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The Role of MRI in the Diagnosis and Management of MS

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Mellen Center Approach: MRI in Multiple Sclerosis

Magnetic resonance imaging (MRI) plays a crucial role in multiple sclerosis (MS) diagnosis, disease monitoring, prognostication, and research. Several important practice guidelines updates for MRI in MS have been published recently, including the 2017 revised McDonald's Criteria[1], Magnetic Resonance Imaging in MS network guidelines[2], and revised recommendations of the Consortium of MS Centers Task Force[3]. This document reflects updated recommendations per Mellen Center consensus based on review of the guidelines.

Initial MRI scan:

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Q: When should an MRI of the brain be obtained?

A: When making the diagnosis of MS, brain and cervical spinal cord MRIs should be obtained in all cases unless specific contraindications. MRI is essential:

- to confirm the suspected diagnosis of MS
- to evaluate for alternative diagnoses
- to serve as a baseline evaluation and staging the disease process

Q: Is an MRI required for the diagnosis of multiple sclerosis, or can other additional testing and clinical features suffice?

A: Yes, MRI should be obtained in all patients unless there is a specific contraindication for obtaining the MRI (for example, presence of MRI-incompatible pacemaker or other electronic devices). In cases where MRIs cannot be obtained, we generally obtain as much supportive testing as possible. We are more cautious regarding the certainty of the diagnosis in such patients, and rely more heavily on lumbar puncture results and other supportive diagnostic testing results such as evoked potentials and optical coherence tomography. If the contraindication for MRI is removed at a later time, we would recommend obtaining an MRI at that point.

Q: Do you ever diagnose MS in a patient with a normal MRI?

A: Per 2017 McDonald criteria, in order to diagnose MS, there needs to be reasonable clinical suspicion, along with supportive MRI and paraclinical evidence. We would be hesitant to diagnosis MS in a patient with a good quality MRI (at least 1.5 Tesla magnet strength or above) showing a normal brain and spinal cord (cervical cord and thoracic cord). However, due to the potential limitations of conventional MRI, particularly with regard to grey matter pathology, there will be rare exceptions to this rule. In most cases, repeatedly normal imaging raises strong doubts about an MS diagnosis, particularly in a patient with long standing neurological disability.

Q: When should an MRI of the cervical and thoracic spine be obtained?

A: We recommend an initial cervical and thoracic spine MRI with and without contrast along with brain MRI in patients suspected of having MS, for diagnosis, to establish disease burden, and to monitor for asymptomatic spinal cord lesions[4,5]. Also, if symptoms or signs could be explained by spinal cord disease, then spinal cord MRI is required to evaluate for non-MS cord pathology. Spinal MRI provides increased specificity in patients with an abnormal brain MRI and increased

sensitivity in patients with a negative brain MRI. This is particularly true in cases where there are non-specific white matter changes due to cerebrovascular risk factors and/or spinal cord compression from degenerative disc disease. Presence of spinal cord lesions have been shown to predict long term disability in patients with CIS and early RRMS[6,7] and therefore this is an important factor in treatment planning. Due to potential issues of artifact and patient motion, the quality of scans is particularly important with spinal MRI. Typically, higher field strengths (1.5 Tesla or higher) are preferred for spinal cord MRI. Routine follow up scans of spinal cord for disease monitoring purposes is recommended but can be challenging due to small anatomical area involved and physiological artifacts that commonly affect quality of the scans.

Q: In which circumstances should a follow-up MRI scan be obtained?

A: It can be useful to monitor sub-clinical disease as well as response to therapy by obtaining MRIs periodically during the course of routine follow up care of MS patients. We obtain repeat MRI in the following circumstances:

- Patients with an MRI typical for MS, in whom we are initiating disease modifying therapy. This serves as a baseline for monitoring therapy.
- Patients on disease modifying therapy. MRI for re-establishing baseline can be obtained at 6 months after disease modifying therapy initiation, and thereafter every 6-12 months individualized according to disease severity, activity when disease modifying therapies are started, as well as type of disease modifying medication (please see the individual Mellen Approaches for the timing of onset of therapeutic effect with each therapy).
- Patients with clinically isolated syndrome, radiologically isolated syndrome who need MRI follow up for diagnosis.
- MS patients who decline therapy, but need monitoring to determine disease activity for future treatment recommendations.
- Patients with a very active initial MRI in which close follow up is needed to assess for radiological stabilization after starting treatment.

Q: Do you recommend an MRI during a relapse of MS?

A: MRIs are not required to diagnose relapses. We do not generally obtain an MRI of the brain or spinal cord during an MS relapse if the symptoms and signs are consistent with MS and there are

no atypical features. The exceptions to this rule would be if the patient is on immunomodulating therapies that increase the risk of progressive multifocal leukoencephalopathy (PML). In addition, if the patient has an altered level of consciousness or other problems such as a severe headache, sudden stroke-like onset, etc., then we would obtain an MRI as soon as possible. Patients whom we are considering switching disease modifying therapy should also obtain MRIs.

Q: What is the Mellen approach to a radiologically-isolated syndrome (RIS), or the incidental finding of classic MS by MRI including enhancing lesions with no clinical symptoms or mild or atypical symptoms?

A: We recommend clinical and imaging follow-up in these situations, depending on the extent and inflammatory nature of the findings. A portion of these individuals will go on to develop clinical signs and symptoms of MS given a long enough time period. A longitudinal follow up study showed that RIS patients have approximately a one in three chance of converting to MS by year 5[8]. The presence of other factors, such as high brain lesion burden, brainstem or cerebellum lesions, spinal cord lesions, contrast-enhancing lesions, CSF oligoclonal bands, or abnormal visual evoked potentials, increase the likelihood of developing clinically definite MS[5], for which treatment with disease modifying therapy may be considered, with benefits and risks to be carefully weighed.

Acquisition/Technical considerations:

Q: What are the technical requirements for obtaining an MRI of the brain and spine?

A: In compliance with published Consortium of MS Centers MRI standardize guidelines, all MRIs should be obtained on machines of at least 1.5 Tesla strength. At Mellen Center, we prefer all MRIs to be performed on 3 Tesla strength machines, especially for spinal cord MRI as higher field strength MRI improves resolution and may increase yield in terms of lesion counts.

All brain MRI scans should include:

If 3D acquisition possible: 3D sagittal T2 FLAIR, 3D T2 weighted sequence, 2D axial diffusion weighted sequence, 3D T1 MPRAGE, axial T1 spin echo post-contrast sequence (if needed).

If unable to perform 3D: 2D axial and sagittal FLAIR, axial fast spin echo T2-weighted sequence, 2D axial diffusion weighted sequence, sagittal T1 spin echo sequence, axial T1 weighted post-contrast sequence (if needed).

All spine MRI scans should include:

Sagittal T2 weighted sequence, sagittal STIR sequence, sagittal T1 weighted sequence, axial T1 weighted sequence, axial T2 weighted sequence, axial and sagittal T1 weighted post-contrast sequences (if needed)

Detailed parameters are available on Consortium of MS Centers website [3]. We further recommend that follow-up MRIs be obtained on the same magnet and with similar software, to allow for 'apples to apples' comparisons rather than attempting comparing slices obtained with gaps to those obtained with no gaps, etc. If contrast is administered for brain MRI, the same dose can be used for post-contrast imaging in the spinal cord as well.

For quantitative analysis such as tissue volume and lesion size, generally 3D sequences are optimal. Volumetric analysis is typically best accomplished using a 3D T2 FLAIR and T1 MPRAGE or equivalent sequence.

Lower field open-MRI scanners are not recommended except in special circumstances (i.e. claustrophobia, implanted devices).

Q: What are the technical requirements for obtaining an MRI of the orbit?

Orbit MRI is not required in asymptomatic patients. However, this may be necessary to confirm optic neuritis or evaluate for other etiologies involving the visual system (e.g., sarcoidosis, compressive lesions, neuromyelitis optica). Coronal STIR or fat-suppressed T2, and post-contrast fat-suppressed T1 with coverage through optic chiasm are the minimal sequences recommended in the Consortium of MS Centers guidelines [3].

Special Issues:

Q: What is the role of contrast agents and their safety?

A: In general contrast agents are safe and we prefer to obtain MRI of the brain and spinal cord with a gadolinium-based contrast agent as an initial diagnostic strategy. Contrast-enhancing lesions assist in satisfying diagnostic criteria of dissemination in time in patients suspected of having MS. They are validated imaging biomarkers of new inflammatory activity, and assist in ensuring that alternative diagnoses are thoroughly evaluated.

The use of IV contrast agents increases the yield of MRI in detecting active lesions and new T2 lesions. Recent studies have demonstrated that the presence of new or enlarging T2 lesions on follow up scans is sufficient as a surrogate for subclinical disease activity and progression [9], and did not perform worse than post-contrast T1 scans at detecting interval change [10]. Also, standardized MRI protocols and high-quality comparable scans between follow-ups increase sensitivity for the evaluation of disease progression.

Contrast can cause allergic reactions that should be treated per standard protocols. Contrast should be generally avoided in pregnancy, although there are no reported adverse effects of contrast on the fetus. It is recommended that a serum creatinine be obtained in individuals as indicated by institutional and American College of Radiology guidelines. We follow our institution's policy for hydration and use of contrast in these patients, which are based on age, GFR, and the presence of risk factors such as diabetes, known renal disease, etc. Contrast can rarely cause nephrogenic sclerosing fibrosis, but this is seen only in patients with severe renal disease and only in a small fraction of patients treated with contrast. Although gadolinium deposition has been reported in brain and other tissues of patients with normal renal function following administration of contrast, there are no known diseases or disorders associated with this finding [11]. We only use macrocyclic gadolinium-based contrast agents (as opposed to linear agents) due to its lower risk of associated gadolinium deposition in body tissues.

Of note, there are no current FDA restrictions on gadolinium-based contrast agent use. The FDA is currently investigating the risk associated with brain deposits following repeated doses of gadolinium-based contrast agents for MRI, and we await further guidance from the FDA on this issue.

Our current approach is to carefully assess the risks and benefit for MRI imaging with contrast and where possible to defer contrast use. For example, in established MS patients with routine MRI

scans every 6-12 months, new T2 lesions and/or enlarged T2 lesions can serve as indicators of disease activity.

Q: Can you obtain an MRI in pregnancy or in a woman who is breast feeding?

A: According to the most recent American College of Obstetrics and Gynecology guidelines [12], there are no precautions or contraindications for non-contrast MRI in pregnant women. There are very rare situations that require obtaining an MRI in a pregnant woman with MS. As mentioned above, the use of contrast is generally avoided during pregnancy, although there is not an absolute contraindication to its use. As very small amounts of gadolinium (<0.04% of the administered dose) is excreted into breast milk, patients who are breast feeding do not need to express their milk after receiving contrast and can continue breast feeding as usual.

Q: Can you perform MRI in MS patients with intrathecal pumps and other implanted devices?

A: We have a protocol for scanning patients who have implanted baclofen pumps. In general, the pump is deactivated by the MRI, and then restarts automatically, but this should always be checked by qualified personnel after the MRI scan. There are conditional protocols that can allow patients with certain deep brain, spine, vagal nerve and bladder stimulators to have MRI scans using specifically approved protocols. We recommend significant caution in scanning these individuals. MRI staff need to review the information for each specific device with regards to MRI compatibility, as protocols and restrictions are evolving with time.

Q: When do you scan patients on natalizumab or other immunomodulating therapies that may increase the risk of PML? What is the protocol you recommend?

A: At each natalizumab infusion visit the TOUCH program requires questioning about new symptoms which might indicate the presence of PML. Early detection of PML improves survival and neurological functional outcomes. We perform MRI of the brain with and without contrast as soon as possible if there are clinical changes of concern in such patients. For routine surveillance, we also obtain routine brain MRIs to assess for clinical efficacy and monitor for PML (for low risk patients, every 6-12 months, for high risk patients, every 3-4 months). As other immunomodulating therapies that may increase PML risk are used, a similar approach should be used. We recommend at least a 3D sagittal FLAIR sequence (or 2D axial and sagittal FLAIR

sequence), and a 2D axial diffusion weighted sequence; post-contrast T1 images may be obtained depending on clinical and radiographic suspicion for PML, and/or PML-related immune reconstitution inflammatory syndromes.

Q: Are there any age-limits for MRI scans?

No, but children younger than 9 years old may require general anesthesia for sedation.

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