COMMENTARY

Harmonizing Magnetic Resonance Imaging Protocols for Veterans With Multiple Sclerosis

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Background: Magnetic resonance imaging (MRI) assists with the diagnosis of multiple sclerosis (MS), allows for timely therapeutic intervention, and for the evaluation of disease progression, treatment effect, and safety. An international task force including representatives from the Veterans Health Administration worked together to update guidelines for imaging the brain, spinal cord, and optic nerve in people with MS.

Observations: This commentary communicates the core message of the 2021 MAGNIMS-CMSC-NAIMS Consensus Recommendations on the Use of MRI in Patients With Multiple Sclerosis as part of the MS Center of Excellence effort to align with contemporary guidelines, apply the highest scientific standards, and achieve consistent outcomes for veterans with MS. To implement and disseminate these proposed recommendations within the Veterans Health Administration, a workgroup was formed at the end of 2020, which discussed a modified version of the 2021 MRI Guidelines to accommodate US Department of Veterans Affairs medical centers that had fewer imaging resources as well as veterans' needs.

Conclusions: Standardized MRI protocols are fundamental for the care of veterans with MS. Mitigating interscan variabilities is recognized as a priority by scientific and clinical expert committees.

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Multiple sclerosis (MS) is a lifelong disease that affects about a million people in the United States.[1,2] Since 1998 more than 45,000 veterans have been diagnosed with MS and about 20,000 are evaluated in the Veterans Health Administration (VHA) annually.[3]

Magnetic resonance imaging (MRI) is a cornerstone for the assessment of persons with multiple sclerosis (pwMS).[4-6] MRI assists with disease diagnosis, allowing for timely therapeutic interventions and with the evaluation of its progression, treatment effect, and safety.[4,5] MRI-based outcomes also are used as primary endpoints in clinical trials.[4,5]

MS has its clinical onset in early adulthood in most individuals and is diagnosed at a mean age of 30 years.[7] As a result, pwMS may receive care and MRIs in different facilities during their lifetime. Mitigating interscan variabilities that can challenge intra- and interperson comparisons is crucial for accurate care. Radiologists may find it difficult to compare scans acquired in different facilities, as dissimilarities in acquisition protocols may mask or uncover focal disease, creating false negative or false positive findings. Moreover, lack of a standardized method to report MRI changes may compromise neurologists' ability to correctly interpret scans and disease progression.

Accordingly, in October 2019, an international task force of neurologists, radiologists, MRI technologists, and imaging scientists with expertise in MS, including representatives from the VHA, worked together to update guidelines for imaging the brain, spinal cord, and optic nerve in pwMS.[8,9] Recognizing the importance of this effort, the VHA Multiple Sclerosis Centers of Excellence (MSCoE), in collaboration with a team of subject matter expert neuroradiologists promptly committed to this effort, advocating the updated consensus recommendations, and favoring their dissemination within the VHA.[10]

As part of this commitment and dissemination effort, in this report we summarize the core points of the newly proposed MRI guidelines and ways to adapt them for use within the VHA. We then discuss key elements for their successful implementation and dissemination, specifically regarding the clinical operations of VHA.

UPDATED GUIDELINES

The 2021 MAGNIMS-CMSC-NAIMS Consensus Recommendations on the Use of MRI in Patients With Multiple Sclerosis covered a broad spectrum of recommendations related to MRI indication, acquisition, and interpretation in MS. The recommendations span 3 major areas: (1) indications for an MRI with/without contrast; (2) summary of the MRI protocol for radiologists and technologists; and (3) interpretation of MRI examinations.

MRI Scan at Different Timepoints of MS

There are 3 crucial milestones within a the lifespan of a pwMS that require an MRI to reach appropriate conclusions and avoid clinical errors. These include the initial diagnosis, the follow-up to monitor disease and/or treatment effect, and the assessment of medication safety.

In the interest of efficiency, MRI protocols may vary slightly depending on these clinical indications. The Table lists core sequences of the

TABLE Recommended Acquisition Protocols

MRI Types	Protocols
Brain	Axial T2-w TSE or FSE[a] Sagittal T2-w FLAIR (fat suppression is optional) Axial T2-w FLAIR (not necessary if sagittal 3D with multiplanar reconstruction obtained) Axial (or 3D sagittal) T1-w postcontrast sequence[b,c] DWI[d,e]
Cervical and thoracic spinal cord[b]	≥ 2 of sagittal TSE, or FSE T2-w, FSE or TSE proton-density, or STIR Sagittal T1-w postcontrast sequence
Optic nerve[b]	Axial and coronal fat suppressed T2-w or STIR Axial and coronal postcontrast T1-w

Abbreviations: 3D, 3-dimensional; DWI, diffusion-weighted image; FLAIR, fluid-attenuated inversion recovery; FSE, fast spin echo; MRI, magnetic resonance image; STIR, short τ recovery; T1-w, T1-weighted; T2-w, T2-weighted; TSE, turbo spin echo; VHA, Veterans Health Administration.
[a]Optional with surveillance MRIs for monitoring disease progression or drug safety if high-quality 3D FLAIR is available.
[b]Optional with surveillance MRIs for monitoring disease progression or drug safety.
[c]VHA committee noted that multislice 2D T1-w could be better than 3D image to mitigate propagation of movement artifacts.
[d]Recommended only in the setting of surveillance MRI to assess drug adverse effects.
[e]VHA radiologists argued that DWI should always be part of the brain MRI protocols when imaging veterans with MS.

updated 2021 consensus recommendations at each timepoint along with the proposed alternatives or preferences from the VHA workgroup.

At the time of diagnosis, both brain and spine (cervical and thoracic) MRIs are recommended. Routine MRI of the optic nerve is considered optional at diagnosis. However, imaging the optic nerve may be useful in specific clinical scenarios when the optic nerve is selectively involved, and the diagnosis or etiology of an optic neuritis is not clear. A repeat brain MRI is advised every 6 to 12 months in patients with clinically or radiologically isolated syndrome who do not fulfill the diagnostic criteria of MS but present risk factors for conversion to MS or paraclinical features of it.

Once the diagnosis is established, brain MRI is recommended for follow-up and for surveillance of drug safety. Spinal cord and optic nerve MRIs are desirable but optional in the follow-up of pwMS and are not required for drug surveillance. Spinal cord MRIs are required at follow-up for patients whose progression cannot be explained by brain MRI features, or who manifest with recurrent spinal cord symptoms, or have spinal cord comorbidities. In these cases, spinal cord MRI also may assist with treatment decisions. Similarly, optic nerve MRI is necessary during follow-up only when optic nerve comorbidities are suspected or when there is progression or reoccurrence of optic nerve–related symptoms.

Brain MRIs are recommended for monitoring drug effect yearly (or at longer intervals, after a few years of disease stability). Conversely, a repeat brain MRI is advised after 6 months if nonsymptomatic radiological disease activity is discovered on surveillance scans.

Abbreviated but more frequent serial brain MRI protocols (eg, every 3 to 4 months) are recommended for pwMS treated with natalizumab and at high risk of developing progressive multifocal leukoencephalopathy (eg, pwMS who are John Cunningham virus [JCV]–positive, and have been treated with natalizumabfor ≥ 18 months, have a JCV antibody index > 0.9, or have a history of immunosuppression). A similar approach is recommended for carryover cases, such as those with high JCV antibody index who are switched to other immunosuppressive treatments.

MRI Field, Scan Resolution, and Coverage

Both 1.5-Tesla (1.5-T) and 3-T scans are believed to be equally effective in imaging pwMS, providing that the 1.5-T scans are good quality. Although imaging at < 1.5 T is not recommended due to suboptimal disease detection, the use of scanners > 3 T is equally discouraged outside the supervision of trained investigators. Signal-to-noise ratio and resolution are key factors impacting scan quality, and their optimization is prioritized over the number of sequences in the updated 2021 consensus recommendations. For brain imaging, a resolution of 1 mm^3 isotropic is preferred for 3-dimensional (3D) imaging and slice thickness ≤ 3 mm without gap (≤ 5 mm with 10-30% gaps for diffusion-weighted imaging only) is recommended for 2D sequences. Images should cover the entire brain

and as much of the cervical spine as possible; images should be prescribed axial for 2D or reformatted axial oblique for 3D using the subcallosal plane as reference. For spine imaging, sites should aim at an in-plane resolution of 1 mm^2; using sagittal slices ≤ 3 mm thick and axial slices ≤ 5 mm thick, both with no gap. Scans should cover the entire cervical and thoracolumbar region inclusive of the conus. For the optic nerve images, slices should be ≤ 2 or 3 mm thick with an in-plane resolution of 1 mm^2. Images should be aligned to the orientation of the optic nerve and chiasms, both of which should be entirely covered.

Postgadolinium Images Use

The discovery of the higher sensitivity of postgadolinium (Gd) T1-weighted (T1-w) MRI relative to high iodine (88.1 g I) computed tomography scans in demonstrating contrast-enhancing MS lesions has revolutionized the way clinicians diagnose and monitor this disease.[11] However, in recent years the role of postcontrast MRI has been debated, considering the potential safety concerns secondary to Gd tissue deposition. For this reason, an intentionally more judicious use of postcontrast MRI is proposed by the consensus recommendations. At disease diagnosis, the use of Gd is advisable to (1) show disease dissemination in time; (2) differentiate the diagnosis based on the Gd pattern; (3) predict short-term disease activity; and (4) characterize activity in the setting of progression. When monitoring pwMS, the use of Gd may be useful in the first year of follow-up, particularly if in the setting of low potency medications or for patients for whom the detection of one or more active lesions would lead to a change in disease-modifying agents. Gd also should be used to first, confirm a clinical exacerbation (if needed); second, further characterize a lesion suggestive of progressive multifocal encephalopathy or monitor this disease over time; and third, monitor lesion burden change in patients with large confluent lesions, the count of which otherwise may be difficult.

MRI During Pregnancy and Lactation

The consensus recommendations state that Gd contrast–enhanced MRI is not absolutely contraindicated during pregnancy, although its use should be limited to strictly necessary situations, particularly those involving differential diagnosis, such as cerebral venous thrombosis or monitoring of possibly enlarging lesion burden. The use of Gd is not contraindicated during lactation, as only a small proportion (< 0.4%) passes into the breast milk, leading to an exposure to < 1% of the permitted Gd dose for neonates.[12,13]

Harmonizing MRI Reports

The consensus recommendations propose reporting the exact lesion count on T2-weighted (T2-w) images when lesions are < 20, or specifying if the number of T2 lesions is between 20 and 50, between 50 and 100, or uncountable, eg, confluent large lesions. Similarly, for the spinal cord, the consensus recommendations propose reporting the exact lesion count on T2-w images when lesions are < 10, or otherwise report that > 10 lesions are seen.

The VHA workgroup proposed reporting a mild, moderate, or severe T2-lesion burden for a T2-lesion count < 20, between 20 and 50, and > 50, respectively. For follow-up MRIs, notation should be made if there is any change in lesion number, indicating the number of new lesions whenever possible. At each timepoint, the presence of active lesions on postcontrast images should be accurately defined.

DISSEMINATION AND IMPLEMENTATION

To implement and disseminate these proposed recommendations within the VHA, a workgroup of neurologists and radiologists was formed in late 2020. A review and discussion of the importance of each of the proposed MRI protocols for veterans with MS was held along with possible modifications to balance the intent of meeting standards of care with resources of individual US Department of Veterans Affairs (VA) medical centers and veterans' needs. The final protocol recommendations were agreed on by group consensus.

In general, this VHA workgroup felt that the current adopted MRI protocols in several VA medical centers (based on previously proposed recommendations) were similar to the ones newly proposed and that implementing changes to meet the 2021 criteria would not be a major challenge.[14,15] Possible regional and nonregional barriers were discussed. The result of these discussions led to a modified version of what could be considered more stringent guidelines to accommodate medical centers that had fewer imaging resources. This modified protocol offers a viable alternative that allows for minimizing heterogeneities while recognizing the capabilities of the available scanner fleet and meeting the needs

of specific centers or veterans. Finally, the workgroup recognized a fundamental obstacle toward this harmonization process in the heterogeneity in vendors and scanner field strength, factors that have previously limited implementation.

The guidelines and proposed changes were then presented to the VA National Radiology Program Office, examined, and discussed for consensus. No changes were felt to be needed, and the recommendation to implement these guidelines in MS regional programs, whenever possible, was deemed appropriate.

At this time, a focused communication plan has been implemented to diffuse the use of this protocol at MS regional programs in the MSCoE network. We will work iteratively with individual sites to practically apply the guidelines, learn about challenges, and work through them to optimize local implementation.

CONCLUSIONS

Standardized MRI protocols are fundamental for the care of veterans with MS. Mitigating interscan variabilities should be recognized as a priority by scientific and clinical expert committees. Several guidelines have been developed over the years to standardize MRI acquisition protocols and interpretations, while updating the same to the latest discoveries.[4,5,8,14,15] The VHA has been historically committed to these international efforts, with the goal to excel in the care of veterans with MS by providing access to state-of-the-art technologies. To this end, the initial Consortium of MS Centers MRI protocol was implemented in several MSCoE VA Regional Program sites a decade ago.[14] Efforts continue to update protocol recommendations as needed and to promote their dissemination across the VHA enterprise.

This commentary is part of the continuous effort of the MSCoE to align with contemporary guidelines, apply the highest scientific standards, and achieve consistent outcomes for veterans with MS. For more important details of the clinical scenarios when additional/optional sequences or scans can be acquired, we advise the reader to refer to the 2021 MAGNIMS-CMSC-NAIMS Consensus Recommendations on the Use of MRI in Patients With Multiple Sclerosis.[8]

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Disclaimer

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