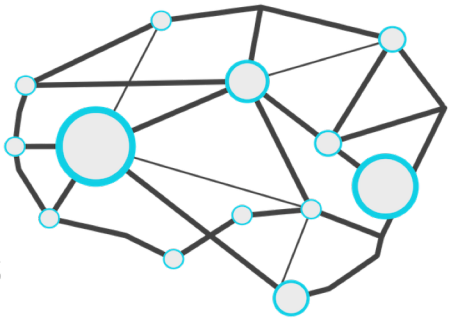
Magnims

Magnetic Resonance Imaging in Multiple Sclerosis



# Update on MAGNIMS guidelines on the use of MRI in the diagnosis and monitoring of multiple sclerosis

## The Value of Spinal Cord MRI

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# Disclosure

- Grant support: UK MS Society, National MS Society, NIHR, EU-H2020, Spinal Cord Research Foundation, Rosetrees Trust, Progressive MS Alliance, Bioclinica & GE Neuro

- Consultancy: Novartis, Teva, Roche, Biogen, Merck

- Editorial work: Associate Editor of Neurology, Editorial Board of Multiple Sclerosis Journal

# 2015 MAGNIMS guidelines for diagnosis of MS

**Spinal cord MRI should always be performed in patients with spinal cord symptoms at disease onset (to satisfy DIS) – there is no need to perform it to demonstrate DIT**

**Spinal cord MRI is helpful when brain MRI results are equivocal or inconclusive**

*A Rovira & MAGNIMS, Nat Rev Neurol 2015*

**Table 2** | Indications for spinal cord MRI for diagnosis of MS

| Situation | Objective |
|---|---|
| Clinically isolated syndrome with spinal cord symptoms | Detect symptomatic and clinically silent lesions<br>Rule out other diseases |
| Clinically isolated syndrome without spinal cord symptoms, but with inconclusive brain MRI (for example, not demonstrating dissemination in space) | Detect clinically silent lesions<br>Increase specificity and sensitivity of diagnosis |
| Strong clinical suspicion of MS, but no findings on brain MRI | Increase sensitivity of diagnosis<br>Investigate possible absence of spinal cord lesions, which could rule out MS |
| Nonspecific brain MRI findings (e.g. perivascular lesions, effects of ageing, incidental findings associated with migraine and/or chronic headache) | Increase sensitivity of diagnosis<br>Investigate possible spinal cord lesions, which could support the diagnosis of MS |
| Radiologically isolated syndrome | Increase specificity of diagnosis<br>Predict risk of conversion to MS |
| Primary progressive MS | Increase sensitivity and specificity of diagnosis<br>Rule out other diseases |

*A Rovira & MAGNIMS, Nat Rev Neurol 2015*

# 2015 MAGNIMS guidelines for monitoring MS

**The use of spinal cord MRI in addition to brain MRI is not recommended for routine monitoring, and should be limited to certain clinical situations (such as unexplained and/or unexpected spinal cord symptoms)**

- Spinal cord MRI is less sensitive than brain MRI for detecting new lesions, particularly with regard to contrast-enhancing lesions
- Technical challenges (vascular and CSF pulsation and difficult to standardize it)

*M Wattjes & MAGNIMS, Nat Rev Neurol 2015*

# New evidence for the use of spinal cord MRI in the diagnosis, prognosis and monitoring

- **Diagnosis**
  - Asymptomatic & symptomatic lesions
  - Spinal cord MRI useful for the differential diagnosis
- **Prognosis**
  - RIS
  - CIS
- **Monitoring**
  - New spinal cord lesions without new brain lesions

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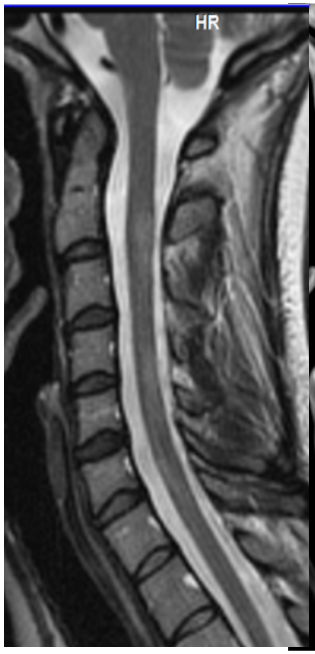
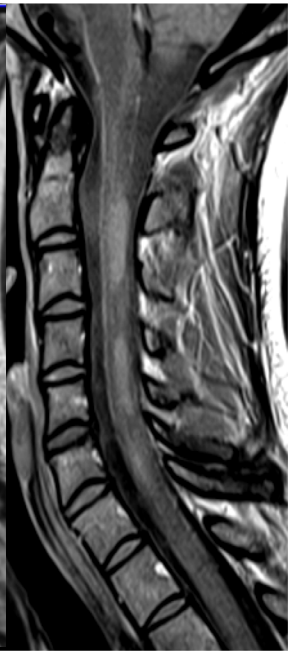
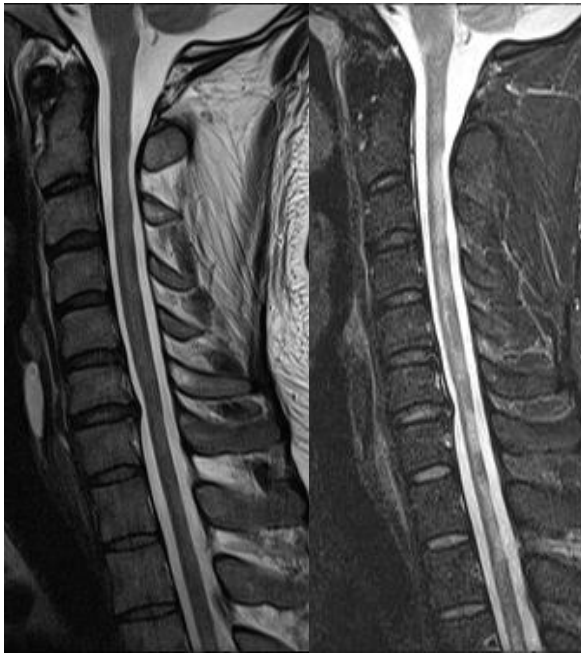
# Recommended spinal cord MRI protocols



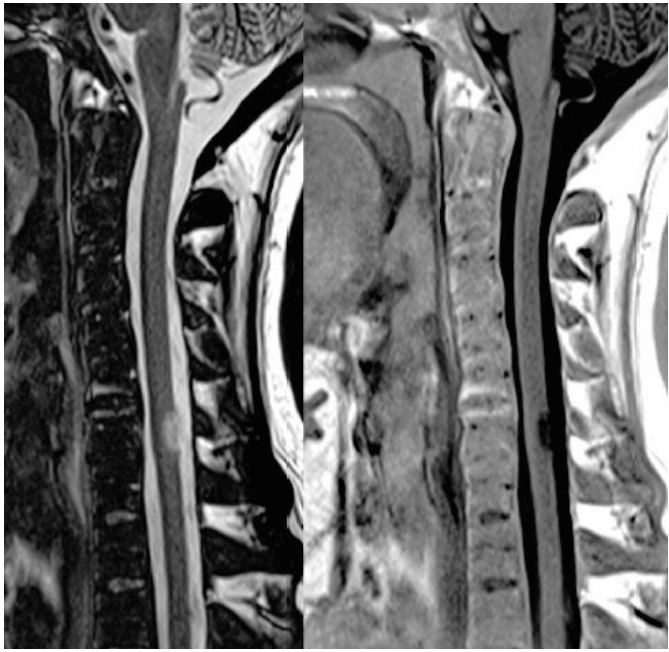

T2



PD



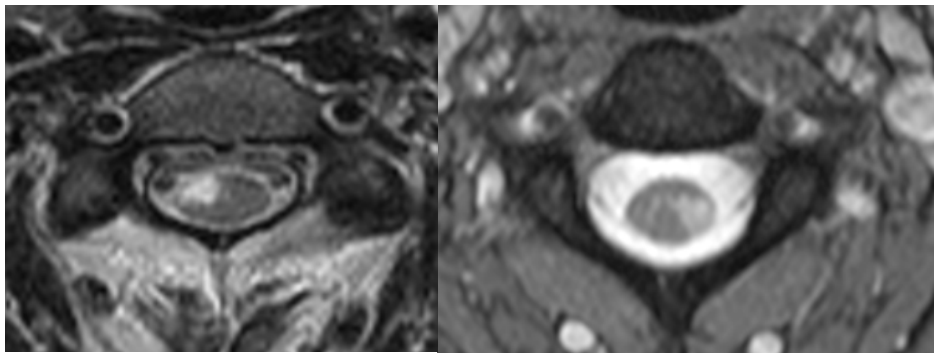
T2 STIR



T2 (or PD) PSIR (or MPRAGE)

At least @ 1.5 T

Resolution: 3 mm sclice thickness (no gap), in-plane 1x1mm

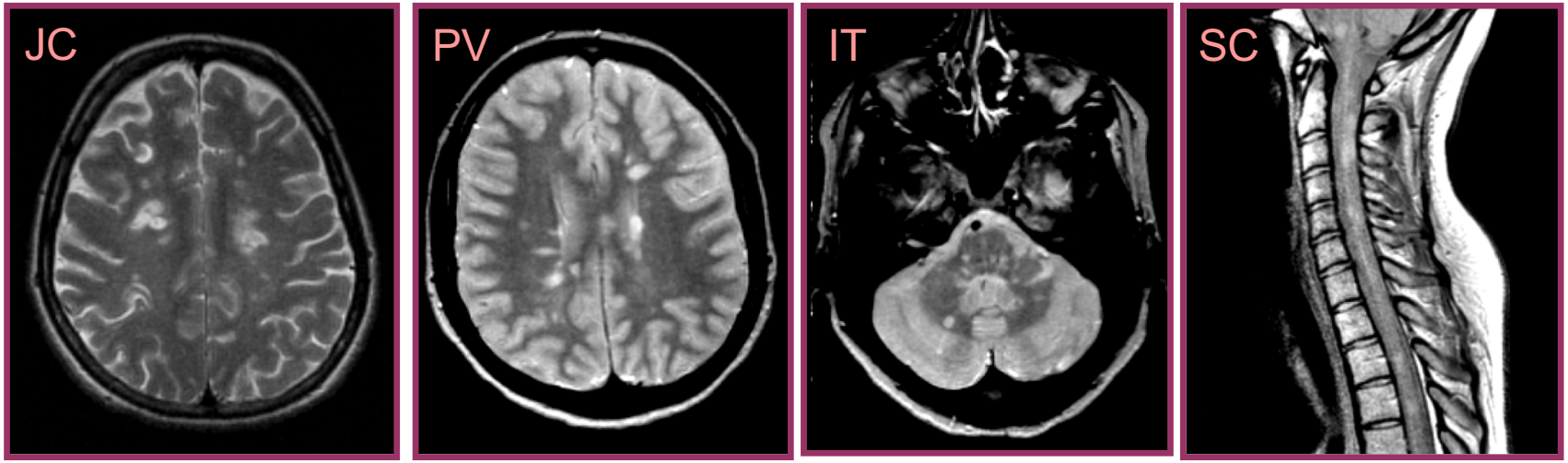


Confirm lesions on axial scans 2D or 3D T2 FSE

*Rovira & MAGNIMS, Nat Rev Neurol 2015; Ciccarelli, Cohen, Reingold, Weishenker, TLN 2018*

# McDonald criteria 2010
# Dissemination in space (DIS)

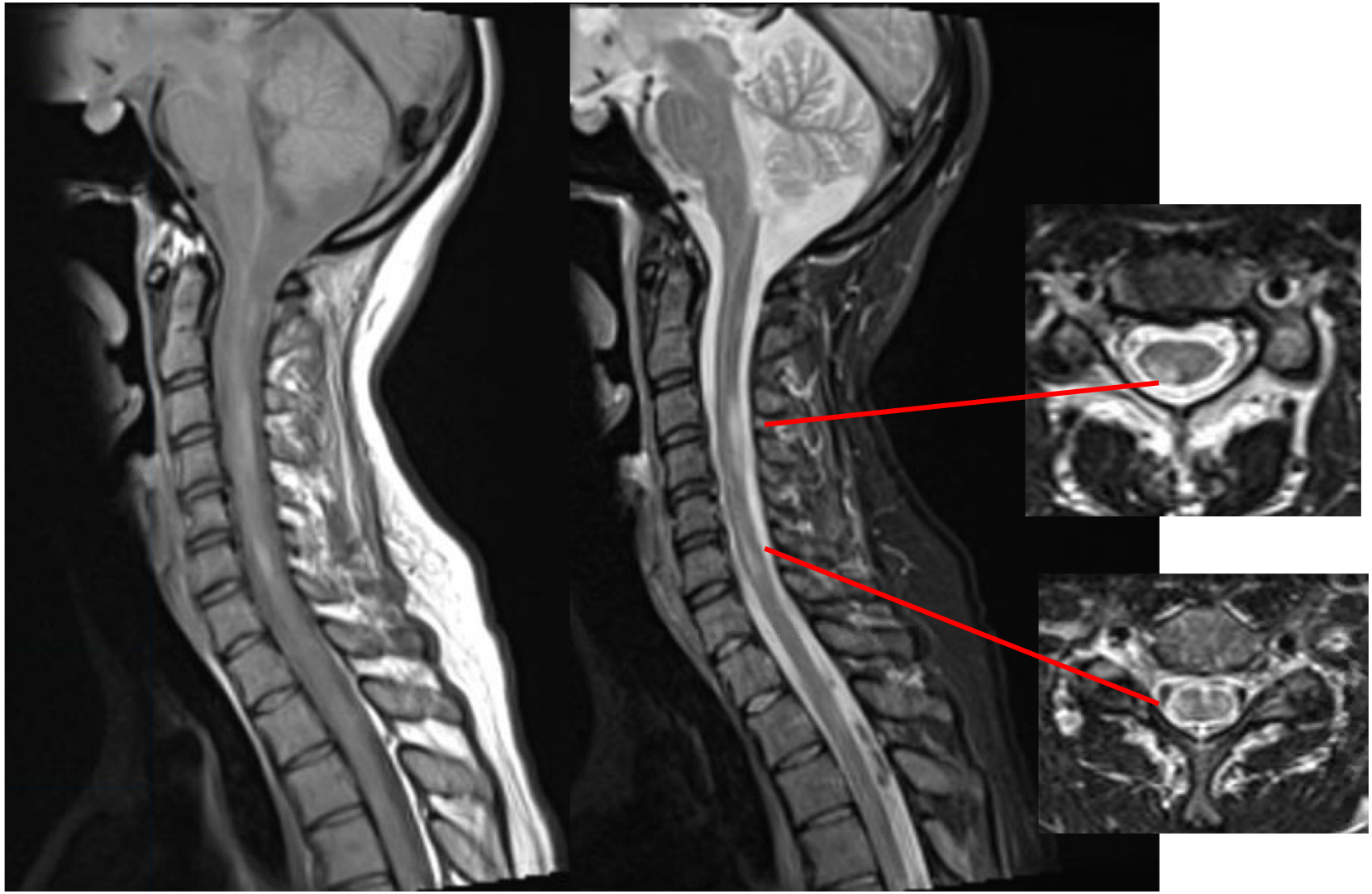
Lesions in 2 out of 4 locations required




When the patient's symptoms are referable to the brainstem/ cerebellum or spinal cord,
then lesions in the symptomatic region are excluded

*Swanton, Lancet Neurol 2007*

# Symptomatic or asymptomatic lesions?



Determining whether a lesion is symptomatic or asymptomatic is sometimes difficult and not always possible

# Including any lesion in the symptomatic region

**Table 1** **Baseline patient characteristics** studied over a mean of 7.3 yrs

| | Brainstem/cerebellar syndrome (n = 20) | Spinal cord syndrome (n = 10) | All patients (n = 30) |
|---|---|---|---|
| Age, y, mean (SD) | 30.6 (8.3) | 32.6 (9.9) | 31.25 (8.8) |
| Female, n (%) | 14 (70) | 4 (40) | 18 (60) |
| No. of lesions in the symptomatic site | | | |
| Normal MRI | 5 | 2 | 7 |
| 1 lesion | 9 | 3 | 12 |
| 2 or more lesions | 6 | 5 | 11 |
| Baseline EDSS score, median | 2.25 | 2 | 2 |

| DIS criteria | Sensitivity | Specificity | Accuracy |
|---|---|---|---|
| **McDonald 2010 (including only asymptomatic lesions)** | 73% | 73% | **73%** |
| **Including any lesion in DIS** | 87% | 73% | **80%** |

*Brownlee, Neurology 2016*

# 2017 revised McDonald criteria

**_Panel_ 5: 2017 McDonald criteria for demonstration of dissemination in space and time by MRI in a patient with a clinically isolated syndrome**

- Dissemination in space can be demonstrated by one or more T2-hyperintense lesions* that are characteristic of multiple sclerosis in two or more of four areas of the CNS: periventricular,† cortical or juxtacortical, and infratentorial brain regions, and the spinal cord
- Dissemination in time can be demonstrated by the 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, with reference to a baseline scan, irrespective of the timing of the baseline MRI

*Unlike the 2010 McDonald criteria, no distinction between symptomatic and asymptomatic MRI lesions is required. †For some patients—eg, individuals older than 50 years or those with vascular risk factors—it might be prudent for the clinician to seek a higher number of periventricular lesions.

*Thompson et al, TLN 2018*

# MRI characteristics of lesions for differential diagnosis

| | Lesion length and location on sagittal images | Location on axial images | T2 signal characteristics | T1 signal characteristics | Gadolinium enhancement |
|---|---|---|---|---|---|
| Multiple sclerosis[34,35] | Usually <1 vertebral segments; consistently <3 vertebral segments* | Multiple, asymmetrical | Hyperintense | Isointense or hypointense in chronic lesions studied with 3T MRI scanners, especially in patients with progressive multiple sclerosis | Present in most acute lesions; variable pattern: homogeneous, but ring-enhancing in about 20% of lesions |
| NMOSD (AQP4)[34,36-39] | About 85% of acute lesions span >3 vertebral segments;† chronic lesions can be short or replaced by long segments of atrophy or myelomalacia (pseudosyrinx) | Usually central; can be unilateral or even peripheral; can vary over the length of the lesion | Hyperintense and in about 90% of patients associated with extremely hyperintense lesions (bright spotty lesions)§ | Usually hypointense in acute lesions | Present in almost all acute lesions; variable pattern, but ring-enhancing in about 30% of lesions |
| NMOSD (MOG)[40] | Acute myelitis spanning >3 vertebral segments; can occur in any part of the spinal cord, but in caudal spinal cord in about 75% of patients with NMOSD (MOG) *vs* 20% of patients with multiple sclerosis | Acute myelitis associated with single, but occasionally multiple, lesions | Hyperintense | Usually hypointense | Usually present but somewhat less frequent than in NMOSD (AQP4) |
| Infarction[41] | About 60% of lesions span >3 vertebral segments; can be normal when performed within first hours after symptom onset | Variable; about 65% of lesions associated with anterior grey matter specific lesions (owl eyes);‡ 30% of lesions with homogenous central grey or entire spinal cord cross-section | Hyperintense; about 40% of lesions have a linear, pencil-like configuration in anterior spinal cord | Commonly evolve into T1 hypointense lesions over months | In about 90% of lesions, there is linear enhancement on sagittal images corresponding to distribution of grey matter in the spinal cord |
| Viral myelitis[42] | Usually spanning >3 vertebral segments | Variable; can be associated with owl eye appearance (enterovirus) or central spinal cord (herpesvirus) | Hyperintense | Variable | Variable |
| Sarcoidosis[43] | Spanning >3 vertebral segments in most patients | Central or entire cross-sectional area | Hyperintense | Hypointense in about 50% of patients | Posterior subpial homogeneous enhancement over long segments of the spinal cord; central canal enhancement common; trident sign on axial images; ring enhancement not seen |
| Spondylotic compressive myelopathy[44] | Variable; can span >3 vertebral segments | Central | Hyperintense | May have disc-like pattern corresponding to site of enhancement | Disc-like (flat pancake) pattern of enhancement at point of maximum spinal cord impingement often present |
| Paraneoplastic myelopathy[45] | Usually over multiple vertebral segments | Symmetrical, tract-specific lesion | Hyperintense | Isointense | Variable; homogeneous gadolinium enhancement in approximately 50% of patients |

*Ciccarelli, Cohen, Reingold, Weishenker; International Conference on Spinal Cord Involvement and Imaging in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorders TLN, 2018*

# New evidence for the use of spinal cord MRI in the diagnosis, prognosis and monitoring

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# Radiologically Isolated Syndrome: predictive role of asymptomatic spinal cord lesions

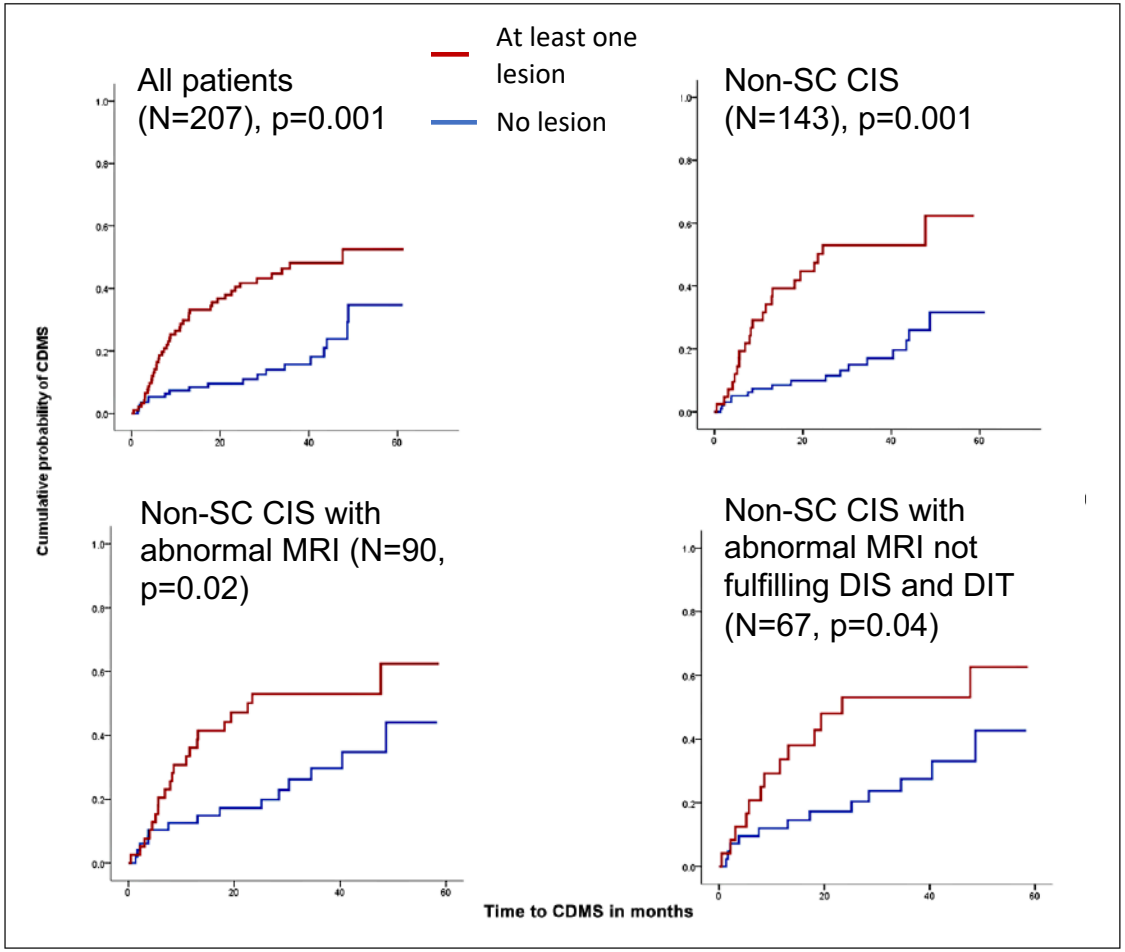
TABLE 1. Comparative Demographics and Clinical Characteristics of the Study Population

| | Nonconverters | All Converters | RIS to CIS/MS (15 yr) | RIS to PPMS (15 yr) | *P* (CIS/MS vs PPMS) |
|---|---|---|---|---|---|
| N | 324 | 128 | 113 | 15 | NA |
| F% | 81 | 71 | 75 | 40 | 0.005[a] |
| Median (yr) age at RIS (range) | 38.6 (14–74) | 32.5 (11–70) | 32.0 (11–70) | 43.3 (20–66) | <0.001[b] |
| Median (yr) follow-up (range) | 2.0 (0–20) | 5.2 (0.2–21.1) | 5.2 (0.2–21.1) | 5.8 (1.1–18.0) | 0.66[b] |
| Median (yr) time to symptomatic MS[c] (range) | NA | 2.4 (2.0–2.8) | 2.3 (1.7–2.9) | 3.5 (1.6–5.4) | 0.21[d] |
| CSF + (%) | 61 | 75 | 73 | 85 | 0.37[a] |
| Spinal cord lesions at the time of RIS (%) | 23 | 69 | 64 | 100* | 0.005[a] |
| (Gd+) spinal cord lesions at the time of RIS (% of all spinal cord lesions) | 3.1 | 17.4 | 19 | 27 | 0.48[a] |

*Lesions lead to progressive disease, but do not cause relapses

*Kantarci, Ann Neurol 2016*

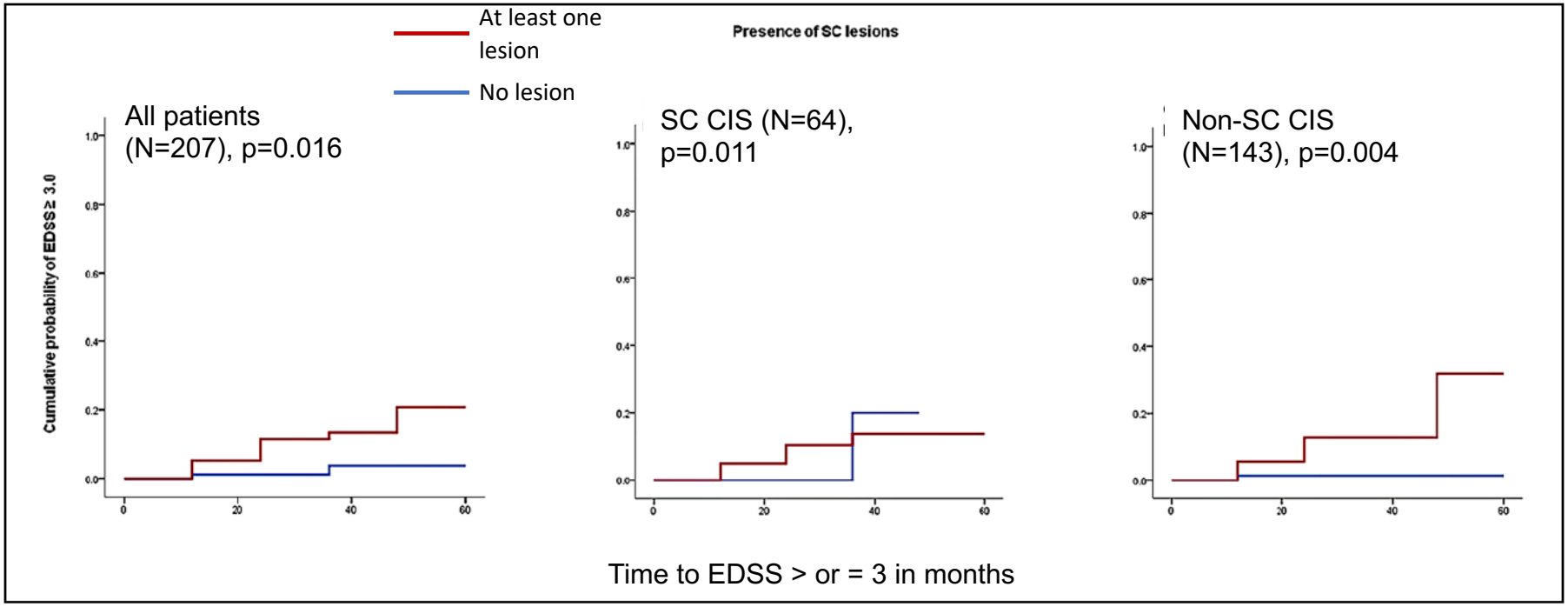
# Spinal cord lesions in CIS predict CDMS - especially in non-SC CIS (asymptomatic lesions)




- Patients who have SC lesions have higher risk of CDMS (2 to 3 times) and will experience a second relapse much sooner
- The risk of CDMS increases with increase lesion number

*Arrambide MSJ 2018*

# Spinal cord lesions in CIS predict disability at follow-up – especially in non-SC CIS




*Arrambide MSJ 2018; Brownlee MSJ 2017*

# Spinal cord lesions in CIS predict SPMS

In 15% of patients

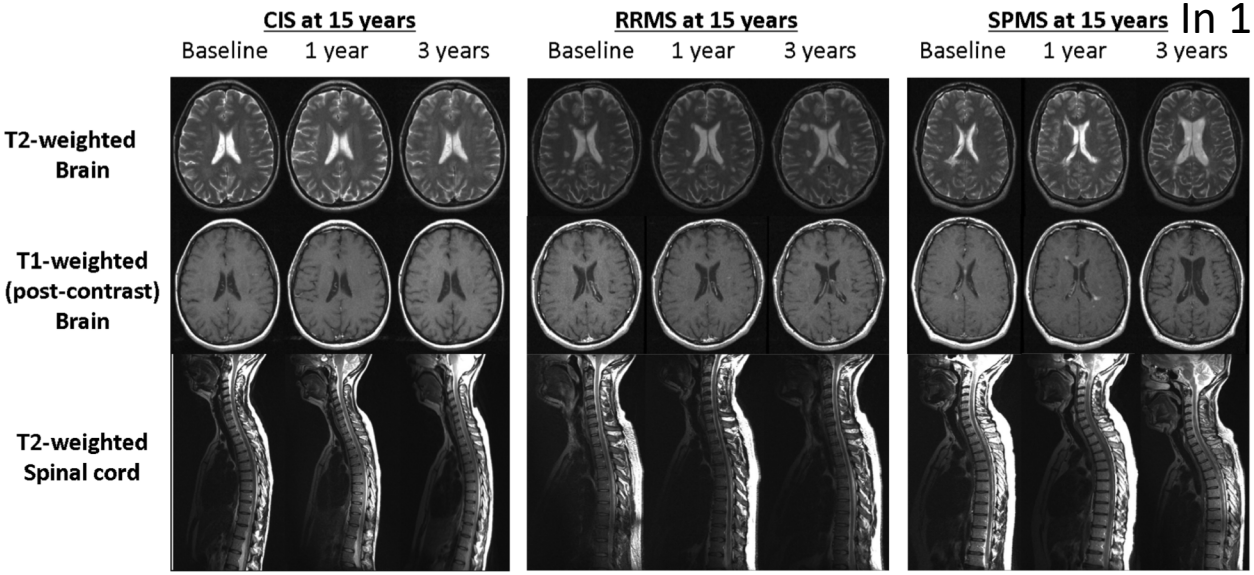



**Table 2** Multivariable logistic regression models investigating early MRI predictors of secondary progressive disease course after 15 years

| | 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 | | |

If no Gad lesions and no spinal cord lesions at onset, the risk of SPMS at 15 years was **5.3%**

If at least 1 spinal cord lesion and 2 or more Gad it was **45.5%**

*Brownlee Brain 2019*

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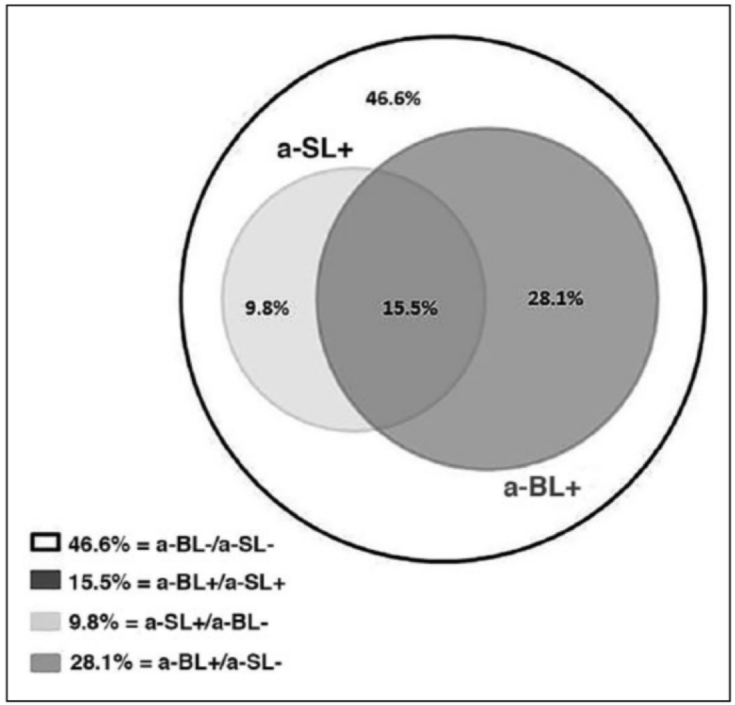
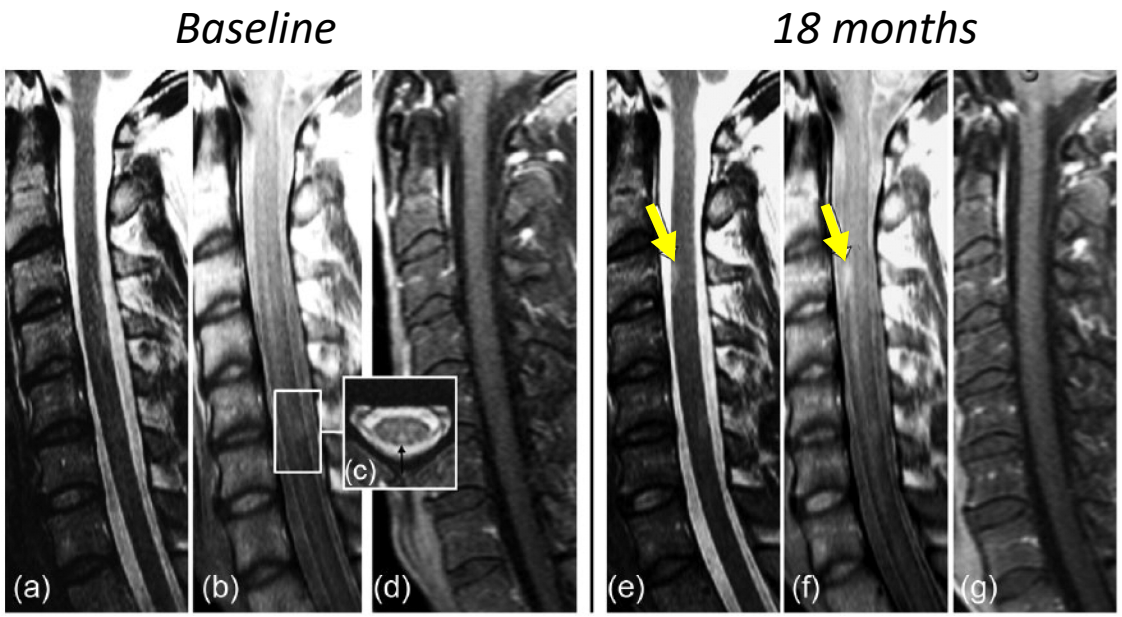
# Spinal cord MRI detects asymptomatic activity

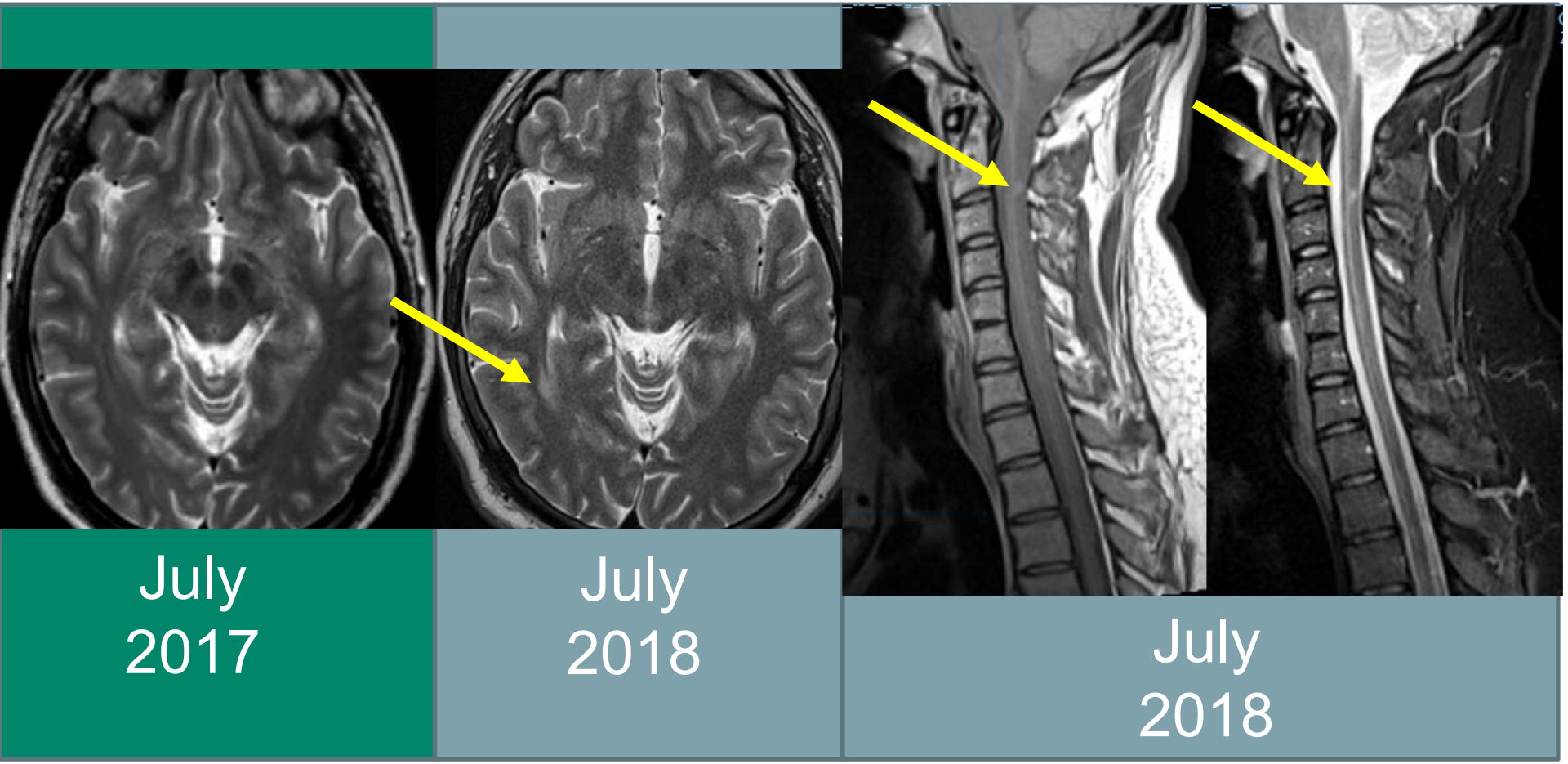
- Asymptomatic spinal cord lesions are seen in 25% of clinically stable RRMS patients
- However, only about 10% patients have subclinical spinal cord lesion activity **alone**




*Zecca, MSJ 2016*

# Case example: concomitant occurrence of new brain and spinal cord lesions



# Limitations of the assessment of new spinal cord lesions with repeat spinal cord MRI in clinical practice

- It increases scanning time
- It elevates costs
- Difficult to perform longitudinal assessments when multiple protocols/scanners; technically challenging; inter-rater differences in scoring the new spinal cord lesions
- **MAGNIMS recommended that spinal cord MRI is not routinely done for monitoring disease activity**

# When to request spinal cord MRI for monitoring of patients in addition to brain MRI?

- Patients with spinal cord phenotype (no or low number of brain lesions)
- Clinical disease progression that cannot be explained by brain MRI (comorbidity in the spinal cord?)
- Spinal cord relapse (typical and atypical)
- Treatment switch decision making: inconclusive clinical presentation and/or brain MRI findings

# Additional considerations

- Asymptomatic spinal cord lesions cause more concerns than brain lesions
- Monitoring spinal cord lesions over time helps to understand the course of MS in individual patients
- Patients with large brain lesion loads, which make it difficult to detect new asymptomatic brain lesions, could be monitored with spinal cord MRI

# Conclusions: MAGNIMS guidelines
# Value of spinal cord MRI

- Important for diagnosis in CIS and prognosis in RIS, CIS and early MS

- Not enough evidence to recommend it routinely to detect DIT

- Not enough evidence to recommend serial spinal cord imaging for routine treatment monitoring
  - Recommended as future area of research
  - Add spinal cord MRI to brain MRI if clinically indicated/specific clinical situations

- Limitations in the assessment of active spinal cord lesions in clinical practice

Magnims

Magnetic Resonance Imaging in Multiple Sclerosis



# 2020 ECTRIMS-MAGNIMS Research Fellowship

**Applications are now open**

Closing date for submission of applications is 01 / February / 2020

MAGNIMS (Magnetic Resonance Imaging in MS) is a European network of academics that share a common interest in the study of multiple sclerosis using magnetic resonance imaging techniques.

## We are MAGNIMS

Such a group has collaborated since 1990 and has collectively made a major contribution to defining the role of MRI in diagnosis and monitoring treatments in MS.