ON-LINE APPENDIX: PICTOGRAPHIC AND TEXTUAL ATLAS OF MRI SCORING TOOL (ADAPTED FROM VERHEY ET AL[1])

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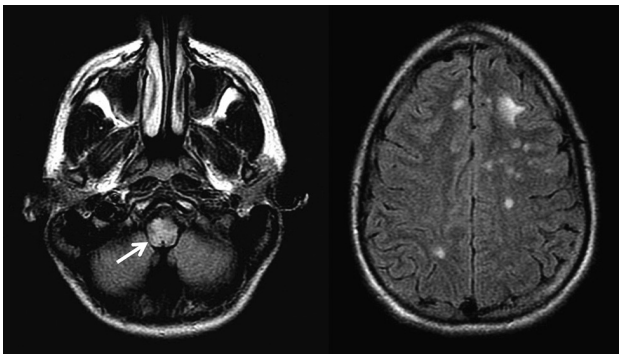
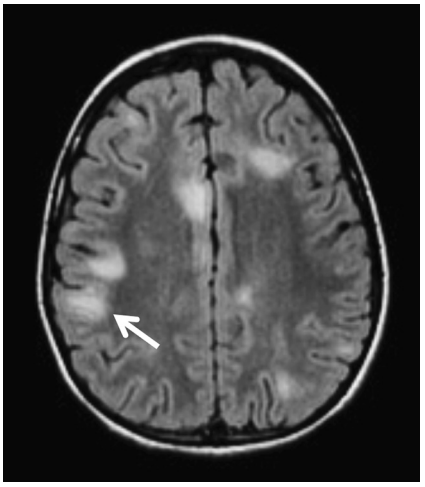
All parameters defined below are dichotomous (ie, present/absent).

1) Lesion count: total number of T2 lesions within the brain. Lesion counts >15 are binned as >15.

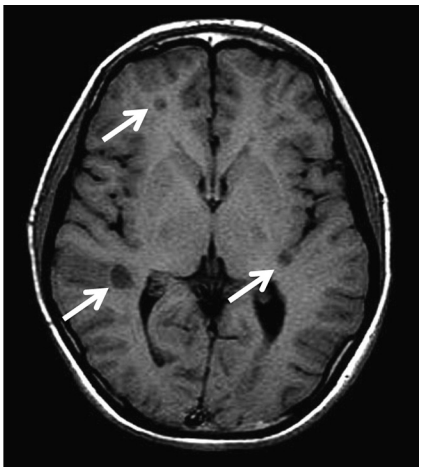
2) Bilateral lesion distribution: scan contains T2 lesions on either side of or spanning the midline in the supratentorial or infratentorial region or both.



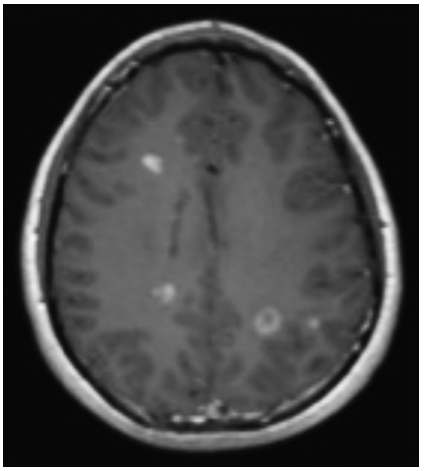
3) Gyral projections: a T2 lesion continuously projecting from subcortical white matter at the depth of a sulcus into a gyrus (or gyri) and abutting the cortical ribbon at the gyral apex.



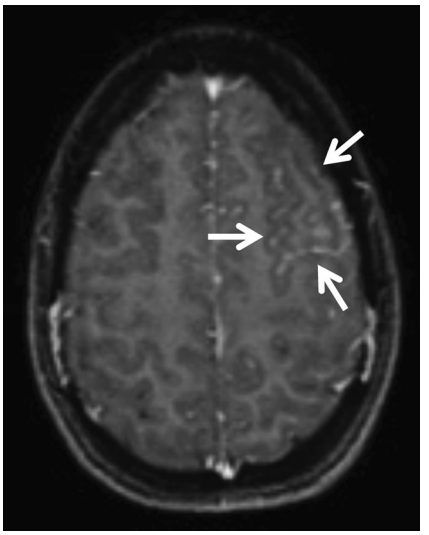
4) T1 hypointensity: abnormal region of white matter with all or a portion of the region being hypointense to cortical gray matter on T1-weighted imaging. It should be nonenhancing on post-contrast images and hyperintense on T2-weighted or FLAIR images. Cross-referencing of T1 hypointense lesions with FLAIR imaging is recommended to exclude perivascular spaces from being scored as T1 hypointense.



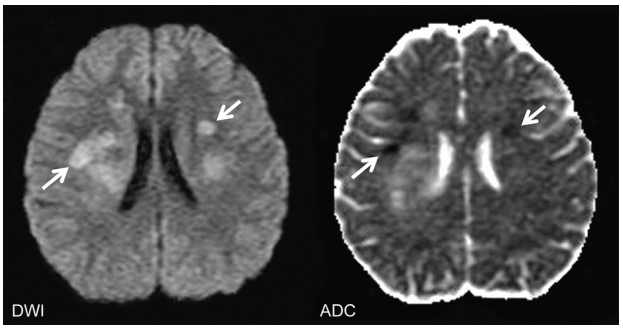
5) Lesional contrast enhancement: nodular or ringlike hyperintense signal on T1-weighted contrast-enhanced imaging (not hyperintense on T1-weighted precontrast imaging) corresponding to T2 lesions.



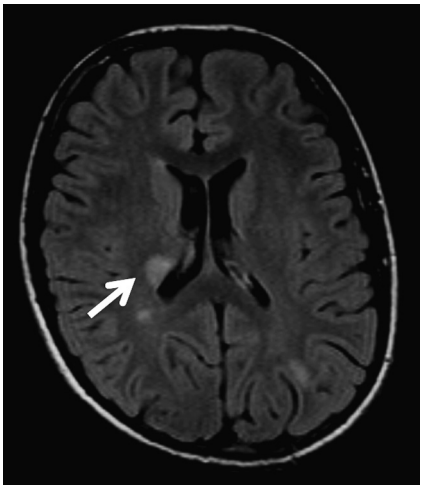
6) Leptomeningeal contrast enhancement: linear or nodular hyperintensity (minimum 3-mm length or diameter) on T1-weighted contrast-enhanced imaging, corresponding anatomically to the arachnoid and pia mater (not hyperintense on T1-weighted precontrast imaging).



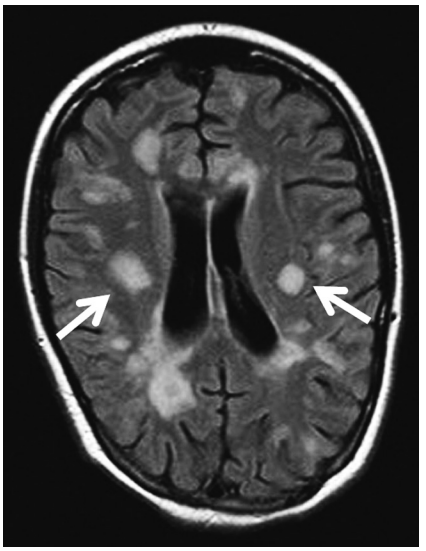
7) Diffusion restriction: hyperintensity on diffusion-weighted imaging corresponding to a T2 lesion and correlated with hypointensity on the apparent diffusion coefficient map.



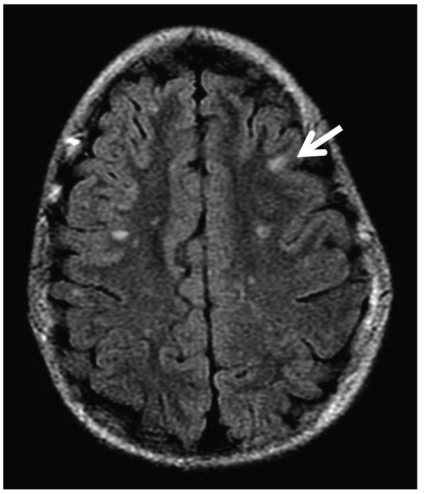
8) Periventricular lesion: white matter T2 lesion abutting any portion of the lateral ventricles only (excludes the third and fourth ventricles). Lesions involving the corpus callosal white matter are included. Lesions within the thalami or basal ganglia (refer to 12 and 13) abutting the lateral ventricles are excluded.



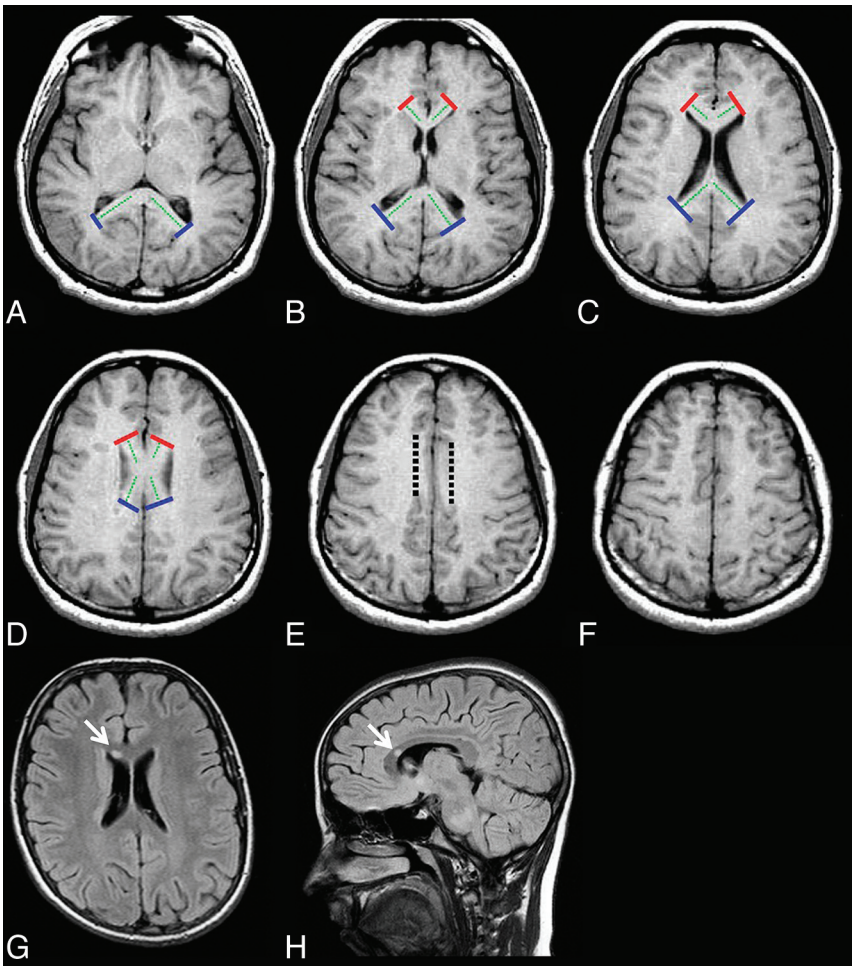
9) Cerebral white matter lesion: supratentorial nonjuxtacortical (refer to 10) and nonperiventricular (refer to 8) white matter T2 lesion. This excludes intracallosal lesions (refer to 11).



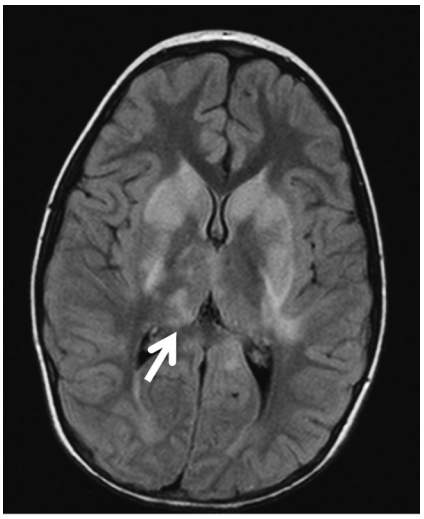
10) Juxtacortical lesion: supratentorial white matter T2 lesion contiguous with the cortical ribbon (ie, involves subcortical U-fibers[2,3]).



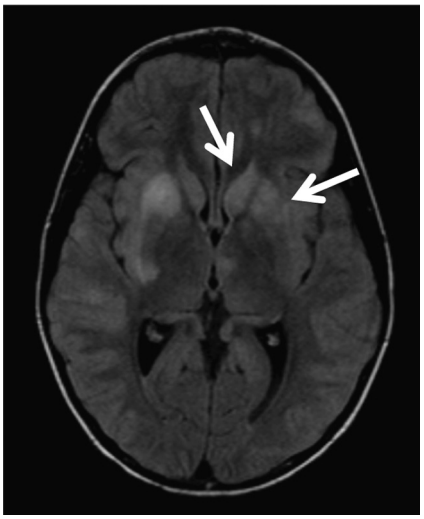
11) Intracallosal lesion: *G, H,* T2 lesion contained entirely within the margins of the corpus callosum (*A–F* in image below, adapted from Callen et al[4]); 1 mm of normal-appearing white matter surrounding lesion is confirmed as intracallosal rather than periventricular (refer to 8). *A–D*, Line (red or blue) drawn from the anterior (or posterior) tip of the lateral ventricle perpendicular to the long axis of the callosal fibers (green lines) and then extending to the cortical ribbon of the midline. *E*, Lateral margin of the lateral ventricle used when the lateral ventricles are no longer visible; medial margin of the lateral ventricle is extrapolated from its location on the most superior axial image showing the lateral ventricles: 1) on the last axial image showing lateral ventricles (note the location of most medial portion of lateral ventricle closest to midline). 2) On each more superior axial section, a line is drawn parallel to interhemispheric fissure that touches this most medial point (extrapolate by viewing the previous slice). 3) The anterior and posterior limits of this line are where the line touches the cortical ribbon of the midline.



12) Thalamic lesion: T2 lesion either entirely or partially contained within the thalamus. Bithalamic lesions are counted as discrete lesions.

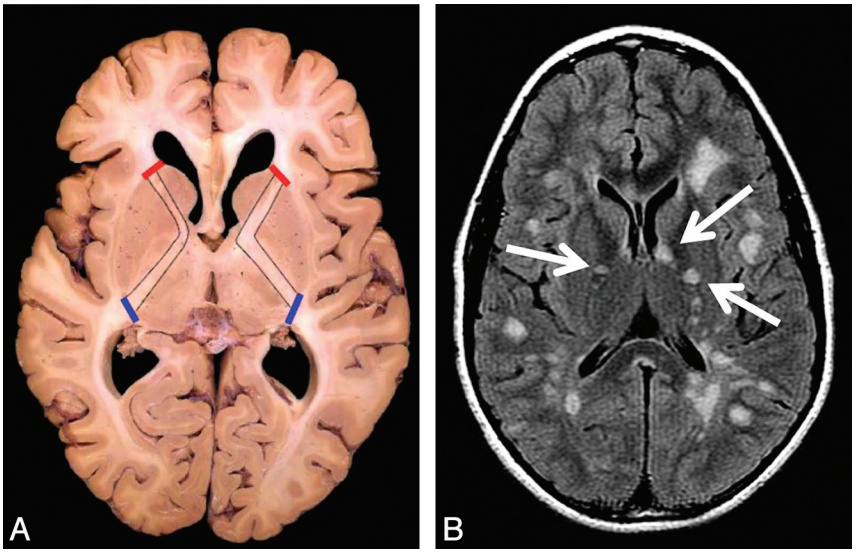


13) Basal ganglia lesion: T2 lesion either entirely or partially contained within the caudate (includes the head and tail), putamen, or globus pallidus (includes the interna and externa).

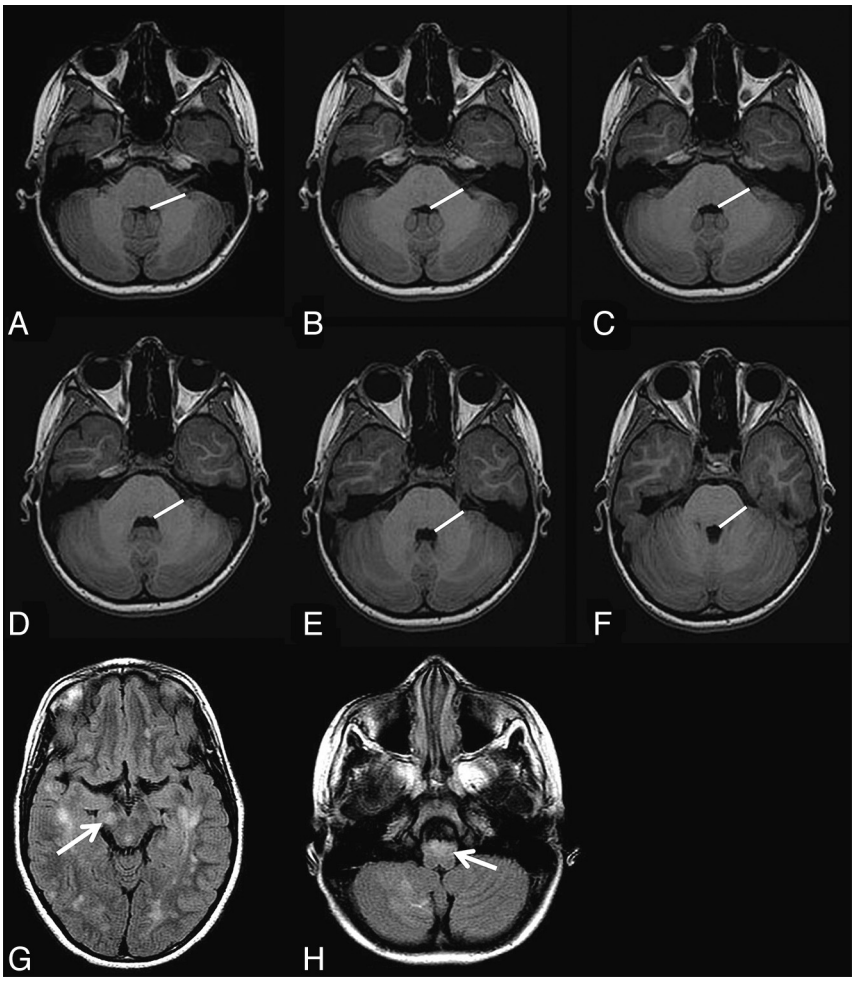


14) Internal capsule lesion: *B*, T2 lesion centered in the anterior or posterior limb of the internal capsule, defined as the supratentorial white matter bounded laterally by the lentiform nuclei and medially by the caudate and thalami (*A* in image below, adapted from Callen et al[4]).

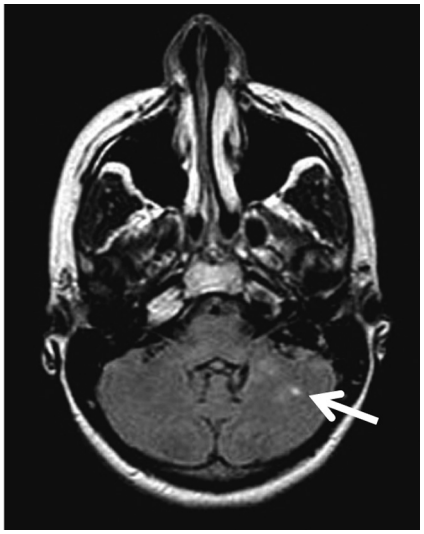
Anterior margin of anterior limb: line drawn from lateral margin of lateral ventricle to the anterolateral aspect of lentiform nucleus. Posterior margin of posterior limb: line drawn from the medial margin of lateral ventricle to the posterolateral aspect of lentiform nucleus, extrapolated from its location of the most superior axial image in which lateral ventricles are visualized.



15) Brain stem lesion: T2 lesion within the brain stem that extends from the most inferior aspect of the medulla oblongata (at the level of the decussation of the pyramids) to the most superior portion of the midbrain (at the level of the red nuclei). The posterior limits of the brain stem are defined below. The limit between the brain stem and cerebellum is defined by a line drawn from the lateral groove of the facial colliculus to the deepest (most posteriorly extending) aspect of the cerebellopontine angle, where cranial nerves 7 and 8 emerge from the pons (*D* and *E*). This line is extrapolated to superior (*A–C*) and inferior (*F*) axial slices.



16) Cerebellar lesion: T2 lesion involving the white or gray matter of any of the following: cerebellar white matter and cortices, dentate nuclei, vermis, flocculus, or nodulus. The anterior limits of the cerebellum are defined in the image above (refer to 15)



SUPPLEMENTARY PANEL: EVIDENCE FOR SCORING TOOL PARAMETERS

1) Lesion count: T2 lesion count is a necessary component in evaluating dissemination in space (DIS) criteria for MS diagnosis. At least 9 T2 lesions are required to meet dissemination in space according to the 2001 and 2005 McDonald criteria.[5,6] This requirement was recently decreased to ≥1 (clinically silent) lesion in 2 of the following regions: periventricular, juxtacortical, infratentorial, and spinal cord.[6] MRI criteria for DIS specific for pediatric-onset MS require at least 5 T2 lesions.[4]

2) Bilateral lesion distribution: Unilateral MRI abnormalities are less common in demyelination and may be more common in vascular occlusive disease or malignancy.

3) Gyral projection: Gyral projection may be a less subjective term to describe the large confluent lesions seen in children with ADEM[7] or very young children presenting with a first attack of MS.[8]

4) T1 hypointensity: T1 hypointense nonenhancing lesions, termed "black holes," have been associated with focal areas of chronic tissue damage on histopathology.[9] The presence of T1 hypointense lesions predicts MS in children with acute demyelination[1] and distinguishes MS from ADEM in children.[10]

5) Lesional contrast enhancement: the presence of asymptomatic contrast-enhancing lesions, when present simultaneously with nonenhancing T2 lesions, fulfills current McDonald criteria for dissemination with time.[6]

6) Leptomeningeal contrast enhancement: Leptomeningeal enhancement may be present in small-vessel primary angiitis of the CNS,[11] in CNS infections,[12,13] and in neoplasm,[14–16] but is not a feature of CNS demyelination.

7) Diffusion restriction: The presence of decreased diffusion supports the diagnosis of an arterial ischemic event,[17-19] in which the clinical presentation may mimic that of acute CNS demyelination.

8) Periventricular lesion: The presence of periventricular lesions is an important aspect in pediatric MS diagnostic criteria[4] and the McDonald criteria for dissemination in space.[5,6] Children with acute CNS demyelination who have ≥1 periventricular lesion on MRI are at high risk for MS diagnosis.[1]

9) Cerebral white matter lesions: The presence of cerebral white matter lesions is included as a parameter to capture those lesions that are nonjuxtacortical and nonperiventricular. The panel deemed it useful in evaluating the overall T2 lesion burden.

10) Juxtacortical lesion: The presence of juxtacortical lesions is a component of the McDonald criteria for DIS.[5,6]

11) Intracallosal lesion: The presence of intracallosal lesions is highly specific for MS but is less sensitive due to its low prevalence in children with MS, especially on MRI scans acquired at onset. This parameter may be thought of as similar to a lesion perpendicular to the long axis of the corpus callosum, a feature proposed by the French group as specific but not sensitive for pediatric-onset MS.[20]

12) Thalamic lesion: Thalamic lesions are frequently reported in children with ADEM.[7,21]

13) Basal ganglia lesion: Basal ganglia lesions are less typically seen in children with MS and, when present, may suggest another diagnosis, such as ADEM[7,21] or metabolic or mitochondrial disorders.[22–28]

14) Internal capsule lesion: Lesions involving the internal capsule were described on MRI scans of children with established MS[4] but may be less prevalent in children with MS at the time of onset.

15) Brain stem lesion: Brain stem lesions are more frequently observed in children with MS compared with adult patients.[29] This parameter is an important component of the pediatric MS criteria for DIS[4] and McDonald criteria for DIS.[5,6]

16) Cerebellar lesion: Cerebellar lesions occur in patients with both pediatric- and adult-onset MS, however, at a greater frequency in children compared with adults.[29]

On-line Table 1: Description of 48 MRI parameters

No.	Parameter	Type	Definition
1	Lesion count	Continuous	T2 lesions counted discretely to 15; if scan has >15 lesions, lesion count is scored as >15
2	Bilateral distribution	Binary	T2 lesions located in both hemispheres or, in the case of 1 brain lesion, the lesion crosses midline
3	Symmetric pattern	Binary	Symmetric T2 lesion pattern on either side of midline
4–7	Lobar location	Binary	T2 lesions located within frontal, temporal, parietal, or occipital lobes
8–11	Vascular territory location	Binary	T2 lesions involving the territory of the anterior cerebral artery, middle cerebral artery, posterior cerebral artery, or vertebrobasilar arteries
12	Cortical gray matter	Binary	T2 lesions located within the cerebral cortical ribbon
13	Juxtacortical	Binary	White matter T2 lesions abutting the cortical ribbon
14	Periventricular	Binary	White matter T2 lesions abutting the lateral ventricle
15	Subcortical	Binary	Nonjuxtacortical and nonperiventricular white matter T2 lesions
16	Intracallosal	Binary	T2 lesions located within the confines of the corpus callosum
17	Internal capsular	Binary	T2 lesions involving the anterior or poster limbs of the internal capsule
18–21	Deep gray matter	Binary	T2 lesions involving the caudate, putamen, globus pallidus, thalamus
22	Cerebellar	Binary	T2 lesions involving the cerebellar white or gray matter
23	Cerebellar peduncle	Binary	T2 lesions involving the superior, middle, or inferior cerebellar peduncles
24–26	Brain stem	Binary	T2 lesions involving the right, left, or midline brain stem
27	Cervical spinal cord	Binary	T2 lesions involving the visible region of the cervical spinal cord on brain MRI
28	Black hole	Binary	Lesions isointense or hypointense to cortical gray matter on T1-weighted imaging that are confirmed as T2-hyperintense
29	Fingerlike projection	Binary	T2 lesion projecting continuously into a gyrus from the subcortical white matter to the juxtacortical white matter at the apex of a gyrus
30	Fingerlike + projection	Binary	Fingerlike projection extending into the cortical gray matter at the gyral apex
31	Dot-dash sign	Binary	T2-weighted irregularity of the ependymal stripe on the undersurface of the corpus callosum, defined as at least 2 dots connected by a dash; the dot is a round hyperintense irregularity of the ependymal undersurface with a diameter larger than the thickness of the dash adjacent to it; the dash is the remaining normal ependymal stripe[30]
32	Target lesion	Binary	T2 lesion with a more hyperintense center relative to the penumbra
33	Diffusion restriction	Binary	Restricted diffusion on DWI and ADC, correlating with a T2 lesion
34	Optic nerve lesion	Binary	T2 lesion along 1 or both optic nerves, anywhere between orbit and optic chiasm
35	Lesion enhancement	Binary	Gadolinium-enhancing lesion, correlating with a T2 lesion
36–39	Optic nerve enhancement	Binary	Contrast enhancement of any: optic nerve, optic nerve sheath, extraoptic fat, or extraoptic muscle
40–42	Other enhancement	Binary	Dural, ependymal, or perineural (excluding optic nerves) enhancement
43–45	Leptomeningeal enhancement	Binary	Contrast enhancement of the arachnoid and pia mater; if present, leptomeningeal enhancement is also scored as linear or nodular
46–47	Compartment of enhancement	Binary	Lesional contrast enhancement present in supratentorial or infratentorial compartments
48	Proportion of discrete lesions	Categorical	Proportion of T2 lesions having well-defined lesion boarders in all planes: 0%–25%, 26%–50%, 51%–75%, 76%–100%

On-line Table 2: Frequency of MRI parameters excluded due to lack of discriminating ability[a]

	ADEM (*n* = 16)		MS (*n* = 27)		SV-cPACNS (*n* = 12)		*P* Value	
	Rater 1	Rater 2	Rater 1	Rater 2	Rater 1	Rater 2	Rater 1	Rater 2
Frontal lobar location	12 (75)	14 (88)	25 (92)	21 (78)	7 (58)	7 (58)	.038	0.340
Temporal lobar location	9 (56)	11 (69)	13 (48)	14 (52)	3 (25)	3 (25)	.246	.151
Parietal lobar location	12 (75)	13 (81)	18 (67)	21 (78)	3 (25)	3 (25)	.020	.003
Occipital lobar location	6 (38)	9 (56)	10 (37)	11 (41)	1 (8)	1 (8)	.191	.060
ACA vascular territory	9 (56)	10 (63)	14 (52)	13 (48)	4 (33)	6 (50)	.5	.930
MCA vascular territory	15 (94)	13 (81)	25 (93)	23 (85)	8 (67)	8 (67)	.06	.263
PCA vascular territory	11 (69)	10 (63)	17 (63)	19 (70)	3 (25)	2 (17)	.05	.005
Vertebrobasilar vascular territory	12 (75)	11 (69)	16 (59)	15 (56)	4 (33)	3 (25)	.09	.128
Cerebellar peduncle	7 (44)	7 (44)	9 (33)	10 (37)	1 (8)	0	.124	.028
Target lesion	0	1 (6)	10 (38)	12 (46)	0	1 (8)	.002[b]	.016
Nodular leptomeningeal enhancement[c]	0	0	0	0	0	0	–	–
Linear leptomeningeal enhancement[c]	1 (100)	2 (100)	2 (100)	1 (100)	2 (100)	1 (100)	–	–
Dural enhancement[d]	0	1 (9)	0	0	0	0	–	.508
Supratentorial lesion enhancement[d]	3 (27)	5 (45)	12 (55)	12 (55)	4 (40)	4 (40)	.370	.841
Infratentorial lesion enhancement[d]	1 (9)	2 (18)	7 (32)	8 (36)	0	1 (10)	.080	.532

Note:—ACA indicates anterior cerebral artery; PCA, posterior cerebral artery; –, not enough variability in frequencies to compute a *P* value.

[a] Numbers represent No. (%). Frequencies of each parameter are compared within each rater separately, as a factor of diagnosis. Significance was defined as $P < .003$, adjusting for multiple comparisons.

[b] Although they were significant after correcting for multiple comparisons, the panel agreed to exclude target lesions due to lack of agreement on a definition.

[c] Leptomeningeal enhancement was present in 5 children (1 with ADEM, 2 with MS, 2 with SV-cPACNS) according to rater 1, and 4 children (2 with ADEM, 1 with MS, 1 with SV-cPACNS) according to rater 2.

[d] Gadolinium was administered in 11 children with ADEM, 22 with MS, and 10 with SV-cPACNS.

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