

CONSORTIUM OF MS CENTERS MRI PROTOCOL AND CLINICAL GUIDELINES FOR THE DIAGNOSIS AND FOLLOW-UP OF MS

2018 REVISED GUIDELINES

Summary of MRI Protocols
and Guidelines Prepared By:



THE CONSORTIUM OF
MULTIPLE SCLEROSIS CENTERS

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PURPOSE

MRI is widely used for the early and accurate diagnosis of multiple sclerosis (MS) and is used increasingly in patient follow-up. Guidelines for a standardized brain and spinal cord MRI protocol had been previously proposed in 2001, 2003, and 2009. More recently, revised recommendations were published (*AJNR* 2016;37:394-401. doi: 10.3174/ajnr.A4539) and subsequently, a letter to the editor addressing concerns regarding the use of gadolinium was published (*AJNR* online: 10.3174/ajnr.A4943). A follow-up consensus meeting was convened in January 2017 to review and update the guidelines with particular attention to the use of gadolinium. The proposed 2018 revised guidelines incorporates new clinical information and imaging techniques that will benefit patients and will be useful for physicians and health care providers.

METHODS

Sponsored by the Consortium of MS Centers, an international group of neurologists, radiologists, and imaging scientists with an expertise in MS from North America and Europe met in Newark, NJ, US, January 11-12, 2017 to revise and update the guidelines and indications for standardized brain and spinal cord MRI for MS including attention to the use of gadolinium, based on new data, survey results and expert opinion. The expert taskforce included representatives of the American Academy of Neurology, the Radiological Society of North America, the American Society of Neuroradiology, the National Institutes of Health, the Magnetic Resonance Imaging in MS (MAGNIMS), and the North American Imaging in Multiple Sclerosis Cooperative (NAIMS). The update reviewed the four imaging protocols: routine brain, progressive multifocal leukoencephalopathy (PML) surveillance, spinal cord, and orbits.

SUMMARY

- » A brain MRI with gadolinium is recommended for the diagnosis of MS
- » A spinal cord MRI is recommended if the brain MRI is non-diagnostic or if the presenting symptoms are referable to the spinal cord
- » A follow-up brain MRI is recommended to:
 - * Demonstrate dissemination in time for diagnosis,
 - * Detect clinically silent disease activity while on treatment,
 - * Safety monitoring including PML surveillance while on treatment,
 - * Evaluate unexpected clinical worsening,
 - * Reassess the original diagnosis,
 - * As a new baseline MRI before starting or modifying therapy,
 - * Every 6 months to 2 years for patients with relapsing MS.
- » **NEW:** Gadolinium-based contrast agents do accumulate in the brain and, to a much lesser degree with macrocyclic agents. While there is no known CNS toxicity, these agents should be used judiciously, recognizing that gadolinium continues to play an invaluable role in specific circumstances related to the diagnosis and follow-up of individuals with MS.
- » The clinical question being addressed should be included in the requisition for the MRI.

BRAIN MRI RECOMMENDATIONS

Baseline studies for patients with a clinically isolated syndrome (CIS) and/or suspected MS:

- * Brain MRI protocol with gadolinium at baseline, and to establish dissemination in time
- * Spinal cord MRI if myelitis, insufficient features on brain MRI to support diagnosis, or age>40 with non-specific brain MRI findings
- * A cervical cord MRI performed simultaneously with the brain MRI could have prognostic value in the evaluation of CIS patients with or without myelitis and would reduce the number of patients requiring a subsequent MRI appointment
- * Orbital MRI if severe optic neuritis with poor recovery

Timing of a follow-up brain MRI protocol for patients with a CIS and/or suspected MS to look for evidence of dissemination in time (i.e. new T2 lesions or gadolinium enhancing lesions):

- * 6-12 months for high risk CIS (e.g. ≥ 2 ovoid lesions on first MRI)
- * 12-24 months for low risk CIS (i.e. normal brain MRI) and/or uncertain clinical syndrome with suspicious brain MRI features (e.g. radiologic isolated syndrome [RIS])

Timing of brain MRI protocol for patients with an established diagnosis of MS:

- * No recent prior imaging available (e.g. patient with established diagnosis of MS and new to your clinical practice)
- * Postpartum to establish a new baseline
- * Prior to starting or switching disease-modifying therapy
- * Approximately 6-12 months after switching disease-modifying therapy to establish a new baseline on the new therapy
- * Every 1-2 years while on disease-modifying therapy to assess for subclinical disease activity (i.e. new T2 lesions or gadolinium enhancing lesions). Less frequent MRI scans required in clinically stable patients after 2-3 years of stable treatment (gadolinium-based contrast optional)
- * Unexpected clinical deterioration or reassessment of original diagnosis (gadolinium-based contrast recommended)
- * The use of gadolinium-based contrast agents is helpful but not essential for detecting subclinical disease activity because new T2 MS lesions can be identified on well-performed standardized MR imaging unless there is a large T2 lesion burden which may obscure new T2 lesions activity.

SPINAL CORD MRI RECOMMENDATIONS

- * Symptoms referable to the spinal cord (myelitis, progressive myelopathy)
- * Older age of onset
- * Recurrent myelitis
- * Limited role for establishing dissemination in time

PML SURVEILLANCE BRAIN MRI PROTOCOL

Timing of PML surveillance brain MRI protocol:

- * At least every 12 months for serum JC virus antibody negative patients on natalizumab
- * Every 3 months (high index) to 6 months (low index) for serum JC virus antibody positive patients and > 18 months on natalizumab

NOTE: the brain MRI protocol for routine monitoring patients on disease-modifying therapies also includes the same sequences (FLAIR and DWI) as the PML surveillance abbreviated MRI protocol.

NEW: WHEN TO USE GADOLINIUM-BASED CONTRAST AGENTS

- » CIS: The use of gadolinium-based contrast agents (GBCA) is indispensable in patients presenting with their first clinical attack (so called “clinically isolated syndrome”) as the use of GBCA allows for an earlier diagnosis by demonstrating lesion dissemination in time (GBCA-enhancing lesion) in addition to lesion dissemination in space, the hallmarks for the diagnosis of MS. Early diagnosis leads to early treatment which may help in preventing disease progression and improve long term prognosis.
- » MS GBCA essential for:
 - * following a patient with highly active disease;
 - * when there is rapidly declining and unexplained and unexpected clinical worsening;
 - * and when there is concern regarding an alternative diagnosis other than MS.
- » MS GBCA optional for: the follow-up monitoring of patients with MS to detect subclinical disease activity which could lead to a change in therapy, the use of GBCA may be helpful within the first two years of treatment onset but is not required because new T2 MS lesions can be identified on well-performed MRI using a standardized protocol unless there is a large T2 lesion burden.
- » Selecting a GBCA is complicated, balancing risks versus benefits pertaining to the patient, the patient population as well as the health care system in general (Davenport, 2018).

PROTOCOL 1: STANDARDIZED BRAIN MRI PROTOCOL (DIAGNOSIS AND ROUTINE FOLLOW-UP OF MS)

Field Strength	Scans should be of good quality, with adequate signal-noise ratio (SNR) and spatial resolution (in slice pixel resolution of $\leq 1\text{mm} \times 1\text{mm}$)
Scan Prescription	Use the subcallosal plane to prescribe or reformat axial oblique slices
Coverage	Whole brain coverage
Slice Thickness and Gap	$\leq 3\text{mm}$, no gap (for 2D acquisition or 3D ¹ reconstruction)
Core Sequences	2D/3D Sagittal & Axial FLAIR ^{1,2} 2D/3D Axial T2 ¹ Axial 2D DWI ³ 3D IR-prep GE ⁴ T1
Gadolinium ⁵ (as required)	Post Gad 2D/3D Axial T1
Additional Sequences	Susceptibility weighted (SWI) Pre Gad 2D/3D Axial T1 Axial proton density

¹ 3D acquisition should be isotropic $\leq 1\text{mm} \times 1\text{mm}$

² FLAIR (Fluid Attenuated Inversion Recovery)

³ DWI (Diffusion Weighted)

⁴ IR-prep GE (Inversion-recovery prepared Gradient Echo); Magnetization Prepared Rapid Acquisition Gradient Echo or MP-RAGE; Turbo Field Echo or TFE

⁵ Single dose of gadolinium-based contrast agent as required (note that the FLAIR or T2 may be performed during the 5 minute minimum delay after gadolinium injection before acquiring the post-gadolinium T1)

PROTOCOL 2: PML SURVEILLANCE BRAIN MRI PROTOCOL

Field Strength	Scans should be of good quality, with adequate signal-noise ratio (SNR) and resolution (in slice pixel resolution of $\leq 1\text{mm} \times 1\text{mm}$)
Scan Prescription	Use the subcallosal plane to prescribe or reformat axial oblique slices
Coverage	Whole brain coverage
Core Sequences ¹	2D/3D Sagittal & Axial FLAIR ² Axial 2D DWI ³
Gadolinium (can be helpful) ⁴	Post Gad 2D/3D Axial T1
Additional Sequences	SWI 2D/3D Axial T2 3D IR-prep GE ⁵ T1 Pre Gad 2D/3D Axial T1 Axial Proton Density
Slice Thickness and Gap	$\leq 3\text{mm}$, no gap (for 2D acquisition or 3D reconstruction)

¹ Typical PML lesions may appear hyperintense on FLAIR, hypointense on T1, high signal intensity on DWI

² FLAIR (Fluid Attenuated Inversion Recovery)

³ DWI (Diffusion Weighted)

⁴ Less than 50% of PML lesions will show contrast enhancement.

⁵ IR-prep GE (Inversion-recovery prepared Gradient Echo); Magnetization Prepared Rapid Acquisition Gradient Echo or MP-RAGE; Turbo Field Echo or TFE

PROTOCOL 3: SPINAL CORD MRI PROTOCOL

Field Strength	Scans should be of good quality, with adequate signal-noise ratio (SNR) and resolution (in slice pixel resolution of $\leq 1\text{mm} \times 1\text{mm}$)
Coverage	Cervical cord coverage ¹
Core Sequences	Two of the following: Sagittal T2 Proton Density STIR ² T1-PSIR ³ Axial T2/T2* through lesions
Slice Thickness and Gap	Sagittal: $\leq 3\text{mm}$, no gap Axial: $\leq 5\text{ mm}$, no gap
Additional Sequences	Sagittal T1 Post Gad T1 ⁴ (sag, axial) Axial T2/T2* entire cervical cord 3D IR-prep GE ⁵ T1

¹Thoracic and conus coverage recommended if symptoms localize to this region to rule out an alternate diagnosis

²STIR (Short Tau Inversion Recovery)

³PSIR (Phase Sensitive T1 Inversion Recovery)

⁴No additional gadolinium necessary if cord examination immediately follows gadolinium enhanced brain MRI

⁵ IR-prep GE (Inversion-recovery prepared Gradient Echo); Magnetization Prepared Rapid Acquisition Gradient Echo or MP-RAGE; Turbo Field Echo or TFE

PROTOCOL 4: ORBIT MRI PROTOCOL

- » May be clinically indicated to confirm optic neuritis and rule out compressive lesions
- » Recommended sequences include coronal STIR or fat-suppressed T2 and a post-gadolinium fat-suppressed T1 with a section thickness of ≤ 2 mm, with coverage to include the optic chiasm
- » Optional sequences may include axial/coronal pre-gadolinium Fat-Sat T1, axial Fat-Sat T2 or STIR, Axial Post-Gad Fat-Sat T1

RECOMMENDATIONS FOR COMMUNICATION

MRI REQUISITION:

The clinician should provide on the request for the standardized MRI brain and/or spinal cord protocol:

- » Clinical questions to be addressed
 - * Diagnosis
 - * Monitoring for management decision
- » Relevant clinical history and physical examination findings
- » Current MS disease-modifying treatment and JC virus status if on natalizumab
- » If known, date and place of previous examinations

MRI REPORT:

Standardized nomenclature/terminology should be used and include:

1. Description of findings
 - * Lesion type, location, size, shape, character, number for diagnostic scan
 - * CIS diagnostic scan: whether meets current MRI dissemination in space or dissemination in time criteria
 - * Qualitative assessment of T2 and brain volume/atrophy
2. MS monitoring or CIS follow up: Comparison with previous studies (new lesions, atrophy)
3. Interpretation (typical for MS, atypical for MS, not MS) and differential diagnosis, if appropriate

NOTE: Structured reports can be helpful (*Alessandrino et al, AJR 2018; Dickerson et al, J Am Coll Radiol 2017*).

RECOMMENDATIONS:

- * Studies should be stored in a DICOM format
- * Copies of MRI studies should be retained permanently and be available
- * It is strongly recommended for patients to keep their own studies on portable digital media

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