# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

Presented by **Alex Rovira** on behalf of

Mike P Wattjes, Olga Ciccarelli, Daniel S Reich, Brenda Banwell, Nicola de Stefano, Christian Enzinger, Franz Fazekas, Massimo Filippi, Jette Frederiksen, Claudio Gasperini, Yael Hacohen, Ludwig Kappos, David K B Li, Kshitij Mankad, Xavier Montalban, Scott D Newsome, Jiwon Oh, Jacqueline Palace, Maria A Rocca, Jaume Sastre-Garriga, Mar Tintoré, Anthony Traboulsee, Hugo Vrenken, Tarek Yousry, Frederik Barkhof, Àlex Rovira on behalf of the Magnetic Resonance Imaging in Multiple Sclerosis study group, the Consortium of Multiple Sclerosis Centres, and North American Imaging in Multiple Sclerosis Cooperative MRI guidelines working group

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M Wattjes et al 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. Lancet Neurol 2021

# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

Objective:

To present updated international consensus 2021 guidelines on MRI in MS, and which now merge recommendations from MAGNIMS, CMSC, and NAIMS.

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# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

- Two independent panels of experts convened on two occasions to update existing guidelines for a standardized MRI protocol.
- MAGNIMS panel convened in Graz, Austria in April 2019.
- CMSC/NAIMS panel met in Newark, NJ, USA in October 2019.
- Subsequently, the leadership of the MAGNIMS, NAIMS/CMSC working groups combined their efforts to reach an international consensus.

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2021 MAGNIMS–CMSC–NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

*Mike P Wattjes, Olga Ciccarelli, Daniel S Reich, Brenda Banwell, Nicola de Stefano, Christian Enzinger, Franz Fazekas, Massimo Filippi, Jette Frederiksen, Claudio Gasperini, Yael Hacohen, Ludwig Kappos, David K B Li, Kshitij Mankad, Xavier Montalban, Scott D Newsome, Jiwon Oh, Jacqueline Palace, Maria A Rocca, Jaume Sastre-Garriga, Mar Tintoré, Anthony Traboulsee, Hugo Vrenken, Tarek Yousry, Frederik Barkhof, Àlex Rovira on behalf of the Magnetic Resonance Imaging in Multiple Sclerosis study group, the Consortium of Multiple Sclerosis Centres, and North American Imaging in Multiple Sclerosis Cooperative MRI guidelines working group**

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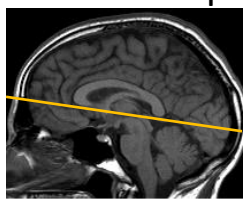
# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

| MRI PROTOCOLS | Brain | Spinal Cord | Optic Nerve |
|---|---|---|---|
| **Field Strength** | ≥1.5 T (preferably 3T) | ≥1.5 T (3T no added value) | ≥1.5 T |
| **Acquisition** | 3D (preferred) or 2D | 2D or 3D | 2D or 3D |
| **Slice Thickness** | 3D: 1mm isotropic [1]<br>2D: ≤3mm, no gap [2] | Sagittal ≤3mm, no gap<br>Axial ≤5mm, no gap | ≤2-3mm, no gap |
| **In-Plane Resolution** | ≤1mm x 1mm | ≤1mm x 1mm | ≤1mm x 1mm |
| **Coverage** | Whole Brain<br>(include as much of cervical cord as possible) | Whole cord<br>(cervical, thoracolumbar including conus) | Optic nerve & chiasm |
| **Axial slice orientation** | Subcallosal plane<br>  | Perpendicular<br>to sagittal axis of cord | Align to optic nerve/chiasm orientation |

**T** = Tesla; **3D** = three dimensional; **2D** = 2 dimensional

[1] Isotropic preferred, if over-contiguous (through-plane and in-plane), not > 1.5 mm with 0.75 mm overlap

[2] Diffusion-weighted imaging, slice thickness should be ≤ 5mm with a 10-30% slice gap

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| Brain Sequences | Diagnostic workup | Follow Up | Safety Monitoring |
|---|---|---|---|
| **Axial $T_2$** | **Recommended** | **Recommended** (Optional if 3D Flair acquired) | **Recommended** (Optional if 3D Flair acquired) |
| **Sagittal & Axial FLAIR** | **Recommended** | **Recommended** | **Recommended** |
| **Post-Gd axial (or 3D sagittal) $T_1$** | **Recommended** | Optional | Optional |
| **Diffusion-weighted imaging** | Optional | Optional (useful for differential Dx) | **Recommended** (for PML detection) |
| DIR or PSIR | Optional (for cortical lesions) | Optional | Optional |
| High-resolution 3D $T_1$ | Optional (for brain atrophy monitoring) | Optional | Not Required |
| Susceptibility-weighted imaging | Optional (for central vein sign) | Not Required | Not Required |

**$T_2$** (TSE/FSE, turbo/fast spin echo)
**Gd** macrocyclic agent, 0.1mm/kg body weight, minimum delay 5-10 minutes
**$T_1$** (TSE/FSE)
**FLAIR** (fluid-attenuated inversion recovery)
**DIR** (double inversion recovery) and **PSIR** (phase-sensitive inversion recovery)
**High resolution 3D $T_1$**
(e.g.MP-RAGE, MP2RAGE magnetization-prepared rapid acquisition of gradient echoes; IR-SPGR, inversion-prepared spoiled gradient; TFE, turbo field-echo)

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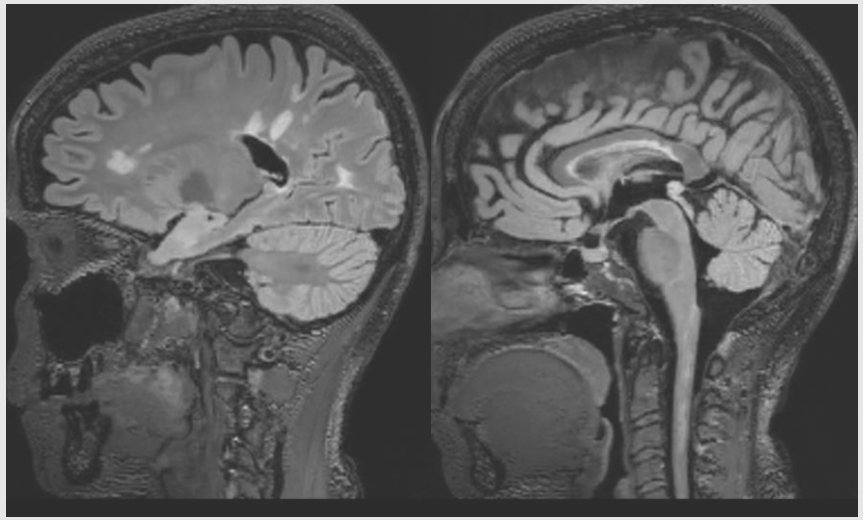
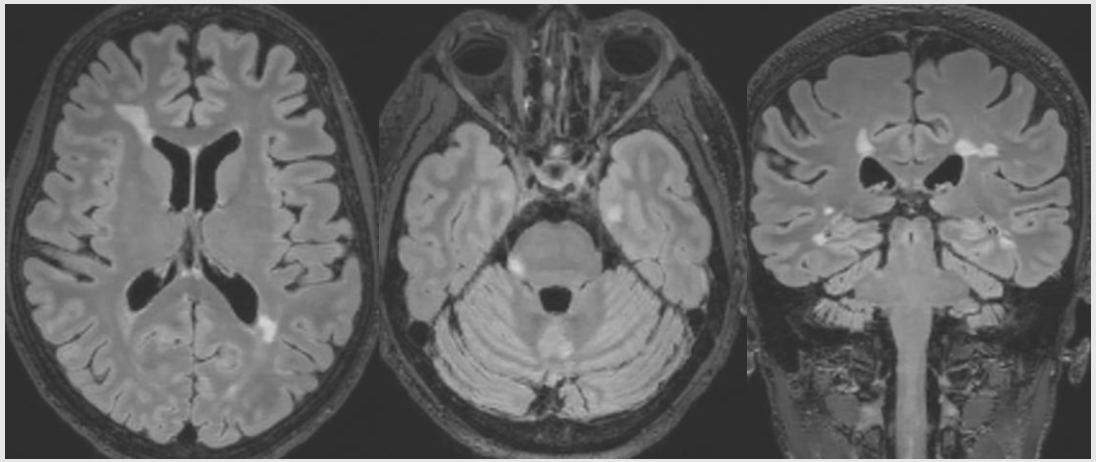
# Standardized MS protocol: 3T

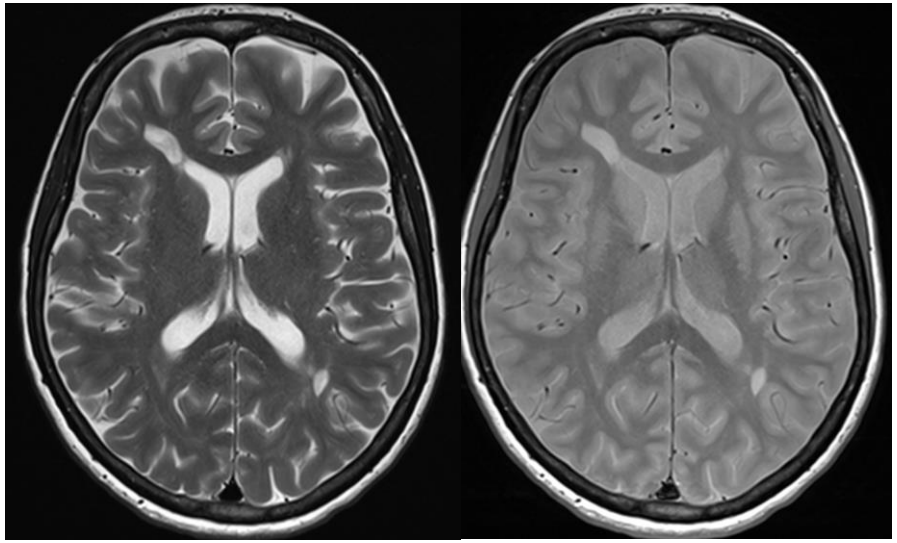
## Basic protocol (total acq. time: 8 min 15 sec)

**3D T2 FLAIR**
Acq: 1.0 x 1.0 x 1.0 mm
TR/TI/TE: 7000/2050/410 ms
Time: 3:58 min

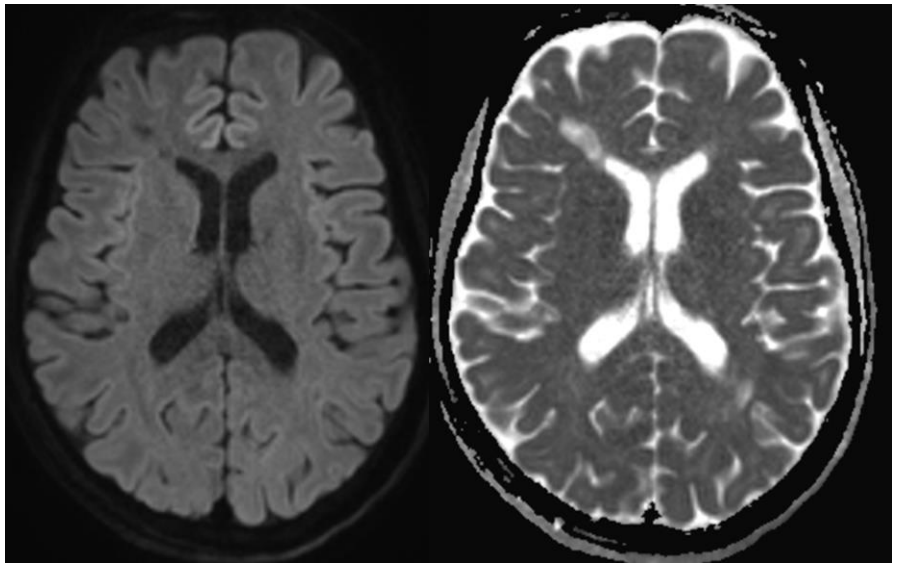




**2D T2 double echo**
Acq: 3 x 1 x 1 mm
TR/TE: 3600/9.4- 94 ms
Time: 2:02 min



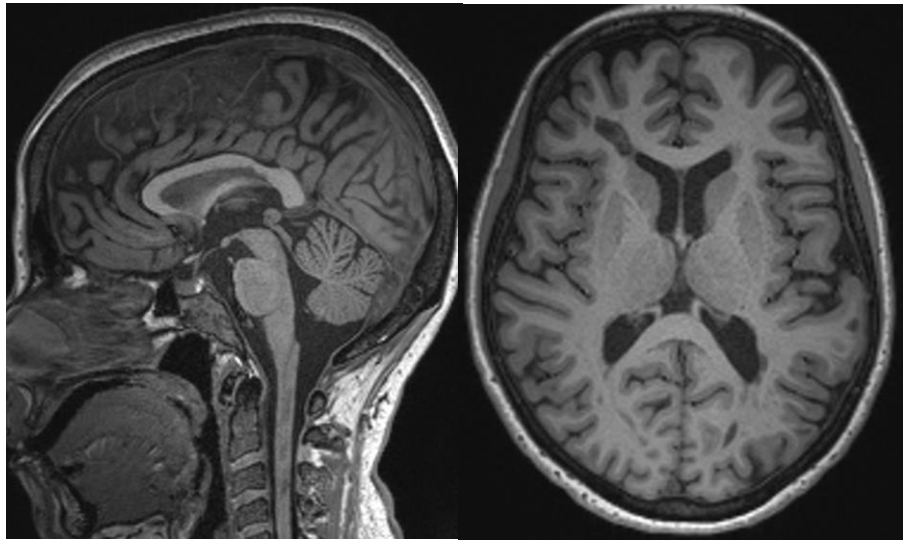
**2D EPI GR**
Acq: 3 x 1 x 1 mm
TR/TE: 3000/63 ms
Time: 2:13 min



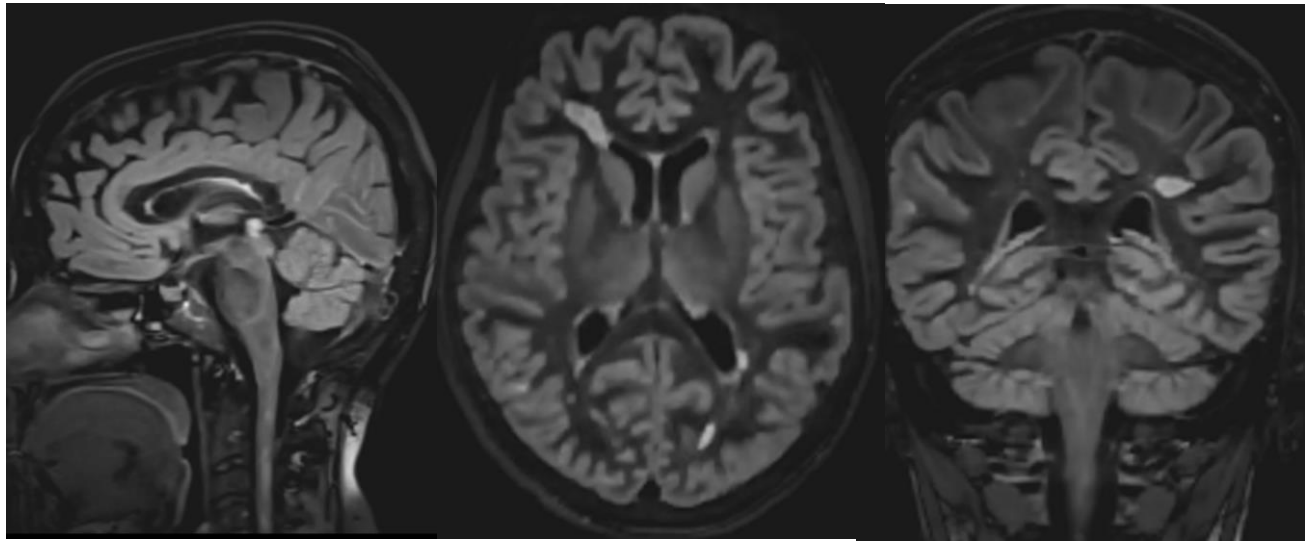
# Standardized MS protocol: 3T

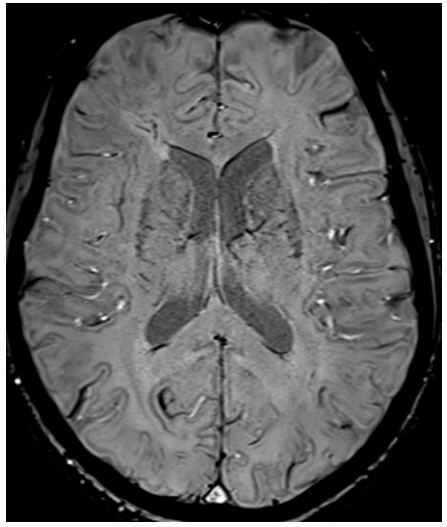
## Optional sequences (total acq. time: 16 min 14 sec)

**3D T1 MPRAGE**
TR/TI/TE: 2300/900/2.98 ms
Acq: 1.0 x 1.0 x 1.0 mm
Time: 5.09 min



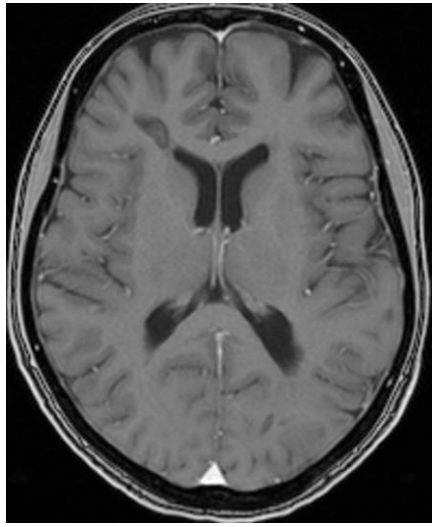
**3D DIR SPACE**
TR/TI/TE: 7500/3000/318 ms
Acq: 1.0 x 1.0 x 1.0 mm
Time: 4.38 min





**3D SWI**
TR/TE: 33/24,6 ms
Acq: 1.0 x 1.0 x 1.0 mm
Time: 3.30 min

**2D GRE T1 with Gad**
TR/TI/TE: 7500/3000/318 ms
Acq: 3.0 x 1.0 x 1.0 mm
Time: 2.57 min



# Assessment of T2LL, new T2, and global / grey matter brain volume

SIEMENS

MSPie
MS PATHS Image Evaluation

REPORT
V2_0_0

NOT FOR CLINICAL USE

**Patient Demographics**

Age: Sex: M

**Review**

Prior: 30-Jun-2020 Current: 18-May-2021

**Relative Disease Burden**

| Total Lesion Volume (mL) | Brain Parenchymal Fraction (BPF) |
|---|---|
| 28.62 | 0.837 |

Moderate / Mild / Severe

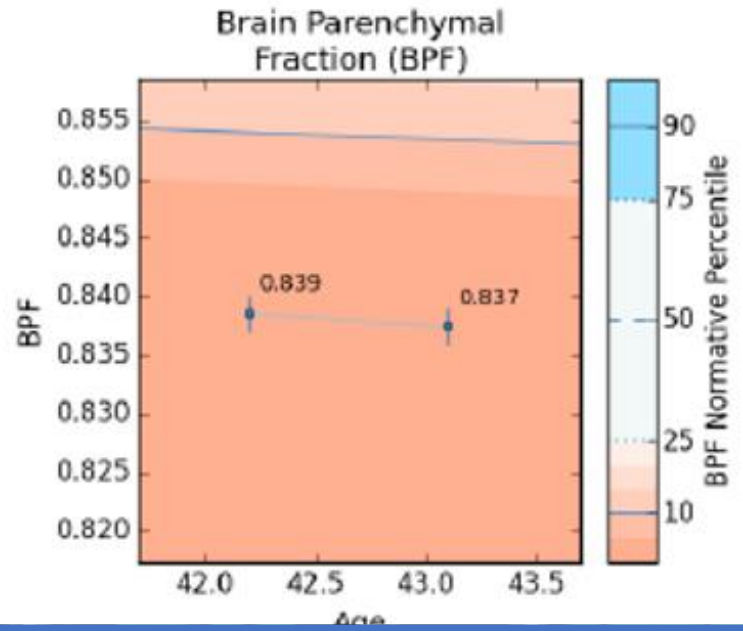
## Morphometry

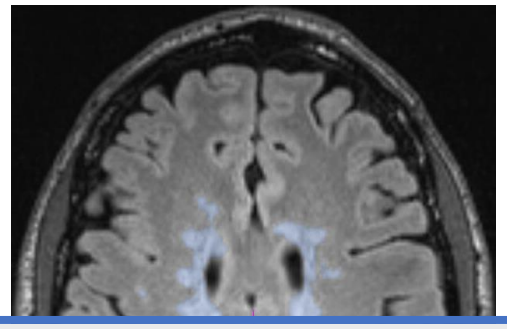
### Brain Volume (normalized)

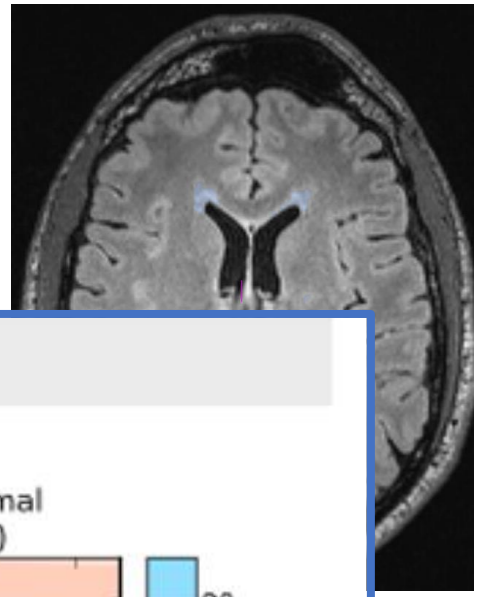
| | Prior 30-Jun-2020 | Current 18-May-2021 | Change since prior (%) |
|---|---|---|---|
| BPF | 0.839 | 0.837 | -0.14 |
| GMF | 0.455 | 0.448 | -1.61 |
| WMF | 0.384 | 0.390 | 1.59 |

### Gray Matter Structure Volume in mL [% of intracran. vol.]

| | Prior 30-Jun-2020 | Current 18-May-2021 | Change since prior (%) |
|---|---|---|---|
| Deep GM | 35.78 [2.60] | 35.62 [2.58] | -0.44 |
| Cortical GM | 475.19 [34.48] | 474.84 [34.42] | -0.07 |
| Thalamus | 11.79 [0.86] | 12.04 [0.87] | 2.05 |



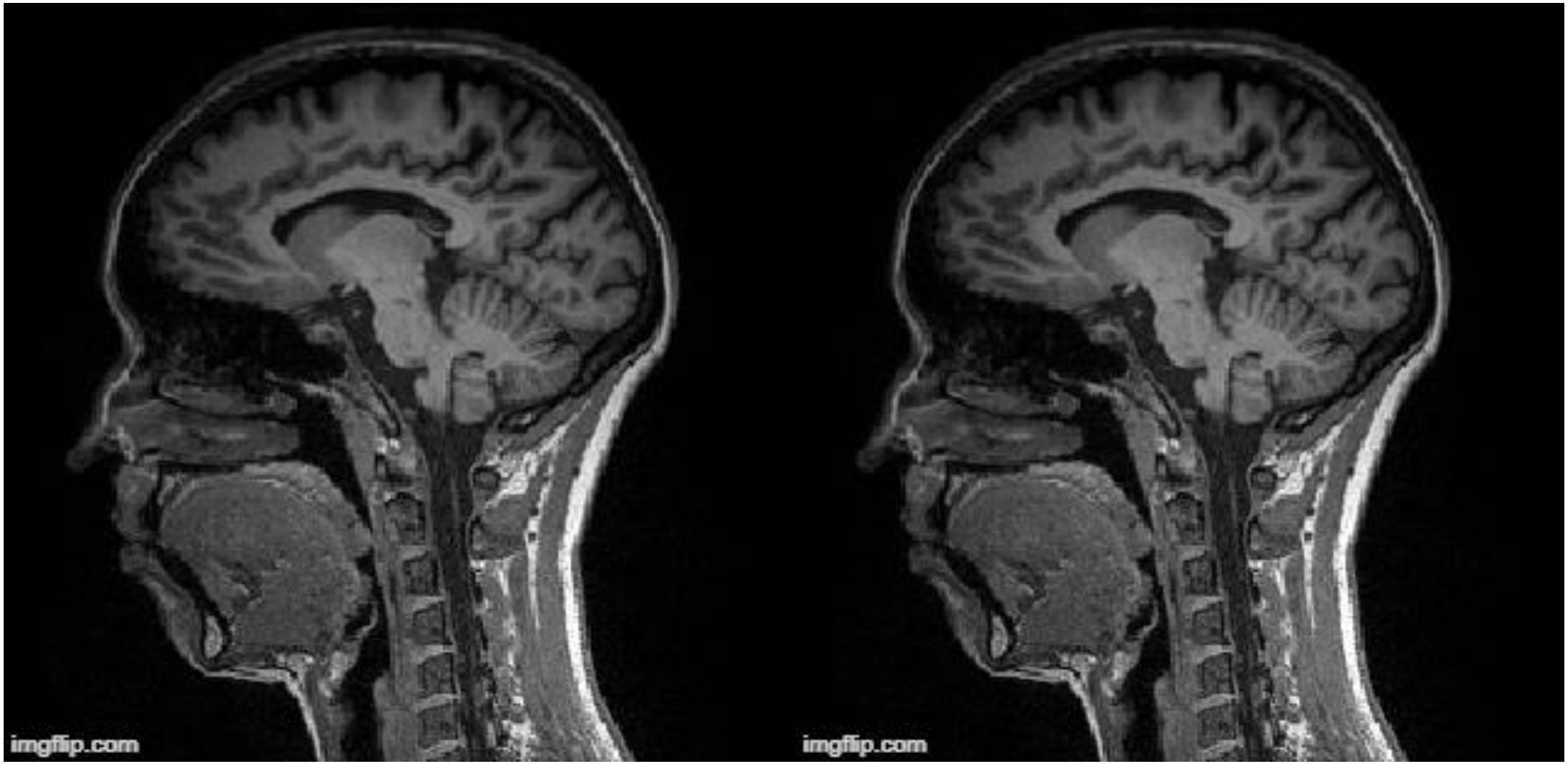




- On-line solution
- Friendly
- Quality control (validation required)
- License

2021-05-27 1/2

# Spinal cord atrophy in MS: automated measure




*Spinal Cord Toolbox*

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| Spinal Cord Sequences | Diagnostic workup | Follow Up | Safety Monitoring |
|---|---|---|---|
| **Sagittal at least 2 of $T_2$, PD or STIR** | **2 sequences Recommended** | Optional | Not Required |
| Sagittal 3D $T_1$ (PSIR, MP-RAGE) cervical only | Optional (substitutes for one of above) | Optional | Not Required |
| Axial T2 or T2* | Optional (through lesions) | Optional | Not Required |
| Pre-Gd Sagittal $T_1$ | Optional | Optional | Not Required |
| Post-Gd Sagittal $T_1$ | **Recommended** | Optional | Not Required |
| Post-Gd axial $T_1$ | Optional | Optional | Not Required |

**$T_2$** (TSE/FSE, turbo/fast spin echo)
**Gd** macrocyclic agent, 0.1mm/kg body weight, minimum delay 5-10 minutes. No additional Gd needed if following Post-Gd brain examination
**$T_1$** (TSE/FSE)
**STIR** (short tau inversion recovery)
**PD** (proton-density, TSE/FSE)
**$T_2$*** ($T_2$ gradient recalled echo)

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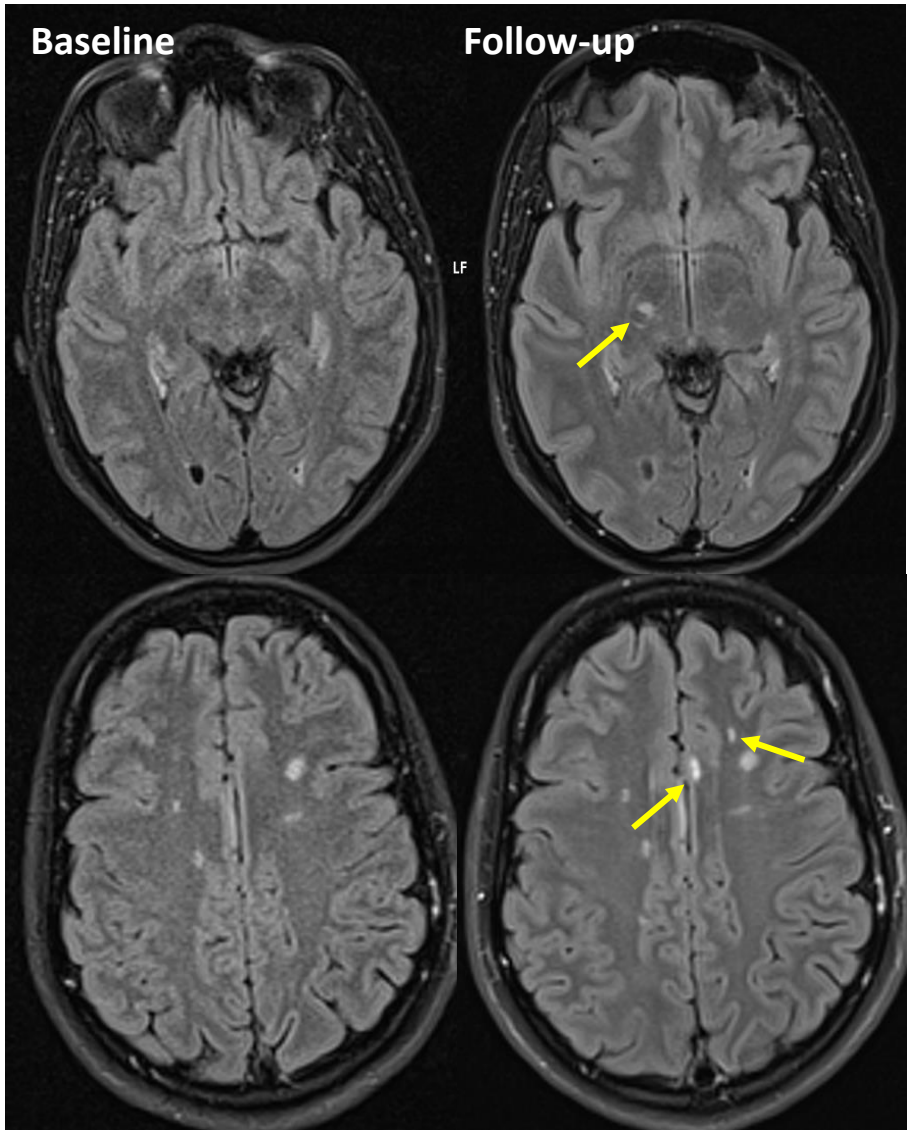
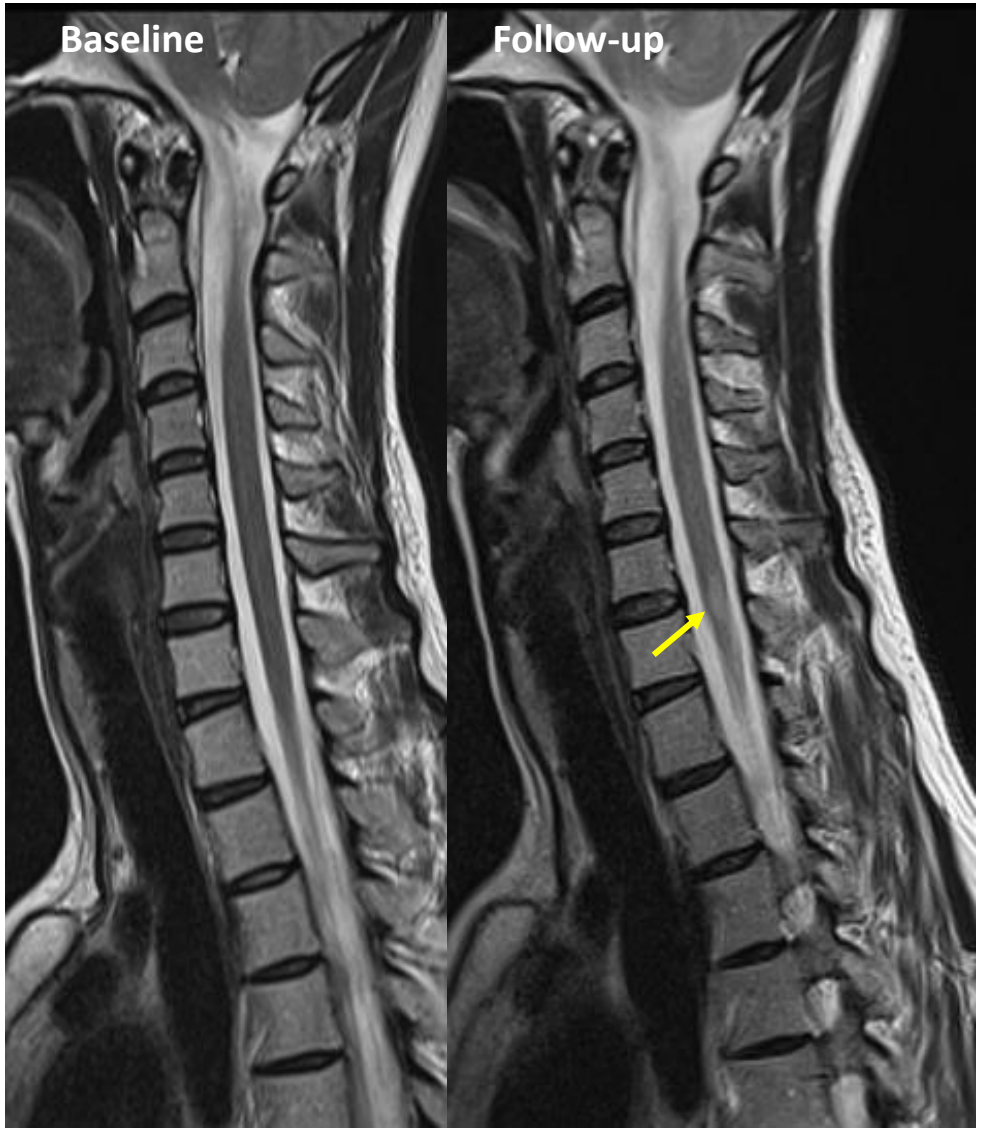
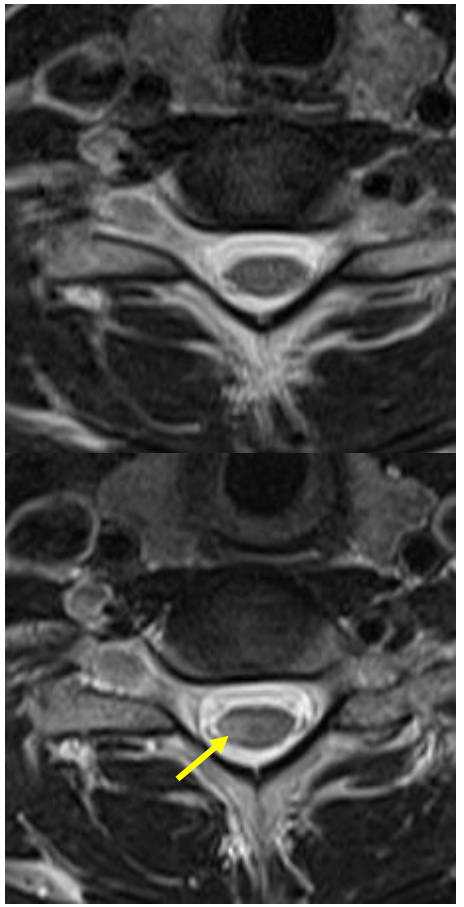
M Wattjes et al. Lancet Neurol 2021

# Spinal cord MRI in monitoring treatment response?



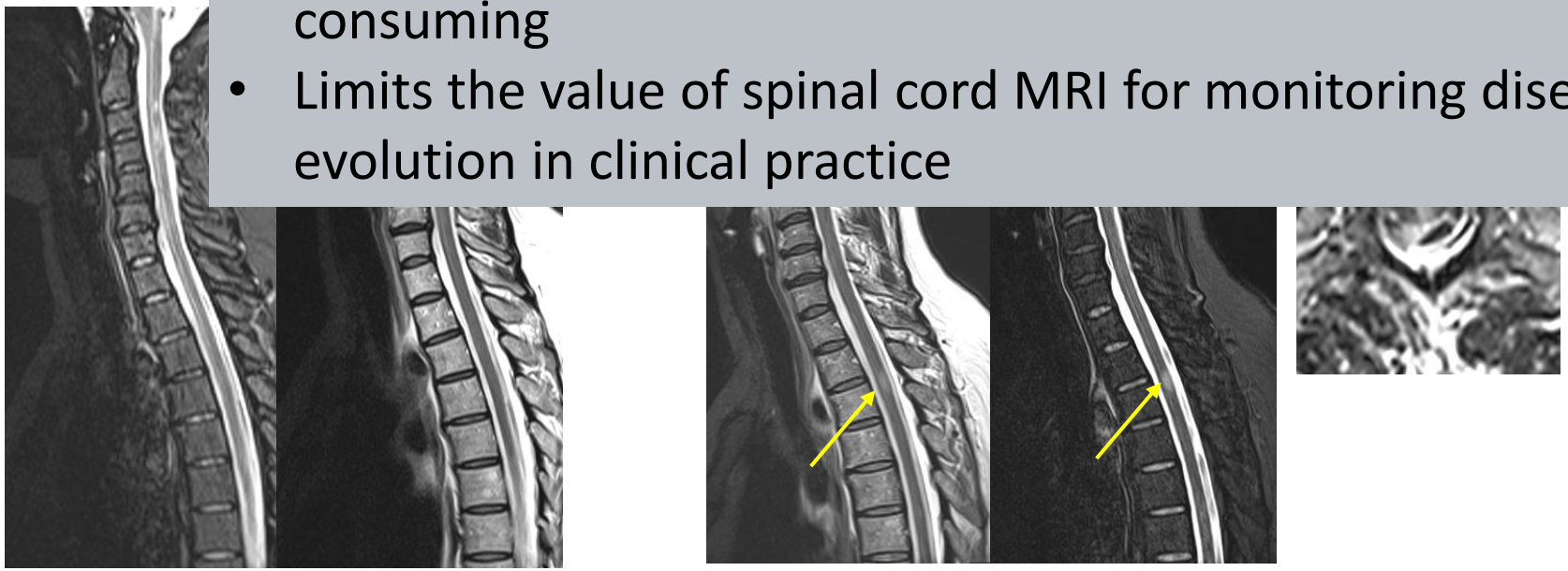



# Spinal cord MRI in monitoring and predicting treatment response

**Adding spinal cord to brain MRI in the routine monitoring of clinically stable RRMS could reveal a significant proportion of disease activity otherwise undetected (weak evidence)**

- Validation studies required
- Acquisition of spinal cord MRI increases the total scanning time
- Challenge
- Absence

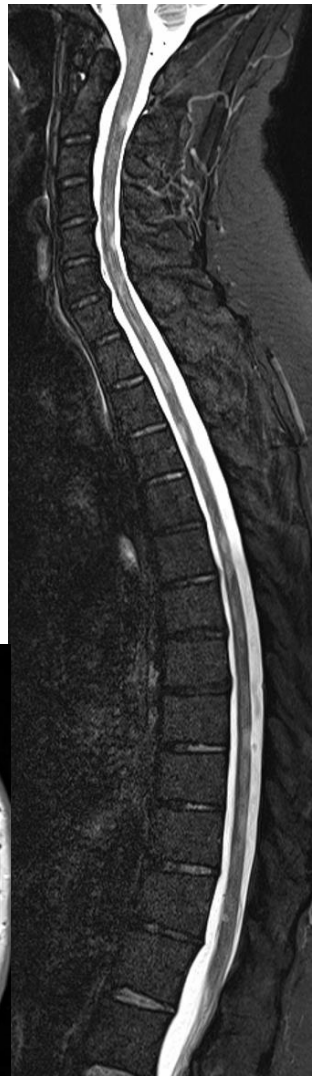
- Spinal cord lesions are prognostically important but difficult to identify and quantify!!!
- Good quality spinal cord MRI is technically challenging and time-consuming
- Limits the value of spinal cord MRI for monitoring disease evolution in clinical practice

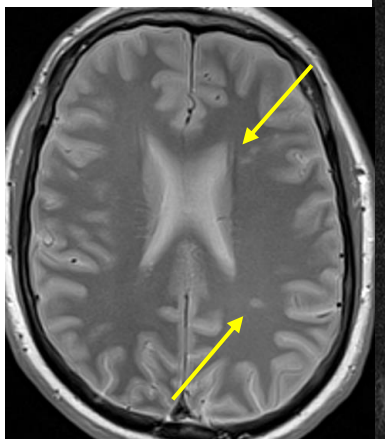


Ciccarelli et al. Lancet Neurol 2019; Wattjes M et al. Nat Rev Neurol. 2015; Rocca et al. Exp Rev Neurother 2020

# Spinal cord MRI in monitoring and predicting treatment response

- Routine spinal cord follow-up MRI **cannot yet be recommended** unless:
  - Significant clinical activity/worsening with no/few changes on brain MRI
  - Spinal cord relapse if detection of (new) lesions could affect treatment decisions
  - Patients with a predominant spinal cord MS phenotype (MRI)
  - Rule out alternative cause for progressive myelopathy





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# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

| Optic Nerve Sequences | Diagnostic workup | Follow Up | Safety Monitoring |
|---|---|---|---|
| Axial & Coronal fat-suppressed $T_2$ or STIR | Optional | Not Required | Not Required |
| Post-Gd Axial & Coronal fat-suppressed $T_1$ | Optional | Not Required | Not Required |

**$T_2$** (TSE/FSE, turbo/fast spin echo)
**Gd** macrocyclic agent, 0.1mm/kg body weight, minimum delay 5-10 minutes. No additional Gd needed if following a Post-Gd brain examination
**$T_1$** (TSE/FSE)
**STIR** (short tau inversion recovery)

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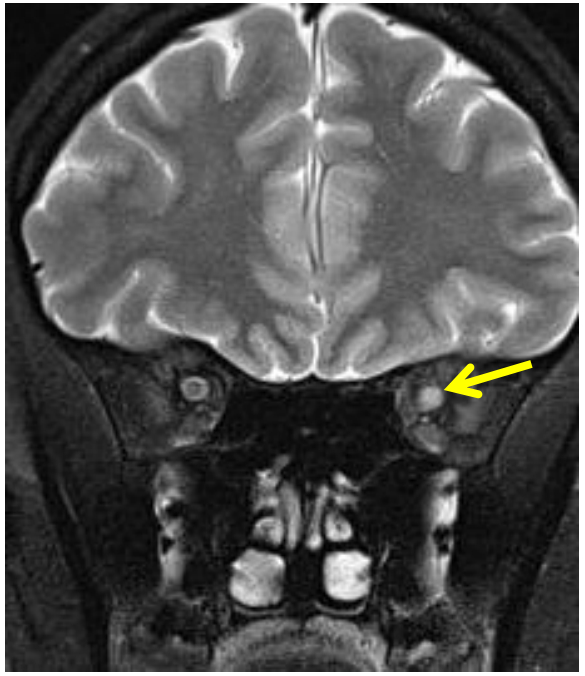
# Optic nerve lesion detection by test (MRI)

Dr A Vidal Jordana

An **abnormal optic nerve MRI** was defined by the presence of a T2 hypersignal in the optic nerve (coronal T2 FS sequence)



**114 / 157 patients (72.6%)** with **optic nerve MRI** performed

(mean time from CIS to MRI 2.9 months, SD 2.6)

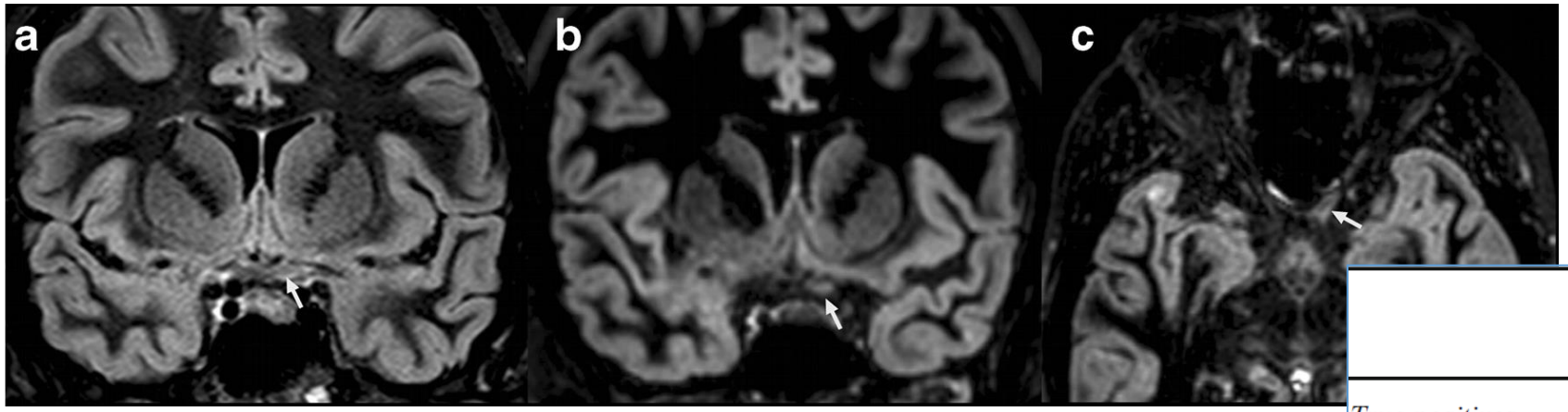
| | Whole cohort (n=112) [a] | ON-CIS (n=55) | Non-ON CIS (n=57) | P-value (ON vs non-ON) |
|---|---|---|---|---|
| **Optic nerve lesion** | 45 (40.2) | 40 (72.7) | 5 (8.8) | <0.001 |

[a] Optic nerve sequence of suboptimal quality in n=2 patients

*Abbreviations (alphabetical order): CIS: clinically isolated syndrome; FS: fat suppression; ON: optic neuritis*

# MRI in Optic Neuritis

- **3D DIR** outperforms 2D STIR for detecting optic nerve lesions



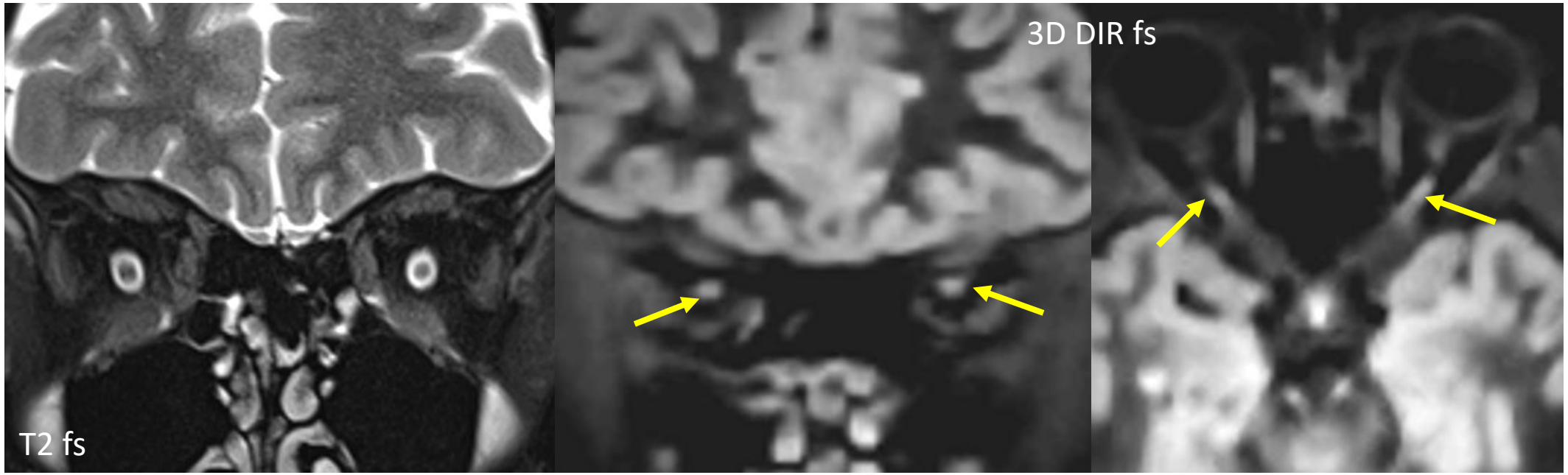

Hodel et al. Eur Radiol 2014

| | 2D STIR FLAIR | DIR 2D coronal reformat | 3D DIR MPR |
|---|---|---|---|
| *True positives* | 37 | 39 | 42 |
| *True negatives* | 16 | 17 | 17 |
| *False positives* | 2 | 1 | 1 |
| *False negatives* | 7 | 5 | 2 |
| *Sensitivity* | 0.84 (0.71-0.97) | 0.88 (0.78-1) | 0.95 (0.89-1) |
| *Specificity* | 0.89 (0.74-1) | 0.94 (0.84-1) | 0.94 (0.84-1) |

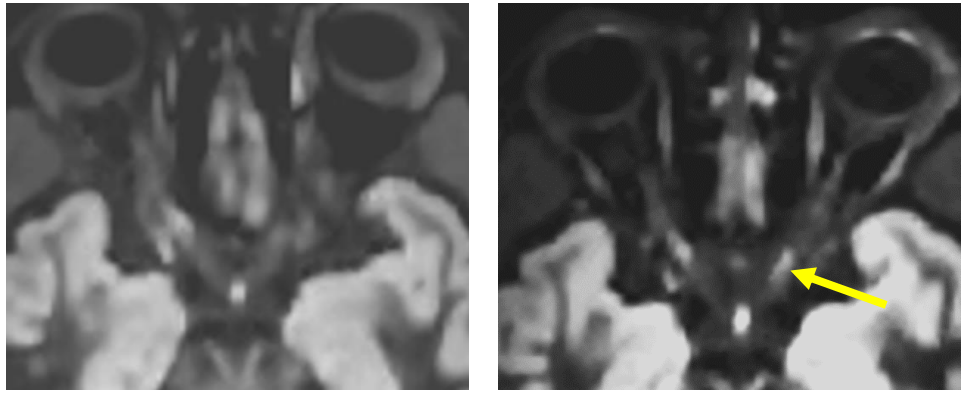
- 3D DIR detects signal changes in **38%** of asymptomatic nerves in CIS patients
- 3D DIR signal changes highly specific for optic nerve pathology (more sensitive than VEPs)

Riederer et al. J Neurol 2019; London et al. Mult Scler J 2019

# MRI in Optic Neuritis: sequences



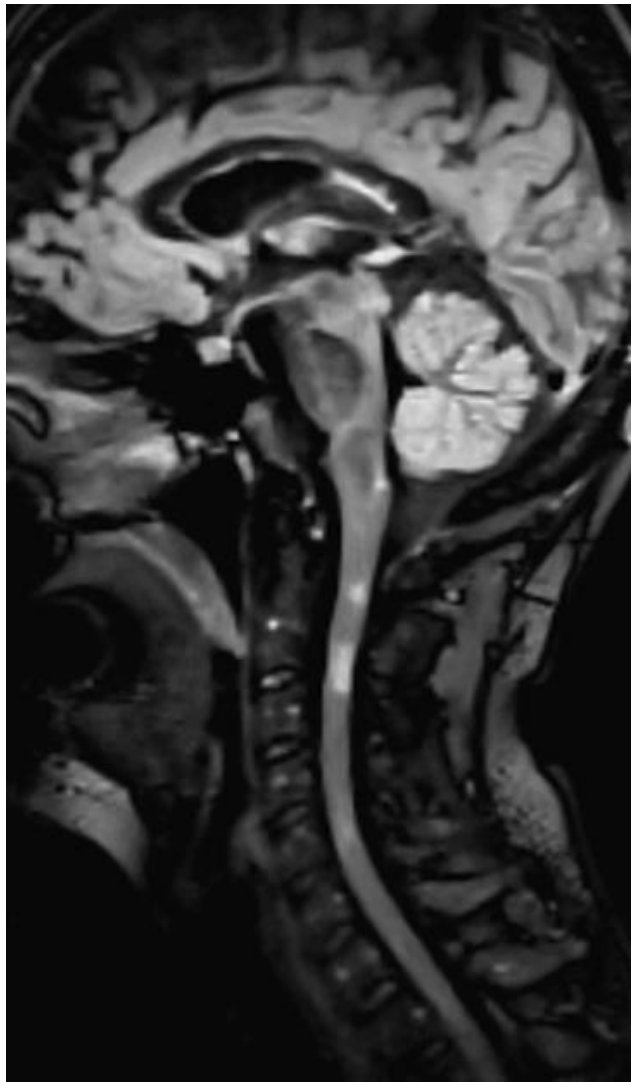

3D DIR fs



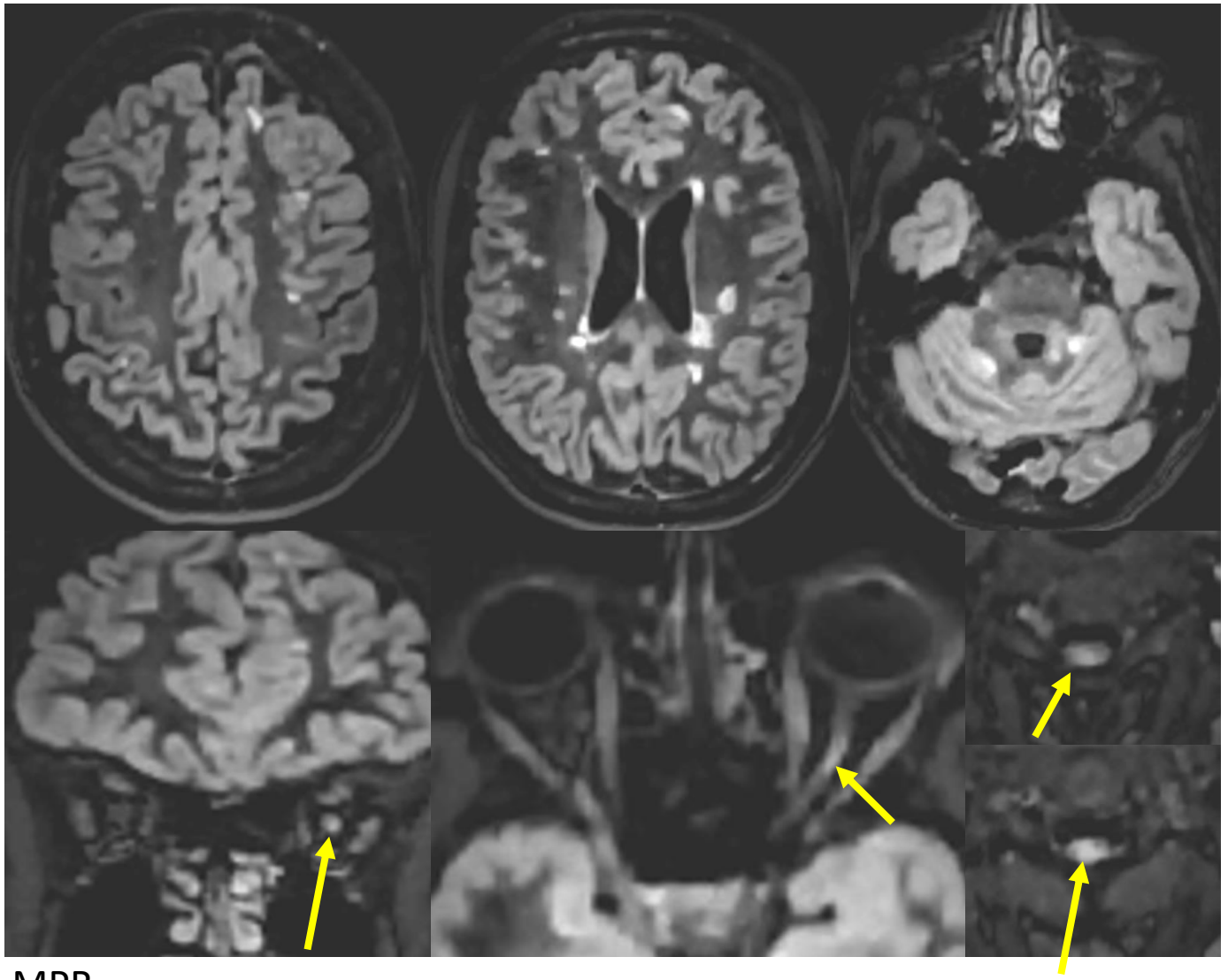
20.10.2021

31.08.2022

# 3D Double Inversion Recovery (DIR): one-step sequence?

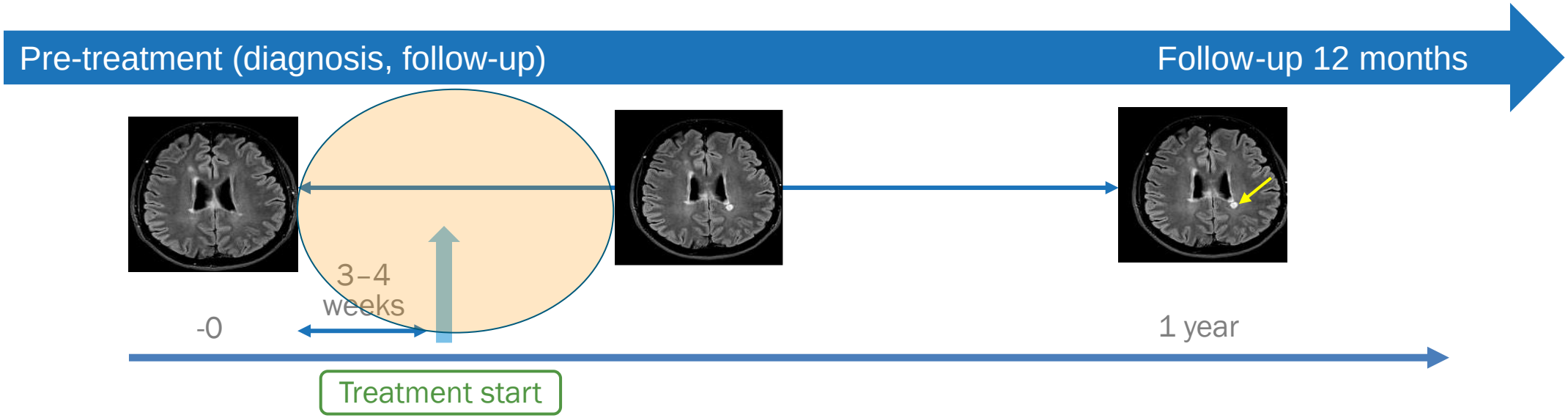


3D DIR
Extended FOV



MPR

# MRI timing




- Disease activity within the first weeks/months after treatment initiation not related to treatment failure:
  - Residual disease activity can reflect a delay in the treatment response
  - Timing of the **rebaseline MRI** based on the pharmacodynamics of DMT (allow sufficient time for drug to start working, usually 3–6 months)
- New T2 lesions are preceded by non-visible **pathological changes already present before treatment initiation**

.

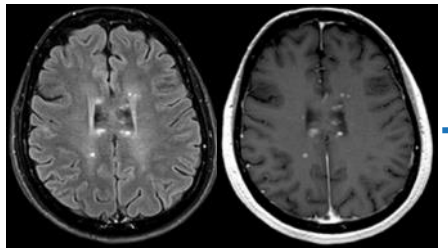
***1.*** *Giovannoni G et al. Mult Scler Relat Disord 2015;4:329–33;* ***2.*** *Freedman MS et al. Can J Neurol Sci. 2013;40:307–23*

# MRI timing

55-year-old woman
CIS March 2018 (polyregional)

Pre-treatment

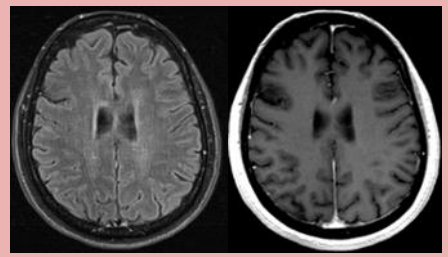
Follow-up 9 months



April 2018

Highly active disease
10 Gd+

Treatment onset
June 2018



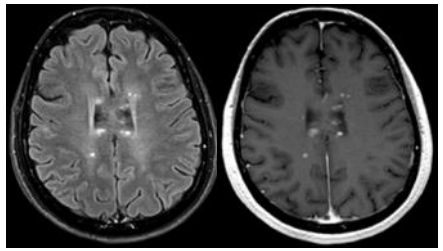
March 2019

4 new T2 lesions
No Gd+

# MRI timing

55-year-old woman
CIS March 2018 (polyregional)

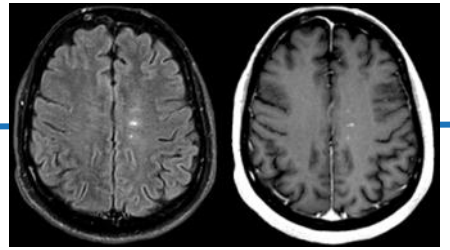
Pre-treatment | Re-baselining 3 months | Follow-up 9 months



April 2018

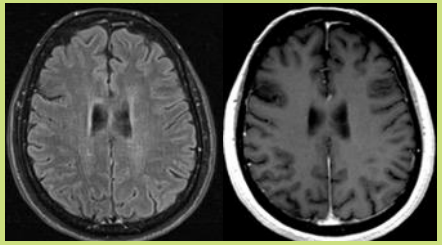
Highly active disease
10 Gd+

Treatment onset
June 2018



September 2018

4 new T2 lesions
2 Gd+

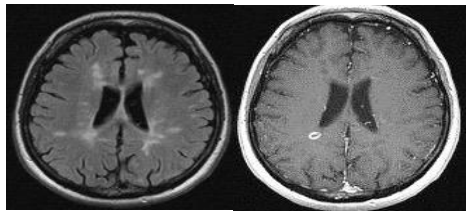


March 2019

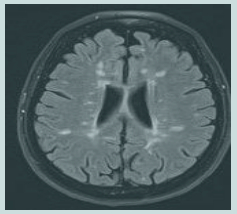
0 new T2 lesions
No Gd+

# MRI timing in monitoring MS

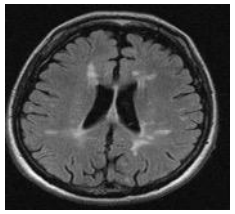
| Initial | Re-Baseline | First follow up[a,b] | Second follow up[a,b] | Follow ups[a,b] |
|---|---|---|---|---|
| Pre-treatment[c] | 3–6 months after treatment onset[d] | 12 months after treatment onset | 24 months after treatment onset | Every year while on treatment[e] |
| **Gd recommended** | **Gd usually not required[f]** | **Gd optional** | **Gd optional** | **Gd optional** |



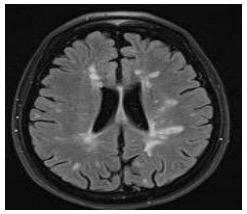
Assess prognostic markers



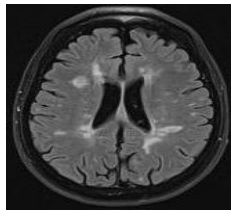
Reference scan



Assess active lesions



Assess active lesions



Assess active lesions

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

[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 (see box 3)*

[c] *Add spinal cord MRI to brain MRI if never performed;*

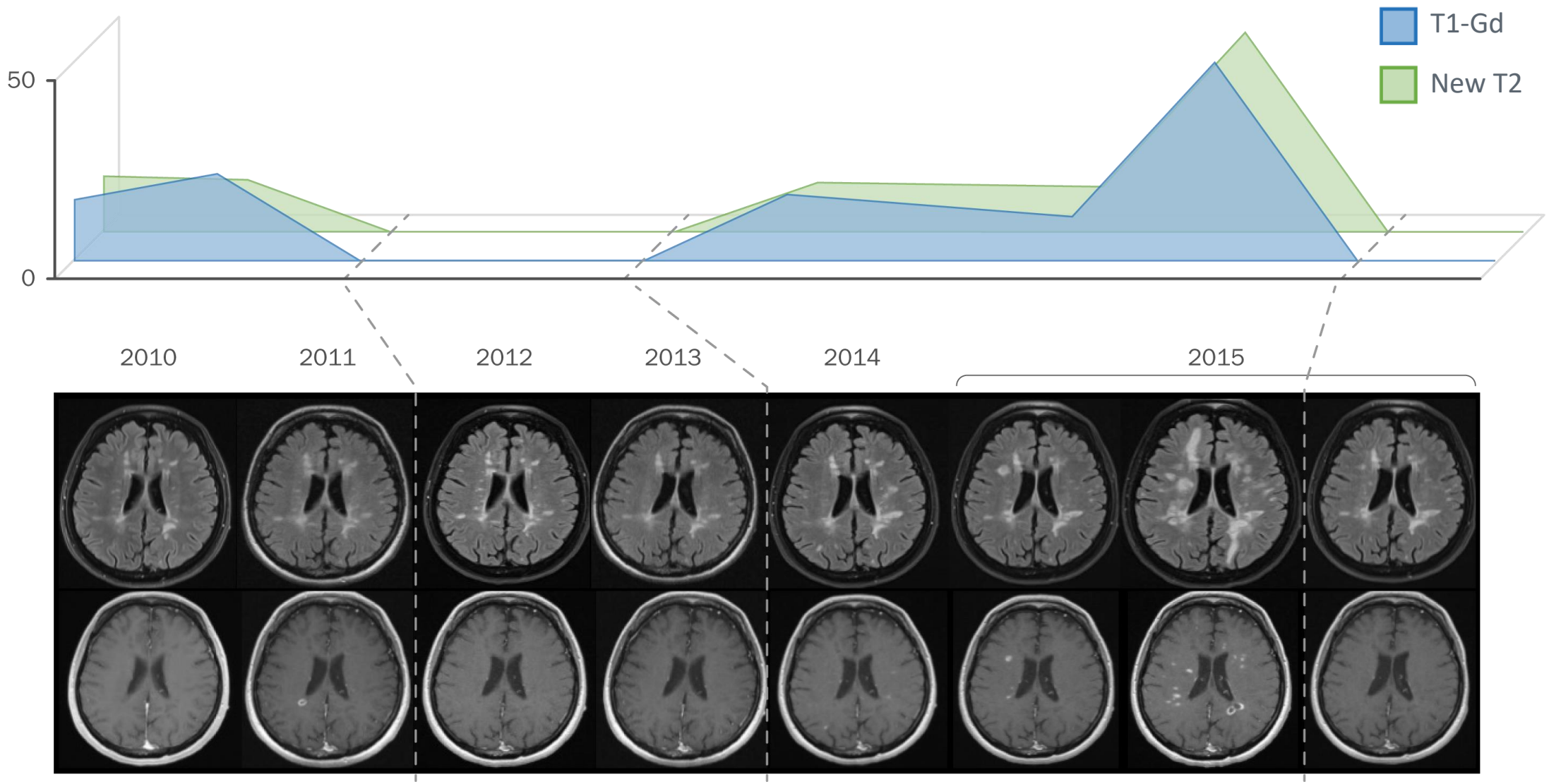
[d] Longer intervals to be considered in patients treated with certain DMTs (up to 9 months with glatiramer acetate, and until completion of the full initial courses with induction therapies)

[e] *Less frequent MRIs in clinically stable patients treated with IFN or GA*

[f] Consider Gd administration in patients with highly active disease at baseline or in patients with unexpected clinical activity after treatment initiation

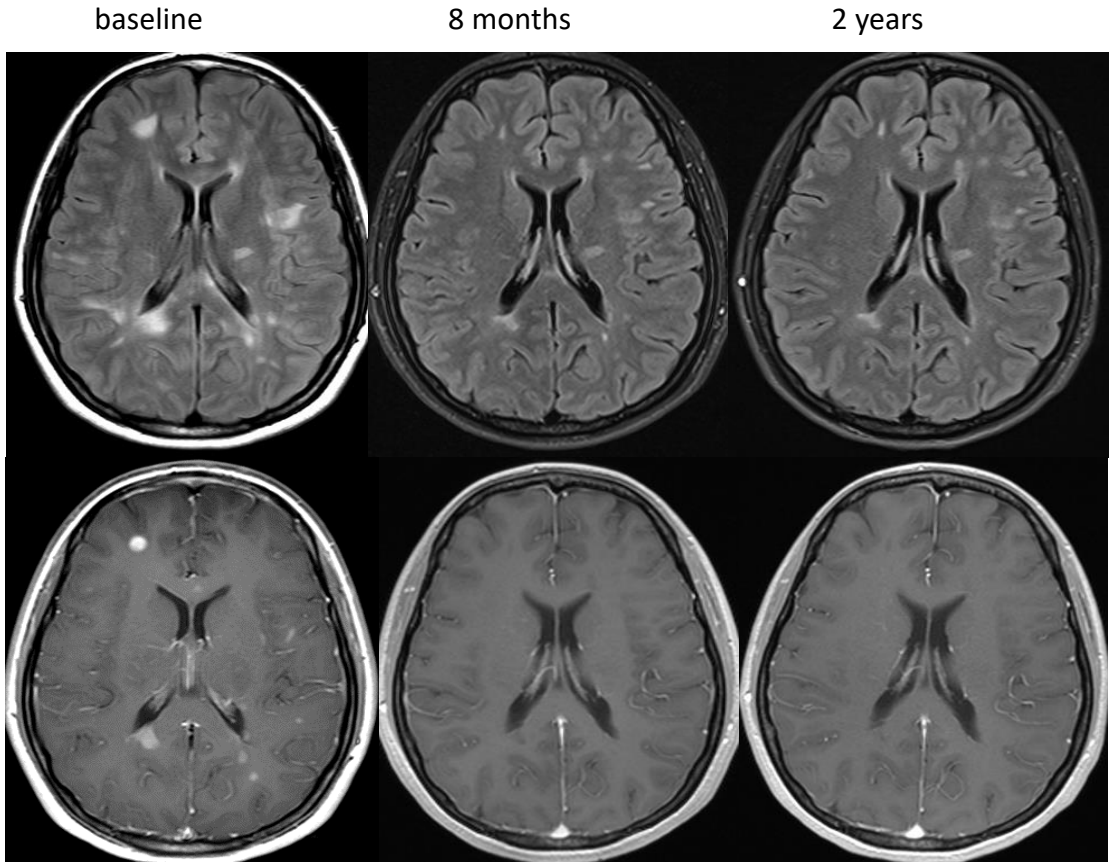
Wattjes, Rovira. Lancet Neurol 2021

# Serial routine assessment of activity at “clinical” intervals (yearly)



# Summary on the use of DMDs in Multiple sclerosis

- Predominant anti-inflammatory effect (Gad and new T2 lesions)
- Increasing use of medium to high-efficacy DMDs (60% at Vall d'Hebron Hospital)
- Majority of patients (>93%) show NO Gad-enhancing lesions on routine follow-up (one year)




- Is cost-effective using GBCAs in routine MRI monitoring?
- Is safe the repetitive injection of GBCAs?

# European Commission decision on use of Gd

- Use Gd only if essential; minimise repetitive Gd imaging when possible
- Use Gd at lowest dose needed
- Only **macrocyclic** agents for CNS studies

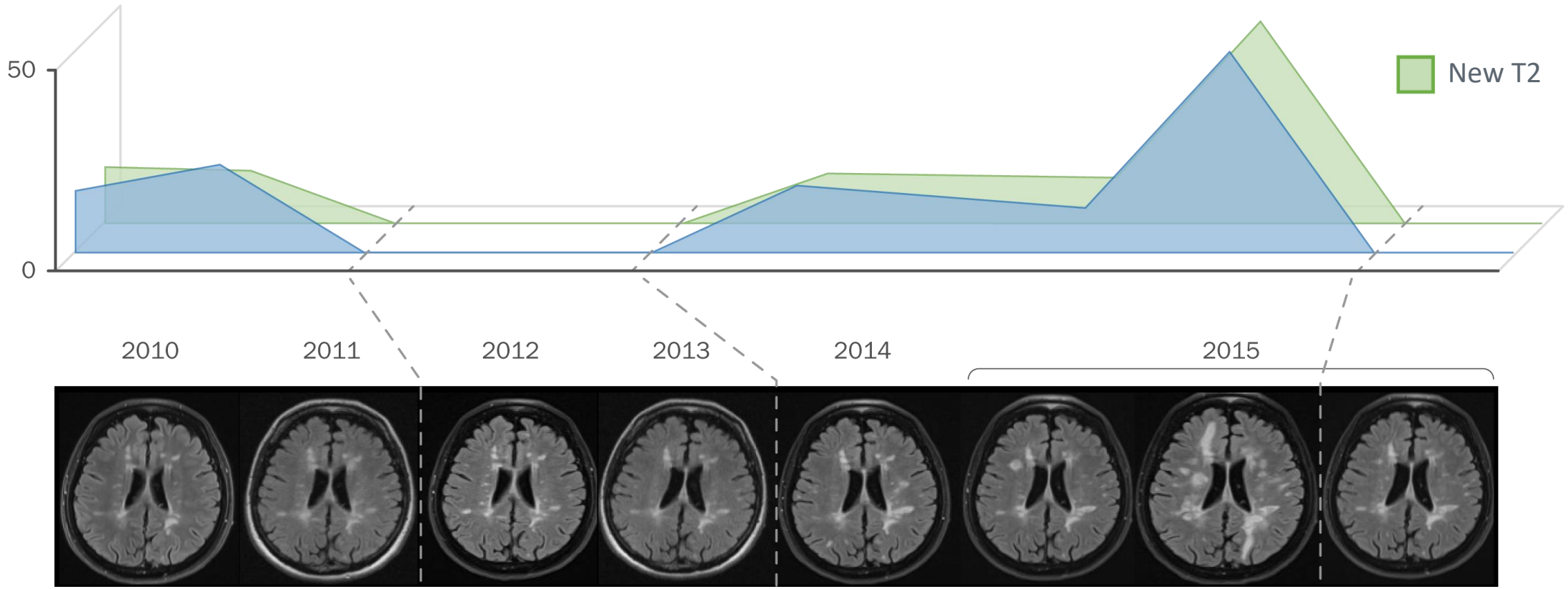
*European Medicines Agency, https://www.ema.europa.eu/en/medicines/human/referrals/gadolinium-containing-contrast-agents (accessed 5 November 2019).*

Despite lack of evidence of the clinical effects (in subjects with normal renal function) we must take special caution in patients at higher risk:

- Patients requiring multiple lifetime doses
- Patients with inflammatory conditions (likely increase Gad deposition)
    - Children, MS, inflammatory bowel disease

Use of GBCAs should be reduced!!!

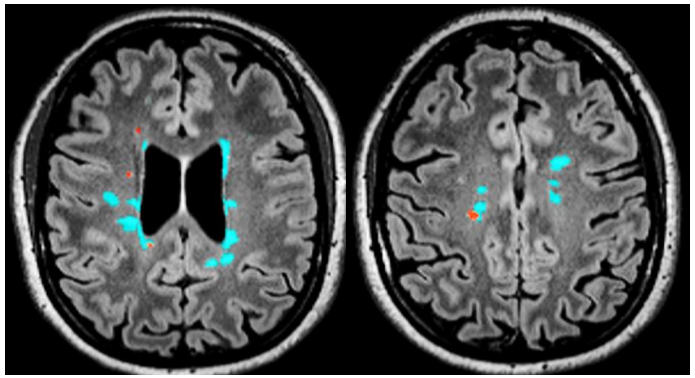
# Serial routine assessment of activity at “clinical” intervals (yearly): only T2?



# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

## Recommendations for the use of GBCAs (monitoring)

| Clinical situation | Indication and objective |
|---|---|
| **Monitoring** | **The use of gadolinium is not recommended**<br><br>• **In case of routine monitoring MRIs in patients without anticipated disease activity**<br>• For PML screening |



**Requirement: a prior and relatively recent and technically comparable brain MRI**

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M Wattjes et al Lancet Neurol 2021

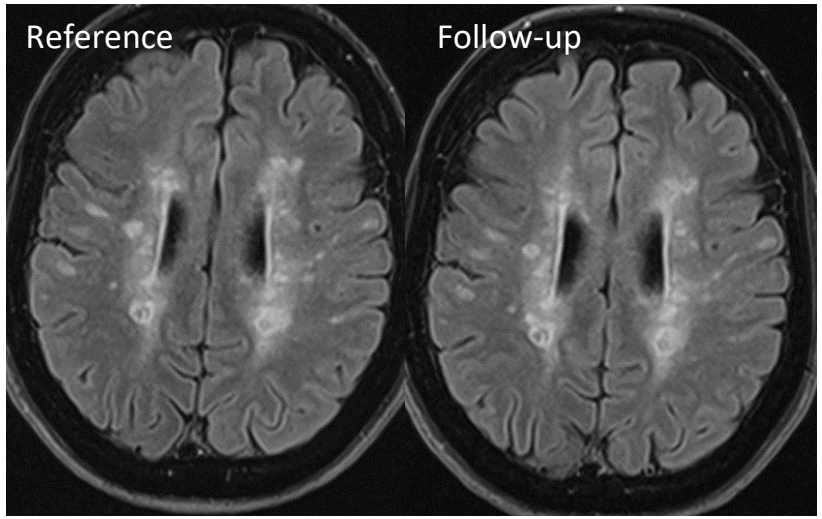
Activity based on new 2 lesions

# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

## Recommendations for the use of GBCAs (monitoring)

| Clinical situation | Indication and objective |
|---|---|
| **Monitoring** | **The use of gadolinium is recommended**<br>• To confirm clinical suspicion of current disease activity is required (MRI should be performed as soon as possible and before steroid treatment), mainly in patients with diffuse and confluent chronic MS lesions<br>• If presence of Gad-enhancing lesion is required to initiate a specific DMD<br>• To detect subclinical activity in patients without a recent reference scan<br>• In the first years (2) in patients receiving low-efficacy DMDs (even if clinically stable)<br>M Wattjes et al Lancet Neurol 2021<br><br>If detection of gadolinium-enhancing lesions could influence treatment decisions (e.g., prompt a switch to a higher efficacy DMT, lack of adherence). |

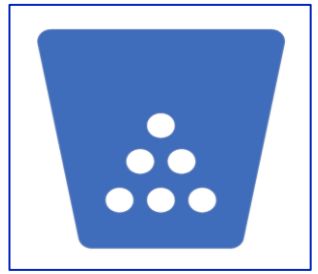
# Active (new/enlarging) T2 lesion counts are routinely used for Assessment of disease activity in Multiple Sclerosis




Visual assessment

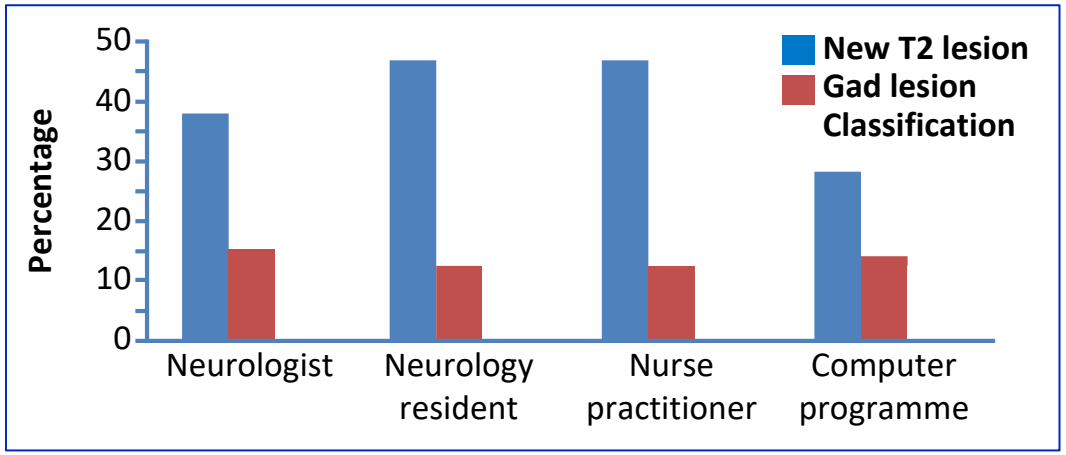
Errors

Low sensitivity
Poor reproducibility



Suboptimal assessment of disease activity

- **Poor quality scans**
  - ✓ Thick slices (>3mm)
  - ✓ Suboptimal repositioning
  - ✓ Non standardized protocol
  - ✓ Movement artifacts
- **Small lesions**
- **Confluent non-active lesions**



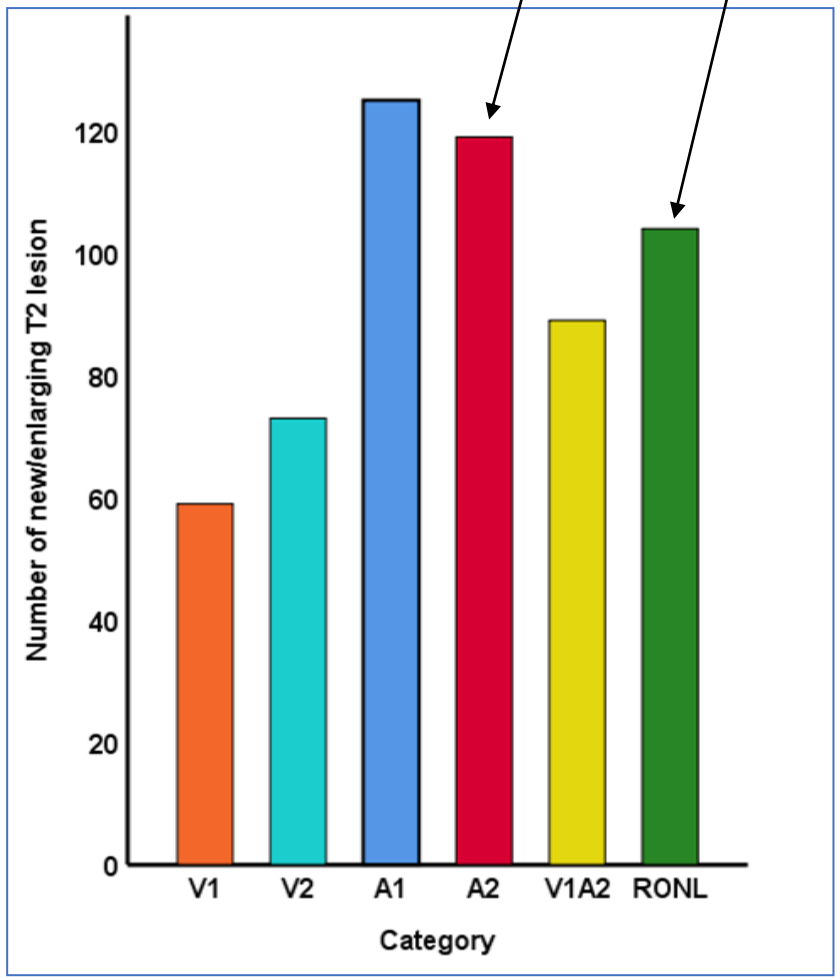

**Concordance analysis:**

- High (0.8-0.96) Gd+
- Intermediate (0.6–0.8) new T2
- Very low(0.0–0.14) enlarged T2

Erbayat Altay E et al. *JAMA Neurol* 2013;70:338–344.

# A supervised approach based on the application of a CNN trained to detect the presence of new T2 lesions in the follow-up scan

AT (CNN) plus visual validation under normal reporting conditions




AT (CNN) plus visual validation under normal reporting conditions

Same scanner (3T) and same sequence

| | V1 | V2 | A1 | A2 | V1A2 |
|---|---|---|---|---|---|
| New T2 lesions | 59 | 73 | 125 | 119 | 89 |
| False negatives | 47* | 31* | 27* | 17* | 15* |
| True positives | 56* | 69* | 77* | 87* | 89* |
| False positives | 3* | 3* | 48* | 32* | 0* |
| Sensitivity (CI) | 54.37 (44.26-64.22) | 69.31 (58.97-77.87) | 74.04 (64.52-82.14) | 83.65 (75.12-90.18) | 85.58 (77.33-91.70) |
| Accuracy (CI) | 52.83 (42.89-62.60) | 67.31 (57.41-76.19) | 50.66 (42.44-58.85) | 63.97 (55.30-72.02) | NA |

Rovira et al. Mult Scler J 2021

# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

## Key messages 1

- Evidence based international consensus recommendations
- Useful for diagnosis, prognosis, and disease monitoring
- Harmonize recommendations from European and North American experts
- MRI protocols are simplified, making them easy to use in clinical practice
- Addresses current limitations of newer sequences diagnosis and quantitative measures for monitoring

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M Wattjes et al 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. Lancet Neurol 2021

# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

## Key messages 2

- 3D-FLAIR brain MRI most important for diagnosis and monitoring
- Gadolinium used restricted to diagnosis and early monitoring
- Spinal cord MRI important for diagnosis and prognosis; dual contrast
- Re-baseline brain MRI after switching treatment (no gadolinium)
- Annual brain MRI while on treatment
- PML monitoring every 3-4 months with abbreviated protocol
- Central vein sign, cortical lesions, brain volume change quantification not yet recommended

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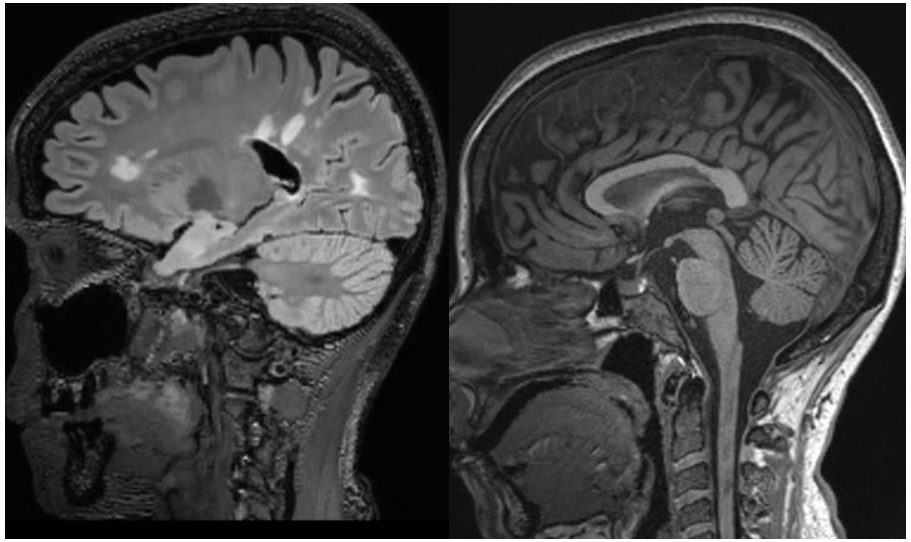
# Take-home message

**The 2021 international recommendations on the use of MRI in multiple sclerosis for diagnostic and monitoring purposes MUST be implemented in ALL our MRI studies**

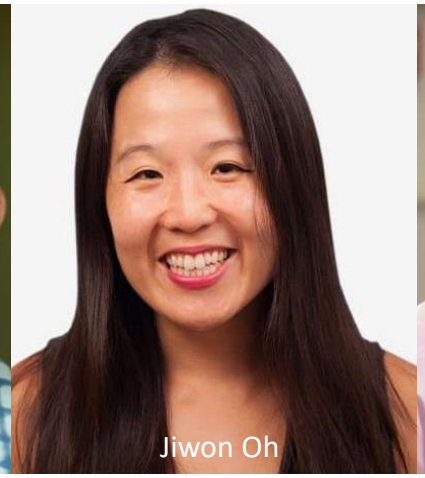
M Wattjes et al. Lancet Neurol 2021




Mike Wattjes


Anthony Traboulsee


David Li


Jiwon Oh


Daniel Reich


Brenda Banwell

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VUmc
Samen kiezen voor beter
VU University Medical Centre – Amsterdam, Netherlands

Vall d'Hebron Hospital
Vall d'Hebron University Hospital – Barcelona, Catalonia

Universitätsspital Basel
University Hospital Basel – Basel, Switzerland

Med Uni Graz
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UCL
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# PROTOCOLO RM ESTANDARIZADO ESCLEROSIS MÚLTIPLE
# 2021 MAGNIMS-CMSC-NAIMS

Lancet Neurology 20: 653-670, 2021

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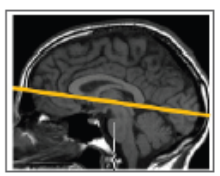
| | CEREBRO | MÉDULA ESPINAL | NERVIO ÓPTICO |
|---|---|---|---|
| **CAMPO MAGNÉTICO** | ≥1,5 T (preferible 3T) | ≥1,5 T | ≥1,5 T |
| **ADQUISICIÓN** | 3D (preferible) o 2D | 2D o 3D | 2D o 3D |
| **GROSOR CORTE** | 3D: 1mm isotrópico[1]<br>2D: ≤3mm, sin gap[2] | Sagital ≤3mm, sin gap<br>Axial ≤5mm, sin gap | ≤2-3mm, sin gap |
| **RESOLUCIÓN EN PLANO** | ≤1mm x 1mm | ≤1mm x 1mm | ≤1mm x 1mm |
| **COBERTURA** | Cerebral completa (incluyendo el segmento proximal de la médula cervical) | Médula completa (cervical, toracolumbar incluyendo el cono) | Nervio y quiasma ópticos |
| **ORIENTACIÓN CORTES AXIALES** (adquisición 2D o reconstrucción 3D) | Plano subcalloso  | Perpendicular al eje sagital de la médula | Alineado a la orientación del nervio/ quiasma óptico |

T = tesla; 3D = 3 dimensiones; 2D = 2 dimensiones

[1] Preferible isotrópico; si sobre contiguo (a través de plano y en plano), no ≥ 1,5 mm con 0,75 mm superposición

[2] Imagen de difusión (DWI): grosor de corte ≤ 5mm con un gap entre cortes no superior a 10-30%

| Cerebro | Dx | Mon | Seg |
|---|---|---|---|
| Axial $T_2$ | | ± | ± |
| Sagital & axial FLAIR (o 3D) | | | |
| Post-Gd axial (o 3D) $T_1$ | | | |
| Imagen de difusión (DWI) | | DDx | |
| DIR o PSIR | | | |
| 3D $T_1$ alta resolución (medición volumen cerebral) | | | |
| Susceptibilidad magnética (SWI) | | | |
| **Nervio óptico** | **Dx** | **Mon** | **Seg** |
| Axial & coronal $T_2$ con supresión grasa o STIR | | | |
| Post-Gd[3] axial coronal $T_1$ con supresión grasa | | | |
| **Médula espinal** | **Dx** | **Mon** | **Seg** |
| Sagital al menos 2: $T_2$, DP o STIR | | | |
| Sagital 3D $T_1$ (PSIR, MPRAGE)[4] sólo cervical | | | |
| Axial $T_2$ o $T_2^*$ | | | |
| Pre-Gd Sagital $T_1$ | | | |
| Post-Gd[3] Sagital $T_1$ | | | |
| Post-Gd[3] axial $T_1$ | | | |

| Recomendado | Opcional | No se requiere |
|---|---|---|

[3] No se requiere nueva inyección de Gd si se obtiene inmediatamente tras el estudio cerebral
[4] Puede substituir una de las siguientes: $T_2$, PD o STIR

**Dx** Diagnóstico de EM
**Mon** Monitorización de actividad de la enfermedad y efectividad del tratamiento modificador de la enfermedad (DMT)
**Seg** Monitorización seguridad para DMT p.e, despistaje de leucoencefalopatía multifocal progresiva (LMP) en pacientes de riesgo

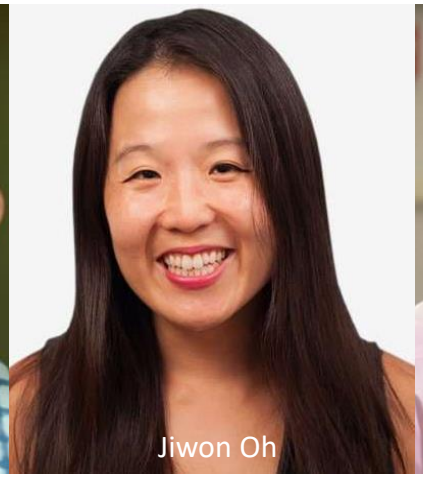
**$T_2$** (TSE/FSE, turbo/fast spin echo)
**±** Axial $T_2$ opcional si 3D FLAIR con reconstrucciones sagital/axial están disponibles
**Gd** agente macrocíclico, 0,1mm/kg peso, retraso mínimo 5-10 minutos
**$T_1$** (TSE/FSE)
**DDx** para diagnóstico diferencial

**FLAIR** (fluid-attenuated inversion recovery), con supresión grasa opcional
**DIR** (double inversion recovery)
**PSIR** (phase-sensitive inversion recovery)

**3D $T_1$ alta resolución** (e.g. MPRAGE/ MP2RAGE magnetization-prepared rapid acquisition of gradient echoes; IR-SPGR, inversion recovery prepared spoiled gradient; TFE, turbo field-echo)

**STIR** (short tau inversion recovery)
**DP** (densidad protónica, TSE/FSE)
**$T_2^*$** ($T_2$ eco de gradiente)







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# What's relevant for your clinical practice?

- A standardized MRI acquisition is essential for both qualitative and quantitative assessment of MRI scans (clinical and research)
- Quantitative measures provide added value to standard qualitative assessments
- Several limitations exist to implement automated tools in clinical practice
- Solutions to these limitations are progressively incorporated

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Vall d'Hebron University Hospital – Barcelona, Catalonia

University Hospital Basel – Basel, Switzerland

Medical University Graz – Graz, Austria

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San Camilo – Forlanini Hospital – Roma, Italy

University of Siena – Siena, Italy

# Gad deposition in CNS

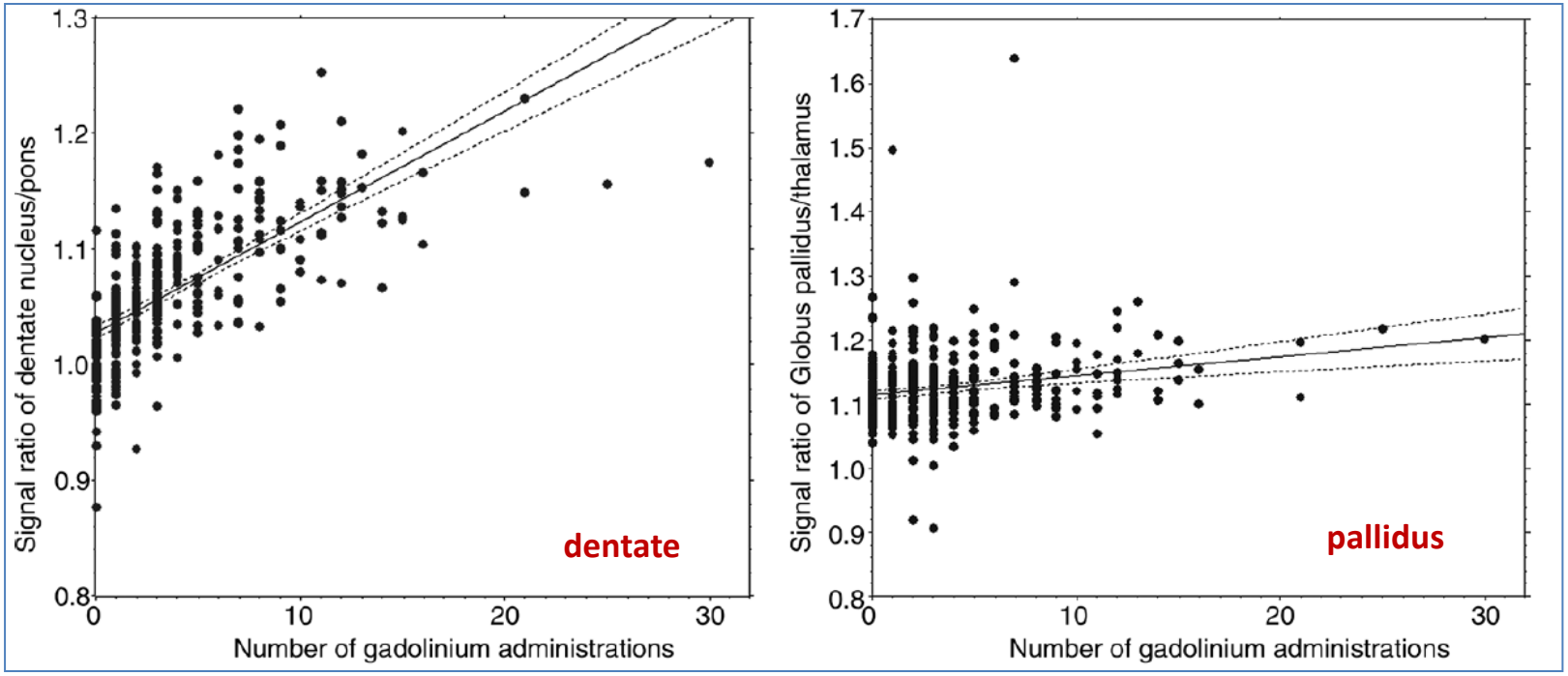
First study that correlated high SI in DN and GP with administration of GBCAs (linear). No clinical data

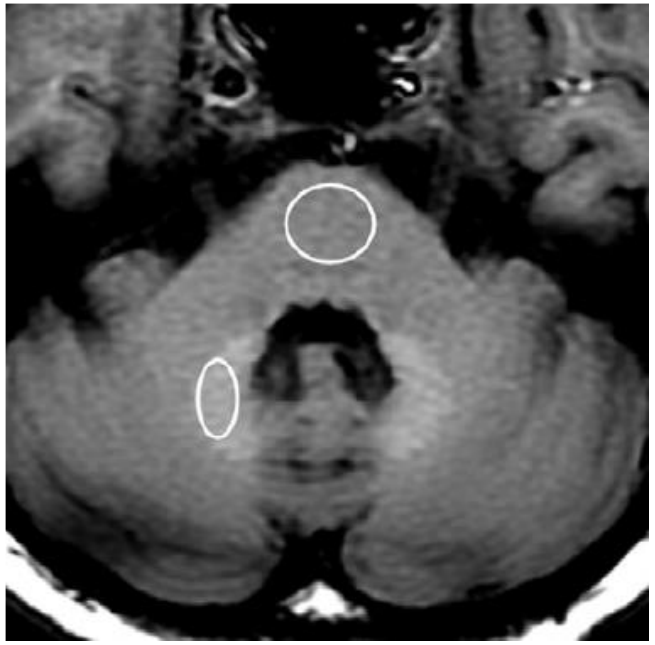
**High Signal Intensity in the Dentate Nucleus and Globus Pallidus on Unenhanced T1-weighted MR Images:** Relationship with Increasing Cumulative Dose of a Gadolinium-based Contrast Material[1]

Radiology

Kanda et al. Radiology 2014

Design
- single center
- retrospective
- 19 patients
- normal liver and renal function
- no prior RT



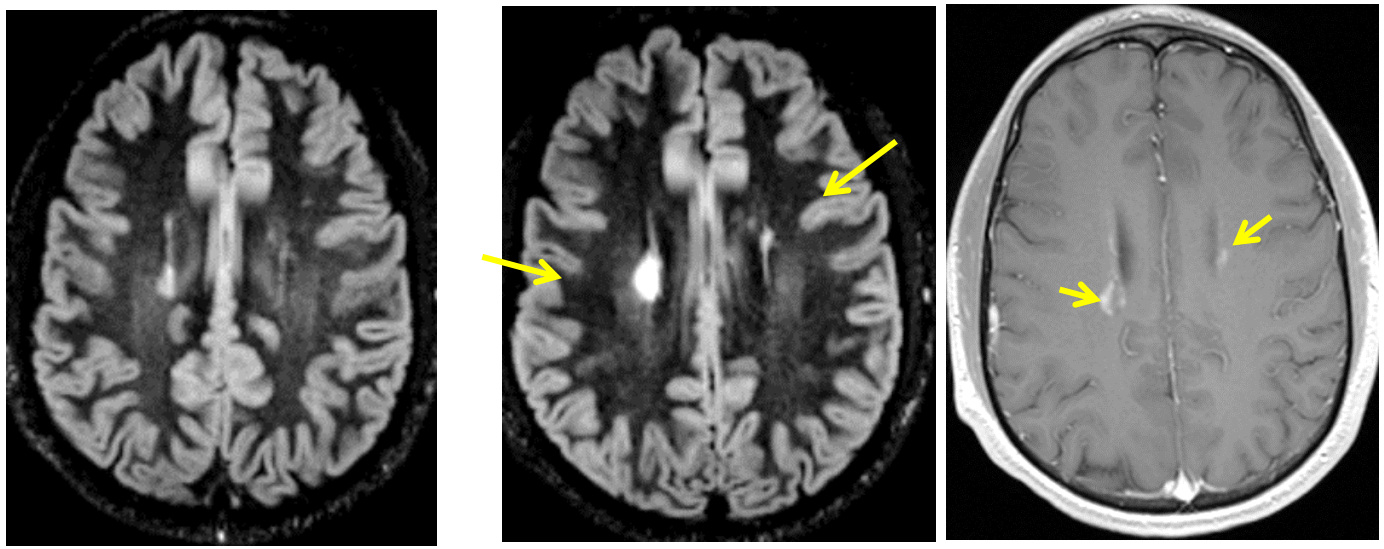
# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

## Recommendations for the use of GBCAs (monitoring)

| Clinical situation | Indication and objective |
|---|---|
| **Monitoring** | **The use of gadolinium is recommended**<br>• To confirm clinical suspicion of current disease activity is required (MRI should be performed as soon as possible and before steroid treatment), mainly in patients with diffuse and confluent chronic MS lesions |

Reference scan

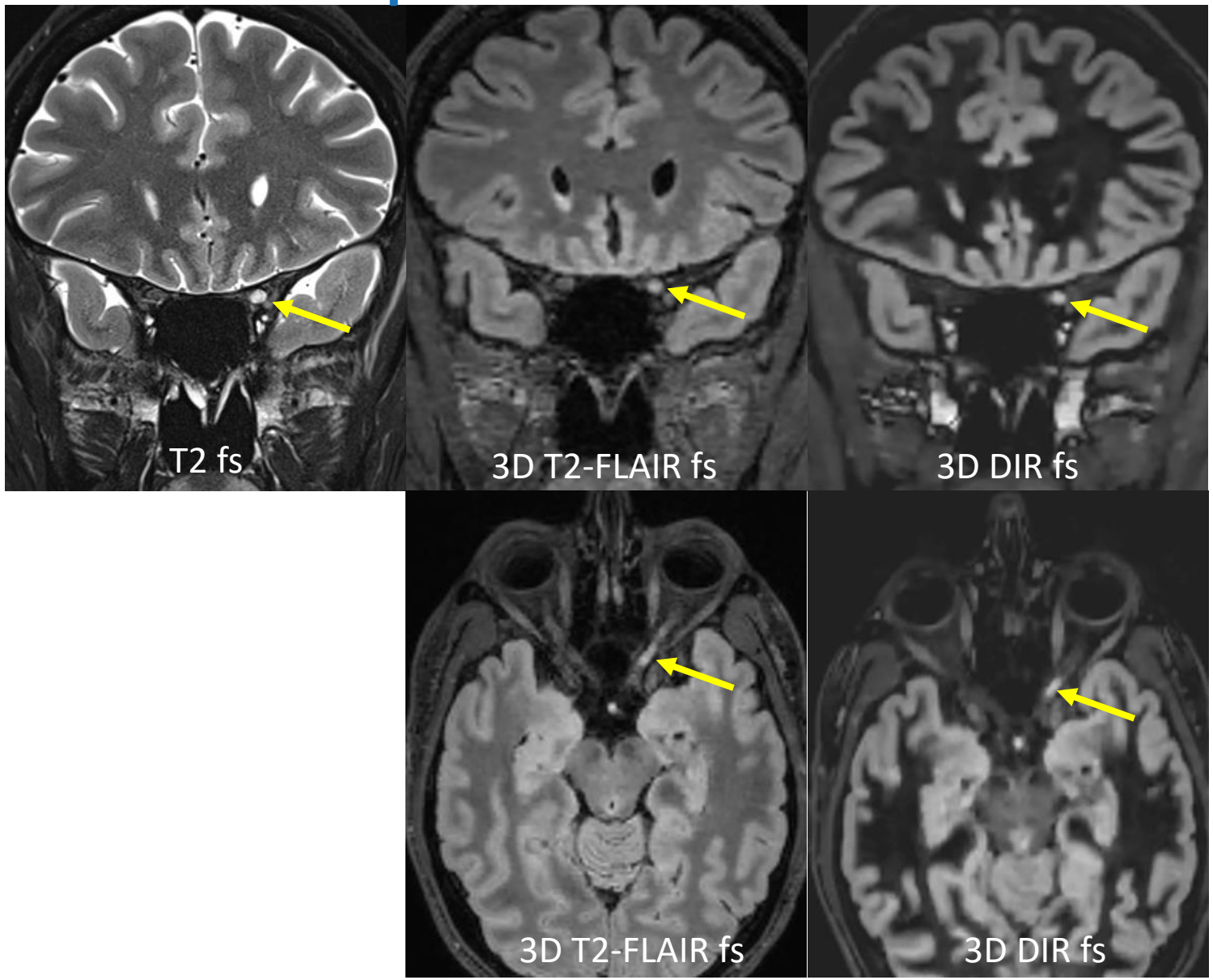
Suspected recent clinical activity



Hospital Vall d'Hebron

M Wattjes et al Lancet Neurol 2021

# MRI in Optic Neuritis: sequences



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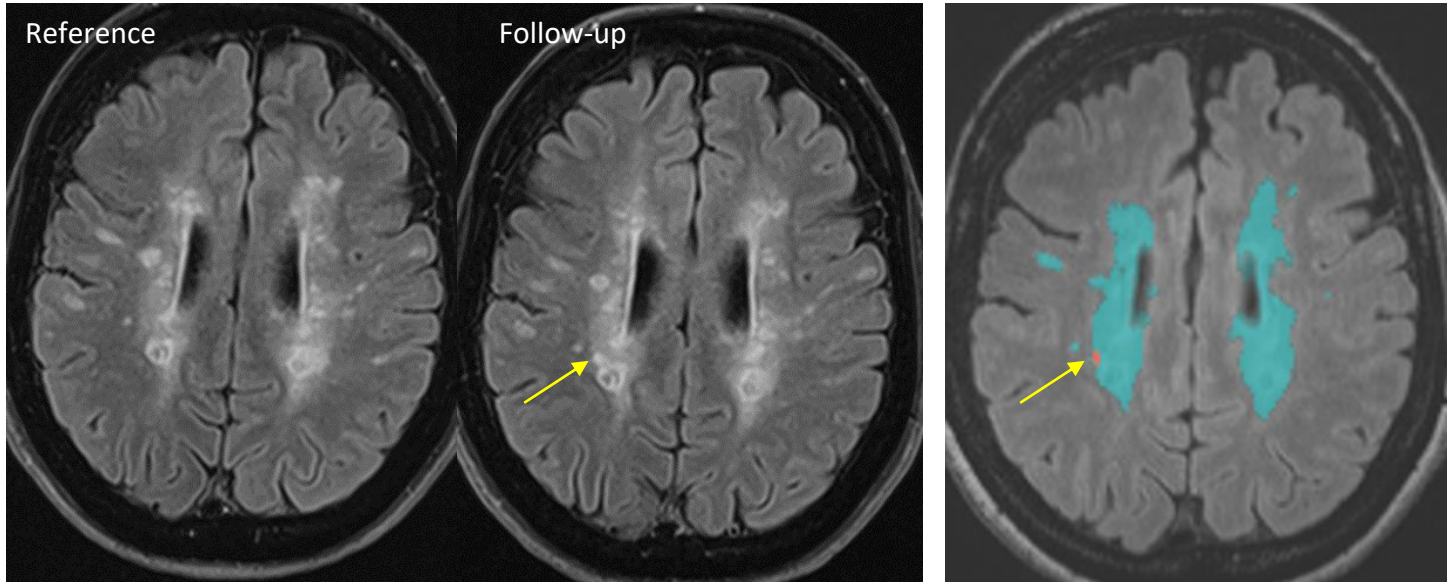
| **Monitoring** | **The use of gadolinium is recommended**<br>• To confirm clinical suspicion of current disease activity is required (MRI should be performed as soon as possible and before steroid treatment), mainly in patients with diffuse and confluent chronic MS lesions |

**Automated co-registration and lesion color-coding (MSPie, Siemens)**

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M Wattjes et al Lancet Neurol 2021

# 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis

| Timing for follow up MRI - Adults | Brain | Spinal Cord |
|---|---|---|
| Clinically Isolated Syndrome | Every 6-12 months<br>To detect new disease activity | Not recommended |
| Radiologic Isolated Syndrome | Every 6-12 months | Not recommended |
| RRMS on treatment | Pretreatment (Gd recommended)<br>3-6 months post start (new baseline)<br>Annually while on treatment | Disability worsening not explained by brain MRI |
| High risk for PML (JCV≥0.9 on natalizumab ≥18months) | Every 3-4 months (abbreviated protocol)<br>During treatment and for 9-12 months post switch | Not recommended |

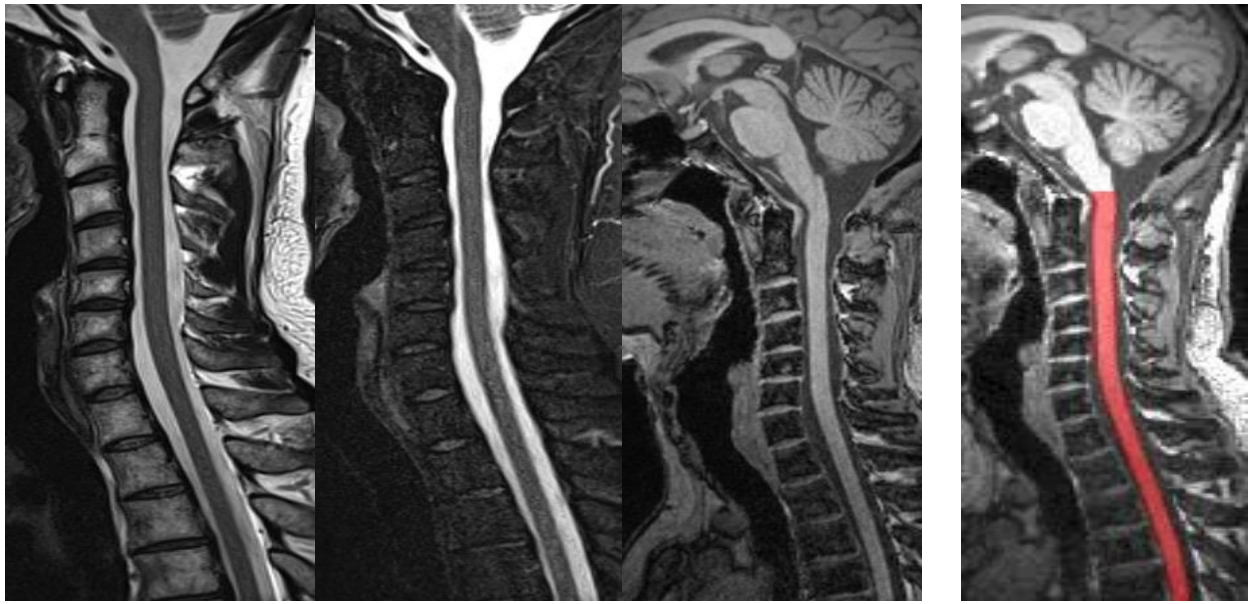
Magnims
Magnetic Resonance Imaging in Multiple Sclerosis

CMSC
THE CONSORTIUM OF MULTIPLE SCLEROSIS CENTERS

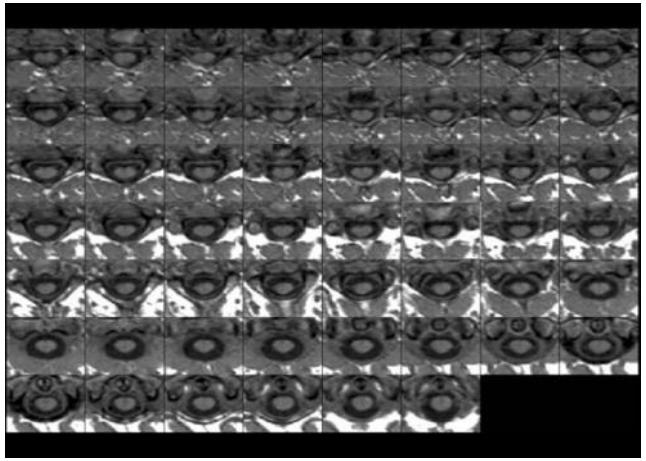
NAIMS
North American Imaging in MS Cooperative

M Wattjes et al 2021 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI in patients with multiple sclerosis. Lancet Neurol 2021

# Spinal cord atrophy in MS: automated measure



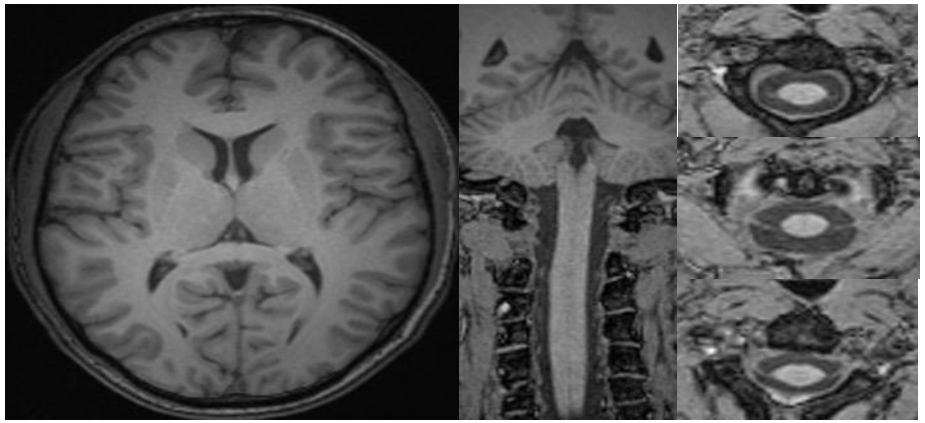
3D IR T1



C1-C5

Cord length: 67.43 mm

Cord volume: 5015.25 $mm^3$



Combined brain and cord atrophy using single 3D-T1

**Spinal cord atrophy can be measured at the cervical level (C2-C3) using brain volumetric scans with sufficient field-of-view**

Caveat: geometric deformity due to non-linear gradients at off-centre position

*Jim v6.0_21, Xinapse Systems®.*

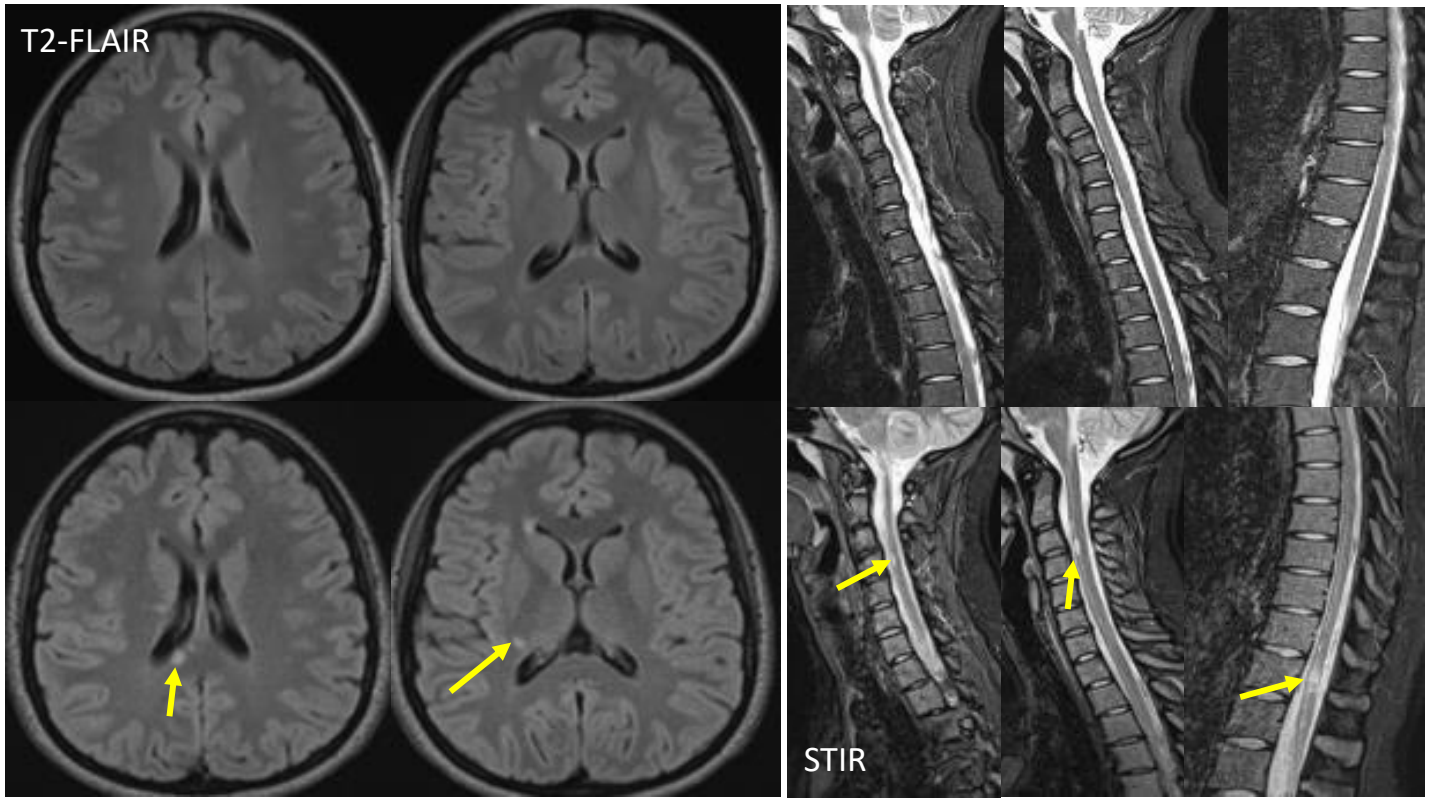
Liu Z et al., Mult Scler Relat Disord. 2015 Jan;4(1):52

# Spinal cord MRI in monitoring and predicting treatment response

## Against

- Spinal MRI shows considerably fewer new lesions than brain MRI
- A relationship exists between development of new brain lesions and spinal cord lesions
- Most are symptomatic
- Serial spinal cord MRI may add little to brain MRI alone in monitoring disease activity and progression

Baseline




1 year follow-up

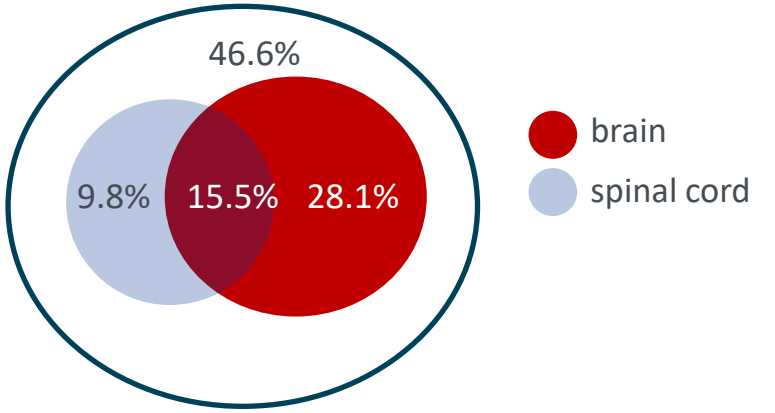
**FLAIR**, fluid-attenuated inversion recovery; **MRI**, magnetic resonance imaging; **STIR**, short-TI inversion recovery.

Thorpe JW et al. Neurology. 1996;46:373–78; Images provided by Dr Rovira.

# Spinal cord MRI in monitoring and predicting treatment response

## In favour

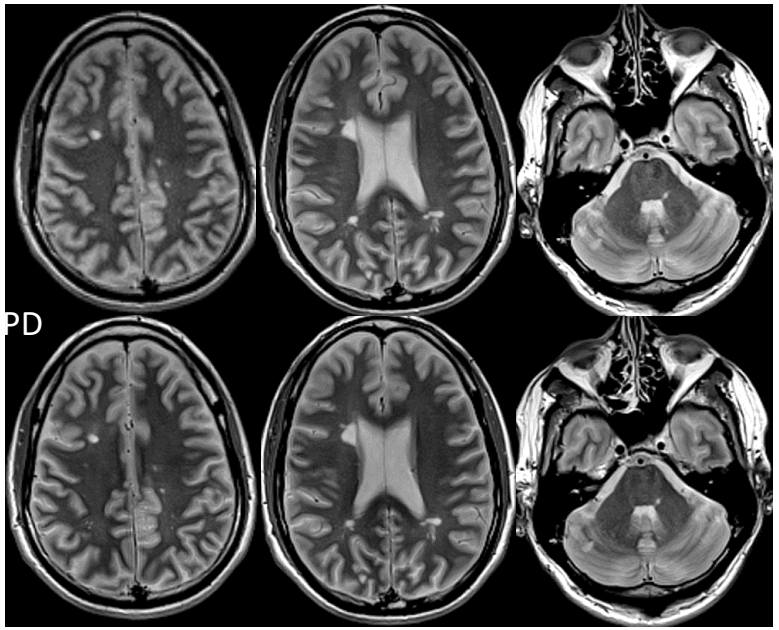
- 103 RRMS patients: **clinically stable**
- Median interval between scans: 17 months
- New asymptomatic lesions



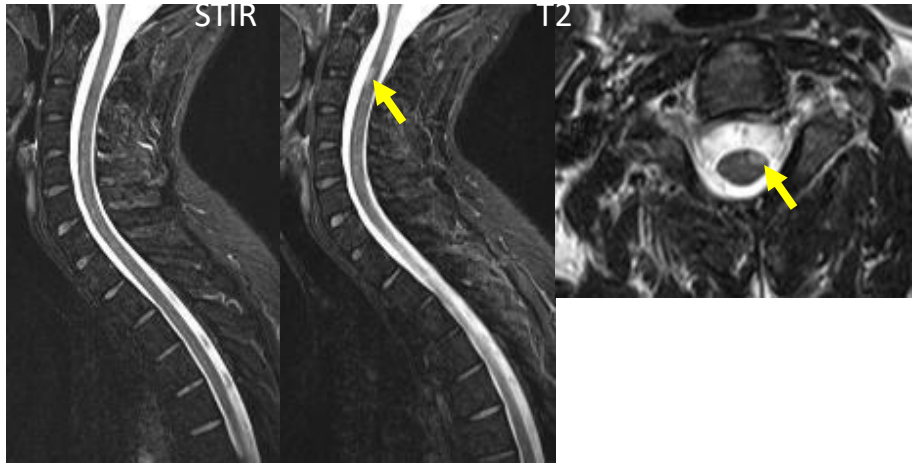

- 43.7% brain
- 25.2% spinal cord
- **9.8% only asymptomatic SC lesions**

- Significant proportion of disease activity only in the SC
- Could have important implications in assessing and predicting treatment response*

Baseline




1 year follow-up




Baseline 1 year follow-up

**PD**, proton density; **RRMS**, relapsing-remitting MS; **SC,** spinal cord; **STIR**, short-TI inversion recovery.

***** Represents the speaker's own view.

Zecca et al. Mult Scler J. 2016;6:782–91; Images courtesy of A. Rovira.

# Gadolinium deposition (2014-2018)

**Table 1. ECF MRI Contrast Agents That Have Been Used in the Clinic**

| ECF agent (trade name) | ECF agent (chemical code) | ECF agent (generic name) | approval date |
|---|---|---|---|
| Dotarem, Clariscan | Gd-DOTA | gadoterate meglumine | 1989 (Europe)<br>2013 (United States) |
| ProHance | Gd-HPDO3A | gadoteridol | 1992 |
| Gadovist (Europe)<br>Gadavist (United States) | Gd-DO3A-butrol | gadobutrol | 1998 (Europe)<br>2011 (United States) |
| Magnevist[a] | Gd-DTPA | gadopentetate dimeglumine | 1988 |
| Omniscan[a] | Gd-DTPA-BMA | gadodiamide | 1993 |
| Optimark[a] | Gd-DTPA-BMEA | gadoversetamide | 1999 |
| Multihance[b,c] | Gd-BOPTA | gadobenate dimeglumine | 2004 |

[a]Agents suspended by the European Medicines Agency in 2017. [b]Agent available for limited, liver-specific indications in the EU. [c]Multipurpose agent that is also suitable for liver imaging.[14]

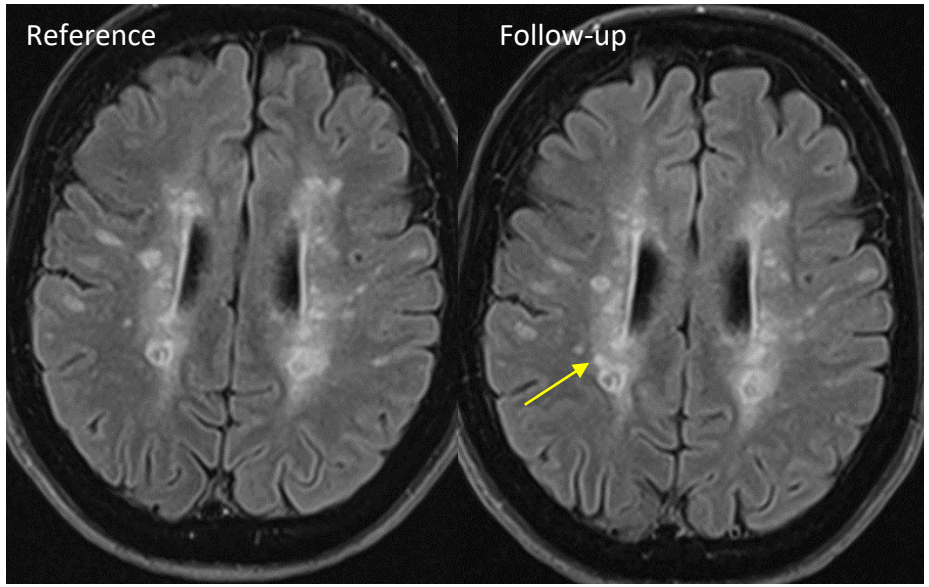
Wahsner et al. Chem Rev 2019

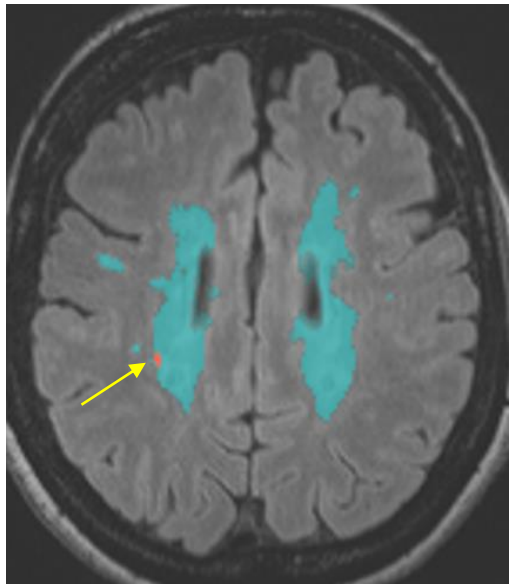
- Higher degree of gadolinium deposition with linear compounds versus macrocyclic
- Macrocyclic agents have higher thermodynamic, kinetic and conditional stability

**Linear** **Macrocyclic**

| | | | Chemical Structure | *Linear* | *Linear* | | | *Macrocyclic* | | *Macrocyclic* |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | *Non-Ionic* | *Ionic* | | | *Non-Ionic* | | *Ionic* |
| | | | Molecule | *gadodiamide* | *gadopentetate dimeglumine* | *gadobenate dimeglumine* | *gadoxetate disodium* | *gadoteridol* | *gadobutrol* | *gadoterate meglumine* |
| Authors | Journal | Year | Marketed as | *Omniscan* | *Magnevist* | *MultiHance* | *Primovist* | *ProHance* | *Gadovist* | *Dotarem* |
| Kanda | Radiology | 2014 | #1 | | | | | | | |
| Errante | Invest Radiol | 2014 | #2 | | | | | | | |
| Kanda | Radiology | 2015 | #3 | | | | | | | |
| Quattrocchi | Invest Radiol | 2015 | #4 | | | | | | | |
| Radbruch | Radiology | 2015 | #5 | | | | | | | |
| Miller | Pediatrics | 2015 | #6 | | | | | | | |
| Ramalho | Radiology | 2015 | #7 | | | | | | | |
| Stojanov | Eur Radiol | 2015 | #8 | | | | | | | |
| Adin | AJNR | 2015 | #9 | | | | | | | |
| McDonald | Radiology | 2015 | #10 | | | | | | | |
| Weberling | Invest Radiol | 2015 | #11 | | | | | | | |
| Radbruch | Invest Radiol | 2015 | #12 | | | | | | | |
| Cao | AJR | 2016 | #13 | | | | | | | |
| Ramalho | Eur Radiol | 2016 | #14 | | | | | | | |
| Ramalho | AJNR | 2016 | #15 | | | | | | | |
| Tedeschi | Eur Radiol | 2016 | #16 | | | | | | | |
| Roberts | AJNR | 2016 | #17 | | | | | | | |
| Tanaka | Eur Neurol | 2016 | #18 | | | | | | | |
| Cao | Invest Radiol | 2016 | #19 | | | | | | | |
| Hu | Pediatric Radiol | 2016 | #20 | | | | | | | |
| Roberts | Brain Develop | 2016 | #21 | | | | | | | |
| Khant | Magn Reson Med Sci | 2016 | #22 | | | | | | | |
| Eisele | Medicine | 2016 | #23 | | | | | | | |
| Radbruch | Invest Radiol | 2016 | #24 | | | | | | | |
| Zhang | Radiology | 2017 | #25 | | | | | | | |
| Eisele | JNNP | 2017 | #26 | | | | | | | |
| Schlemm | Mult Scler | 2017 | #27 | | | | | | | |
| Radbruch | Radiology | 2017 | #28 | | | | | | | |
| Kuno | Radiology | 2017 | #29 | | | | | | | |
| Bae | Eur Radiol | 2017 | #30 | | | | | | | |
| Radbruch | Radiology | 2017 | #31 | | | | | | | |
| Flood | Radiology | 2017 | #32 | | | | | | | |
| Langner | Eur Radiol | 2017 | #33 | | | | | | | |
| Kahn | Radiology | 2017 | #34 | | | | | | | |
| Ichikawa | Invest Radiol | 2017 | #35 | | | | | | | |
| Conte | Eur Radiol | 2017 | #36 | | | | | | | |
| Tedeschi | Magn Reson Med Sci | 2017 | #37 | | | | | | | |
| Espagnet | Ped Radiol | 2017 | #38 | | | | | | | |
| Forslin | AJNR | 2017 | #39 | | | | | | | |
| Roberts | Neurology | 2017 | #40 | | | | | | | |
| Schneider | AJNR | 2017 | #41 | | | | | | | |
| Eisele | J Neuroimaging | 2017 | #42 | | | | | | | |
| Tibussek | Radiology | 2017 | #43 | | | | | | | |
| Splendiani | Radiol med | 2017 | #44 | | | | | | | |
| Lee | Plos One | 2017 | #45 | | | | | | | |
| Bjørnerud | Radiology | 2017 | #46 | | | | | | | |
| Yoo | Invest Radiol | 2017 | #47 | | | | | | | |
| Muller | Clin Neuroradiol | 2017 | #48 | | | | | | | |
| Kromrey | Eur Radiol | 2017 | #49 | | | | | | | |
| Renz | Invest Radiol | 2018 | #50 | | | | | | | |
| Lee | Plos One | 2017 | #51 | | | | | | | |

# Automated co-registration and lesion color-coding (MSPie, Siemens)



Images from Alex Rovira, Hospital Vall d'Hebron

MSPie
MS PATHS Image Evaluation

REPORT
V2_0_0

NOT FOR CLINICAL USE

## Patient Demographics

Age: Sex: F

## Review

**Prior:** 03-Dec-2020 **Current:** 07-Jun-2021
Brain segmentation: ACCEPTED
Lesion segmentation: ACCEPTED

## Relative Disease Burden

| Total Lesion Volume (mL) | Brain Parenchymal Fraction (BPF) |
|---|---|
| 40.96 | 0.818 |

New or Enlarged Lesions: 1
BPF Change Since Prior: -0.50%

## T2 Lesions Metrics

T2 Lesion Volume (mL)

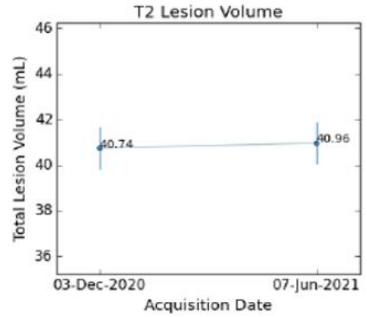
| | Prior 03-Dec-2020 | Current 07-Jun-2021 | Change since prior (%) |
|---|---|---|---|
| **Total** | **40.74** | **40.96** | **0.54** |
| Juxtacortical | 0.92 | 1.01 | 9.62 |
| Periventricular | 39.70 | 39.81 | 0.27 |
| Infratentorial | 0.01 | 0.01 | 6.25 |
| Others | 0.10 | 0.13 | 23.53 |

T2 Lesion Fraction (lesion volume / brain volume, %)

| | | |
|---|---|---|
| T2 lesion fraction | 3.71 | 3.77 |

New/Enlarged T2 Lesions Since Prior

| | Count | Volume(mL) |
|---|---|---|
| **Total** | **1** | **0.022** |
| # Lesions < 0.003mL | 0 | 0 |
| # Lesions >= 0.003mL | 1 | 0.022 |




## Morphometry

Brain Volume (normalized)

| | Prior 03-Dec-2020 | Current 07-Jun-2021 | Change since prior (%) |
|---|---|---|---|
| BPF | 0.822 | 0.818 | -0.50 |
| GMF | 0.477 | 0.473 | -0.93 |
| WMF | 0.345 | 0.345 | 0.08 |

Gray Matter Structure Volume in mL [% of intracran. vol.]

| | Prior 03-Dec-2020 | Current 07-Jun-2021 | Change since prior (%) |
|---|---|---|---|
| Deep GM | 33.43 [2.31] | 33.37 [2.29] | -0.17 |
| Cortical GM | 461.77 [31.89] | 451.32 [31.04] | -2.26 |
| Thalamus | 11.98 [0.83] | 12.16 [0.84] | 1.50 |