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## Standardized MR Imaging Protocol for Multiple Sclerosis: Consortium of MS Centers Consensus Guidelines

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## CONSENSUS STATEMENT

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# Standardized MR Imaging Protocol for Multiple Sclerosis: Consortium of MS Centers Consensus Guidelines

**M**R imaging has played an important role in contributing to our understanding of the natural history of multiple sclerosis (MS) in the brain and spinal cord, including its expression as both a focal (plaque) and more diffuse disease affecting normal-appearing white and gray matter, the latter detected by using quantitative MR techniques.<sup>1</sup> A set of conventional measures (T2 burden of disease [BOD], T2 lesion, and T1 gadolinium-enhancing lesion counts) are routinely used in phase II and III MS clinical trials as primary and secondary outcome measures, respectively, and there is expanding use of enhancing lesion counts in phase I clinical trials as a “safety” measure. MR imaging activity (a new lesion) has recently been accepted by an International Panel (IP) of MS experts as a criterion that can be used to establish evidence of disease dissemination in time (DIT) after a clinically isolated syndrome (CIS) in lieu of a second clinical attack.<sup>2</sup> This new MR imaging lesion allows a formal clinical diagnosis of MS, provided specific MR imaging-derived dissemination in space (DIS) criteria are also met.<sup>2</sup> This use of MR imaging to establish the diagnosis of MS has the important effect of accelerating the diagnosis by months or even years.<sup>3–5</sup> A positive MR imaging is also used as a factor for decision to treat, without additional evidence for DIT, by many neurologists, particularly in North America, when a patient presents with a classic CIS and characteristic lesions on MR imaging.<sup>6,7</sup> Less formally, MR imaging is increasingly used in practice to measure subclinical disease, on the basis of its greater sensitivity compared with clinical measures. On average MR imaging is about

5–10-fold more sensitive to ongoing demyelination than clinical measures.

As MR imaging is used more and more for diagnosis and management decisions, limiting factors have been the lack of (1) a standardized protocol for how MR imaging should be used for patients with MS or suspected to have MS, (2) for when to use MR imaging, and (3) the minimum standard.

Recognizing the central role of MR imaging for diagnosis, in clinical trials, and to follow disease activity and injury, an international group of neurologists and radiologists met in Vancouver, British Columbia, on November 3–4, 2001. The meeting was sponsored by the Consortium of Multiple Sclerosis Centers (CMSC). The goal was to develop recommendations and guidelines for a standardized MR imaging protocol for the diagnosis and follow-up of MS patients. Formal follow-up meetings and discussion of the CMSC consensus guidelines criteria in 12 platform presentations at major neurology and radiology venues across 4 continents and more than 30 regional meetings have provided a forum for discussion and refinement of the original guidelines.

The purpose of this report is to present these recommendations and guidelines to the entire imaging community. Translation from population data (clinical trials and natural history studies) to the individual patient is not necessarily straightforward or without risk. The hope is that the imaging community will assume a leadership role in implementing these standardized guidelines into routine clinical practice, but also provide an opportunity for further discussions of future revisions particularly as the quantitative measures of normal-appearing central nervous system (CNS) tissues become feasible in a clinical environment, beyond the cornerstone of the conventional measures discussed here.

For this overview the CMSC consensus criteria for standardized MR imaging in MS are provided in bold text. Comments by the consensus panel and authors follow the recommendations as additional supporting information for the reader.

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**Table 1: Brain MR imaging protocol**

	Sequence	Diagnostic Scan for Clinically Isolated Syndrome	MS Baseline or Follow-up Scan	Comment
1	3 plane (or other) scout	Recommended	Recommended	Set up axial sections through subcallosal line*
2	Sagittal Fast FLAIR	Recommended	Optional	Sagittal FLAIR sensitive to early MS pathology, such as in corpus callosum
3	Axial FSE PD/T2	Recommended	Recommended	TE <sub>1</sub> minimum (eg, ≤30 ms) TE <sub>2</sub> (usually ≥80 ms) PD series sensitive to infratentorial lesions that may be missed by FLAIR series
4	Axial Fast FLAIR	Recommended	Recommended	Sensitive to white matter lesions and especially juxtacortical–cortical lesions
5	Axial pregadolinium T1	Optional	Optional	Considered routine for most neuroimaging studies
6	3D T1	Optional	Optional	Some centers use this for atrophy measures.
7	Axial gadolinium-enhanced T1	Recommended	Optional	Standard dose of 0.1 mmol/kg injected over 30 s; scan starting minimum 5 min after start of injection

**Note.**—FSE indicates fast spin-echo (or turbo spin-echo); PD, proton density-weighted (long TR, short TE sequence); T2, T2-weighted (long TR, long TE sequence); T1, T1-weighted (short TR, short TE sequence). Section thickness for sequences 3–6 is ≤3 mm with no intersection gaps when feasible. Partition thickness for 3D sequence 6 is ≤1.5 mm. In-plane resolution is approximately ≤1 × 1 mm.

\* The subcallosal line joins the undersurface of the front (rostrum) and back (splenium) of the corpus callosum.

**Table 2: Spinal cord MR imaging protocol**

When Acquired Immediately Following an Enhanced Brain MRI*			When Acquired without a Preceding Enhanced Brain MRI		
Sequence	Recommendation		Sequence	Recommendation	
1	3 plane (or other scout)	Recommended	1	3 plane (or other scout)	Recommended
2	Postcontrast sagittal T1	Recommended	2	Precontrast sagittal T1	Recommended
3	Postcontrast sagittal FSE PD/T2†	Recommended	3	Precontrast sagittal FSE PD/T2†	Recommended
4	Postcontrast axial T1	Through suspicious lesions	4	Precontrast Axial FSE PD/T2‡	Through suspicious lesions
5	Postcontrast axial FSE PD/T2‡	Through suspicious lesions	5	3D T1§	Optional
6	Postcontrast 3D T1§	Optional	6	Postcontrast-enhanced sagittal T1	Recommended
			7	Postcontrast-enhanced axial T1	Through suspicious lesion(s)

**Note.**—FSE indicates fast spin-echo (or turbo spin-echo); PD, proton density-weighted (long TR, short TE sequence); T2, T2-weighted (long TR, long TE sequence); T1, T1-weighted (short TR, short TE sequence).

\* Indications are (1) main presenting symptoms are at the level of the spinal cord, and these have not resolved (2) if the brain MRI results are equivocal. No additional intravenous contrast is required if the spinal cord study immediately follows the contrast-enhanced brain MRI, as gain is very limited. The segment to be studied (cervical and/or thoracic) is based on clinical findings. Sagittal section thickness is 3-mm (no gap).

† PD series may depict lesions less apparent on heavily T2-weighted series.

‡ Increases confidence in the findings of sagittal series; may provide classic lesion characteristics.

§ For volumetric analysis if desired.

||Standard dose of 0.1 mmole/kg injected over 30 s; scan starting 5 min after start of injection.

## Consensus

### *I. Initial Evaluation after a CIS or Based on Past History That Is Suspicious*

**When available, an MR imaging study that meets the standardized protocol should be acquired as part of the initial evaluation** (Tables 1 and 2).

CIS is a common term in use today, though some prefer “monosymptomatic attack.” Most patients diagnosed with MS present with or retrospectively recall symptoms or signs consistent with an optic neuritis, usually acute and unilateral with loss of central vision, pain on eye movement, and an afferent pupil defect; a brain stem syndrome (eg, internuclear ophthalmoplegia); or a spinal cord syndrome with partial transverse myelitis with ascending numbness and/or paresthesia, hyperreflexia, tight bandlike sensations localizing to the affected cord segment, with motor, bowel, or bladder involvement. Other suggestive features for MS include trigeminal neuralgia, Lhermitte phenomenon, spasticity, tremor, and ataxia.<sup>8</sup>

The phrase, when available, was introduced in recognition that MR imaging is not universally available in Third World nations. The diagnosis of MS is clinical and can be established without MR imaging.

Details of the MR imaging component of the IP criteria are provided in Table 3. These criteria are based on counting lesions of specific types. In the early stages of MS, particularly at the time of a CIS, lesion counts are simple and can be performed rapidly with good reproducibility provided scan quality is adequate.

Whereas the early literature on which the DIS criteria were derived included variable section thickness (5–10 mm), intersection gaps, and low-field (<1T) imaging, several, recent studies suggest that these quantitative (lesion count) criteria remain valid on the basis of more modern imaging technique.<sup>9</sup>

The IP criteria (most often referred to as the McDonald criteria) are not the only documented MS predictive criteria in common use. For example, many MS neurologists, particularly in North America, will initiate immunomodulatory treatment based on a well-documented CIS accompanied by a positive MR imaging with 2 or more characteristic T2-lesions ≥3 mm in diameter, one of which is either periventricular or ovoid.<sup>6,7</sup> These patients are at high risk for second clinical attack, or may accumulate additional subclinical MR imaging lesions suggestive of ongoing demyelination.<sup>10</sup> For this set of individuals, standardized MR imaging is also important to minimize errors in interpretation of the MR imaging.

**Table 3: International panel MR imaging criteria<sup>2</sup>**

Magnetic resonance imaging criteria for dissemination in space

Three of 4 of the following:

1. One gadolinium-enhancing lesion or 9 T2-hyperintense lesions if there is no gadolinium-enhancing lesion
2. At least one infratentorial lesion
3. At least one juxtacortical lesion
4. At least 3 periventricular lesions

(Note: One spinal cord lesion can be substituted for one brain lesion.)

Magnetic Resonance Imaging Criteria for Dissemination of Lesions in Time

1. If a first scan occurs 3 mo or more after the onset of the clinical event, the presence of an enhancing lesion is sufficient to demonstrate dissemination in time, provided that it is not at the site implicated in the original clinical event. If there is no enhancing lesion at this time, a follow-up scan is required. The timing of this follow-up scan is not crucial, but 3 mo is recommended. A new T2 or enhancing lesion at this time then fulfills the criterion for dissemination in time.
2. If the first scan is performed less than 3 mo after the onset of the clinical event, a second scan done 3 mo or more after the clinical event showing a new enhancing lesion provides sufficient evidence for dissemination in time. However, if no enhancing lesion is seen at this second scan, a further scan not less than 3 mo after the first scan that shows a new T2 lesion or an enhancing lesion will suffice.

## II. Baseline MR Imaging Evaluation

**For a patient who already has a diagnosis of MS, it is appropriate that the baseline evaluation include an MR imaging that meets the standardized protocol. This is in addition to a complete neurologic history and examination.**

Misdiagnosis of MS is becoming less frequent with the use of brain and spinal cord MR imaging to exclude MS mimickers, such as neoplasm, spinal stenosis, or vascular malformation. More difficult and more clinically problematic is distinguishing MR imaging lesions due to overlapping pathology, such as that caused by Sjögren syndrome, systemic lupus erythematosus, Lyme disease, or sarcoidosis. The IP report discusses these pathologies and includes strong recommendations regarding exclusion of alternative diagnoses through history, clinical evaluation, and appropriate laboratory studies.<sup>2</sup> It is important that a diagnosis of MS not be made simply on the basis of MR imaging findings without the appropriate clinical signs and symptoms.

## III. Indications for Spinal MR Imaging

**A. If the main presenting symptoms are at the level of the spinal cord, and have not resolved, spinal cord MR imaging and brain MR imaging are required.**

**B. If the results of the brain MR imaging are equivocal and the diagnosis of MS is still being entertained, spinal cord imaging may be justified.**

Recommendation (A) includes spinal cord MR imaging to exclude mimicking or secondary pathology. Even when spinal cord lesions are observed, the guidelines suggest baseline brain MR imaging to demonstrate characteristic lesions.

With respect to (B), the lesions from MS in the spinal cord have been well described in the literature; 50%–90% of clinically definite MS patients will have lesions on spinal cord MR imaging.<sup>11</sup> These lesions are more common in the cervical than the thoracic cord. Characteristic features include (vertical) length of lesion  $\leq 2$  vertebral segments, and asymmetry on axial sections.<sup>12</sup> T2-hyperintense lesions do not develop in the spinal cord from normal aging and are very uncommon from small vessel disease such as that related to hypertension, diabetes, and atherosclerotic risk factors.<sup>12</sup> Nevertheless, some caution is justified in the interpretation of spinal cord findings in isolation as brain MR imaging findings tend to be more definitive and characteristic for MS and more likely to be present than those in the spinal cord which represents a small

fraction of the total CNS tissue. Spinal cord evaluation may be compromised by pulsation and other motion artifacts, and in practice false-negative and false-positive interpretations are not rare.

Recommendation (B) is provided with the understanding that spinal cord imaging provides a relatively low but certainly not zero yield at the time of a CIS when there is no clinical evidence of myelopathy and the brain MR imaging is normal. A positive cord MR imaging with characteristic lesions improves confidence in the diagnosis or presumptive diagnosis (which may lead to more careful follow-up). Spinal cord MR imaging may establish additional lesions such that the IP criteria for DIS are fulfilled, because they allow substitution of a spinal cord lesion for a brain lesion.

## IV. Follow-Up MR Imaging

A. In the absence of clinical indications, routine follow-up MR imaging scans are not recommended, regardless of whether the patient is being treated. Clinical indications for follow-up MR imaging are (1) unexpected clinical worsening or when the clinician has a concern about the patient's course, (2) reassessment of disease burden for the initiation of treatment, and (3) suspicion of a secondary diagnosis.

Routine follow-up scans are defined as those requested on a regular—for example, annual—basis in the absence of the qualifying factors described below. The recommendations provide flexibility in the use of MR imaging that are based on current clinical practice patterns by many experienced MS neurologists. Many members of the consensus panel expressed hope that with increasing experience by using standardized MR imaging, and its use in establishing baseline disease in individuals (as opposed to populations), there will be a re-evaluation of these relatively conservative recommendations and consideration in the future for routine (perhaps annual) follow-up MR imaging in MS.

The principal basis for this consensus finding was related to the uncertainty in interpreting the results of new, routinely scheduled MR imaging. For example, because all therapies are only partially effective, an increase in MS lesion numbers in an individual being treated with an immunomodulatory therapy may reflect partially effective or completely ineffective therapy but alternatively could be a smaller increase than might have occurred had there been no therapy.

The approved therapies for MS—glatiramer acetate (Cop-

axone), interferon beta-1a (Avonex and Rebif), interferon beta-1b (Betseron) for relapsing disease, and mitoxantrone (Novantrone) for progressive relapsing disease are only partially effective, reducing MR imaging lesions by 30%–90% and relapse frequency on the order of about 30%–60%.<sup>13</sup> When more effective therapy becomes available, it is anticipated that routine MR imaging will provide results that can be more objectively interpreted. There is new literature that addresses MR imaging criteria in assessing the effectiveness of therapy and identifying non or poor responders,<sup>14,15</sup> but these criteria have not as yet been prospectively tested in independent data bases.

Today, with current therapy, in a clinically silent individual without cognitive deterioration, stable MR imaging generally supports a good interval course; many new lesions in a clinically silent individual are a potential red flag suggesting consideration of change in current therapy or the need for more frequent follow-up, and a major increase in lesion numbers in a modestly (clinically) active patient or a patient with indeterminate (sensory) findings suggests therapy be re-evaluated.

It should be noted that many expert MS neurologists use routine follow-up MR imaging in their clinical practice, and there were strong minority dissenting opinions expressed in the consensus meetings.

B. If follow-up MR imaging is to be obtained, it should be performed according to the standardized protocol and compared with previous studies.

On follow-up, with good imaging in the same plane and with reasonably close section selection based on thin non-gapped sections, the radiologist can provide several measures that are of value in following lesions in the brain. These include (1) number of new or enlarging T2-hyperintense lesions and, if contrast-enhanced MR imaging is acquired (see below), (2) the number of enhancing lesions.

In addition, the imaging review can comment on T1 hypointense lesions or so called “black holes” as absent-mild-moderate-severe. T1 black holes when truly chronic are focal areas of relatively severe tissue injury, including axonal injury, matrix destruction, and myelin loss.<sup>16</sup> Acute MS lesions may appear T1 hypointense as a result of transient edema: these are not true T1-black holes. T1 hypointensity may linger months after an acute event with such lesions evolving to isointensity (loss of edema or repair) or persisting as chronic, permanent hypointensity. A true T1 black hole is a chronic hypointensity. These lesions in reality cannot be determined with complete certainty on a single MR imaging, because, by definition, they should be persistent for at least 6 months.<sup>17</sup> In routine clinical practice, however, T1 black holes are assumed to be any lesions that are hypointense on postgadolinium-enhanced T1-weighted scans. Such hypointensities are unlikely to be acute on a contrast-enhanced scan, the exception being if the patient has received high dose corticosteroids within hours to weeks of the MR imaging, because enhancement based on blood-brain barrier disruption can be rapidly reversed in some individuals and some lesions (false-positive T1 black hole).

Brain volume loss is also evaluated qualitatively and may be described by using an ordinal scale (mild-moderate-severe) based on global assessment of ventricle size and sulcal width. Volume loss (atrophy) is the net result of loss of axons, myelin, and changes in the supporting tissue matrix. Atrophy correlates modestly with disability in MS populations,<sup>18</sup> less so in

individuals. Volume loss can be transient related to hydration, nutritional status, or use of corticosteroids.

Much has been learned about the disease from quantitative analyses of T2-lesion volume (BOD), change in BOD, counts of new or enlarging T2 lesions over time, and enhancing lesions evaluated monthly or annually in patients enrolled in therapeutic trials. These simple measures have been instrumental in the approval process of the MS therapies by providing objective support for the clinical outcomes. T2-hyperintense lesions predict MS (second clinical attack) over short and long intervals, and change in T2 BOD predicts long-term disability in populations.<sup>19</sup>

For the spinal cord, scan quality, lesion size, and lesion (tissue) contrast typically make analysis of change in number over time difficult or unreliable, unless change is dramatic.

## V. Contrast-Enhanced MR Imaging

A. Regarding the use of gadolinium-chelate, enhanced MR imaging is recommended for suspected MS for purposes of diagnosis and initial diagnostic evaluation.

There are several factors contributing to this recommendation. Confounding diagnoses may be less well visualized, or even missed, without contrast-enhanced MR imaging (leptomeningeal disease, meningioma, other mass lesions, vascular malformation). More important, the identification of enhancing lesions is an important component of the IP criteria providing evidence for disease DIT and DIS. Enhancing lesions at the time of a CIS are a strong independent predictor of future clinical attacks and a diagnosis of MS,<sup>10,20,21</sup> probably as identification of an enhancing lesion is more likely with more active disease.

Conventional doses of gadolinium-chelate (0.1 mmol/kg, 20 mL maximum) are recommended with a minimum delay of 5 minutes following injection. Although it is well documented that greater doses (and delayed imaging) will increase lesion conspicuity and lesion number,<sup>22</sup> for routine clinical care in an individual there is no evidence that supports higher doses at this time.

Although a greater dose of MR contrast may convert an individual from not MS to MS, to date there have been no formal tests of this strategy to predict MS. The cost of additional MR contrast is not inconsequential.

B. Enhanced MR imaging is considered optional for the baseline evaluation (in individuals already diagnosed with MS).

The standard of care is variable. Some MS neurologists routinely use enhanced MR imaging in their baseline assessment, but others do not. Enhancing lesions are a surrogate marker for focal disruption of the blood-brain barrier associated with macroscopic inflammation, an early (though probably not the earliest) stage in focal MS lesions. New enhancing lesions remain conspicuous from about 1 week through about 16 weeks, most <4 weeks.<sup>23</sup> It is likely that inflammation is also microscopic (below MR imaging resolution), but there are no practical and no established quantitative methodologies for evaluating microscopic inflammation in vivo. There is controversy regarding inflammation in MS—notably related to “good” (potentially reparative) versus “bad” (proinflammatory, injurious) inflammation.<sup>24</sup> Nevertheless, the current at least partially effective MS therapies are thought to exert



much of their effect through anti-inflammatory mechanisms, and inflammation, dysfunction, and electrical disturbances are well correlated in functionally exquisite parts of the CNS, which suggests that much of the MR imaging–detected inflammation is undesirable. Inflammation is notably associated with axonal transection and other markers for axonal injury (amyloid precursor protein).<sup>25</sup>

C. Enhanced MR imaging is considered optional for the follow-up of MS.

Although the standard of care in many MS centers is to acquire routine enhanced MR imaging to aid in treatment decisions, there is insufficient evidence to conclude that enhancement alone should drive treatment decisions.

## **VI. Acquisition Standards**

MR imaging of the brain or spinal cord should be performed (if possible) at  $\geq 1\text{T}$  to optimize image quality and tissue contrast

A minority of participants were of the opinion there was insufficient evidence to support the superiority of  $\geq 1\text{T}$  over lower field strength (eg,  $0.3\text{T}$ – $0.5\text{T}$ ) scanners for the clinical imaging of MS.<sup>26–28</sup> The higher field strength systems do provide consistently higher image quality, by virtue of better signal intensity to noise for similar scan times and with thinner sections. This benefit would be most apparent for the evaluation of the spinal cord and for examining patients less able to cooperate with longer scanning times. Lower-field-strength magnets with an open configuration, however, may be the only option for examining extremely claustrophobic patients.

With the introduction of  $3\text{T}$  MR imaging systems into clinical practice, several questions arise, including the comparability of  $3\text{T}$  versus  $<3\text{T}$  imaging data (ie, whether  $3\text{T}$  detects more pathology when routine imaging sequences are used, sensitivity of  $3\text{T}$  MR imaging to contrast enhancement, and whether  $3\text{T}$  imaging at the time of a CIS require change in DIS criteria).

## **VII. Referral Indications and Documentation**

The referring physician should indicate on the request for the “standardized MR imaging” one of the following: (1) suspected MS; (2) baseline evaluation of MS; (3) follow-up of MS.

This simple classification is in keeping with the technical recommendations for standardized MR imaging as outlined in Tables 1 and 2 and helpful for the IP criteria as well (Table 3).

In practice, cases are not infrequently presented to radiology services with less-definitive, more-encompassing indications such as a clinical sign and/or symptom with MS listed in the differential among other potential etiologies. The decision to use the standardized (MS) protocol may not be an optimal or straightforward choice in all cases, though the protocol even when used in non-MS evaluations provides a fairly thorough evaluation for most first-time evaluations.

## **VIII. The Radiology Report**

The radiology report should use everyday language and be consistent. The report should include (1) a description of the findings, (2) a comparison with previous MR imaging scans, and (3) interpretation and differential diagnosis.

Although no specific recommendations were generated, following from the discussion above, and based on the new IP

criteria, a simple lesion characterization and terminology was discussed as likely to be helpful in patient care.

As discussed above, the report would include a count of the number of enhancing lesions when feasible, T2-hyperintense lesions, and consideration of T1-hypointense lesions and atrophy (eg, a scale of mild-moderate-severe). When feasible (in the earlier stages of MS before lesions become confluent), a count of the new T2-hyperintense lesions provides a metric of change over time.

A statement could be provided regarding T2-lesion volume: mild (few lesions); moderate (multiple lesions, early or near confluent); and severe (many, confluent lesions).

In view of the IP criteria, terminology for describing T2 lesions at diagnosis would include periventricular (touching ventricle surfaces), total T2 (all locations), juxtacortical-cortical (touching cortical gray matter), and infratentorial (cerebellum, medulla-pons-midbrain).

A quantitative measure of total lesion volume and brain and spinal cord atrophy was considered (optimistically) optional, with very few facilities capable at this time of providing these measures for clinical evaluation.

For future consideration, a reporting table, optional for use, would be developed. In most hospital and clinic environments, particularly as electronic data management and PACS are implemented, a reporting table may provide an opportunity to summarize data in individual patients over time, but this will require individual (center) efforts.

## **IX. Copy of the MR Imaging Studies**

A. A copy of these MR imaging studies should be retained permanently and be available. In addition, it may be useful for patients to keep their own studies on portable electronic media.

Because of the chronic nature of MS, which spans several decades, it is expected that many patients may change location for their care or MR imaging. At many centers, film or digital data are destroyed after several years or difficult to retrieve in a timely fashion. Consequently, a personal MR imaging file that is always with the patient is beneficial and increasingly feasible with portable media such as recordable CD, DVD, and USB keys, to allow for comparison with previous studies.

B. Studies should be stored in a standard format (eg, digital imaging and communications in medicine [DICOM]).

Comparison of prior studies is feasible by using workstations or film. If standardized studies can be loaded on a workstation, in native format, comparison with prior studies is feasible and simplified.

Viewer software (programs included with CDs, for example), while common, may be more difficult to use for direct comparisons with prior studies.

## **Discussion in the Imaging and Neurology Community since the original Presentations of these Consensus Recommendations**

Since the last consensus meeting, this work has been presented at North American, European, and Australian scientific sessions and in poster forums, as well as at less-formal venues sponsored by pharmaceutical companies, grand rounds, etc. In general, acceptance by the neurology community has been excellent, whereas anecdotal experience suggests the imaging

community has been more cautious in embracing these guidelines.

Strong concerns and questions have been raised regarding only a few issues.

1. Spinal cord imaging: The methodology for standard clinical imaging of the spinal cord for MS or myelopathy varies between practices, ranging from the gold-standard multiecho conventional spin-echo acquisition (though relatively rare today), fast spin-echo imaging (proton and T2-weighted), and fast-STIR sequences.<sup>29-32</sup> The literature is not definitive in suggesting the best sequence, because there are few studies comparing pulse sequences and study design issues render the results difficult to interpret (determination of false-positive findings). In the end, what guides selection of a spinal cord sequence may be experience with a particular sequence, instrument limitations or advantages, and other nonquantifiable factors. The choice of fast spin-echo sequence by the consensus groups likely reflects the experience of the consensus group, but by no means suggests that other sequences (fast-STIR) may not have advantages as well.

It should be noted that, with the rare exception of borderline brain MR at the time of a CIS, the spinal cord examination is not used to provide a quantitative count of lesions. The accuracy and reproducibility of counting lesions in the spinal cord is not optimal, and the spinal cord represents only a small fraction of total CNS tissue. Qualitative assessment of the spinal cord (lesion size, shape, distribution, and change over time) are important in the evaluation of MS. The use of non-standardized sequences (fast-STIR) should provide comparable information to recommended sequences for these purposes.

2. Sagittal imaging of the brain. The recommendation for sagittal fast-fluid-attenuated inversion recovery (FLAIR) imaging of the brain was also based on practice patterns. Several experienced imagers have suggested alternative sequences (T1-weighted spin-echo or T2-weighted fast spin-echo) to achieve sharper margins between corpus callosum and surrounding tissues to evaluate midline structures and corpus callosum size. These potential advantages were weighed against the use of FLAIR contrast in providing greater conspicuity of early lesions<sup>33</sup> and characteristic MS patterns. Some sites may elect to acquire a quick T1- or T2-weighted series in addition to the recommended sagittal fast-FLAIR series.

3. At the time of the initial consensus meeting, contiguous 3-mm-thick axial brain sections were recommended to increase the accuracy of lesion counting.<sup>34,35</sup> Concern was raised regarding the increase in scan time necessary to do this, and the matter was reconsidered, ultimately resulting in rewording the recommendation of section thickness to “3 mm, or 5 mm if 3 mm imaging is not possible.”

4. FLAIR axial strategy. One strategy employed to decrease scan time is to acquire the fast-FLAIR axial series after injection of contrast, during the recommended interval (5 minutes) before acquiring the T1-weighted postcontrast-enhanced series. This makes efficient use of otherwise “dead” time.<sup>36</sup> Although there may be some disadvantages (possibility of increasing blood-motion induced ghosting), the postcontrast FLAIR may be advantageous in increasing conspicuity of enhancing lesions (T1 and T2 effects), and some groups use this approach in routine imaging.

5. T1 precontrast. This sequence was not originally listed as required but is an option that many will elect to assist in determining enhancement.

6. Magnetization transfer (MT) postcontrast enhanced series. Although an appropriate MT pulse increases contrast-to-noise for enhanced lesions, optimal use requires a pre-MT pulse acquisition, and some sequences with MT are accompanied by increased noise from pulsation artifacts. This is not a commonly used option.

7. “Advanced” quantitative imaging. While the literature strongly underscores the importance in MS of abnormality of the normal-appearing white matter and gray matter<sup>1</sup> detected by MT imaging, diffusion imaging (apparent diffusion coefficient or fractional anisotropy), T1 and T2 relaxation imaging, whole brain and regional atrophy measures, and proton (<sup>1</sup>H-) MR spectroscopy, these methods have not been shown as yet to be practical in the clinical environment in individual patients. Few doubt that these methods will become important in the future in clinical care as they are validated in formal studies and technique, standardization, and quality control issues are addressed.

8. These recommendations for MS are most valuable in diagnosis and follow-up of early MS in individuals characterized by a CIS and a relapsing course. After approximately 10 years, more than half of these patients (untreated) enter a secondary progressive stage with fewer relapses, fewer new or enhancing lesions, and yet progressive disability. In the secondary progressive stage of disease, the standardized criteria, based on focal lesions, may become less helpful in following individuals.

In primary progressive MS (progressive from onset), occurring in 10%–15% of the MS population, enhancing and new lesions do occur, but far less frequently than in relapsing MS. There is speculation that in many of these individuals, lesion burden increase is more so by lesion expansion than by addition of new lesions, but many individuals show patterns indistinguishable from relapsing MS. Severe spinal cord involvement is common. At this time, there are no specific alternative recommendations for imaging patients with a diagnosis of primary progressive MS.<sup>37</sup>

9. In some centers that use fast-FLAIR and heavily T2-weighted fast spin-echo imaging, proton-weighted imaging is no longer acquired for brain pathology indications. An advantage of the proton attenuation–density series, included in the standardized MS scan, is greater sensitivity to important lesions in the posterior fossa, an area where fast-FLAIR may not infrequently fail.<sup>38</sup>

10. These recommendations may not be applicable to evaluation of pediatric MS, though most characteristics will overlap. Further studies are required to address the issues of optimal imaging standardization in pediatric MS.<sup>39</sup>

## Conclusions

The development of consensus guidelines is a challenging process that, when done well, balances advantages and disadvantages. In this case, the advantages of standardized indications and imaging are to allow diagnosis and follow-up within and between imaging centers and practices. Disadvantages include compromises in choosing methodology, removing choice, and in some cases asking practices to move from the

methodology in which they have the most experience. Ultimately, although initially slightly painful, the hope is that standardization will benefit the individual MS patient, which after all is the goal of any medical imaging. These recommendations are provided with the understanding that they will likely require modification as instrument capabilities change, new pulse sequences are developed, and more quantitative methodologies become validated in individuals and feasible in practice.

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