#### American College of Radiology ACR Appropriateness Criteria® Demyelinating Diseases

<u>Variant: 1</u> Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI cervical and thoracic spine without and with IV contrast	Usually Appropriate	0
MRI head without and with IV contrast	Usually Appropriate	0
MRI cervical and thoracic spine with IV contrast	May Be Appropriate	0
MRI cervical and thoracic spine without IV contrast	May Be Appropriate	0
MRI head without IV contrast	May Be Appropriate	0
MRI lumbar spine without and with IV contrast	May Be Appropriate	0
MRI orbits with IV contrast	May Be Appropriate	0
MRI orbits without and with IV contrast	May Be Appropriate	0
MRI orbits without IV contrast	May Be Appropriate	0
MRI head with IV contrast	Usually Not Appropriate	0
MRI lumbar spine with IV contrast	Usually Not Appropriate	0
MRI lumbar spine without IV contrast	Usually Not Appropriate	0
CT head with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without and with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT lumbar spine with IV contrast	Usually Not Appropriate	<b>∵</b> ••
CT lumbar spine without IV contrast	Usually Not Appropriate	<b>∵</b> ••
CT orbits with IV contrast	Usually Not Appropriate	<b>૽ ૽</b>
CT orbits without and with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT orbits without IV contrast	Usually Not Appropriate	<b>∵</b> ••
CT cervical and thoracic spine with IV contrast	Usually Not Appropriate	<b>∵</b> • • • •
CT cervical and thoracic spine without and with IV contrast	Usually Not Appropriate	<b>∵</b> • • • •
CT cervical and thoracic spine without IV contrast	Usually Not Appropriate	<b>∵ ∵ ∵</b>
CT lumbar spine without and with IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>

### <u>Variant: 2</u> Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI cervical and thoracic spine without and with IV contrast	Usually Appropriate	0
MRI head without and with IV contrast	Usually Appropriate	0
MRI cervical and thoracic spine with IV contrast	May Be Appropriate	0
MRI cervical and thoracic spine without IV contrast	May Be Appropriate	0
MRI head without IV contrast	May Be Appropriate	0
MRI lumbar spine without and with IV contrast	May Be Appropriate	0
MRI head with IV contrast	Usually Not Appropriate	0
MRI lumbar spine with IV contrast	Usually Not Appropriate	0

Usually Not Appropriate	0
Usually Not Appropriate	0
Usually Not Appropriate	0
Usually Not Appropriate	0
Usually Not Appropriate	<b>※ ※</b>
Usually Not Appropriate	<b>⊗ ⊗</b>
Usually Not Appropriate	<b>⊗ ⊗</b>
Usually Not Appropriate	<b>*</b>
Usually Not Appropriate	<b>**</b>
Usually Not Appropriate	<b>⊗ ⊗</b>
Usually Not Appropriate	<b>⊗ ⊗</b>
Usually Not Appropriate	<b>⊗ ⊗</b>
Usually Not Appropriate	
Usually Not Appropriate	<b>∵</b>
Usually Not Appropriate	<b>∵</b>
Usually Not Appropriate	<b>∵</b>
	Usually Not Appropriate

## <u>Variant: 3</u> Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI cervical and thoracic spine without and with IV contrast	Usually Appropriate	0
MRI cervical and thoracic spine without IV contrast	Usually Appropriate	0
MRI head without and with IV contrast	Usually Appropriate	0
MRI head without IV contrast	Usually Appropriate	0
MRI cervical and thoracic spine with IV contrast	May Be Appropriate	0
MRI head with IV contrast	Usually Not Appropriate	0
MRI lumbar spine with IV contrast	Usually Not Appropriate	0
MRI lumbar spine without and with IV contrast	Usually Not Appropriate	0
MRI lumbar spine without IV contrast	Usually Not Appropriate	0
MRI orbits with IV contrast	Usually Not Appropriate	0
MRI orbits without and with IV contrast	Usually Not Appropriate	0
MRI orbits without IV contrast	Usually Not Appropriate	0
CT head with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without and with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT lumbar spine with IV contrast	Usually Not Appropriate	<b>૽ ૽</b>
CT lumbar spine without IV contrast	Usually Not Appropriate	<b>૽ ૽</b>
CT orbits with IV contrast	Usually Not Appropriate	<b>∵ ∵</b>
CT orbits without and with IV contrast	Usually Not Appropriate	���
CT orbits without IV contrast	Usually Not Appropriate	���
CT cervical and thoracic spine with IV contrast	Usually Not Appropriate	<b>∵</b>
CT cervical and thoracic spine without and with IV contrast	Usually Not Appropriate	<b>∵</b>
CT cervical and thoracic spine without IV contrast	Usually Not Appropriate	<b>∵ ∵ ∵</b>
CT lumbar spine without and with IV contrast	Usually Not Appropriate	<b>∵ ∵ ∵</b>

### <u>Variant: 4</u> Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI cervical and thoracic spine without and with IV contrast	Usually Appropriate	0
MRI head without and with IV contrast	Usually Appropriate	0
MRI orbits without and with IV contrast	Usually Appropriate	0
MRI cervical and thoracic spine with IV contrast	May Be Appropriate	0
MRI cervical and thoracic spine without IV contrast	May Be Appropriate	0
MRI head without IV contrast	May Be Appropriate	0
MRI orbits with IV contrast	May Be Appropriate (Disagreement)	0
MRI orbits without IV contrast	May Be Appropriate	0
MRI head with IV contrast	Usually Not Appropriate	0
MRI lumbar spine with IV contrast	Usually Not Appropriate	0
MRI lumbar spine without and with IV contrast	Usually Not Appropriate	0
MRI lumbar spine without IV contrast	Usually Not Appropriate	0
CT head with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without and with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without IV contrast	Usually Not Appropriate	<b>⊗ ⊗</b>
CT lumbar spine with IV contrast	Usually Not Appropriate	<b>⊗ ⊗</b>
CT lumbar spine without IV contrast	Usually Not Appropriate	<b>૽ ૽</b>
CT orbits with IV contrast	Usually Not Appropriate	<b>૽ ૽</b>
CT orbits without and with IV contrast	Usually Not Appropriate	<b>∵</b>
CT orbits without IV contrast	Usually Not Appropriate	<b>∵</b>
CT cervical and thoracic spine with IV contrast	Usually Not Appropriate	<b>૽ ૽</b>
CT cervical and thoracic spine without and with IV contrast	Usually Not Appropriate	<b>⊗ ⊗ ⊗</b>
CT cervical and thoracic spine without IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>
CT lumbar spine without and with IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>

## <u>Variant: 5</u> Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI brachial plexus without and with IV contrast	Usually Appropriate	0
MRI cervical and thoracic spine without and with IV contrast	Usually Appropriate	0
MRI lumbar spine without and with IV contrast	Usually Appropriate	0
MRI lumbosacral plexus without and with IV contrast	Usually Appropriate	0
MRI brachial plexus without IV contrast	May Be Appropriate (Disagreement)	0
MRI cervical and thoracic spine without IV contrast	May Be Appropriate	0
MRI head without and with IV contrast	May Be Appropriate	0
MRI lumbar spine without IV contrast	May Be Appropriate (Disagreement)	0
MRI lumbosacral plexus with IV contrast	May Be Appropriate	0
MRI lumbosacral plexus without IV contrast	May Be Appropriate (Disagreement)	0
MRI brachial plexus with IV contrast	Usually Not Appropriate	0
MRI cervical and thoracic spine with IV contrast	Usually Not Appropriate	0

MRI head with IV contrast	Usually Not Appropriate	0
MRI head without IV contrast	Usually Not Appropriate	0
MRI lumbar spine with IV contrast	Usually Not Appropriate	0
MRI orbits with IV contrast	Usually Not Appropriate	0
MRI orbits without and with IV contrast	Usually Not Appropriate	0
MRI orbits without IV contrast	Usually Not Appropriate	0
CT head with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without and with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT head without IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT lumbar spine with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT lumbar spine without IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT orbits with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT orbits without and with IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT orbits without IV contrast	Usually Not Appropriate	<b>※ ※</b>
CT cervical and thoracic spine with IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>
CT cervical and thoracic spine without and with IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>
CT cervical and thoracic spine without IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>
CT lumbar spine without and with IV contrast	Usually Not Appropriate	<b>※ ※ ※</b>

#### **Panel Members**

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#### **Summary of Literature Review**

#### Introduction/Background

Demyelinating diseases of the central nervous system (CNS) represent a diverse group of disorders characterized by inflammation, damage, and loss of myelin sheaths that surround nerve fibers in the brain and spinal cord. These conditions can be classified into primary demyelinating diseases, such as multiple sclerosis (MS) and other idiopathic inflammatory-demyelinating diseases (IIDDs) and secondary demyelinating diseases resulting from infectious, ischemic, metabolic, or toxic causes [1].

The spectrum of IIDD encompasses a broad range of CNS disorders that can be differentiated according to their severity, clinical course, and lesion distribution, as well as their imaging, laboratory, and pathological findings [1]. The spectrum includes monophasic, multiphasic, and progressive disorders, ranging from highly localized forms to multifocal or diffuse variants [1]. Relapsing-remitting (RR) and secondary progressive (SP) MS are the 2 most common forms of IIDD [1]. MS can also have a progressive course from onset (primary progressive) [1].

Fulminant forms of IIDD include a variety of disorders that have in common the severity of the clinical symptoms, an acute clinical course, and atypical findings on MRI [1]. The classic fulminant IIDD, Marburg disease, is extremely rare [1]. Baló's concentric sclerosis and acute disseminated

encephalomyelitis (ADEM) can also present with severe acute attacks [1]. Some IIDDs have a restricted topographic distribution, as is the case with neuromyelitis optica spectrum disorders (NMOSD), which can have a monophasic course, but more often follows a relapsing course [1].

MS is a progressive inflammatory, demyelinating, and neurodegenerative autoimmune disease characterized pathologically by perivascular infiltrates of mononuclear inflammatory cells, demyelination, and axonal loss and gliosis, with the formation of focal and diffuse abnormalities in the brain and spinal cord [1]. The disease mainly affects the optic nerves, brainstem, spinal cord, and cerebellar and periventricular white matter, although cortical and subcortical gray-matter damage is also prominent, resulting in chronic progressive disability for the majority of people with the disorder [1].

Optic neuritis (ON) is an acute inflammatory disease of the optic nerve that typically presents with either an acute or subacute onset [2, 3]. ON typically presents with temporary loss of vision in the affected eye, a scotoma (usually in or near the center of the visual field), pain in the eyeball that often occurs with eye movements, abnormal color vision, and unusual flashes of light (phosphenes) [2, 3]. The diagnosis of ON is made clinically and consists of a classic triad of visual loss, periocular pain, and dyschromatopsia [2, 3].

Acute transverse myelitis (ATM) and acute partial TM may be the first manifestations of NMO and MS, respectively [2, 3]. Symmetric onset is less characteristic of MS and should suggest NMO [2, 3]. MS-associated TM typically appears with asymmetric sensory symptoms due to posterolateral spinal cord lesions and motor deficits [2, 3].

Several laboratory tests are crucial for diagnosing and differentiating demyelinating diseases. The serum autoantibody NMO-immunoglobulin G (IgG), defined by Lennon et al, was recognized as a specific biomarker for NMO and the NMOSD [2, 3]. Its target antigen is the water channel aquaporin-4 (AQP4), suggesting that NMO may represent a novel autoimmune channelopathy [2, 3]. NMO-IgG seropositivity was 76% sensitive and 94% specific for NMO [2, 3].

Cerebrospinal fluid (CSF) analysis provides important diagnostic information. In NMO, pleocytosis (≥50 leukocytes/mm³) is considered to be a major supportive criterion [2, 3]. Oligoclonal bands (OCBs), being present in 22.7% of patients, are the second most frequent CSF abnormality in NMO [2, 3]. In contrast, OCBs are found in 80% to 90% of MS patients [2, 3]. CSF pleocytosis (>50 leukocytes/mm³) is often present in NMO, whereas OCBs are seen less frequently (20%-40%) than in MS patients (80%-90%) [2, 3].

The McDonald diagnostic criteria for MS were originally introduced in 2001 and have been revised multiple times, most recently at the 40th Congress of the European Committee for Treatment and Research in Multiple Sclerosis in 2024. The updated McDonald criteria have incorporated new MRI features that enhance diagnostic accuracy for MS [4, 5]. These criteria now include assessment of the central vein sign, which can differentiate MS from other demyelinating conditions with 94% accuracy at 3T MRI, particularly when present in at least 6 lesions and especially valuable in patients age 50 or older [4, 5]. Additionally, paramagnetic rim lesions have been recognized as important diagnostic features, present in 48% of clinically isolated syndrome, 59% of RRMS, and 38% of progressive MS cases, where the presence of more than one lesion plus dissemination in time or CSF findings can support MS diagnosis [6].

Treatment strategies for demyelinating diseases vary depending on the specific condition. Distinguishing NMO from MS is critical, particularly in the early stages, since the treatment and prognosis of these disorders differ [1]. Some evidence suggests that MS-modifying treatments such as interferon- $\beta$ , natalizumab, and laquinimod exacerbate NMO [1]. On the other hand, multiple immunosuppressants (such as azathioprine and mitoxantrone) as well as 4 FDA-approved monoclonal antibodies (ravulizumab-cwvz, eclulizumab, inebilizumab, and satralizumab) have been shown to be effective in preventing NMO relapses [1, 7-10].

Treatment with high-dose corticosteroids may accelerate visual recovery in ON, but has little impact on long-term visual outcome [2, 3]. Since there is evidence of early axonal damage in acute demyelinating ON, disease-modifying drugs should be considered in patients at a high risk of developing MS in the future as prophylaxis against permanent neurological impairment [2, 3].

#### **Special Imaging Considerations**

Advanced MRI techniques have significantly improved the diagnosis and monitoring of MS [11-13]. Conventional MRI remains crucial, but newer methods offer enhanced sensitivity and specificity [11-13]. These include magnetization transfer imaging, MR spectroscopy, diffusion tensor imaging (DTI), and functional MRI, which provide more detailed information about MS lesion characteristics, pathophysiology, and degree of atrophy [11-13]. These techniques allow for better visualization of brain and spinal cord involvement, detection of occult disease, and quantification of tissue atrophy [11-13]. These advanced imaging modalities also offer improved assessment of treatment responses in RRMS and potential endpoints for clinical trials in progressive phenotypes [11-13].

DTI can detect microstructural changes in both lesions and normal-appearing tissue, providing insights into demyelination and axonal loss [11-13]. For example, in RRMS, DTI metrics in normal-appearing spinal cord differ significantly from healthy controls, with lower fractional anisotropy in lateral, posterior, and central regions [11-13]. DTI abnormalities are detectable in early stages of MS and become more pronounced with disease progression [11, 12, 14].

Artificial intelligence applications in MS extend to lesion segmentation, biomarker identification, and outcome prediction [15, 16]. The segmentation of white matter lesions in MS patients is crucial for diagnosis and monitoring [15, 16]. These methods demonstrate competitive accuracy in MS lesion segmentation while offering additional benefits such as whole-brain segmentation and topological constraints [15, 16].

Volumetric analysis in MS diagnosis and follow-up has shown promise [17]. Brain volume loss, particularly in white matter, correlates with clinical parameters like disability status and fatigue [17]. Automated MRI brain volumetry software can reveal connections between segmental volume changes and clinical outcomes [17].

Perfusion imaging has emerged as a tool in MS research and diagnosis [18]. Studies have shown that acute MS lesions exhibit hyperperfusion indicative of inflammation [18]. Conversely, normal-appearing white matter in MS patients typically demonstrates normal to decreased perfusion compared to healthy controls [18].

#### **Initial Imaging Definition**

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

• There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

• There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously wherein each procedure provides unique clinical information to effectively manage the patient's care).

#### **Discussion of Procedures by Variant**

### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

The goal of imaging of adult patients with acute or subacute sensorimotor or brainstem symptoms is to diagnose or exclude demyelinating disease in the CNS. This imaging information improves patient outcome by helping to determine whether there is evidence of demyelinating disease and thereby guiding timely management.

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### A. CT cervical and thoracic spine with IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine with IV contrast for initial evaluation of suspected CNS demyelinating disease. The available literature consistently indicates that CT imaging for suspected demyelinating disease of the CNS is not the preferred imaging modality because of its limited soft tissue characterization and poor visualization of the spinal cord when compared to MRI [1]. MRI is superior to CT for detecting and characterizing brain and spine demyelinating lesions [1].

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### B. CT cervical and thoracic spine without and with IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine without and with IV contrast for initial evaluation of suspected CNS demyelinating disease.

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. C. CT cervical and thoracic spine without IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine without IV contrast for initial evaluation of suspected CNS demyelinating disease.

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### D. CT head with IV contrast

There is no relevant literature to support the use of CT head with IV contrast for initial evaluation

of suspected CNS demyelinating disease.

### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### E. CT head without and with IV contrast

There is no relevant literature to support the use of CT head without and with IV contrast for initial evaluation of suspected CNS demyelinating disease.

### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### F. CT head without IV contrast

Head CT without IV contrast can demonstrate imaging findings which may mimic clinical symptoms of demyelinating disease, such as intracranial hemorrhage, mass and mass effect, or infarct. However, there is no relevant literature to support the use of CT head without IV contrast for initial evaluation of suspected CNS demyelinating disease.

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. G. CT lumbar spine with IV contrast

There is no relevant literature to support the use of CT lumbar spine with IV contrast for initial evaluation of suspected CNS demyelinating disease.

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### H. CT lumbar spine without and with IV contrast

There is no relevant literature to support the use of CT lumbar spine without and with IV contrast for initial evaluation of suspected CNS demyelinating disease.

### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### I. CT lumbar spine without IV contrast

There is no relevant literature to support the use of CT lumbar spine without IV contrast for initial evaluation of suspected CNS demyelinating disease.

### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### J. CT orbits with IV contrast

CT orbits with IV contrast can demonstrate retrobulbar masses and inflammatory processes, which may mimic a clinical presentation of demyelinating disease. However, CT demonstrates poor contrast resolution relative to MRI and is suboptimal in assessing the optic nerves themselves compared with MRI. There is no relevant literature to support the use of CT orbits with IV contrast for initial evaluation of suspected CNS demyelinating disease.

### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

#### K. CT orbits without and with IV contrast

There is no relevant literature to support the use of CT orbits without and with IV contrast for initial evaluation of suspected CNS demyelinating disease.

#### Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect

#### demyelinating disease of the central nervous system. Initial imaging. L. CT orbits without IV contrast

There is no relevant literature to support the use of CT orbits without IV contrast for initial evaluation of suspected CNS demyelinating disease.

Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging.

M. MRI cervical and thoracic spine with IV contrast

Limited literature supports the use of postcontrast MRI of the spine alone. The available evidence indicates that both pre- and postcontrast imaging should be performed together for initial imaging. On the other hand, postcontrast only T1- and T2-weighted imaging of the spine can sometimes be performed to help with overall examination time and patient tolerance when scanning multiple body parts and when evaluating primarily for intradural rather than spinal column disease.

Specifically in the setting of suspected MS, spinal cord MRI is recommended by the Consortium of MS Centers Task Force if the brain MRI is nondiagnostic or if the presenting symptoms localize to the spinal cord [24]. The proposed spinal cord MRI protocol includes sagittal T1-weighted (optional), sagittal T2-weighted, sagittal PD or T2 STIR or phase-sensitive T1 inversion recovery, axial T2/T2\*-weighted imaging, and postcontrast gadolinium-enhanced T1-weighted imaging [24]. As a minimum, coverage should include the cervical cord in MS because clinically silent MS lesions are more common and better visualized there. It may not be necessary to examine the thoracic cord routinely unless there are clinical symptoms or signs at that level. When spinal cord imaging is performed at the same time as brain imaging with gadolinium, no additional contrast is required [24].

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. N. MRI cervical and thoracic spine without and with IV contrast

Available literature supports the use of MRI cervical and thoracic spine without and with intravenous (IV) contrast for initial evaluation of suspected CNS demyelinating disease, particularly when spinal cord involvement is suspected based on clinical findings.

MRI of the brain and the spinal cord, and together with the clinical and laboratory findings, can accurately classify demyelinating diseases in most cases [1]. The high sensitivity of MRI in depicting brain and spinal cord demyelinating plaques has made this technique the most important paraclinical tool in current use, not only for the early and accurate diagnosis of MS, but also for understanding the natural history of the disease and monitoring and predicting the efficacy of disease-modifying treatments [1].

The initial imaging modality used to investigate suspected CNS demyelinating disease is a MRI scan of the brain and spinal cord, since it is highly sensitive in detecting characteristic lesions associated with demyelination, particularly in conditions like MS [1, 19]. Other demyelinating diseases of the CNS can often be distinguished from each other based on appearance on brain MRI in conjunction with clinical lab testing [20-22]. For example, area postrema syndrome clinically may suggest NMO, in which case a brain MRI with and without IV contrast could be used for

further evaluation of the dorsal medulla/area postrema for demyelinating lesions [20]. In myelin oligodendrocyte glycoprotein antibody-associated disorders (MOGAD), MRI demonstrates characteristic features such as perineural optic nerve enhancement and spinal cord H-sign [21, 22].

The diagnosis of MS relies heavily on MRI information, especially when there is a clinically isolated syndrome suggestive of demyelination [1]. MRI can be used to show dissemination in space (lesions in 2 of 4 locations; juxtacortical, periventricular, infratentorial, or spinal cord) and to demonstrate dissemination in time (enhancement or new T2 lesions at follow-up) [1]. With the 2024 update of the McDonald criteria, optic nerve is a fifth location that can be used to establish dissemination in space, and central vein sign on T2\*-weighted MRI (6 or more) can be used to establish dissemination in time.

Spinal cord abnormalities are found in 74% to 92% of established MS cases, depending on the clinical phenotype [1]. Asymptomatic spinal cord lesions are found in 30% to 40% of patients with clinically isolated syndrome, even when presenting symptoms do not involve the spinal cord clinically [1]. MS spinal cord lesions characteristically have a cigar shape on sagittal scans and rarely exceed 2 vertebral segments in length, contrasting with the longitudinally extensive lesions seen in NMO [1]. On cross-section, they typically occupy the lateral and posterior white-matter columns and rarely occupy more than half the cross-sectional area [1].

Contrast enhancement in spinal cord lesions is less frequent than in brain lesions, occurring 4 to 10 times less frequently, which may be partially explained by the smaller volume of spinal cord compared to brain [1]. High doses of gadolinium and long postinjection delays can increase detection of active spinal cord lesions [1].

MRI of the brain and spinal cord is used in the diagnostic workup of NMOSD, with characteristic lesion patterns observed [20, 23]. NMOSD is characterized by longitudinally extensive TM (lesions extending over 3 or more contiguous segments and occasionally the entire spinal cord) and bilateral ON [1]. The cord lesions are centrally located (preferential central gray-matter involvement) and affect much of the cross-section on axial images [1]. The presence of very hyperintense spotty lesions on T2-weighted images ("bright spotty sign") is a specific feature that helps differentiate NMO from MS [1]. Spinal cord lesions in MS are usually short and peripheral, whereas NMOSD lesions are centrally located and longitudinally extensive.

In MOGAD, MRI demonstrates characteristic features such as perineural optic nerve enhancement, longitudinally extensive spinal cord lesions, and spinal cord H-sign [21, 22]. MOGAD typically presents with bilateral or longitudinally extensive ON and cortical/subcortical brain lesions. MOGAD features include fluffy poorly demarcated lesions possibly with pontine/thalamic involvement intracranially [21, 22].

Specifically in the setting of suspected MS, spinal cord MRI is recommended by the Consortium of MS Centers Task Force if the brain MRI is nondiagnostic or if the presenting symptoms localize to the spinal cord [24]. The proposed spinal cord MRI protocol includes sagittal T1-weighted (optional), sagittal T2-weighted, sagittal PD or T2 short tau inversion recovery (STIR) or phase-sensitive T1 inversion recovery, axial T2/T2\*-weighted imaging, and postcontrast gadolinium-enhanced T1-weighted imaging [24]. As a minimum, coverage should include the cervical cord in MS because clinically silent MS lesions are more common and better visualized there. It may not

be necessary to examine the thoracic cord routinely unless there are clinical symptoms or signs at that level. When spinal cord imaging is performed at the same time as brain imaging with gadolinium, no additional contrast is required [24].

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. O. MRI cervical and thoracic spine without IV contrast

The available literature supports the use of MRI cervical and thoracic spine without IV contrast but indicates that contrast-enhanced imaging is preferred for initial imaging.

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. P. MRI head with IV contrast

Regarding contrast-enhanced brain MRI, the available evidence indicates that both pre- and postcontrast imaging should be performed together.

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. Q. MRI head without and with IV contrast

The literature strongly supports the use of MRI head without and with IV contrast for initial evaluation of suspected CNS demyelinating disease, and particularly for suspected MS. MRI is the most sensitive imaging technique for detecting MS plaques throughout the brain, with proton density (PD) or T2-weighted images showing areas of high signal intensity in the periventricular white matter in >90% of MS patients [1]. The McDonald criteria for MS include lesions in 4 specific locations: cortico/juxtacortical, periventricular, infratentorial, and spinal cord regions [1]. Contrast enhancement is routinely used in MS studies to provide a measure of inflammatory activity in vivo. Gadolinium enhancement varies in size and shape, usually lasting a few weeks, and incomplete ring enhancement with the open border facing gray-matter is a common finding in active MS plaques [1]. This enhancement pattern helps distinguish inflammatory-demyelinating lesions from other focal lesions such as tumors or abscesses which have closed ring enhancement [1].

MRI of the brain and the cord, together with the clinical and laboratory findings, can accurately classify demyelinating diseases in most cases [1]. The high sensitivity of MRI in depicting brain and spinal cord demyelinating plaques has made this technique the most important paraclinical tool in current use, not only for the early and accurate diagnosis of MS, but also for understanding the natural history of the disease and monitoring and predicting the efficacy of disease-modifying treatments [1].

The diagnosis of MS relies heavily on MRI information, certainly when there is a clinically isolated syndrome suggestive of demyelination [1]. MRI can be used to show dissemination in space (lesions in 2 of 4 locations; juxtacortical, periventricular, infratentorial, or spinal cord) and to demonstrate dissemination in time (enhancement or new T2 lesions at follow-up) [1]. With the 2024 update of the McDonald criteria, optic nerve is a fifth location that can be used to establish dissemination in space, and central vein sign on T2\*-weighted MRI (6 or more) can be used to establish dissemination in time.

The 2017 McDonald criteria showed similar overall diagnostic accuracy to the 2010 McDonald criteria, with higher adjusted hazard ratio for development of clinically definite MS [25]. The

inclusion of symptomatic lesions and requirement of a minimum of 3 lesions to define periventricular involvement could be considered in future criteria revisions [25]. The updated McDonald criteria have incorporated new MRI features that enhance diagnostic accuracy for MS [4, 26]. These criteria now include assessment of the central vein sign, which can differentiate MS from other demyelinating conditions with 94% accuracy at 3T MRI, particularly when present in at least 6 lesions and especially valuable in patients age 50 or older [4, 5]. Additionally, paramagnetic rim lesions have been recognized as important diagnostic features, present in 48% of clinically isolated syndrome, 59% of RRMS, and 38% of progressive MS cases, where the presence of more than 1 lesion plus dissemination in time or CSF findings can support MS diagnosis [6, 27].

The pathophysiology of demyelinating diseases varies depending on the specific condition. In MS, the disease process involves both acute and chronic MS plaques that appear hyperintense on T2/fluid-attenuated inversion recovery (FLAIR) sequences, reflecting their increased tissue water content [1]. The signal increase indicates edema, inflammation, demyelination, reactive gliosis, and/or axonal loss in proportions that differ from lesion to lesion [1]. MRI of the brain including PD or T2-weighted MRI show areas of high signal intensity in the periventricular white matter in >90% of MS patients [1]. Histopathological studies have shown that a substantial portion of the total brain lesion load in MS is located within the cerebral cortex [1]. In MS, lesions tend to affect specific regions of the brain, including the periventricular white matter, the inferior surface of the corpus callosum, the corticojuxtacortical regions, the temporal lobes, and the infratentorial regions [1]. Focal involvement of the periventricular white matter in the anterior temporal lobes is typical for MS and rarely seen in other white matter disorders [1]. MS plagues are generally round to ovoid in shape and range from a few millimeters to >1 cm in diameter [1]. They are typically discrete and focal at the early stages of the disease, but become confluent as the disease progresses, particularly in the posterior hemispheric periventricular white matter [1]. The vast majority of MS patients have at least 1 ovoid periventricular lesion, whose major axis is oriented perpendicular to the outer surface of the lateral ventricles [1]. The ovoid shape and perpendicular orientation derive from the perivenular location of the demyelinating plagues noted on histopathology (Dawson's fingers)[1]. In NMO, the pathological differences from MS are significant [2, 3]. The pathological hallmark in MS is sharply demarcated demyelinating plaques with relatively preserved axons, whereas in NMO, both axons and myelin are involved, resulting in necrotic cavitation [2, 3]. According to the proposed pathogenesis of NMO, an unknown antigenic stimulus in the periphery leads to the production of circulatory NMO-IgG [2, 3]. The AQP4-antibody binds to a cell-surface antigen, the extracellular domain of AQP4, and once the antibodies cross the blood-brain barrier, they bind to AQP4 on astrocyte foot processes and activate the lytic complement cascade [2, 3].

The clinical presentation of demyelinating diseases varies significantly depending on the specific condition and affected anatomical regions. Serial MRIs are often required to monitor disease progression and response to treatment in MS [24].

Brain MRI with gadolinium-based IV contrast is used for the diagnosis of MS, one of the most common demyelinating diseases [24]. Gadolinium-based contrast detects the breakdown of the blood-brain barrier that occurs with new development of demyelinating lesions and re-activation of old lesions [24]. Specific sequences such as FLAIR and T2-weighted images are helpful in visualizing areas of demyelination in all forms of demyelinating disease [24]. Most newly enhancing lesions will leave residual T2 hyperintensity after the enhancement resolves [24]. The average

duration of enhancement for individual brain lesions is 3 weeks, with most enhancing for 2 to 6 weeks [24].

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. R. MRI head without IV contrast

The literature supports the use of MRI head without IV contrast but indicates that contrast-enhanced imaging is preferred for initial imaging. The use of IV contrast is helpful in assessing for active demyelinating lesions [24]. Particularly in the setting of suspected MS, brain MRI with gadolinium is recommended for the diagnosis of MS by the Consortium of MS Centers Task Force [24].

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. S. MRI lumbar spine with IV contrast

Limited literature supports the use of postcontrast MRI lumbar spine imaging in CNS demyelinating disease, for example when there is specific clinical concern for conus medullaris involvement. Depending on institutional preference, postcontrast only T1- and T2-weighted imaging of the spine can sometimes be performed to help with overall examination time and patient tolerance when scanning multiple body parts and when evaluating primarily for intradural not vertebral disease.

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. T. MRI lumbar spine without and with IV contrast

The literature indicates that demyelinating diseases of the CNS predominantly involve the brain and spinal cord, so the usefulness in imaging the lumbar spine is limited since thoracic spine imaging would most likely be sufficient in capturing abnormalities of the distal thoracic spinal cord relating to demyelinating lesions [24]. MRI of the lumbar spine without and with IV contrast could be indicated if there is suspected involvement at the level of the conus medullaris in the upper lumbar spine, or if clinical symptoms suggest involvement of the lumbar spine or cauda equina nerve roots [24]. The literature emphasizes that specifically in the setting of suspected MS, spinal cord MRI is recommended by the Consortium of MS Centers Task Force if the brain MRI is nondiagnostic or if the presenting symptoms localize to the spinal cord [24]. As a minimum, coverage should include the cervical cord in MS, because clinically silent MS lesions are more common and better visualized there [24]. It may not be necessary to examine the thoracic cord routinely unless there are clinical symptoms and/or signs at that level [24]. When MRI lumbar spine is performed, imaging of the spine with the use of IV contrast is preferred in initial imaging to assess for findings of active demyelination as well as to exclude other possible etiologies of the patient's symptoms [24]. In summary, the available literature provides only limited support for MRI lumbar spine in initial CNS demyelinating disease assessment, with preference given to brain and cervical/thoracic spine imaging as the primary modalities, whereas lumbar spine MRI remains an option if there is clinical suspicion of lumbar nerve root involvement.

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. U. MRI lumbar spine without IV contrast

Limited literature supports the use of noncontrast MRI of the lumbar spine imaging in suspected

CNS demyelinating disease, for example when there is clinical concern for conus medullaris involvement.

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. V. MRI orbits with IV contrast

Limited literature supports the use of postcontrast MRI of the orbits for suspected demyelinating disease. However, the available evidence indicates that both pre- and postcontrast imaging should be performed together. If acute sensory symptoms include visual abnormalities and pain localizing to the orbit, MRI of the orbits may be considered in initial imaging evaluation for suspected demyelinating disease [24]. Many demyelinating diseases of the CNS are known to involve the optic nerves and can present with symptoms of ON [24]. The suggested sequences for orbital MRI in the setting of ON and suspected MS include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of ≤2 mm, with coverage through the optic chiasm [24].

## Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. W. MRI orbits without and with IV contrast

The literature supports the use of MRI orbits without and with IV contrast when orbital symptoms are present. If acute sensory symptoms include visual abnormalities and pain localizing to the orbit, MRI of the orbits may be considered in initial imaging evaluation for suspected demyelinating disease [24]. Many demyelinating diseases of the CNS are known to involve the optic nerves and can present with symptoms of ON [24]. The suggested sequences for orbital MRI in the setting of ON and suspected MS include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of ≤2 mm, with coverage through the optic chiasm [24].

# Variant 1:Adult. Acute or subacute sensorimotor or brainstem symptoms. Suspect demyelinating disease of the central nervous system. Initial imaging. X. MRI orbits without IV contrast

The literature supports the use of MRI orbits without IV contrast but indicates that contrast-enhanced imaging is preferred. If acute sensory symptoms include visual abnormalities and pain localizing to the orbit, MRI of the orbits may be considered in initial imaging evaluation for suspected demyelinating disease [24]. A key finding on orbital MRI of acute ON is optic nerve enhancement, which requires the administration of IV contrast [24].

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

The goal of imaging is to diagnose or exclude demyelinating disease in the CNS, particularly the spinal cord [28]. TM is associated with several demyelinating diseases, including MS, NMOSD, and ADEM [28]. TM can also occur as an idiopathic condition or in connection with autoimmune diseases like systemic lupus erythematosus and Sjögren's syndrome [28]. The clinical presentation of TM involves acute onset of motor, sensory, and autonomic dysfunction [28].

The approach to diagnosis should consider clinical history, physical examination findings, and imaging results to differentiate between various etiologies such as demyelinating, infectious, vascular, and neoplastic causes. Follow-up guidelines may vary depending on the specific disease context in which TM occurs. Treatment typically involves immunomodulating therapy, such as

high-dose IV corticosteroids or plasma exchange. Although prognosis varies, early aggressive treatment may improve outcomes [28].

Diagnostic criteria include distinguishing between acute complete and partial TM, as this may indicate etiology and relapse risk. AQP4 autoantibody testing is crucial for diagnosing NMO. Other potential tests include CSF examination for cells or OCBs and brain MRI to assess for white matter lesions.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### A. CT cervical and thoracic spine with IV contrast

Although CT could demonstrate degenerative changes or other pathology of the spinal column, which may lead to spinal cord compression and mimic a clinical presentation of TM, there is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### B. CT cervical and thoracic spine without and with IV contrast

Although CT could demonstrate degenerative changes or other pathology of the spinal column, which may lead to spinal cord compression and mimic a clinical presentation of TM, there is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM. CT is less sensitive than MRI for detection of spinal cord lesions in TM [28, 29]. MRI is superior to CT to demonstrate cord swelling/expansion, a key finding in ATM [28, 29]. Imaging with IV contrast to assess lesion extent and exclude other pathologies is a cornerstone of TM evaluation [28, 29].

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### C. CT cervical and thoracic spine without IV contrast

Although CT could demonstrate degenerative changes or other pathology of the spinal column, which may lead to spinal cord compression and mimic a clinical presentation of TM, there is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### D. CT head with IV contrast

There is no relevant literature to support the use of CT head imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### E. CT head without and with IV contrast

There is no relevant literature to support the use of CT head imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### F. CT head without IV contrast

There is no relevant literature to support the use of CT head imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### G. CT lumbar spine with IV contrast

Although CT could demonstrate degenerative changes or other pathology of the spinal column, which may lead to spinal cord or cauda equina nerve root compression and mimic a clinical presentation of TM, there is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### H. CT lumbar spine without and with IV contrast

Although CT could demonstrate degenerative changes or other pathology of the spinal column, which may lead to spinal cord or cauda equina nerve root compression and mimic a clinical presentation of TM, there is no relevant literature to support the use of any CT imaging modality for initial evaluation of suspected TM. CT is less sensitive than MRI for detection of spinal cord lesions in TM, and it does not provide a diagnostic evaluation of the cauda equina nerve roots [28, 29]. MRI is superior to CT to demonstrate cord swelling/expansion, a key finding in ATM [28, 29]. It is crucial to image the entire spine with IV contrast to assess lesion extent [28, 29].

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### I. CT lumbar spine without IV contrast

Although CT could demonstrate degenerative changes or other pathology of the spinal column, which may lead to spinal cord or cauda equina nerve root compression and mimic a clinical presentation of TM, there is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### J. CT orbits with IV contrast

CT of the orbits does not assess the spinal cord and cannot provide a diagnostic evaluation for TM. There is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### K. CT orbits without and with IV contrast

CT of the orbits does not assess the spinal cord and cannot provide a diagnostic evaluation for TM. There is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### L. CT orbits without IV contrast

CT of the orbits does not assess the spinal cord and cannot provide a diagnostic evaluation for TM. There is no relevant literature to support the use of any CT imaging for initial evaluation of suspected TM.

Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level.

### Suspect transverse myelitis. Initial imaging. M. MRI cervical and thoracic spine with IV contrast

Limited literature supports performance of MRI with only postcontrast sequences; however, the available evidence indicates that both pre- and postcontrast imaging should be performed together. On the other hand, postcontrast only T1- and T2-weighted imaging of the spine can sometimes be performed to help with overall examination time and patient tolerance when scanning multiple body parts and when evaluating primarily for intradural not vertebral disease.

MRI of the cervical and thoracic spine is indicated in the setting of suspected TM [24]. CT is less sensitive than MRI for detection of spinal cord lesions in TM [28, 29]. Gadolinium contrast detects the breakdown of the blood-brain barrier that occurs with new demyelinating lesion development and re-activation of old lesions [24]. MRI is superior to CT to demonstrate cord swelling/expansion, a key finding in ATM [28, 29]. It is crucial to image the entire spine with IV contrast to assess lesion extent and exclude other pathologies [28, 29].

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### N. MRI cervical and thoracic spine without and with IV contrast

The literature strongly supports the use of MRI cervical and thoracic spine without and with IV contrast for initial evaluation of suspected TM. Contrast-enhanced MRI of the cervical and thoracic spine is indicated in the setting of suspected TM [24]. CT is less sensitive than MRI for detection of spinal cord lesions in TM [28, 29]. Gadolinium contrast detects the breakdown of the blood-brain barrier that occurs with new demyelinating lesion development and re-activation of old lesions [24]. MRI is superior to CT to demonstrate cord swelling/expansion, a key finding in ATM [28, 29]. It is crucial to image the entire spine with IV contrast to assess lesion extent and exclude other pathologies [28, 29].

MRI is used in the diagnosis of TM [28, 29]. MRI can reveal increased signal intensity on T2weighted images, often with cord swelling [28, 29]. Contrast enhancement is common, but not universal [28, 29]. Patterns of cord involvement may provide clues into the underlying cause of TM [28, 29]. Idiopathic TM often presents with centrally located hyperintensity spanning 3 to 4 vertebral segments and focal peripheral enhancement [28, 29]. Spinal MRI findings can help differentiate between demyelinating diseases, with longitudinally extensive TM being characteristic of NMOSD [29]. MRI can reveal increased signal intensity on T2-weighted images, often with cord swelling. Patterns of cord involvement may provide clues into the underlying cause of TM. Idiopathic TM often presents with centrally located hyperintensity spanning 3 to 4 vertebral segments and focal peripheral enhancement. MRI of the brain and spinal cord is considered essential in the diagnostic workup of NMOSD, with characteristic lesion patterns observed [20, 23]. In MOGAD, MRI demonstrates characteristic features such as spinal cord H-sign [21, 22]. NMOSD is characterized by extensive, longitudinally extensive TM [20, 23]. Spinal cord lesions in MS are usually short-segment and peripheral, whereas NMOSD lesions are centrally located and longitudinally extensive with additional T2 hyperintense spotty lesions [20, 23]. MOGAD features include fluffy poorly demarcated lesions [21, 22].

Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### O. MRI cervical and thoracic spine without IV contrast

The literature supports the use of MRI cervical and thoracic spine without IV contrast but indicates that contrast-enhanced imaging is preferred. MRI of the cervical and thoracic spine is indicated in the setting of suspected TM [24]. CT is less sensitive than MRI for detection of spinal cord lesions in TM [28, 29]. Gadolinium contrast detects the breakdown of the blood-brain barrier that occurs with new demyelinating lesion development and re-activation of old lesions [24]. MRI can reveal increased signal intensity on T2-weighted images, often with cord swelling. Contrast enhancement is common but not universal [28, 29].

Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### P. MRI head with IV contrast

Regarding contrast-enhanced brain MRI, the available evidence indicates that both pre- and postcontrast imaging should be performed together.

Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### Q. MRI head without and with IV contrast

The literature supports the use of MRI head without and with IV contrast as adjunctive imaging when TM is suspected. When ATM is suspected, MRI of the spinal cord is crucial [25]. MRI of the brain in addition to the spine may be helpful in finding a specific diagnosis relating to the patient's ATM as well as excluding other potential causes of the patient's symptoms [25]. MRI of the brain and spinal cord is highly sensitive in detecting characteristic lesions associated with demyelination, particularly in conditions like MS [1, 19]. Brain MRI also plays a role in predicting risk of conversion to MS [25]. The use of IV contrast is helpful in detecting active demyelinating lesions [24].

The brain MRI findings in TM vary depending on the underlying etiology and associated demyelinating conditions. In MS-associated TM, brain lesions tend to affect specific regions including the periventricular white matter, the inferior surface of the corpus callosum, the corticojuxtacortical regions, the temporal lobes (particularly anterior temporal lobes), and the infratentorial regions [1]. MRI of the brain including PD or T2-weighted MRI show areas of high signal intensity in the periventricular white matter in >90% of MS patients [1]. Regarding NMOassociated TM, MRI of the brain and spinal cord is considered essential in the diagnostic workup of NMOSD, with characteristic lesion patterns observed [20, 23]. In contrast to MS, where periventricular lesions are discrete, oval-shaped, and perpendicular to the ependymal lining due to their perivenular distribution (Dawson's fingers), NMO lesions are not oval-shaped, located immediately adjacent to the lateral ventricles following the ependymal lining in a disseminated pattern, and are often edematous and heterogeneous [20, 23]. In MOGAD, MRI demonstrates characteristic features such as fluffy, poorly demarcated lesions possibly with pontine/thalamic involvement intracranially [21, 22]. Demyelinating diseases of the CNS can often be distinguished from each other based on appearance on brain MRI in conjunction with clinical lab testing [20-22]. For example, area postrema syndrome clinically may suggest NMO, in which case a brain MRI without and with IV contrast could be used for further evaluation of the dorsal medulla/area postrema for demyelinating lesions [20].

The literature supports the use of MRI head without and with IV contrast as adjunctive imaging when TM is suspected [24, 25]. However, the literature also supports the use of MRI head without IV contrast as adjunctive imaging but indicates that contrast-enhanced imaging is preferred [24,

25]. In summary, brain MRI plays a crucial complementary role to spinal cord imaging in TM evaluation, particularly for determining the underlying etiology, predicting MS conversion risk, and excluding alternative diagnoses.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### R. MRI head without IV contrast

The literature supports the use of MRI head without IV contrast as adjunctive imaging but indicates that contrast-enhanced imaging is preferred. When ATM is suspected, MRI of the spinal cord is crucial [25]. MRI of the brain in addition to the spine may be helpful in finding a specific diagnosis relating to the patient's ATM [25]. The use of IV contrast is helpful in detecting active demyelinating lesions as well as excluding other potential causes of the patient's symptoms [24]. MRI of the brain and spinal cord is highly sensitive in detecting characteristic lesions associated with demyelination, particularly in conditions like MS [1, 19].

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### S. MRI lumbar spine with IV contrast

Insufficient literature supports the use of MRI lumbar spine with IV contrast for initial imaging in patients with suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### T. MRI lumbar spine without and with IV contrast

Insufficient literature supports the use of MRI lumbar spine without and with IV contrast for initial imaging in patients with suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### **U. MRI lumbar spine without IV contrast**

Insufficient literature supports the use of MRI lumbar spine without IV contrast for initial imaging in patients with suspected TM.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### V. MRI orbits with IV contrast

There is insufficient evidence to support MRI orbits with IV contrast in the initial imaging of patients with suspected TM. MRI of the orbits could be performed as an adjunctive imaging test if the patient presents with concurrent visual symptoms. The recommended sequences for orbital MRI in the setting of ON and suspected MS include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of ≤2 mm, with coverage through the optic chiasm [24].

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### W. MRI orbits without and with IV contrast

There is insufficient evidence to support the use of MRI orbits in the initial imaging assessment for TM. The available literature indicates that in the setting of suspected ATM, the likelihood of orbit involvement is low if there is absence of pain localized to the orbit or visual impairments [24]. This

suggests that orbital imaging would not typically be indicated unless specific visual symptoms are present. However, the literature provides some support for orbital imaging as an adjunctive test in specific circumstances: many demyelinating diseases of the CNS that are associated with TM are also known to involve the optic nerves and can present with symptoms of ON [24]. TM can be associated with NMOSD, where optic nerve involvement is more common. NMO is an autoimmune inflammatory disorder of the CNS with a predilection for the optic nerves and spinal cord [1]. The discovery of an NMO-specific autoantibody directed against AQP4-antibody binds, the major water channel in the CNS, clearly identified NMO as a disease separate from MS [1].

When MRI orbits is performed in the context of suspected demyelinating disease, the recommended sequences for orbital MRI in the setting of ON and suspected MS include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of  $\leq 2$  mm, with coverage through the optic chiasm [24].

In summary, there is insufficient evidence to support MRI of the orbits in initial TM assessment, with its use as an adjunctive imaging examination is primarily justified when patients present with concurrent visual symptoms suggestive of optic nerve involvement or when there is clinical suspicion for NMOSD. The primary imaging focus for TM remains on spinal cord evaluation rather than orbital structures.

### Variant 2:Adult. Acute or subacute sensorimotor symptoms below a spinal cord level. Suspect transverse myelitis. Initial imaging.

#### X. MRI orbits without IV contrast

There is insufficient evidence to support MRI orbits without IV contrast in the initial imaging of patients with suspected TM. MRI of the orbits could be performed as an adjunctive imaging test if the patient presents with concurrent visual symptoms. The recommended sequences for orbital MRI in the setting of ON and suspected MS include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of  $\leq 2$  mm, with coverage through the optic chiasm.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

The goal of imaging in this scenario is to reassess the extent of known demyelinating disease in patients without progressive neurologic findings on clinical examination. Radiologic follow-up in demyelinating diseases varies by condition [30, 31]. This imaging information improves patient outcome by helping to determine whether there is progression or improvement of demyelinating disease, thereby guiding management. This imaging information benefits the patient by reducing potential delay in appropriate treatment and by hastening patient recovery.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### A. CT cervical and thoracic spine with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### B. CT cervical and thoracic spine without and with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### C. CT cervical and thoracic spine without IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### D. CT head with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### E. CT head without and with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### F. CT head without IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### **G. CT lumbar spine with IV contrast**

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### H. CT lumbar spine without and with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### I. CT lumbar spine without IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### J. CT orbits with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### K. CT orbits without and with IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### L. CT orbits without IV contrast

There is no relevant literature to support the use of any CT imaging for surveillance imaging in known demyelinating disease.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### M. MRI cervical and thoracic spine with IV contrast

The literature supports various MRI approaches for surveillance imaging depending on the specific demyelinating disease and clinical context, and particularly when detection of active lesions is necessary for guiding management decisions. Specifically in the setting of MS, routine follow-up imaging of the spinal cord is indicated in monitoring patients with spinal cord phenotype (no or few brain lesions) for the detection of active spinal cord lesions [30]. In MOGAD, routine MRI of the brain, spine, or orbits is not typically part of clinical practice, as lesions often resolve after acute attacks [22, 33]. However, a single MRI scan after an attack may be useful to establish a new baseline for future comparison [22, 33]. For NMOSD, routine spinal cord and brain MRI during follow-up is indicated [22, 33]. No specific imaging interval is detailed in clinical practice guidelines for routine imaging in NMO or MOGAD in the absence of new neurological symptoms.

Limited literature supports the use of postcontrast MRI of the spine alone. The available evidence indicates that both pre- and postcontrast imaging should be performed together for initial imaging. On the other hand, postcontrast only T1- and T2-weighted imaging of the spine can sometimes be performed to help with overall exam time and patient tolerance when scanning multiple body parts and when evaluating primarily for intradural not vertebral disease.

In surveillance imaging of known CNS demyelinating disease, contrast is recommended if showing disease activity with presence of gadolinium enhancing lesions is required to initiate or change a specific disease-modifying treatment [30]. However, this recommendation inherently assumes that both pre- and postcontrast sequences will be obtained for proper comparison. Contrast-enhanced T1-weighted images are routinely used in the study of MS to provide a measure of inflammatory activity in vivo [1]. MRI-based disease activity is 5–10 times more frequent than clinical evaluation of relapses, suggesting that most of the enhancing lesions are clinically silent [1].

## Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### N. MRI cervical and thoracic spine without and with IV contrast

There is a role for MRI of the cervical and thoracic spine in the surveillance of known CNS demyelinating disease in patients with stable neurologic examinations without new neurologic symptoms.

Available literature supports various MRI approaches for surveillance imaging depending on the specific demyelinating disease and clinical context. There is limited evidence supporting the use of MRI cervical and thoracic spine imaging with and without IV contrast in surveillance imaging of known CNS demyelinating disease in clinically stable patients. The literature indicates that spinal cord involvement is common in established demyelinating disease, making surveillance imaging clinically relevant. The prevalence of spinal cord abnormalities is as high as 74% to 92% in established MS, and depends on the clinical phenotype of MS [1]. Asymptomatic spinal cord lesions are found in 30% to 40% of patients with a clinically isolated syndrome, even if the presenting symptoms do not involve the spinal cord clinically [1]. In MS, routine follow-up imaging of the spinal cord is indicated in monitoring patients with spinal cord phenotype (no or few brain lesions) for the detection of active spinal cord lesions [30].

Postcontrast MRI shows disease activity with presence of gadolinium enhancing lesions, which is required to initiate or change a specific disease-modifying treatment [30]. Contrast enhancement is important for detecting disease activity but is less frequent in the spinal cord than the brain. Active lesions are rarer in the spinal cord than the brain and are more frequently associated with new clinical symptoms [1]. Subclinical disease activity with contrast-enhancing lesions is 4 to 10 times less frequent in the spinal cord than the brain, a fact that may be partially explained by the large volume of brain as compared with spinal cord [1].

The decision regarding contrast use could be based on treatment implications. The presence of disease activity with gadolinium enhancing lesions may lead to initiation of or change in a specific disease-modifying treatment [30]. Higher doses of gadolinium and longer postinjection delay can increase the detection of active spinal cord lesions [1]. In summary, whereas spinal cord MRI has a defined role in surveillance of known CNS demyelinating disease, particularly in patients with spinal cord phenotype MS, the evidence suggests that contrast-enhanced imaging is primarily indicated when treatment decisions depend on detecting active disease activity rather than for routine surveillance in stable patients.

There is clear evidence supporting MRI as the preferred imaging modality over CT for surveillance imaging in known demyelinating disease. MRI is the most sensitive imaging technique for detecting MS plaques throughout the spinal cord [1]. PD or T2-weighted MRI (especially acquired using the FLAIR sequence) show areas of high signal intensity in the periventricular white matter in >90% of MS patients [1]. MRI is superior to CT for detecting and characterizing spine demyelinating lesions [1]. CT imaging for suspected demyelinating disease of the CNS is not the preferred imaging modality because of its limited soft tissue characterization when compared to MRI [1]. The high sensitivity of MRI in depicting spinal cord demyelinating plagues has made this technique the most important paraclinical tool in current use, not only for the early and accurate diagnosis of MS, but also for understanding the natural history of the disease and monitoring and predicting the efficacy of disease-modifying treatments [1]. Contrast-enhanced T1-weighted images are routinely used in the study of MS to provide a measure of inflammatory activity in vivo [1]. MRI-based disease activity is 5 to 10 times more frequent than clinical evaluation of relapses, suggesting that most of the enhancing lesions are clinically silent [1]. MRI can effectively demonstrate cord swelling, a key finding in ATM, as well as other focal spinal cord demyelinating lesions [1]. In summary, the literature consistently demonstrates that MRI's superior sensitivity for detecting demyelinating lesions, ability to assess disease activity through enhancement patterns,

and capacity to visualize characteristic lesion morphology and distribution make it the preferred imaging modality for surveillance of known demyelinating disease compared to CT.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### O. MRI cervical and thoracic spine without IV contrast

Available literature supports various MRI approaches for surveillance imaging depending on the specific demyelinating disease and clinical context. Specifically in the setting of MS, routine followup imaging of the spinal cord is indicated in monitoring patients with spinal cord phenotype (no or few brain lesions) for the detection of active spinal cord lesions [30]. There is very limited literature support for the use of MRI cervical and thoracic spine imaging without IV contrast in surveillance of known CNS demyelinating disease in stable patients. The literature supports the use of MRI cervical and thoracic spine without IV contrast for routine surveillance, but imaging of the spine with the use of IV contrast is preferred to assess for findings of active demyelination [24]. For patients with stable clinical examinations, routine surveillance spine MRI without IV contrast may be sufficient for monitoring structural changes and lesion burden, whereas contrast-enhanced studies could be reserved for situations where detection of active inflammation would potentially alter treatment management. The literature indicates that spinal cord involvement is common in established demyelinating disease, making surveillance imaging clinically relevant. The prevalence of spinal cord abnormalities is as high as 74% to 92% in established MS, and depends on the clinical phenotype of MS [1]. Asymptomatic spinal cord lesions are found in 30% to 40% of patients with a clinically isolated syndrome, even if the presenting symptoms do not involve the spinal cord clinically [1].

Noncontrast MRI can detect structural changes and lesion burden in the spinal cord. In RRMS, the spinal cord lesions are typically multifocal [1]. In SPMS, the abnormalities are more extensive and diffuse and are commonly associated with spinal cord atrophy [1]. In primary progressive MS, spinal cord abnormalities are quite extensive as compared with brain abnormalities [1]. Active lesions are rarer in the spinal cord than the brain and are more frequently associated with new clinical symptoms [1]. Subclinical disease activity with contrast-enhancing lesions is 4 to 10 times less frequent in the spinal cord than the brain, a fact that may be partially explained by the large volume of brain as compared with spinal cord [1]. Although noncontrast MRI cervical and thoracic spine imaging can provide valuable information about structural changes, lesion burden, and atrophy in surveillance of known CNS demyelinating disease, the available evidence suggests that contrast-enhanced imaging is preferred when the goal is to detect subclinical disease activity that might influence treatment decisions.

Recent large studies suggest that the incremental value of contrast in routine surveillance of stable patients is limited, with few management changes resulting from its use. Routine brain and cervical spine MRI detected new isolated cervical spinal cord lesions in only <;2% of clinically stable people with MS. Developing new asymptomatic cervical spinal cord lesions was associated with concomitant new brain lesions and did not confer an independent increased risk of relapse or disability worsening. Performing spine MRI may not be warranted for routine monitoring in most people with MS, and performing only brain MRI may be sufficient to capture the vast majority of clinically silent disease activity [32].

Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance

#### imaging.

#### P. MRI head with IV contrast

There is no relevant literature to support the use of MRI head with IV contrast for surveillance imaging of patients with known demyelinating disease and a stable neurologic examination.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### Q. MRI head without and with IV contrast

The literature supports various MRI approaches for surveillance imaging depending on the specific demyelinating disease and clinical context.

In MOGAD, routine MRI of the brain, spine, or orbits is not typically part of clinical practice, as lesions often resolve after acute attacks [22, 33]. However, a single MRI scan after an attack (not specified with or without IV contrast) may be useful to establish a new baseline for future comparison [22, 33]. For NMOSD, routine spinal cord and brain MRI during follow-up is recommended [22, 33]. Gadolinium contrast-enhancement of spinal cord lesions is detected in only 25% of MOG-TM cases compared to lesions in MS (75%) or AQP4-TM (80%) [22]. Of note, spinal cord MRI can initially be normal in up to 10% of MOGAD patients with myelitis attacks [22].

In clinically isolated syndrome, initial brain MRI with gadolinium is recommended by the Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) group within 3 months, followed by additional studies at 1 and 3 years; new T2 lesions at 3 months have been shown to predict conversion to MS [30]. Follow-up imaging to establish a MS diagnosis when the first MRI does not fulfill the criteria is recommended as follows: Brain MRI is recommended every 6-12 months in clinically isolated syndrome and subclinical MS radiologically isolated syndrome with risk factors for conversion to MS and paraclinical features of MS [30]. Use of gadolinium is not recommended routinely for follow-up when initial brain MRI is not diagnostic for MS [30].

For routine follow-up in MS with stable examination, baseline brain MRI (with gadolinium if required by drug label) is recommended by the 2021 MAGNIMS-Consortium of Multiple Sclerosis Centres (CMSC)-North American Imaging in Multiple Sclerosis Cooperative (NAIMS) consensus recommendations before starting or switching disease-modifying treatment [30]. New baseline brain MRI usually at 3 to 6 months after treatment onset is recommended to avoid misinterpretation of lesions that developed before therapeutic onset [30]. Yearly brain MRI while the patient is on the disease-modifying treatment is indicated for routine follow-up [30]. In MS with stable neurologic examination, follow-up brain MRI with gadolinium is recommended to demonstrate dissemination in time and ongoing clinically silent disease activity while on treatment, to re-assess the original diagnosis, and as a new baseline before starting or modifying therapy in the setting of MS [24, 31]. Contrast is recommended by the 2021 MAGNIMS-CMSC-NAIMS consensus guidelines if showing disease activity with presence of gadolinium enhancing lesions is required to initiate or change a specific disease-modifying treatment [30]. Gadolinium enhancement varies in size and shape, usually lasting a few weeks, although steroid treatment shortens this period [1]. For MS, MRI protocols for regular follow-up are described with intervals ranging from 6 months to 2 years [31]. Gadolinium use is limited to defined situations in the context of a stable neurologic examination, such as when new treatment is initiated, approximately 6 months after switching disease-modifying therapy to establish a new baseline on the new therapy, or when previous images are unavailable. A proposed progressive multifocal

leukoencephalopathy (PML) surveillance protocol includes T2 FLAIR and DWI sequences only [24, 31]. Specifically in the setting of MS, the use of gadolinium-based contrast agents is recommended in the first year of follow-up (ie, after treatment initiation) if a new baseline MRI scan (ie, usually 3-6 months after treatment initiation) was not obtained, particularly in patients on interferon beta or glatiramer acetate (which are less effective in reducing MRI activity than are other therapies). Contrast is also recommended if detection or confirmation of clinical disease activity is required in patients without a recent reference brain MRI scan (done <3-6 months ago). MRI should be ideally done as soon as possible and before steroid treatment. Contrast is recommended if showing disease activity with presence of gadolinium enhancing lesions is required to initiate or change a specific disease-modifying treatment. Contrast is indicated in patients with diffuse and confluent chronic MS lesions (ie, large lesion burden), in which detection of disease activity is required but difficult to show on the basis of new or enlarged T2 lesions. Contrast is recommended for PML screening if there has been a suspicious lesion detected on the standard monitoring or screening brain MRI scan, as well as in monitoring of PML and detection and monitoring of PML-IRIS.

Gadolinium-enhanced MRI on first follow-up scan after treatment initiation could be considered in the absence of a new baseline scan. Yearly brain MRI while the patient is on the disease-modifying treatment is recommended for routine follow-up; longer intervals could be considered in clinically stable patients after the first few years of treatment, particularly if safety monitoring is not required. Specifically in the setting of MS, routine follow-up imaging of the spinal cord is indicated in monitoring patients with spinal cord phenotype (no or few brain lesions) for the detection of active spinal cord lesions. It is indicated in treatment switch decision making in the setting of inconclusive clinical presentation or brain MRI findings or the detection of active spinal cord lesions and exclusion of possible comorbidity involving the spinal cord.

Gadolinium contrast detects the breakdown of the blood-brain barrier that occurs with new demyelinating lesion development and re-activation of old lesions. In the setting of MS, the average duration of enhancement for individual brain lesions is 3 weeks, with most enhancing for 2 to 6 weeks. Rarely, MS lesions in the brain show persistent enhancement for >3 months with single-dose gadolinium. Most newly enhancing lesions will leave residual T2 hyperintensity after the enhancement resolves.

In ON, treatment typically involves corticosteroids to speed up visual recovery, whereas disease-modifying drugs are used to reduce recurrence and severity of attacks, particularly in cases associated with MS. Gadolinium-enhanced MRI can predict short-term visual improvement, with lesion length correlating with posttreatment visual acuity. MRI techniques can provide valuable information in ON follow-up and MS risk assessment. Close follow-up, including regular consultations and yearly brain MRI, is suggested for patients with factors favoring MS conversion. These factors include the following: The presence of brain lesions on baseline MRI is the strongest predictor of MS conversion. In the Optic Neuritis Treatment Trial, 72% of patients with one or more lesions on baseline brain MRI developed MS during follow-up, compared with only 25% of patients with no lesions [1]. The cumulative probability of developing MS in the 15 years after the onset of ON was 50%, and was strongly related to the presence of lesions on a baseline noncontrast-enhanced MRI of the brain [1]. The presence and number of spinal cord lesions at baseline are significant and independent predictors of higher disability and MS conversion [1]. Among patients without lesions on MRI, baseline factors associated with a substantially lower risk for MS included

male gender, optic disc swelling, and certain atypical features of ON [1]). Female gender is consistently identified as a risk factor for MS conversion [1]. The female/male ratio for MS converters is 2:1 [1]. Age at presentation also influences conversion risk, with younger patients having higher conversion rates [1]. The type of ON presentation affects conversion risk. Recurrent retrobulbar-type ON increases the risk of MS development [1]. The presence of prior nonspecific neurological symptoms is identified as a risk indicator for the development of MS [1]. CSF abnormalities have significant prognostic value for MS conversion. In 1976, Stendahl-Brodin and Link reported that 30% of patients with isolated ON had OCBs in CSF and, 6 years later, 81.8% developed MS, compared with only 4.2% without OCBs [1]. The CSF-IgG index is a significant predictor for the development of clinically definite MS [1]. Elevated CSF-IgG index is identified as a risk indicator for the development of MS [1]. For patients presenting with spinal cord symptoms, specific factors increase MS conversion risk. The risk factors for conversion to MS after spinal cord involvement include a family history for MS, severe impairment at onset, MS-typical lesions on brain MRI, abnormal IgG-index and the presence of CSF-specific OCBs [1]. Family history for MS was the highest risk factor [1]. Complete TM carries a low risk for MS (2%-8%), whereas incomplete transection carries a much higher risk (72%-80%) [1]. The risk of MS has been demonstrated to be higher after acute partial TM than after other CISs, such as ON [1]. Geographic and ethnic factors significantly influence MS conversion rates. Although the conversion rate to clinically definite MS has ranged from 13% to 87% in Europe and the United States, the cumulative probability of MS conversion over a 5-year period was 14.2% in Taiwan, 8.3% in Japan, and 12% in Mexico [1]. The conversion rate to MS in Asia and South America was relatively low compared with European and United States studies [1]. Both ethnic and regional factors may be playing a role in the wide range of MS conversion rates in different countries [1].

Follow-up guidelines for TM vary depending on the specific disease context in which TM occurs. Therapies can significantly reduce gadolinium-enhancing lesions, indicating suppression of active inflammation. However, brain and spinal cord atrophy may still progress, correlating with increased disability.

Natalizumab, a highly effective MS therapy, is associated with an increased risk of PML. Early PML detection is challenging due to heterogeneous MRI findings, including various patterns of inflammation and contrast enhancement. PML-immune reconstitution inflammatory syndrome (IRIS) is a potential complication following natalizumab cessation, with contrast enhancement being the most common early imaging sign, typically presenting as patchy or punctate patterns in the PML lesion periphery. Other MRI characteristics of PML-IRIS include new perivascular T2 hyperintense lesions and meningeal inflammation.

Brain MRI plays a crucial role in monitoring disease activity and progression in patients with known demyelinating disease, even when they are clinically stable. MRI-based disease activity is 5 to 10 times more frequent than clinical evaluation of relapses, suggesting that most of the enhancing lesions are clinically silent [1]. This indicates that subclinical disease activity can occur without corresponding clinical symptoms, making routine surveillance imaging important for disease monitoring. The high sensitivity of MRI in depicting brain and spinal cord demyelinating plaques has made this technique the most important paraclinical tool in current use, not only for the early and accurate diagnosis of MS, but also for understanding the natural history of the disease and monitoring and predicting the efficacy of disease-modifying treatments [1].

Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance

#### imaging.

#### R. MRI head without IV contrast

The literature supports various MRI approaches for surveillance imaging depending on the specific demyelinating disease and clinical context. There are specific clinical scenarios where MRI brain without IV contrast would be preferred over contrast-enhanced imaging for surveillance in known demyelinating disease without new neurologic symptoms.

In patients who require long-term routine follow-up of a chronic demyelinating disease, such as in the setting of MS, a noncontrast MRI could be considered as well to minimize repeated gadolinium load [30] if baseline imaging is available. Specifically in the setting of MS, the use of gadolinium-based contrast agents is not recommended to show dissemination in time on serial MRI scans in case of standard monitoring for subclinical disease activity, if a previous and recent (ie, within approximately 1 year) MRI scan is available that was done with similar technical parameters. It is not recommended in new baseline (ie, usually 3–6 months after treatment initiation) MRI scan, in short follow-up MRI (ie, within 6 months) done to confirm disease activity in patients with isolated MRI activity on the previous MRI scan, or for PML screening. It is also strictly contraindicated during pregnancy and indicated only if essential for patient management during lactation [30].

Use of gadolinium is not recommended routinely for follow-up when initial brain MRI is not diagnostic for MS [30]. This indicates that in patients with known demyelinating disease where the initial diagnosis was not definitively established through MRI criteria, routine surveillance can be performed without IV contrast. For routine follow-up in MS, baseline brain MRI (with gadolinium if required by drug label) is recommended before starting or switching disease-modifying treatment [30]. This suggests that contrast may only be necessary when specifically required by medication protocols rather than for routine surveillance. Yearly brain MRI while the patient is on the disease-modifying treatment is recommended for routine follow-up [30]. The literature does not specify that contrast is mandatory for this routine yearly surveillance imaging. New baseline brain MRI usually at 3-6 months after treatment onset is recommended to avoid misinterpretation of lesions that developed before therapeutic onset [30]. Contrast is suggested if showing disease activity with presence of gadolinium enhancing lesions is required to initiate or change a specific disease-modifying treatment [30].

The clinical scenario where MRI brain without IV contrast would be useful for surveillance includes routine follow-up imaging in stable patients on established disease-modifying therapy where treatment decisions do not depend on detecting active enhancement. However, when contrast is deemed necessary, it should always be performed in conjunction with precontrast imaging rather than as a contrast-only study.

In MS, new baseline brain MRI usually at 3–6 months after treatment onset is recommended to avoid misinterpretation of lesions that developed before therapeutic onset. Longer intervals are to be considered in patients who are treated with disease-modifying therapies that are slow acting. New baseline MRI usually at 3–6 months after treatment initiation is recommended without gadolinium unless highly active disease at baseline or unexpected clinical activity. In patients who show MRI disease activity that is not associated with clinical activity on a follow-up scan, a new MRI scan without gadolinium 6 months later may be considered. However detecting new or enlarging T2 lesions compared with a previous study would also indicate new inflammatory activity in the setting of known demyelinating disease even in the absence of gadolinium enhancement

A proposed PML surveillance protocol includes T2 FLAIR and DWI sequences only [24, 31] and can be used to detect PML in the presymptomatic phase for at-risk patients on some disease-modifying therapies.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### S. MRI lumbar spine with IV contrast

There is insufficient literature to support the use of MRI lumbar spine in surveillance of CNS demyelinating disease in patients with stable neurologic examination. The literature indicates that demyelinating diseases of the CNS predominantly involve the brain and spinal cord, but the usefulness in imaging the lumbar spine is limited since thoracic spine imaging would most likely be sufficient in capturing most abnormalities of the lower spinal cord relating to demyelinating lesions [1]. In MS, routine follow-up imaging of the spinal cord is indicated in monitoring patients with spinal cord phenotype (no or few brain lesions) for the detection of active spinal cord lesions [30]. It is also indicated in patients with worsening disability that cannot be explained by brain MRI for the detection of active spinal cord lesions and the exclusion of possible comorbidity involving the spine [30]. However, the literature does not specifically support routine lumbar spine surveillance imaging in stable patients, as the prevalence of spinal cord abnormalities is as high as 74% to 92% in established MS, and depends on the clinical phenotype of MS [1], with most abnormalities occurring in the cervical and thoracic regions rather than the lumbar region.

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### T. MRI lumbar spine without and with IV contrast

There is insufficient literature to support the use of MRI lumbar spine in surveillance of CNS demyelinating disease in patients with stable neurologic examination. The literature indicates that demyelinating diseases of the CNS predominantly involve the brain and spinal cord, but the usefulness in imaging the lumbar spine is limited since thoracic spine imaging would most likely be sufficient in capturing most abnormalities of the lower spinal cord relating to demyelinating lesions [1].

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### **U. MRI lumbar spine without IV contrast**

There is insufficient literature to support the use of MRI lumbar spine in surveillance of CNS demyelinating disease in patients with stable neurologic examination. The literature indicates that demyelinating diseases of the CNS predominantly involve the brain and spinal cord, but the usefulness in imaging the lumbar spine is limited since thoracic spine imaging would most likely be sufficient in capturing most abnormalities of the lower spinal cord relating to demyelinating lesions [1].

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### V. MRI orbits with IV contrast

The available literature provides insufficient support for routine MRI orbits surveillance in stable

CNS demyelinating disease patients. Orbital imaging should primarily be reserved for patients who develop new visual symptoms or have chronic progressive optic nerve symptoms, rather than being part of routine surveillance in clinically stable patients. There is no indication for obtaining orbital MRI with IV contrast in surveillance imaging. The literature indicates that when contrast is used, both pre- and postcontrast imaging should be performed together to properly assess for enhancement patterns [24].

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### W. MRI orbits without and with IV contrast

There is insufficient literature to support the use of MRI orbits in surveillance of CNS demyelinating disease in patients with stable neurologic examination.

The literature indicates that in MS, routine monitoring of the optic nerves is recommended with new visual symptoms that are suggestive of comorbidity affecting the optic nerve [30]. However, this recommendation specifically applies to patients with new symptoms rather than stable patients undergoing routine surveillance. The literature also indicates that routine monitoring of the optic nerves is recommended with chronic progressive optic nerve symptoms, and patients with repeated isolated optic nerve relapses [30]. These scenarios involve patients with ongoing or recurrent symptoms rather than stable examinations. The primary indication for orbital MRI in surveillance would be in patients with new visual symptoms. Many demyelinating diseases of the CNS are known to involve the optic nerves and can present with symptoms of ON [24]. In MOGAD, routine MRI of the brain, spine, or orbits is not typically part of clinical practice, as lesions often resolve after acute attacks. However, a single MRI scan after an attack may be useful to establish a new baseline for future comparison.

The recommended sequences for orbital MRI in the setting of ON include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of ≤2 mm, with coverage through the optic chiasm [24]. When orbital MRI is performed, the literature supports the use of MRI orbits without and with IV contrast. The use of IV contrast is preferred particularly when evaluating for active ON, given that a finding on orbital MR of acute ON is optic nerve enhancement [24].

### Variant 3:Adult. Known demyelinating disease. Stable neurologic examination. Surveillance imaging.

#### X. MRI orbits without IV contrast

There is no relevant literature to support the use of MRI orbits without IV contrast for surveillance imaging in patients with known demyelinating disease and a stable neurologic examination.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

The goal of imaging is to assess for acute change or progression in the setting of known demyelinating disease. This imaging information improves patient outcome by helping to determine whether there is worsening of demyelinating disease versus a secondary acute process and thereby guiding timely management. This imaging information benefits the patient by reducing potential delay in appropriate treatment and by hastening patient recovery.

Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### A. CT cervical and thoracic spine with IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### B. CT cervical and thoracic spine without and with IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine without and with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### C. CT cervical and thoracic spine without IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine without IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### D. CT head with IV contrast

There is no relevant literature to support the use of CT head with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### E. CT head without and with IV contrast

There is no relevant literature to support the use of CT head without and with IV contrast for initial imaging evaluation of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### F. CT head without IV contrast

There is no relevant literature to support the use of CT head without IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### **G. CT lumbar spine with IV contrast**

There is no relevant literature to support use of CT lumbar spine with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### H. CT lumbar spine without and with IV contrast

There is no relevant literature to support the use of CT lumbar spine without and with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating

disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### I. CT lumbar spine without IV contrast

There is no relevant literature to support the use of CT lumbar spine without IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### J. CT orbits with IV contrast

There is no relevant literature to support the use of CT orbits with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### K. CT orbits without and with IV contrast

There is no relevant literature to support the use of CT orbits without and with IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### L. CT orbits without IV contrast

There is no relevant literature to support the use of CT orbits without IV contrast for initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### M. MRI cervical and thoracic spine with IV contrast

Limited literature supports the use of postcontrast MRI of the spine alone. The available evidence indicates that both pre- and postcontrast imaging should be performed together for initial imaging. On the other hand, postcontrast only T1- and T2-weighted imaging of the spine can sometimes be performed to help with overall examination time and patient tolerance when scanning multiple body parts and when evaluating primarily for intradural rather than extradural or vertebral disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### N. MRI cervical and thoracic spine without and with IV contrast

Available literature supports the use of MRI cervical and thoracic spine without and with IV contrast for evaluation of new or progressive neurologic deficits in known demyelinating disease.

For patients with established MS developing new or progressive neurologic deficits, MRI of the cervical and thoracic spine with and without IV contrast could detect active disease activity, assess for new lesions, and guide treatment decisions. This is particularly important given that subclinical disease activity occurs much more frequently than clinically apparent relapses [1]. High doses of gadolinium and a long postinjection delay can increase the detection of active spinal cord lesions

[1], making the presence of contrast enhancement particularly valuable in the assessment of new symptoms in established MS patients. In patients with established MS who develop new or progressive neurologic symptoms, spinal MRI is recommended selectively: one set of guidelines from the Consortium of MS Centers Task Force advises such imaging when brain MRI is nondiagnostic [24] or when symptoms point to spinal cord involvement, whereas another calls for full spine imaging in cases of clinical progression as noted by Sasiadek et al [34]. In MS, routine follow-up imaging of the spinal cord is indicated in patients with worsening disability that cannot be explained by brain MRI for the detection of active spinal cord lesions and the exclusion of possible comorbidity involving the spine or spinal cord [30]. Active lesions are rarer in the spinal cord than the brain and are more frequently associated with new clinical symptoms [1]. Contrast is recommended by the 2021 MAGNIMS-CMSC-NAIMS consensus guidelines if showing disease activity with the presence of gadolinium enhancing lesions is required to initiate or change a specific disease-modifying treatment [30]. It is indicated in patients with repeated spinal cord relapse for the detection of active spinal cord lesions and exclusion of alternative diagnosis or possible comorbidity involving the spinal cord. It is indicated in atypical spinal cord relapse or atypical spinal cord symptoms or signs suggestive of comorbidity for the detection of active spinal cord lesions and the exclusion of alternative diagnosis or possible comorbidity involving the spinal cord [30].

Some guidelines recommend routine use of gadolinium at key timepoints [24], whereas others reserve contrast for scenarios such as relapse, high lesion burden, or differential diagnosis [35]. In select recommendations, macrocyclic gadolinium agents are preferred to reduce risk [26]. In summary, clinical practice guidelines support a tailored imaging approach that uses routine brain MRI for all patients, adds spinal MRI when clinical findings warrant, and employs contrast—whether routine or selective—in accordance with the patient's clinical status and treatment context [24].

In MOGAD, an MRI scan after an attack may be useful to establish a new baseline for future comparison, but this is not specific to the clinical scenario of new or progressive neurologic symptoms. For NMOSD, routine spinal cord and brain MRI during follow-up is recommended [22, 33], though no specific imaging interval is detailed for routine imaging in NMO or MOGAD in the absence of new neurological symptoms. Spinal cord MRI is indicated when patients with established NMO/MOGAD develop new TM symptoms. The spinal cord lesions in NMO typically extend over 3 or more contiguous vertebral segments and occasionally the entire spinal cord (longitudinally extensive spinal cord lesions); they are centrally located (preferential central graymatter involvement) and affect much of the cross-section on axial images [1].

In ON, treatment typically involves corticosteroids to speed up visual recovery, while disease-modifying drugs are used to reduce recurrence and severity of attacks, particularly in cases associated with MS. Gadolinium-enhanced MRI can predict short-term visual improvement, with lesion length correlating with post-treatment visual acuity. MRI techniques can provide valuable information in ON follow-up and MS risk assessment. Close follow-up, including regular consultations and yearly brain MRI, is recommended for patients with factors favoring MS conversion [2, 3, 36]. Please refer to the ACR AC narrative on ON for further details [37].

Treatments can significantly reduce gadolinium-enhancing lesions, indicating suppression of active inflammation. However, brain and spinal cord atrophy may still progress, correlating with increased

disability.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### O. MRI cervical and thoracic spine without IV contrast

Available literature supports the use of MRI cervical and thoracic spine without IV contrast but indicates that contrast-enhanced imaging is preferred. In MS, routine follow-up imaging of the spinal cord is indicated in patients with worsening disability that cannot be explained by brain MRI for the detection of spinal cord lesions [30]. However, the use of IV contrast is helpful in detecting active demyelinating lesions [24].

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### P. MRI head with IV contrast

There is no relevant literature to support the use of MRI head with IV contrast alone in initial imaging of new or progressive neurologic deficits in patients with known demyelinating disease.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### Q. MRI head without and with IV contrast

Available literature strongly supports the use of MRI head without and with IV contrast for evaluation of new or progressive neurologic deficits in known demyelinating disease. The high sensitivity of MRI in depicting brain and spinal cord demyelinating plaques has made this technique the most important paraclinical tool in current use [1].

The literature strongly supports the use of MRI head without and with IV contrast for evaluation of new or progressive neurologic deficits in established MS. Patients with established MS who develop new or progressive neurologic symptoms are advised to undergo brain MRI in all cases [24]. For patients with established MS developing new or progressive neurologic deficits, MRI brain with and without IV contrast detects active disease activity, assesses for new lesions, and guides treatment decisions. This is particularly important given that subclinical disease activity occurs much more frequently than clinically apparent relapses [1]. Contrast-enhanced T1-weighted images are routinely used in the study of MS to provide a measure of inflammatory activity in vivo [1]. Gadolinium-based contrast detects the breakdown of the blood-brain barrier that occurs with new development of demyelinating lesions and re-activation of old lesions [24]. High doses of gadolinium and a long postinjection delay can increase the detection of active spinal cord lesions [1], making contrast enhancement particularly valuable in the assessment of new symptoms in established MS patients. In MS, follow-up brain MRI with gadolinium is recommended to evaluate unexpected clinical worsening and dissemination in time [24, 31]. Contrast is recommended by the 2021 MAGNIMS-CMSC-NAIMS consensus guidelines if detection or confirmation of clinical disease activity is required in patients without a recent reference brain MRI scan [30]. For MS, protocols for regular follow-up are described with intervals ranging from 6 months to 2 years, particularly when unexpected clinical worsening occurs [31]. In MS patients who show MRI disease activity that is not associated with clinical activity on a follow-up scan, a new MRI scan without gadolinium 6 months later may be considered [30].

The literature strongly supports the use of MRI brain and spine imaging for patients with established NMO and MOGAD who develop new or progressive neurologic deficits. Brain MRI

abnormalities exist in a significant proportion (50%-85%) of patients with NMO [1]. Brain MRI lesions are often asymptomatic, but sometimes are associated with symptoms even at disease onset [1]. The brain syndromes in NMO include autoimmune endocrinopathy, hypothalamic dysfunction, intractable hiccup/nausea, focal symptoms (especially brainstem), encephalopathy accompanied with corpus callosum lesions [1]. For NMOSD, routine spinal cord and brain MRI during follow-up is recommended [22, 33]. In MOGAD, an MRI scan after an attack may be useful to establish a new baseline for future comparison. Clinical presentation can include monophasic or recurrent episodes of ON, myelitis, brain stem syndromes, ADEM, and symptoms of encephalitis such as seizures. MOGAD patients are often scanned after a first presentation of ON, longitudinally extensive TM and/or other clinical symptoms; thus, most imaging findings are cross-sectional and follow-up imaging data is scant [22]. During the acute and subacute phase, the lesions are tumefactive and show contrast uptake [1]. MRI of the affected optic nerve demonstrates swelling and loss of blood–brain barrier integrity with gadolinium enhancement that can extend into the optic chiasm [1].

In a patient with TM and new or progressive neurologic deficits, MRI of the brain may be useful in assessing for conversion to MS. Clinicians increasingly rely on MRI findings for treatment decisions, with even one new T2 lesion in MS potentially prompting therapy changes. Various MRI techniques provide insights into disease progression, axonal injury, and brain atrophy, contributing to improved clinical decision-making in the setting of demyelinating disease. Natalizumab, a highly effective MS therapy, is associated with an increased risk of PML, which may present with a wide variety of neurologic deficits. Early PML detection is challenging due to heterogeneous MRI findings, including various patterns of inflammation and contrast enhancement. PML-IRIS is a potential complication following natalizumab cessation, with contrast enhancement being the most common early imaging sign, typically presenting as patchy or punctate patterns in the PML lesion periphery [38, 39]. Other MRI characteristics of PML-IRIS include new perivascular T2 lesions and meningeal inflammation. Treatments can significantly reduce gadolinium-enhancing lesions, indicating suppression of active inflammation. However, brain and spinal cord atrophy may still progress, correlating with increased disability.

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### R. MRI head without IV contrast

The available literature supports the use of MRI head without IV contrast when a diagnosis of demyelinating disease has been established and there are worsening clinical symptoms, but indicates that contrast-enhanced imaging is preferred. In MS, follow-up brain MRI is recommended to evaluate unexpected clinical worsening [24, 31]. However, the use of IV contrast is helpful in detecting active demyelinating lesions and confirming disease activity [24, 30].

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### S. MRI lumbar spine with IV contrast

There is insufficient evidence to support the use of MRI lumbar spine with IV contrast as initial imaging in patients with known demyelinating disease and new or progressive neurologic deficits. In MS, follow-up imaging of the spinal cord with cervical spine and/or thoracic spine MRI may be indicated in patients with worsening disability that cannot be explained by brain MRI [30].

Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### T. MRI lumbar spine without and with IV contrast

There is insufficient evidence to support the use of MRI lumbar spine without and with IV contrast as initial imaging examination in patients with known demyelinating disease and new or progressive neurologic deficits. In MS, follow-up imaging of the spinal cord with cervical spine and/or thoracic spine MRI may be indicated in patients with worsening disability that cannot be explained by brain MRI [30].

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### **U. MRI lumbar spine without IV contrast**

There is insufficient evidence to support the use of MRI lumbar spine with IV contrast as initial imaging in patients with known demyelinating disease and new or progressive neurologic deficits. In MS, follow-up imaging of the spinal cord with cervical spine and/or thoracic spine MRI may be indicated in patients with worsening disability that cannot be explained by brain MRI [30].

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### V. MRI orbits with IV contrast

Evaluation of the optic nerves is recommended with new visual symptoms that are suggestive of comorbidity affecting the optic nerve [30]. The reader is directed to the ACR Appropriateness Criteria® topic on "Vision Loss" for additional discussion of ON [37].

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### W. MRI orbits without and with IV contrast

The literature supports the use of MRI orbits without and with IV contrast when new visual symptoms are present in known demyelinating disease suggestive of comorbidity localizing to the optic nerve, chronic progressive optic nerve symptoms, and patients with repeated isolated optic nerve relapses [30]. The recommended sequences for orbital MRI in the setting of ON include a coronal STIR or fat-suppressed T2 and a postgadolinium fat-suppressed T1 with a section thickness of  $\leq 2$  mm, with coverage through the optic chiasm [24]. The reader is directed to the ACR Appropriateness Criteria® topic on "Vision Loss" for additional discussion of ON [37].

### Variant 4:Adult. Known demyelinating disease. New or progressive neurologic deficits. Initial imaging.

#### X. MRI orbits without IV contrast

The literature supports the use of MRI orbits without IV contrast but indicates that contrast-enhanced imaging is preferred. In MS, evaluation of the optic nerves is recommended with new visual symptoms with prechiasmatic localization [30]. However, the use of IV contrast is preferred particularly when evaluating for active ON, given that a key finding is optic nerve enhancement [24]. The reader is directed to the ACR Appropriateness Criteria® topic on "Vision Loss" for additional discussion of ON [37].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

The goal of imaging is to diagnose or exclude demyelinating disease in the peripheral nervous system. This imaging information improves patient outcome by helping to determine whether there is demyelinating disease and thereby guiding timely management. This imaging information benefits the patient by reducing potential delay in appropriate treatment and by hastening patient

recovery.

Peripheral nervous system demyelinating diseases include conditions such as Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), anti-MAG (myelin-associated glycoprotein) peripheral neuropathy, polyneuropathy-organomegaly-endocrinopathy-monoclonal gammopathy-skin (POEMS) syndrome, and Charcot-Marie-Tooth (CMT) disease, and other inflammatory neuropathies [40, 41]. These conditions primarily affect peripheral nerve roots, plexuses, and peripheral nerves rather than the CNS [40, 41]. These conditions can be caused by infectious agents, genetic factors, and immune-related mechanisms. The diagnosis relies on clinical presentation, electrophysiological studies, CSF analysis, and imaging [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### A. CT cervical and thoracic spine with IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine with IV contrast for initial evaluation of suspected peripheral nervous system demyelinating disease. CT imaging is not the preferred imaging modality for peripheral demyelinating diseases because of its limited soft-tissue characterization and poor visualization of nerve roots and peripheral nerves when compared to MRI [1]. MRI is superior for detecting nerve root enhancement and thickening associated with peripheral demyelinating conditions [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### B. CT cervical and thoracic spine without and with IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine without and with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### C. CT cervical and thoracic spine without IV contrast

There is no relevant literature to support the use of CT cervical and thoracic spine without IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease. Although CT may demonstrate degenerative changes or other abnormalities that could result in spinal cord or nerve root compression, it has limited soft-tissue characterization and poor visualization of nerve roots and peripheral nerves when compared with MRI [1]. MRI is superior for detecting nerve root enhancement and thickening associated with peripheral demyelinating conditions [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### D. CT head with IV contrast

There is no relevant literature to support the use of CT head with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease. Peripheral demyelinating diseases primarily affect the peripheral nervous system rather than the CNS [40, 41]. CT imaging of the head would not be expected to provide relevant diagnostic information for peripheral demyelinating conditions [1]. To directly assess the peripheral nervous system

demyelinating disease, the location of interest should be imaged such as the cervical plexus, brachial plexus, or lumbosacral plexus. Some peripheral demyelinating diseases could be associated with white matter changes in the brain. Although brain imaging could be helpful, it might not be useful for initial imaging.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### E. CT head without and with IV contrast

There is no relevant literature to support the use of CT head without and with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### F. CT head without IV contrast

There is no relevant literature to support the use of CT head without IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### **G. CT lumbar spine with IV contrast**

There is no relevant literature to support the use of CT lumbar spine with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### H. CT lumbar spine without and with IV contrast

There is no relevant literature to support the use of CT lumbar spine without and with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### I. CT lumbar spine without IV contrast

There is no relevant literature to support the use of CT lumbar spine without IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### J. CT orbits with IV contrast

There is no relevant literature to support the use of CT orbits with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### K. CT orbits without and with IV contrast

There is no relevant literature to support the use of CT orbits without and with IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### L. CT orbits without IV contrast

There is no relevant literature to support the use of CT orbits without IV contrast for initial evaluation of patients with suspected peripheral nervous system demyelinating disease.

# Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### M. MRI brachial plexus with IV contrast

Insufficient evidence supports the use of postcontrast MRI of the brachial plexus alone for initial imaging of patients with suspected demyelinating disease of the peripheral nervous system. Instead, the available evidence indicates that both pre- and postcontrast imaging should be performed together. MRI of the brachial plexus may be indicated in patients with suspected peripheral demyelinating disease presenting with upper extremity weakness [40, 41].

# Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### N. MRI brachial plexus without IV contrast

The literature supports the use of MRI brachial plexus without IV contrast for initial imaging of patients with suspected demyelinating disease of the peripheral nervous system but indicates that contrast-enhanced imaging is preferred. MRI of the brachial plexus may be indicated in patients with suspected peripheral demyelinating disease presenting with upper extremity weakness [40, 41]. However, the use of IV contrast is helpful in detecting nerve enhancement and inflammation associated with peripheral demyelinating conditions [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### O. MRI brachial plexus without and with IV contrast

Available evidence supports the use of MRI brachial plexus without and with IV contrast for evaluation of suspected peripheral nervous system demyelinating disease. MRI can be useful in the evaluation of peripheral demyelinating diseases, particularly for imaging plexuses and proximal nerve segments [40, 41]. In GBS and chronic inflammatory demyelinating polyneuropathy (CIDP), MRI may demonstrate nerve enhancement, thickening, and signal abnormalities in the brachial plexus region [40, 41].

The diagnosis and treatment of CIPD remains challenging. For treatment, IV immunoglobulin (IVIg) or corticosteroids are recommended as initial therapy for typical CIDP and variants, with plasma exchange recommended if these are ineffective. IVIg is suggested as first-line treatment for motor CIDP. Key MRI features in CIDP include thickening of spinal nerve roots, peripheral nerves in the lumbar and brachial plexuses, and bilateral trigeminal nerves. MRI reveals significant hypertrophy of lumbosacral nerve roots and sciatic nerves in CIDP patients compared to controls. MRI, along with ultrasound (US), can detect increased cross-sectional area of nerves, which correlates with conduction velocity and amplitude in electrophysiological studies. Notably, aggressive CIDP cases show marked increases in T2 signal of plexuses and peripheral nerves. The diagnosis of CIDP rests upon a combination of clinical, electrodiagnostic, and laboratory features with exclusions to eliminate other disorders that may mimic CIDP. CSF examination, US of proximal median nerve segments, cervical spinal roots, and the brachial plexus or MRI of spinal roots, brachial or lumbar plexus, and a trial of immunotherapy with objective assessment of endpoints may assist the diagnosis. Most commonly, the disease begins with paraesthesia and weakness in the distal limbs as well as difficulty walking. The clinical examination shows progressive symmetric proximal and distal muscle weakness, sensory loss, and decreased or absent deep tendon reflexes. The disease

course is steadily progressive for more than 8 weeks, but can be RR. In contrast with GBS, cranial nerves are less frequently affected and respiratory or autonomic involvement is exceptional. Criteria for CIDP have been most closely linked to electrodiagnostic criteria for detection of peripheral nerve demyelination. The European Academy of Neurology/Peripheral Nerve Society guideline suggest to use US in adult patients to diagnose CIDP in patients fulfilling diagnostic criteria for possible CIDP but not for CIDP. The diagnosis of CIDP may be more likely if there is nerve enlargement of at least 2 sites in proximal median nerve segments and/or the brachial plexus. Enlargement mainly of proximal nerve segments in arm nerves and spinal nerve roots are the most characteristic feature in CIDP. The European Academy of Neurology/Peripheral Nerve Society guideline suggest not to use MRI in adult patients to diagnose CIDP except in patients fulfilling diagnostic criteria for possible CIDP but not for CIDP. CIDP may be more likely if there is enlargement and/or increased signal intensity of nerve roots on T2-weighted MRI sequences with fat suppression. MRI of the brachial and lumbosacral plexus may aid in the diagnosis of CIDP by showing nerve root hypertrophy, increased signal intensity or contrast enhancement. A condition in which MRI may be considered in patients fulfilling only possible electrodiagnostic criteria is when US results are noncontributory. In children with suspected CIDP, systematic studies on MRI are lacking, inherited demyelinating neuropathies are more prevalent than CIDP and can also show nerve size increase. Before concluding that US or MRI abnormalities are supportive of CIDP, there should be no laboratory/clinical features that suggest other diseases such as multifocal motor neuropathy, demyelinating CMT disease, immunoglobulin M paraproteinemic neuropathy (especially with anti-MAG antibodies), POEMS syndrome, diabetic radiculoplexus neuropathy, amyloid neuropathy, neuralgic amyotrophy, leprosy, neurofibromatosis, or neurolymphomatosis [40].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### P. MRI cervical and thoracic spine with IV contrast

Insufficient evidence supports the use of postcontrast MRI of the cervical and thoracic spine alone for initial imaging of patients with suspected demyelinating disease of the peripheral nervous system. The available evidence indicates that both pre- and postcontrast imaging should be performed together. MRI of the cervical and thoracic spine may be indicated in patients with suspected peripheral demyelinating disease to evaluate nerve roots [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### Q. MRI cervical and thoracic spine without and with IV contrast

The literature supports the use of MRI cervical and thoracic spine without and with IV contrast for initial imaging of patients with suspected peripheral nervous system demyelinating disease. In GBS and CIDP, MRI may demonstrate nerve root enhancement, thickening, and signal abnormalities in the cervical and thoracic regions [40, 41]. The nerve roots may show enhancement and thickening in these peripheral demyelinating conditions [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### R. MRI cervical and thoracic spine without IV contrast

The literature supports the use of MRI cervical and thoracic spine without IV contrast for initial imaging of patients with suspected demyelinating disease of the peripheral nervous system but

indicates that contrast-enhanced imaging is preferred. MRI can be useful in the evaluation of peripheral demyelinating diseases for imaging nerve roots [40, 41]. However, the use of IV contrast is helpful in detecting nerve root enhancement associated with peripheral demyelinating conditions [40, 41].

# Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### S. MRI head with IV contrast

There is insufficient evidence to support the use of MRI head with IV contrast in the initial imaging of patients with suspected demyelinating disease of the peripheral nervous system. Although peripheral demyelinating diseases primarily affect the peripheral nervous system, brain MRI may occasionally be considered as an adjunct imaging test to exclude CNS involvement or alternative diagnoses [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### T. MRI head without and with IV contrast

There is insufficient evidence to support the use of MRI head without and with IV contrast in the initial imaging of patients with suspected demyelinating disease of the peripheral nervous system, though it may be useful in certain clinical situations when patients present with cranial nerve deficits. Although peripheral demyelinating diseases primarily affect the peripheral nervous system, brain MRI may occasionally be considered as an adjunct imaging test to exclude CNS involvement or alternative diagnoses [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### **U. MRI head without IV contrast**

There is insufficient evidence to support the use of MRI head without IV contrast in the initial imaging of patients with suspected demyelinating disease of the peripheral nervous system. Although peripheral demyelinating diseases primarily affect the peripheral nervous system, brain MRI may occasionally be considered as an adjunct imaging test to exclude CNS involvement or alternative diagnoses [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### V. MRI lumbar spine with IV contrast

There is limited evidence to support the use of MRI lumbar spine with IV contrast alone in the initial imaging of patients with suspected demyelinating disease of the peripheral nervous system. The available evidence indicates that both pre- and postcontrast imaging should be performed together. MRI of the lumbar spine may be indicated in patients with suspected peripheral demyelinating disease to evaluate the cauda equina and nerve roots [40, 41]. However, in practice, MRI should be performed both without and with IV contrast if IV contrast is being used [24].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### W. MRI lumbar spine without and with IV contrast

In demyelinating diseases of the peripheral nervous system such as GBS and CIDP, MRI lumbar spine without and with IV contrast may demonstrate cauda equina and nerve root enhancement, thickening, and signal abnormalities [40, 41]. The cauda equina and nerve roots may show

enhancement and thickening in these peripheral demyelinating conditions [40, 41].

GBS is a rare immune-mediated disorder of peripheral nerves and nerve roots, often triggered by infections. The European Academy of Neurology/Peripheral Nerve Society have developed evidence-based guidelines for GBS diagnosis and treatment using Grading of Recommendations, Assessment, Development and Evaluation methodology. Although not explicitly mentioned in current guidelines, contrast-enhanced spinal MRI can be a valuable supplementary diagnostic tool, especially when clinical and electrophysiological findings are inconclusive. Treatment recommendations include IVIg or plasma exchange. GBS is an acute inflammatory demyelinating polyneuropathy. Besides weakness and sensory disturbances, patients may have cranial nerve involvement, respiratory insufficiency, autonomic dysfunction, and pain. GBS is more likely if there is a history of recent diarrhea or respiratory infection; CSF examination is valuable. Electrodiagnostic testing is advised to support the diagnosis. Anti-GQ1b antibody testing should be considered when Miller Fisher syndrome is suspected. Nodal-paranodal antibodies should be tested when autoimmune nodopathy is suspected. MRI or US imaging should be considered in atypical cases. Changing the diagnosis to acute-onset CIPD should be considered if progression continues after 8 weeks from onset. About 5% of patients initially diagnosed with GBS later turn out to have acute-onset CIPD and should be treated as for CIDP. The European Academy of Neurology/Peripheral Nerve Society guideline suggest against using nerve MRI or US as routine add-on tests for the diagnosis of GBS with a typical presentation. The presence of MRI nerve root enhancement is supportive of GBS, but does not rule out other causes of polyradiculopathy. The most common MRI finding in GBS is enhancement of the cauda equina nerve roots. This enhancement indicates a breakdown of the blood-nerve barrier due to inflammatory infiltration. Though MRI can be a useful supplementary diagnostic tool for GBS, further controlled studies are needed to confirm its specificity. When the disease course is considered compatible with acuteonset CIPD, the presence of widespread nerve enlargement on nerve US or MRI may favor the diagnosis of acute-onset CIPD, but is not specific for the diagnosis. Whole spine MRI with IV contrast may aid in ruling out spinal cord compression, TM, spinal cord tumorsm or other mimics. Nerve MRI or US should only be considered if the diagnosis of GBS is uncertain, possibly to rule out other causes. Abnormal nerve MRI and US may help to localize the pathology to the nerve roots, but the tests lack specificity and does not rule out GBS when normal. In Bickerstaff brainstem encephalitis, a form of Miller Fisher syndrome variant, brain MRI may show white matter changes [41].

# Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging. X. MRI lumbar spine without IV contrast

The literature supports the use of MRI lumbar spine without IV contrast to evaluate for lesions affecting the cauda equina nerve roots but indicates that contrast-enhanced imaging is preferred. MRI can be useful in the evaluation of peripheral demyelinating diseases for imaging the cauda equina and nerve roots [40, 41]. However, the use of IV contrast is helpful in detecting nerve root enhancement associated with peripheral demyelinating conditions [40, 41].

# Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### Y. MRI lumbosacral plexus with IV contrast

Insufficient evidence supports the use of postcontrast MRI of the lumbosacral plexus alone for initial imaging of patients with suspected demyelinating disease of the peripheral nervous system.

Instead, the available evidence indicates that both pre- and postcontrast imaging should be performed together. MRI of the lumbosacral plexus may be indicated in patients with suspected peripheral demyelinating disease presenting with lower extremity weakness [40, 41].

# Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### Z. MRI lumbosacral plexus without and with IV contrast

MRI can be useful in the evaluation of peripheral demyelinating diseases, particularly for imaging plexuses and proximal nerve segments [40, 41]. In demyelinating diseases of the peripheral nervous system such as GBS and CIDP, MRI may demonstrate nerve enhancement, thickening, or signal abnormalities in the lumbosacral plexus region [40, 41].

The diagnosis and treatment of CIDP remain challenging. For treatment, IVIg or corticosteroids are recommended as initial therapy for typical CIDP and variants, with plasma exchange recommended if these are ineffective. IVIg is suggested as first-line treatment for motor CIDP. Key MRI features in CIDP include thickening of spinal nerve roots, peripheral nerves in the lumbar and brachial plexuses, and bilateral trigeminal nerves. MRI reveals significant hypertrophy of lumbosacral nerve roots and sciatic nerves in CIDP patients compared to controls. MRI, along with US, can detect increased cross-sectional area of nerves, which correlates with conduction velocity and amplitude in electrophysiological studies. Notably, aggressive CIDP cases show marked increases in T2 signal of plexuses and peripheral nerves. The diagnosis of CIDP rests upon a combination of clinical, electrodiagnostic, and laboratory features with exclusions to eliminate other disorders that may mimic CIDP. CSF examination, US of the proximal median nerve segments, cervical spinal roots, and the brachial plexus or MRI of spinal roots, brachial or lumbar plexus, and a trial of immunotherapy with objective assessment of endpoints may assist the diagnosis. Most commonly, the disease begins with paresthesia and weakness in the distal limbs as well as difficulty walking. The clinical examination shows progressive symmetric proximal and distal muscle weakness, sensory loss, and decreased or absent deep tendon reflexes. The disease course is steadily progressive for more than 8 weeks, but can be RR. In contrast with GBS, cranial nerves are less frequently affected and respiratory or autonomic involvement is exceptional. Criteria for CIDP have been most closely linked to electrodiagnostic criteria for detection of peripheral nerve demyelination. The European Academy of Neurology/Peripheral Nerve Society guideline suggest to use US in adult patients to diagnose CIDP in patients fulfilling diagnostic criteria for possible CIDP but not for CIDP. Enlargement, mainly of the proximal nerve segments in arm nerves and spinal nerve roots, are the most characteristic feature in CIDP. The European Academy of Neurology/Peripheral Nerve Society guideline suggest not to use MRI in adult patients to diagnose CIDP except in patients fulfilling diagnostic criteria for possible CIDP but not for CIDP. CIDP may be more likely if there is enlargement and/or increased signal intensity of nerve roots on T2-weighted MRI sequences with fat suppression. MRI of the brachial and lumbosacral plexus may aid in the diagnosis of CIDP by showing nerve root hypertrophy, increased signal intensity, or contrast enhancement. A condition in which MRI may be considered in patients fulfilling only possible electrodiagnostic criteria is when US results are noncontributory. In children with suspected CIDP, systematic studies on MRI are lacking, inherited demyelinating neuropathies are more prevalent than CIDP and can also show nerve size increase. Before concluding that US or MRI abnormalities are supportive of CIDP, there should be no laboratory/clinical features that suggest other diseases such as multifocal motor neuron disease, demyelinating CMT disease, immunoglobulin M paraproteinemic neuropathy (especially with anti-MAG antibodies), POEMS syndrome, diabetic radiculoplexus neuropathy, amyloid neuropathy, neuralgic amyotrophy, leprosy, neurofibromatosis,

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### [. MRI lumbosacral plexus without IV contrast

The literature supports the use of MRI lumbosacral plexus without IV contrast for initial imaging of patients with suspected demyelinating disease of the peripheral nervous system but indicates that contrast-enhanced imaging is preferred. MRI of the lumbosacral plexus may be indicated in patients with suspected peripheral demyelinating disease presenting with lower extremity weakness [40, 41]. However, the use of IV contrast is helpful in detecting nerve enhancement and inflammation associated with peripheral demyelinating conditions [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### \. MRI orbits with IV contrast

No relevant literature supports the use of MRI orbits with IV contrast for initial imaging of patients with suspected peripheral nervous system demyelinating disease. Peripheral nervous system demyelinating diseases primarily affect nerve roots, plexuses, and peripheral nerves, rather than the optic nerves, which are part of the CNS [40, 41].

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

### ]. MRI orbits without and with IV contrast

There is no relevant literature to support the use of MRI orbits without and with IV contrast for initial imaging of patients with suspected peripheral nervous system demyelinating disease.

### Variant 5:Adult. Acute or chronic symmetric weakness. Suspect demyelinating disease of the peripheral nervous system. Initial imaging.

#### ^. MRI orbits without IV contrast

There is no relevant literature to support the use of MRI orbits without IV contrast for initial imaging of patients with suspected peripheral nervous system demyelinating disease.

### **Summary of Highlights**

Variant 1: For initial imaging of adult patients with acute or subacute sensorimotor or brainstem symptoms in whom demyelinating disease of the CNS is suspected, MRI head without and with IV contrast is recommended to look for causative demyelinating lesions of the brain and for active enhancement. MRI cervical and thoracic spine without and with IV contrast is a complementary procedure that can be performed at the same time to look for additional demyelinating lesions of the spinal cord (cervical cord coverage is often higher yield than thoracic cord coverage).

Variant 2: For initial imaging of adult patients with acute or subacute sensorimotor symptoms below a spinal cord level in whom TM is suspected, MRI cervical and thoracic spine without and with IV contrast is recommended to look for causative demyelinating lesions of the spinal cord and for active enhancement. MRI head without and with IV contrast is a complementary procedure that can be performed at the same time to look for additional demyelinating lesions of the brain.

Variant 3: For surveillance imaging of adult patients with known demyelinating disease and stable

neurologic examination, MRI head without and with IV contrast and MRI cervical and thoracic spine without and with IV contrast are recommended as complementary procedures to look for new or enhancing lesions of the CNS (subclinical progression). Alternatively, when there is low clinical suspicion for active enhancing disease, MRI head without IV contrast and MRI cervical and thoracic spine without IV contrast can also be recommended as complementary procedures to look for new lesions of the CNS in clinically stable patients (noncontrast alternative). The choice of brain, cervical cord, and thoracic cord coverage will depend on the locations of the patient's known disease.

Variant 4: For initial imaging of adult patients with known demyelinating disease and new or progressive neurologic deficits, MRI head without and with IV contrast, MRI orbits without and with IV contrast, MRI cervical and thoracic spine without and with IV contrast are recommended as complementary procedures to look for causative demyelinating lesions of the brain, optic nerves, spinal cord and for active enhancement. The choice of brain, orbits, cervical cord, and thoracic cord coverage will depend on the suspected localization of the patient's neurologic deficits.

Variant 5: For initial imaging of adult patients with acute or chronic symmetric weakness in whom demyelinating disease of the peripheral nervous system is suspected, MRI cervical and thoracic spine without and with IV contrast, MRI lumbar spine without and with IV contrast, MRI brachial plexus without and with IV contrast, and MRI lumbosacral plexus without and with IV contrast are recommended as complementary procedures to look for causative demyelinating lesions of the spinal/peripheral nerves and for active enhancement. The choice of spine and plexus coverage will depend on the suspected localization of the patient's weakness. MRI head without and with IV contrast may be appropriate when demyelinating disease of the cranial nerves is suspected (e.g., Miller Fisher variant of GBS).

### **Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at <a href="https://acsearch.acr.org/list">https://acsearch.acr.org/list</a>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at <a href="https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria">https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria</a>.

### **Appropriateness Category Names and Definitions**

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate		The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable riskbenefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.

May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

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#### **Disclaimer**

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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