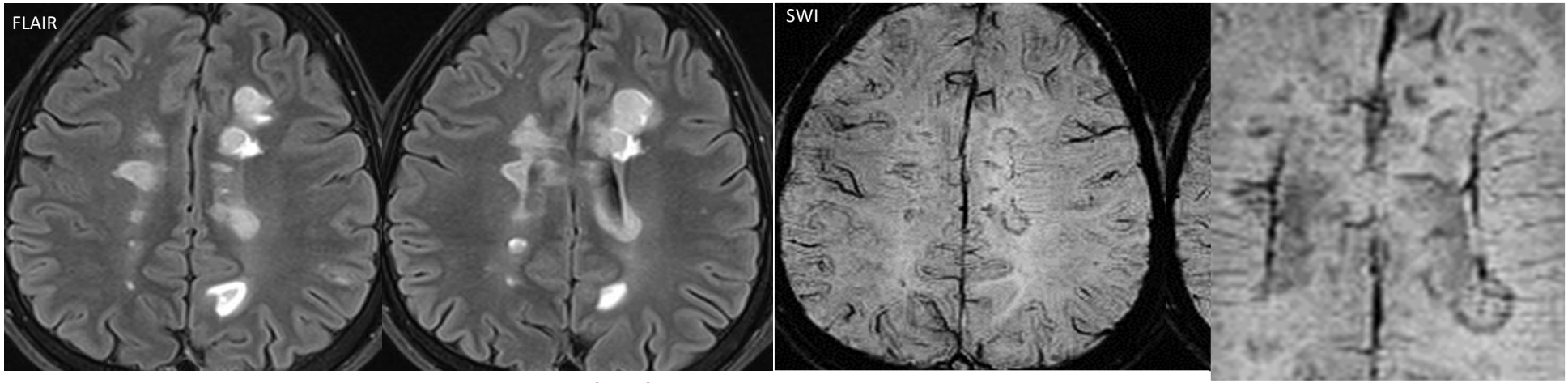
Magi et al. Ann Neurol 2018



The “central vein sign” differentiates inflammatory CNS vasculopathies from MS at standard clinical magnetic field strengths.

Susceptibility-weighted MR imaging in MS

Intralesional susceptibility signal (ISS) in MS (3T)



Intralesional susceptibility signal (ISS)

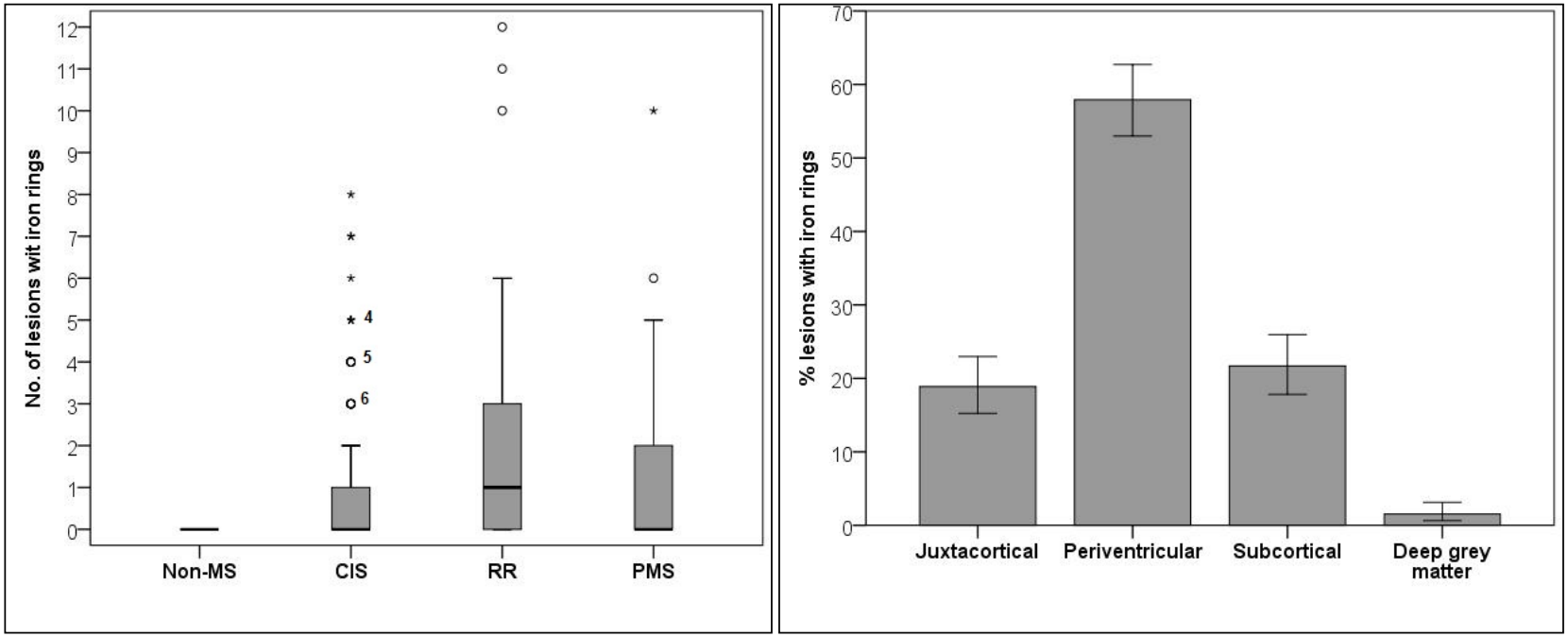
50% of T2 lesions

Rovira et al. Multiple Sclerosis Journal 2015; 21 (S11):209

Likely represents iron-rich macrophages / microglia
Myelin loss also contributes

Hagemeier et al. J Magn Reson Imaging 2012;36:73-83; Bian et al. Mult Scler 2013;19:69-75

Hypointense rims: MS versus other CNS disorders

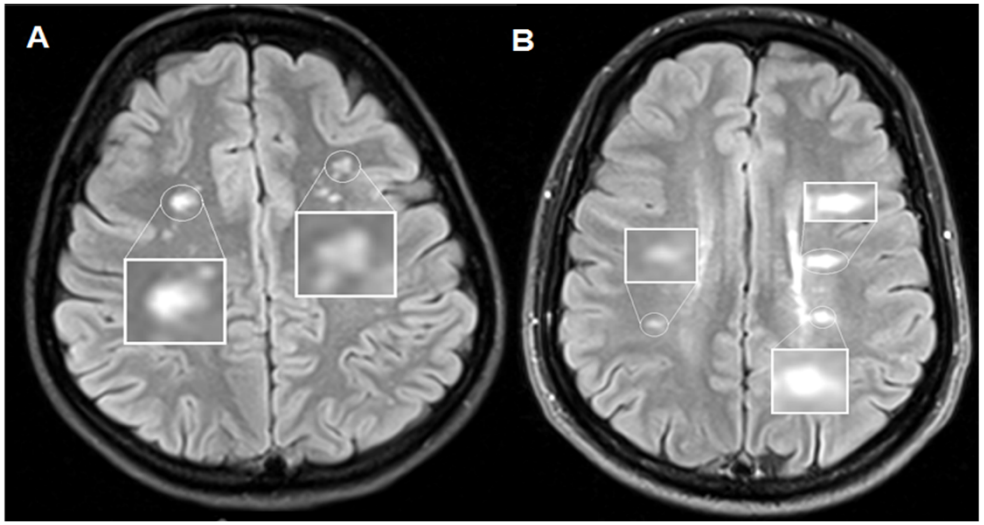


48% of CIS, 59% of RR and 39% of PMS patients had at least one lesion with an IR

Rim positive lesions were more likely to be found **periventricularly** than in other locations (X^2 (3) = 263.8, p<0.001)

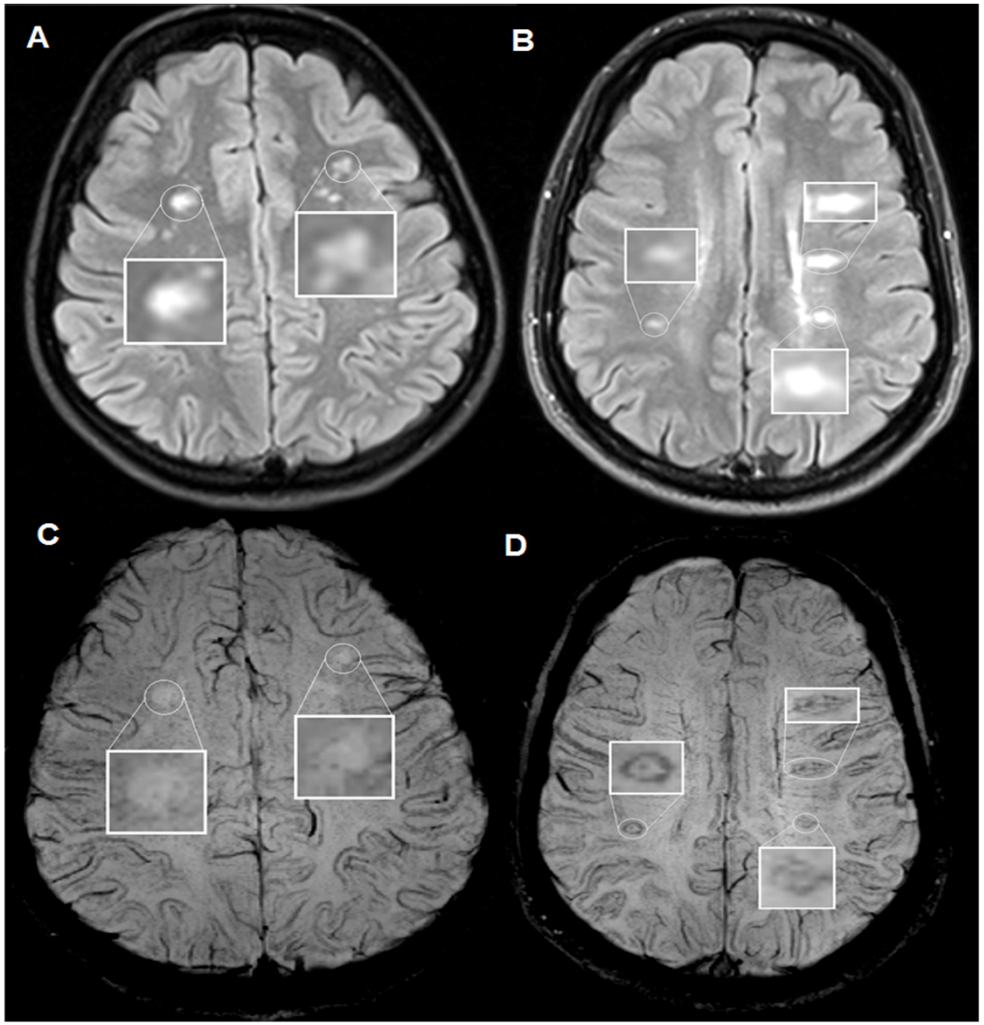
Clarke, Rovira et al. ECTRIMS 2019

Susceptibility-weighted MR imaging in MS



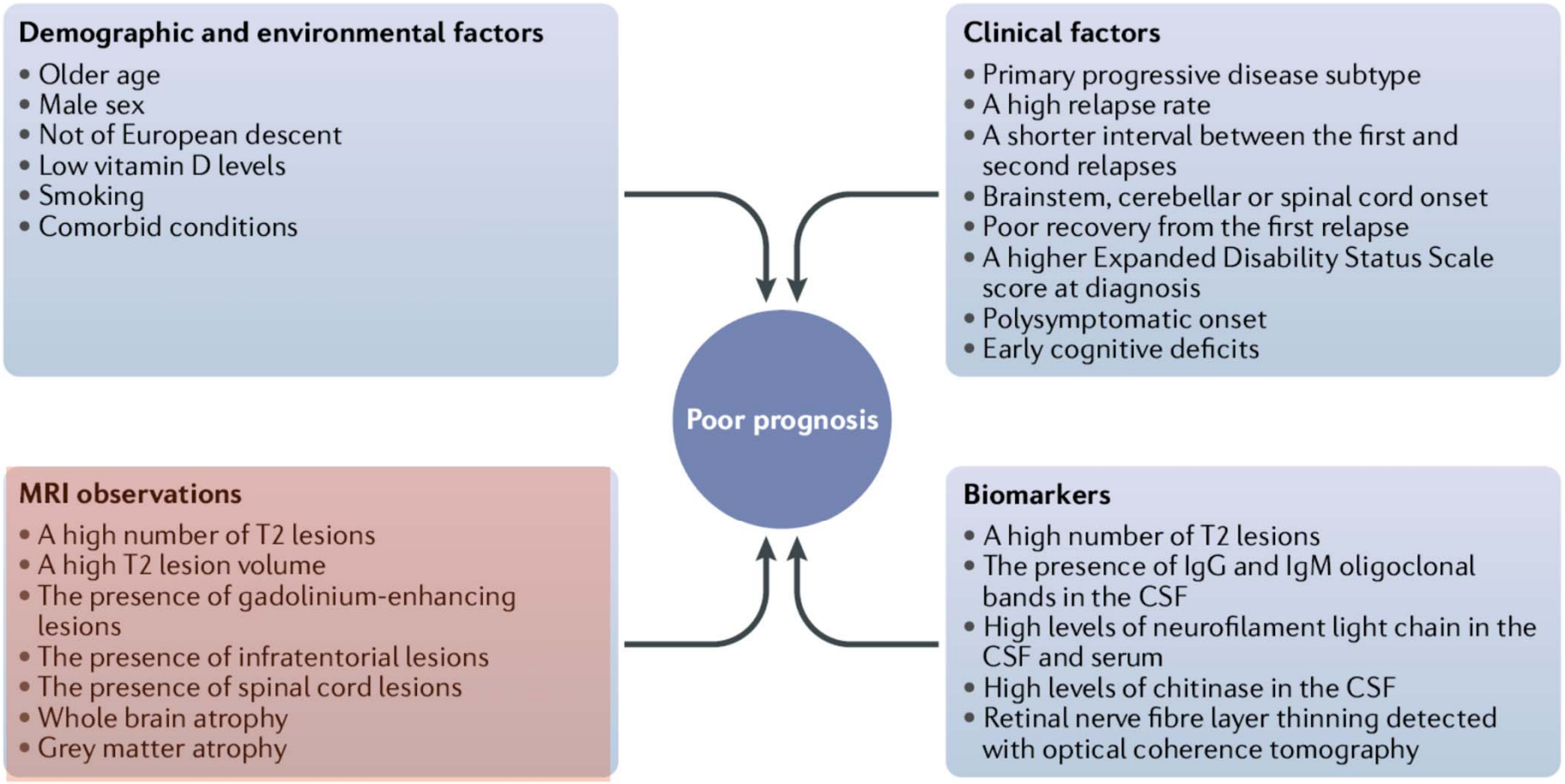
Susceptibility-weighted MR imaging in MS

Systemic vasculitis



MS

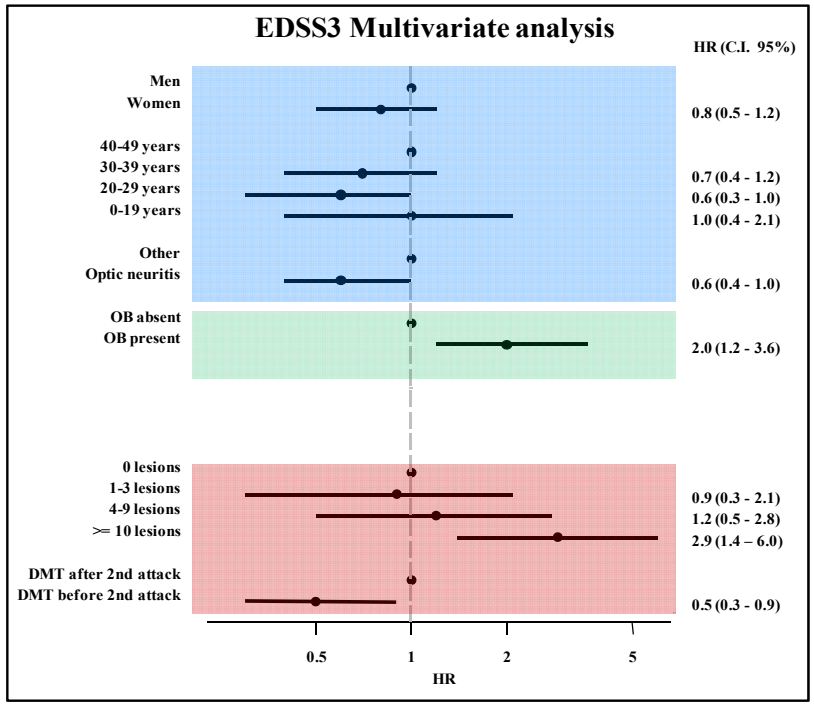
Prognostic factors: relapses, disability worsening



Rotstein, Montalban. Nat Rev Neurol 2019

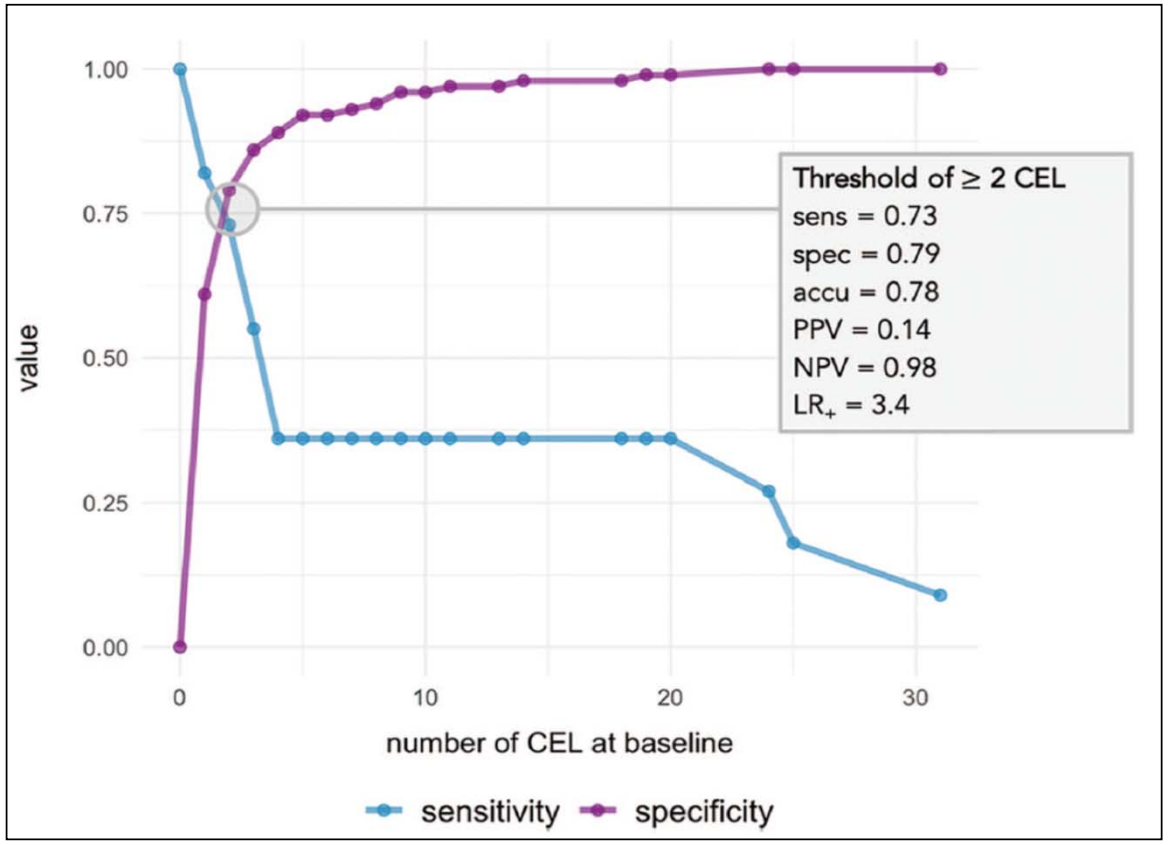
Prognostic factors at disease onset: The Barcelona inception cohort

- Study design: Barcelona inception cohort
- Sample size: 1,015 CIS patients
- Follow-up: 6.75 years (mean)
- Final outcomes: reaching EDSS score of 3.0 or more



Tintoré, Rovira et al. Brain 2015

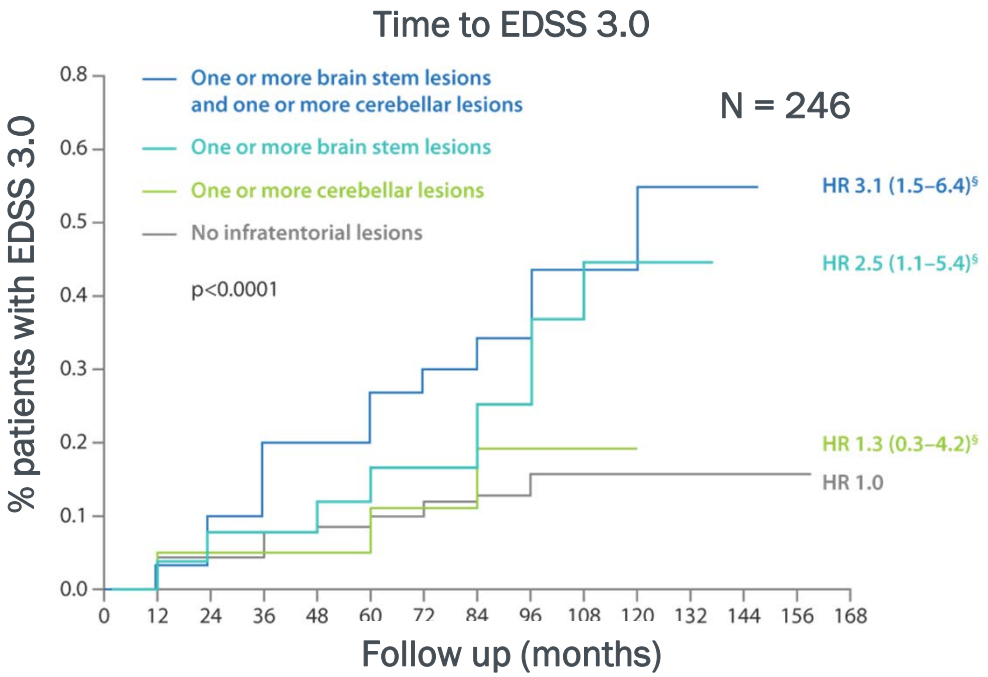
- Study design: Barcelona inception cohort
- Sample size: 401 CIS patients
- Follow-up: 10 years (mean)
- Final outcomes: reaching EDSS score of 6.0 or more

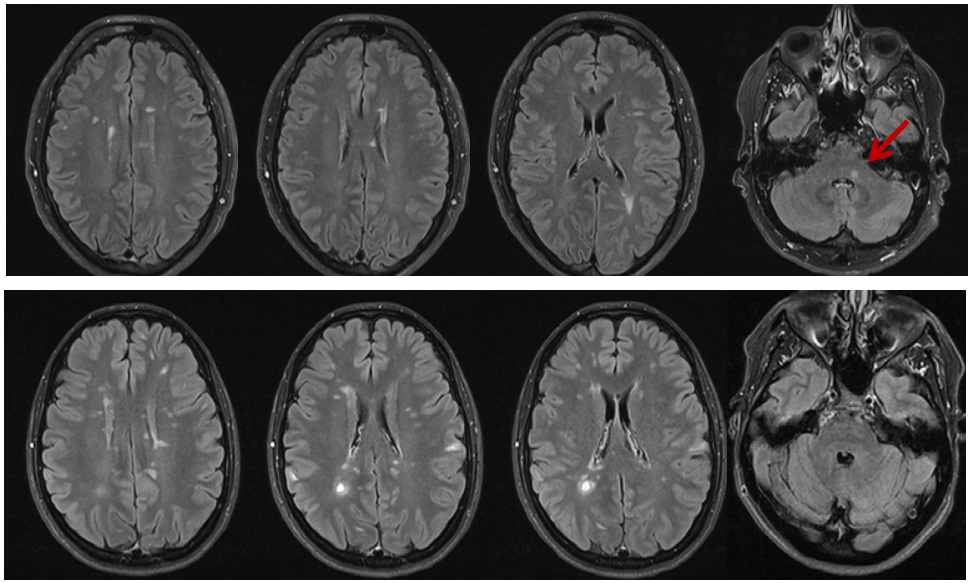


Tintoré et al., Mult Scler J 2019

Prognostic factors at disease onset: topography of lesions

The Barcelona inception cohort



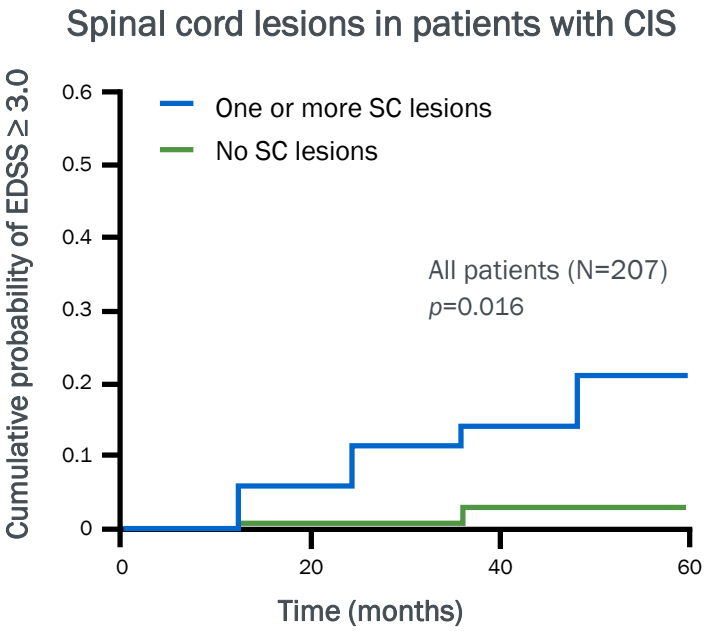


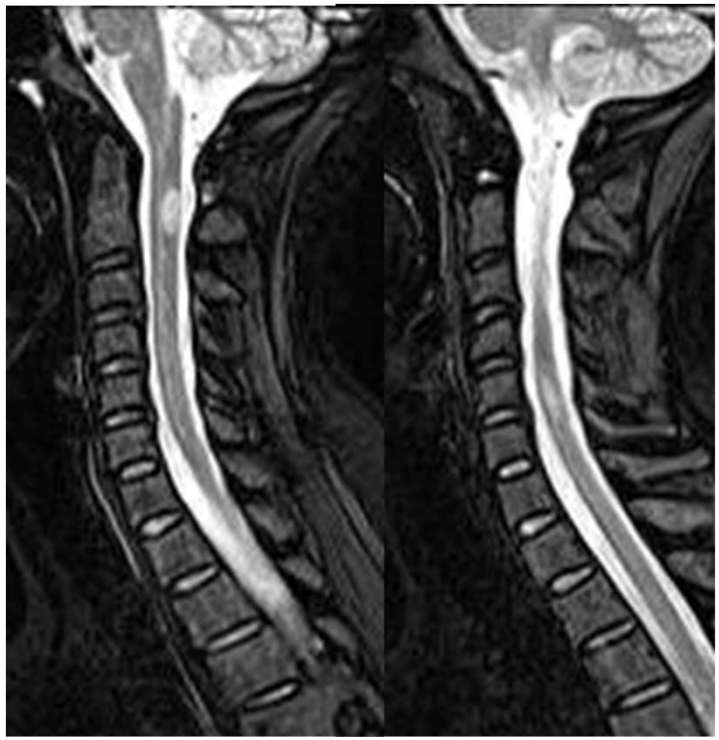
Topography of lesions can predict patients at risk of faster disability progression; presence of infratentorial lesions increases the risk for disability

Prognostic factors at disease onset: The Barcelona inception cohort

Vall d'Hebron Hospital

Topography of lesions can predict patients at risk of faster disability progression

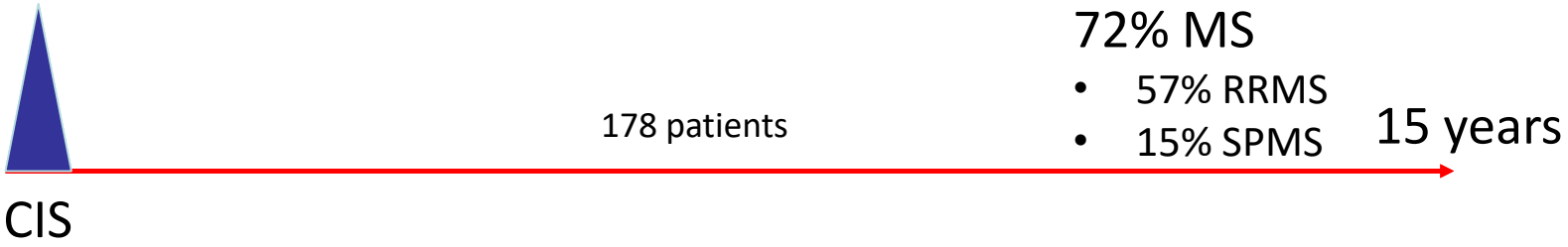


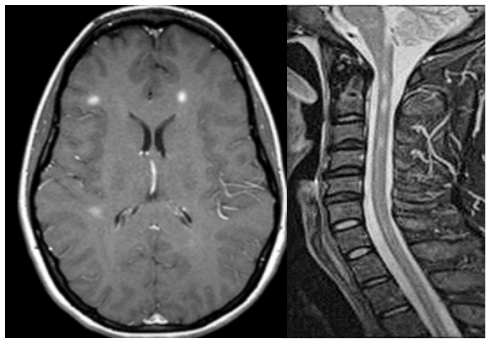


The presence of at least one SC lesion at the time of the CIS is associated with short-term disability and further contributes to estimate the risk of disability accumulation, particularly in non-SC CIS.

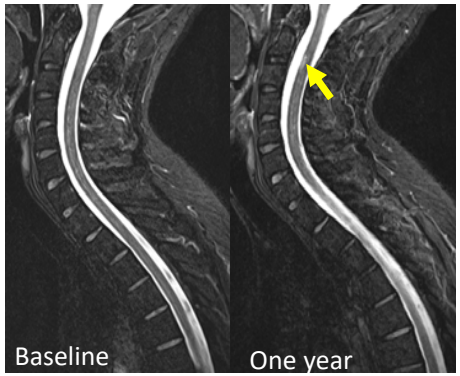
Arrambide, Rovira et al. MSJ 2017

Early MRI predictors long term outcome (CIS)





Baseline MRI



Baseline MRI model:

Gad lesions (≥2) and spinal cord lesions (≥ 1) were independently associated with higher odds of conversion to SPMS at 15 years (C-statistic 0.76).

Table 2 Multivariable logistic regression models investigating early MRI predictors of secondary progressive disease course after 15 years

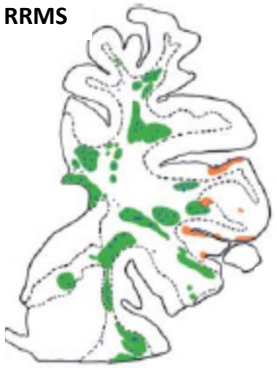
	Odds ratio	95% CI	P	C-statistic	Accuracy (95% CI)
Baseline (n = 164)				0.76	85% (79%, 90%)
Baseline GdE lesions (versus 0)					
1	1.33	0.35, 5.07	0.678		
⩾2	3.16	1.08, 9.23	0.035		
⩾1 baseline spinal cord lesions (versus 0)	4.71	1.72, 12.92	0.003		
Baseline–1 year (n = 136)				0.86	91% (85%, 95%)
Baseline GdE lesions (versus 0)					
1	2.31	0.47, 11.40	0.306		
⩾2	4.58	1.19, 17.71	0.027		
⩾1 new spinal cord lesions (versus 0)	5.72	1.67, 19.56	0.005		
⩾1 new infratentorial lesions (versus 0)	7.02	2.06, 23.94	0.002		
Baseline–3 years (n = 121)				0.89	88% (81%, 94%)
⩾1 new spinal cord lesions (versus 0)	38.68	4.67, 320.53	0.001		
⩾1 new infratentorial lesions (versus 0)	3.28	0.87, 12.31	0.079		

Brownlee et al. Brain 2019

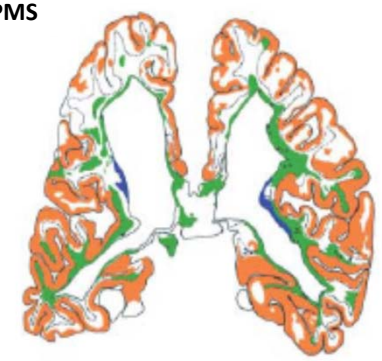
Grey matter pathology and neurodegeneration

Cortical lesions

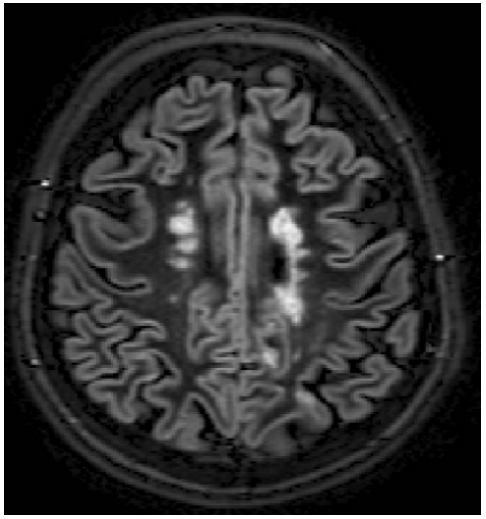
RRMS



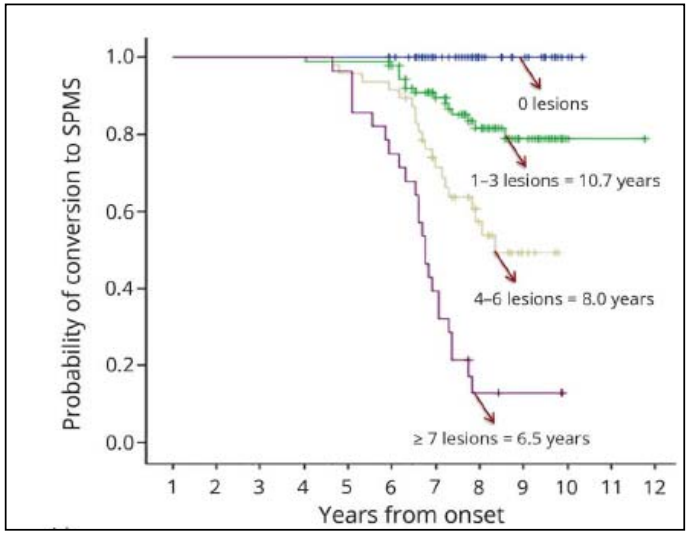
SPMS



Kutzelnigg et al., Brain 2005



Evolution to SPMS



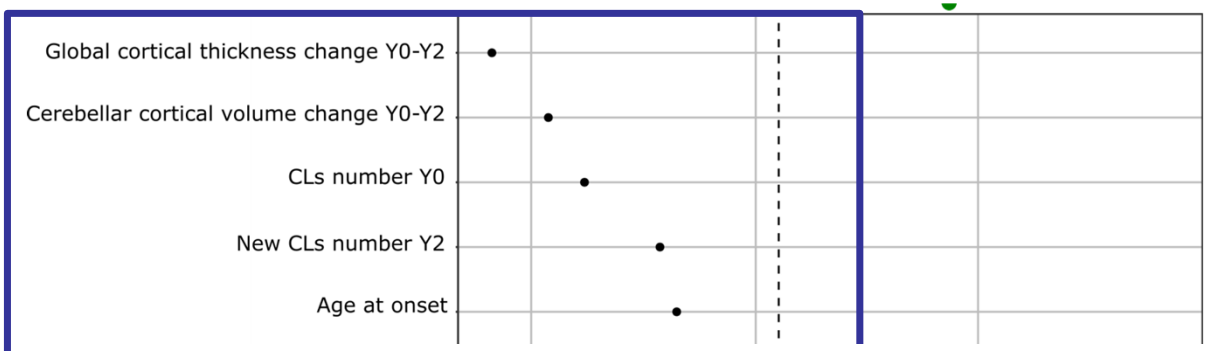
Scalfari et al.,Neurology 2018

Phenotype	CLs prevalence	CLs accumulation
RIS	Up to 40%	?
CIS	Up to 52%	28% patients (3y FU)
RRMS	Up to 64%	43-58% patients (3y-7y FU) (≈0.8-0.9 new CLs/patient/yr)
SPMS	Up to 74%	**47-48% patients** (3y-7y FU) (≈1.0 new CLs/patient/yr)
PPMS	Up to 84% (DIR) Up to 88% (PSIR)	15-58% patients (1y-2y FU) (≈0.8-1.6 new CLs/patient/yr)
Pediatric MS	Less than 12%	?

Filippi et al., Lancet Neurol 2019

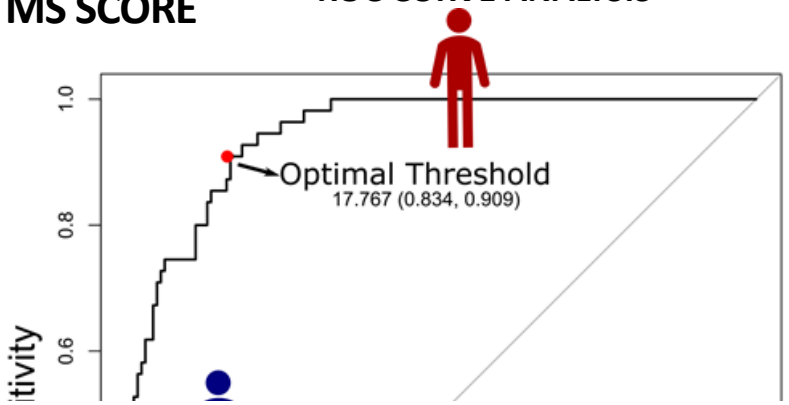
Predictors of disability worsening: Machine learning approach (Random Survival Forest)

THE MOST SIGNIFICANT PREDICTIVE FACTORS
BY USING MACHINE LEARNING APPROACH

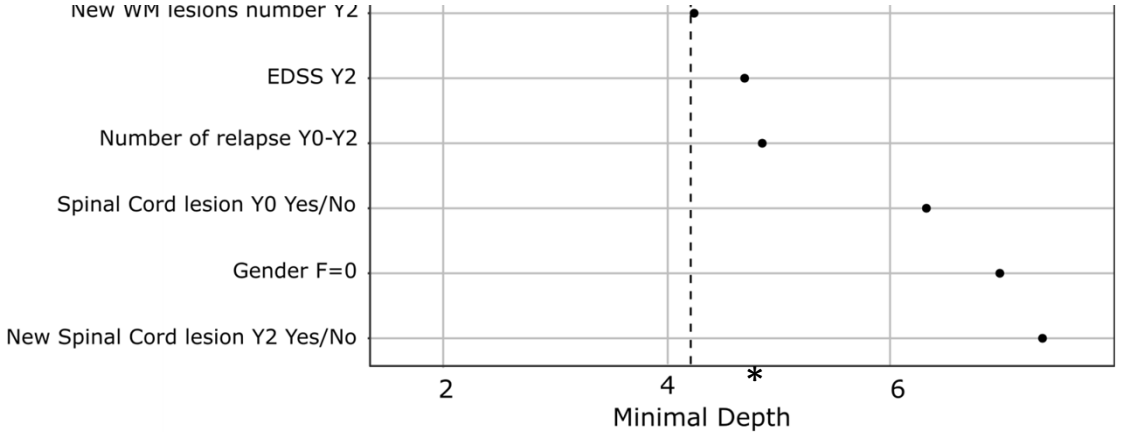


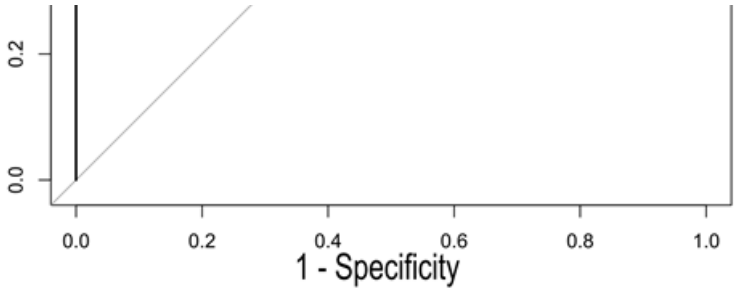
PROGRESSIVE MS SCORE

ROC CURVE ANALYSIS



The severity of the early focal and global cortical pathology is a strong predictor of the conversion to the progressive phase.



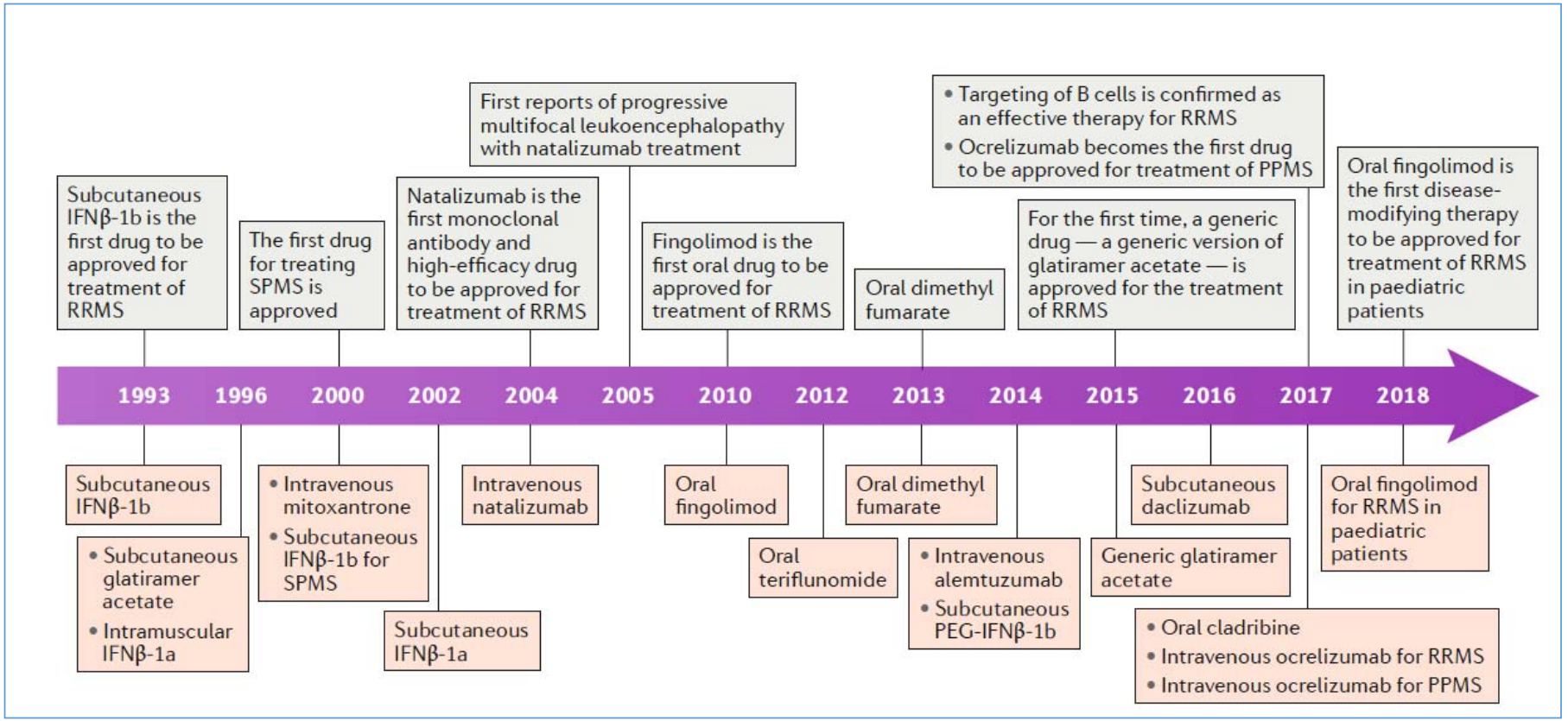


Specificity	Sensitivity	Accuracy
87%	92%	88%

*Measure used to calculate the size of the variables' predictiveness included in the ML model.
The lower the MD the higher was the predictive effect

Courtesy of Pisani , Calabresi et al. (Verona) ECTRIMS 2019

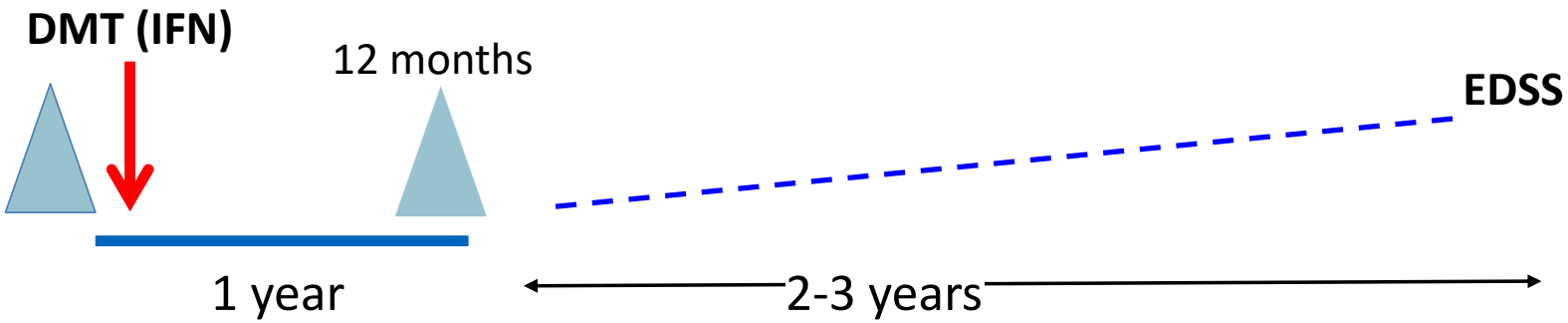
Treatment options in Multiple Sclerosis (DMDs)



- 13 disease modifying treatments
- Different MoA, efficacy, safety profile, adherence, tolerance, cost, administration…

Tintoré et al. Nat Rev Neurol. 2018

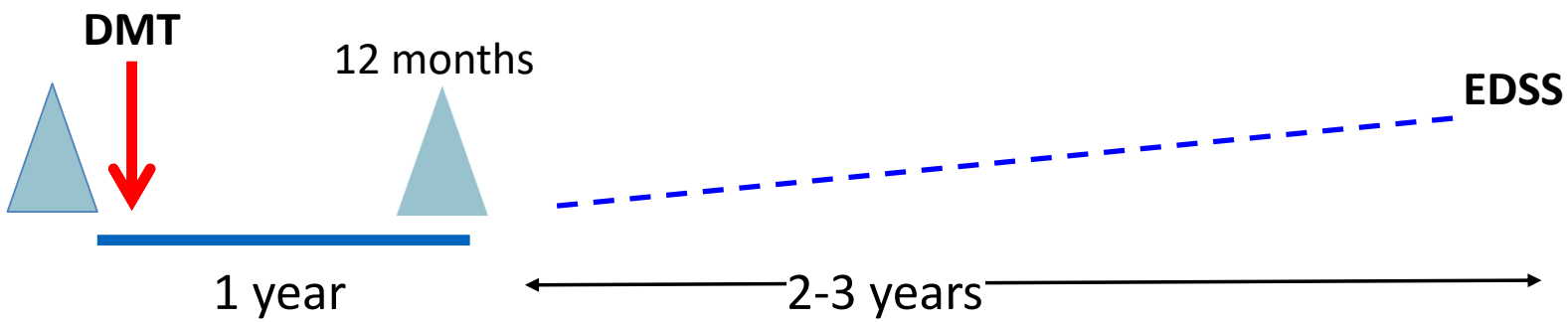
MRI as a predictors of treatment response



- **Clinical measures**
  - Relapse rate /severity
  - Confirmed disability progression

- **Radiological biomarkers**
  - Number of new / enlarging T2 lesions
  - Number of Gd+ lesions

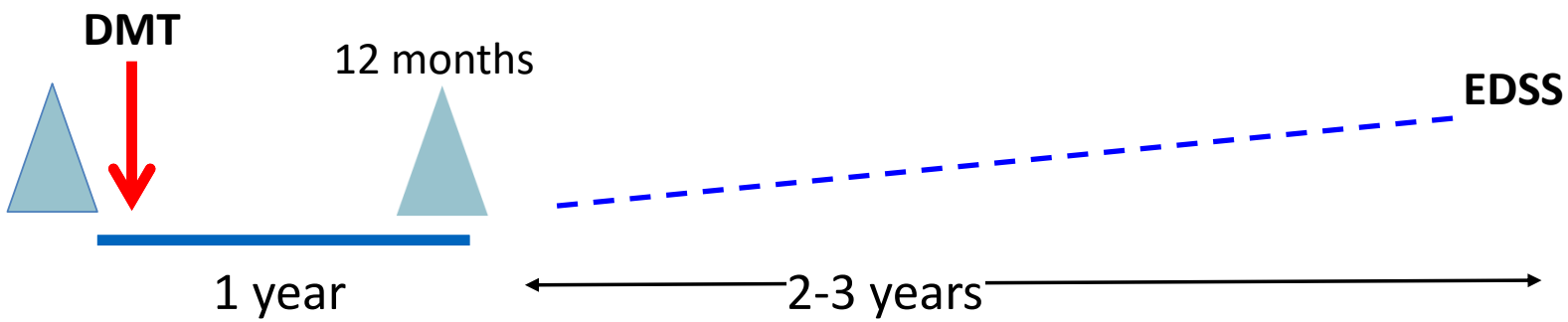
Predictors of treatment response: short-term data



MRI activity (new T2/Gad T1)
Relapses
EDSS worsening
Neuropsychology and quality of life
Demographics
Baseline and follow-up data

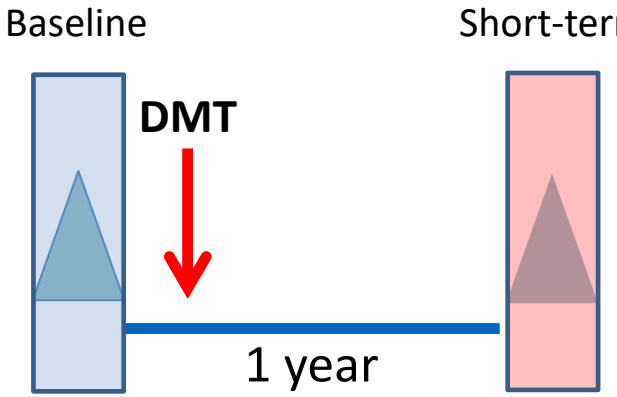
- **Rio score** (Río et al. Mult Scler 2009;15:848-53)
- **Modified Rio score** (Sormani et al. Mult Scler 2012;19:605-12)
- **MSBase Study Group** (Kalincik et al. Brain 2017; 140: 2426-43)
- **Prosperini et al.** (Prosperini et al Mult Scler 2014;20:566-76)
- **Canadian model** (Freedman et al. Can J Neurol Sci. 2013;40:307-23)
- **German model** (Stangel et al. Ther Adv Neurol Disord 2015;8:3-13)
- **NEDA** (Havrdova et al. Neurology 2010; 74 (suppl 3):S3-S7.)
- **MAGNIMS score** (Sormani et al. Neurology 2016; 87: 134)

Predictors of treatment response: short-term data



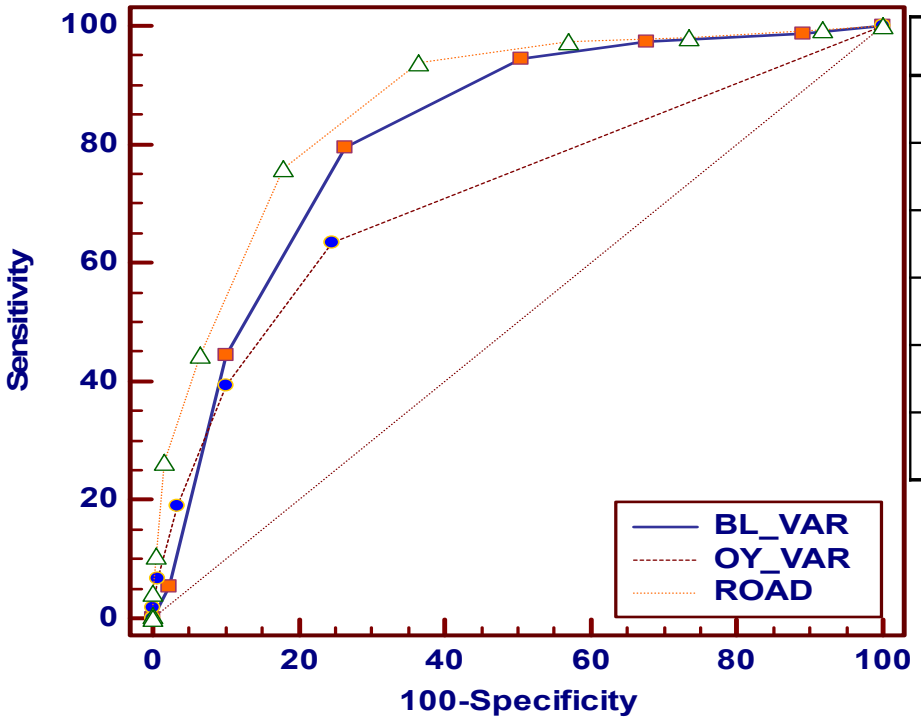
- **Limitations**
  - ✓ Ignore baseline measures and fluid biomarkers
  - ✓ Require at least one-year follow-up
  - ✓ Tested only in injectable first-line therapies (IFN, GA)

RoAD score (Risk of ambulatory disability)



	Variable	Category
Baseline factors	Sex	Female Male
	Age, years	<30 30-40 >40 mean (SD) median [interval]
	Disease duration, years	<2 2-5 5 mean (SD) median [interval]
	EDSS score	<1.5 1.5-2.0 >2.0 mean (SD) median [interval]
	Relapses in previous year	1 2 ≥3 mean (SD) median [interval]
	Gadolinium-enhancing lesions	0 1 ≥2 mean (SD) median [interval]

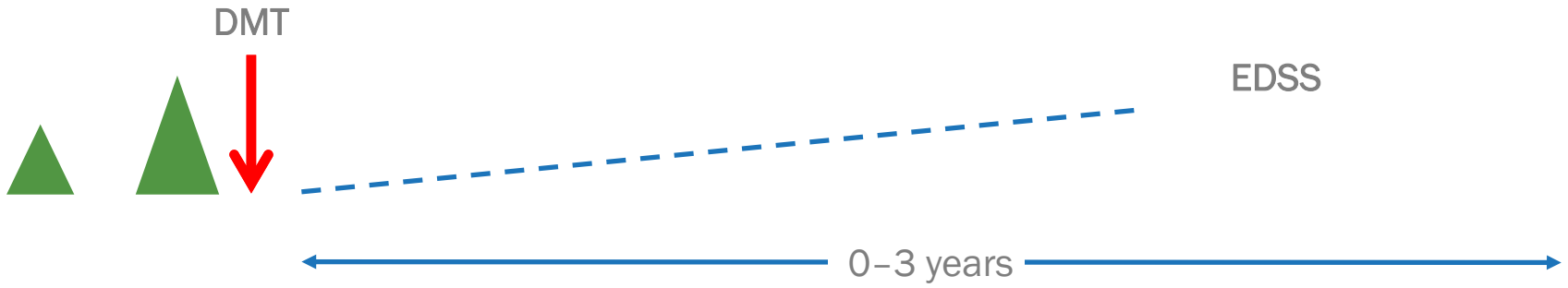
	Variable	Category
One-year factors	≥1-point EDSS worsening	No Yes
	Relapses	0 1 ≥2 mean (SD) median [interval]
	Gadolinium-enhancing lesions	0 1 ≥2 mean (SD) median [interval]
	New T2-hyperintense lesions	0 1 2 ≥3 mean (SD) median [interval]



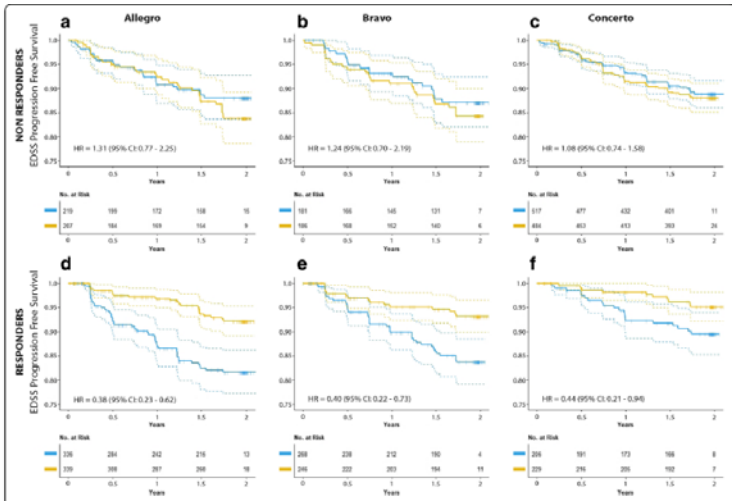
	RoAD score
AUC	0.87
Best cut-off	>4
Sensitivity	**76%**
Specificity	**82%**
PPV	**39%**
NPV	**96%**

Gasperini, Prosperini, Rovira et al.

Predictors of treatment response: baseline data only



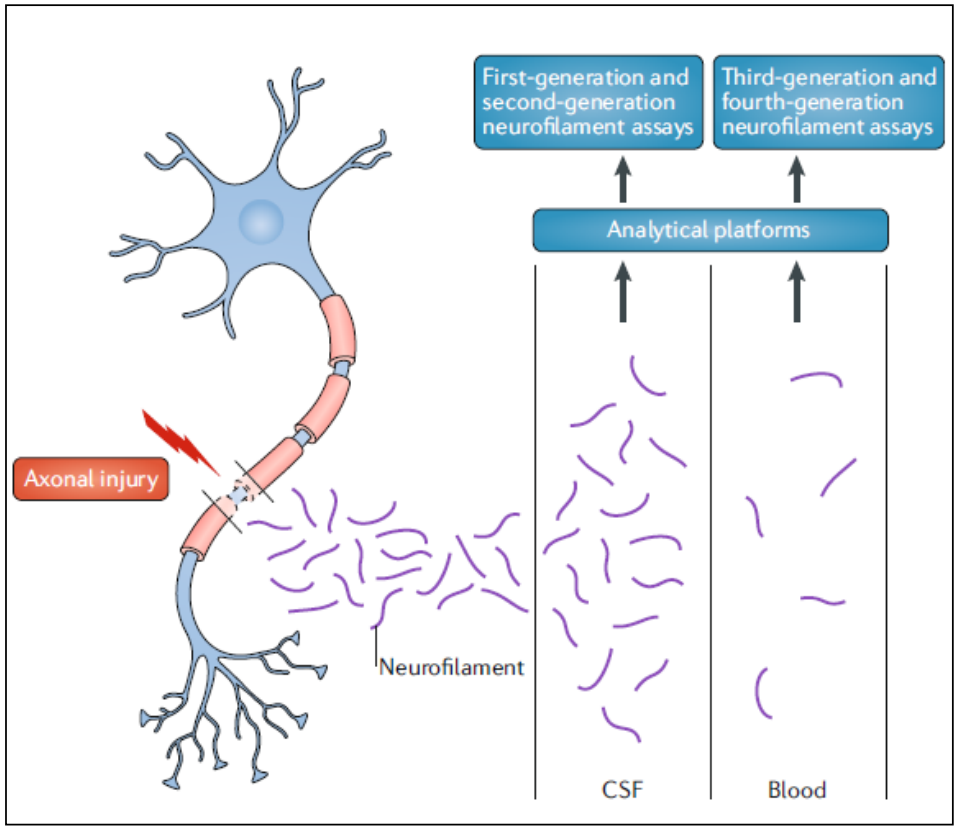
- Baseline patients' characteristics could identify patients with larger/lower benefits from treatment
- Data from RCTs could be used for creating models to identify predictors of largest benefit to treatment response



- Linear combination of age, sex, previous relapses, brain volume, and MRI lesion activity.
- This method can be applied to any RCT to create a treatment-specific score.
- Addition of fluid biomarkers (NfL) should be considered

Bovis et al. BMC Medicine (2019) 17:113

NfL as a biomarker of MS



Capture both inflammatory and degenerative process (T2, Gad, atrophy)

Measure of neuro-axonal damage

- Focal/diffuse
- Brain and spinal cord

Accesible, easy and quick to measure

Good correlation with clinical endpoints

Prognostic marker of disease activity

Responsive to MS therapy

- Prediction of treatment response?

- MS diagnosis: McDonald 2017 criteria
- MAGNIMS guidelines 2020
- New MRI features: leptomeningeal enhancement, central vein, iron rims/dots
- MR: prognosis; prediction of treatment response
- Competitor: Neurofilaments light chain (NfL)