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MAGNETIC RESONANCE

Multiple sclerosis imaging in clinical practice: a European-wide survey of 428 centers and conclusions by the ESNR Working Group

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Abstract

Objectives To evaluate compliance with the available recommendations, we assessed the current clinical practice of imaging in the evaluation of multiple sclerosis (MS).

Methods An online questionnaire was emailed to all members and affiliates. Information was gathered on applied MR imaging protocols, gadolinium-based contrast agents (GBCA) use and image analysis. We compared the survey results with the Magnetic Resonance Imaging in MS (MAGNIMS) recommendations considered as the reference standard.

Results A total of 428 entries were received from 44 countries. Of these, 82% of responders were neuroradiologists. 55% performed more than ten scans per week for MS imaging. The systematic use of 3 T is rare (18%). Over 90% follow specific protocol recommendations with 3D FLAIR, T2-weighted and DWI being the most frequently used sequences. Over 50% use SWI at initial diagnosis and 3D gradient-echo T1-weighted imaging is the most used MRI sequence for pre- and post-contrast imaging. Mismatches with recommendations were identified including the use of only one sagittal T2-weighted sequence for spinal cord imaging, the systematic use of GBCA at follow-up (over 30% of institutions), a delay time shorter than 5 min after GBCA administration (25%) and an inadequate follow-up duration in pediatric acute disseminated encephalomyelitis (80%). There is scarce use of automated software to compare images or to assess atrophy (13% and 7%). The proportions do not differ significantly between academic and non-academic institutions.

Conclusions While current practice in MS imaging is rather homogeneous across Europe, our survey suggests that recommendations are only partially followed.

Clinical relevance statement Hurdles were identified, mainly in the areas of GBCA use, spinal cord imaging, underuse of specific MRI sequences and monitoring strategies. This work will help radiologists to identify the mismatches between their own practices and the recommendations and act upon them.

Key Points

- *While current practice in MS imaging is rather homogeneous across Europe, our survey suggests that available recommendations are only partially followed.*
- *Several hurdles have been identified through the survey that mainly lies in the areas of GBCA use, spinal cord imaging, underuse of specific MRI sequences and monitoring strategies.*

Keywords Multiple sclerosis · Magnetic resonance imaging · Contrast media · Gadolinium

Abbreviations

ADEM	Acute disseminated encephalomyelitis
CIS	Clinically isolated syndrome
DIR	Double inversion recovery
DWI	Diffusion-weighted imaging
ESNR	European Society of Neuroradiology
GBCA	Gadolinium-based contrast agents
GRE	Gradient recalled echo
MAGNIMS	Magnetic Resonance Imaging in MS

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MS	Multiple sclerosis
PD	Proton density
PSIR	Phase sensitive inversion recovery
STIR	Short tau inversion recovery
TSE	Turbo spin echo

Introduction

Multiple sclerosis (MS) is a prevalent neurological disease that requires the frequent use of MRI for both the initial diagnosis and follow-up of the disease. The 2017 revisions of the McDonald criteria on MS reinforced the importance of brain and spinal cord MRI [1].

The available recommendations in MS imaging [2–9] contribute to improving both the diagnostic performance and the safety of MRI. However, their clinical impact is directly dependent on the applicability in the daily routine. Indeed, adoption of a standardized MRI protocol is a major challenge because of differences in health-care systems and clinical practices between countries in Europe.

To what extent these suggested protocols are applied in clinical settings across Europe is still unknown. The European Society of Neuroradiology (ESNR) therefore sought to assess the current clinical practice of imaging in the evaluation of MS patients and determine potential hurdles to act upon.

To this end, a pan-European survey was distributed among ESNR members and affiliates, addressing the applied MRI protocols and image analysis. The results of this survey as well as conclusions by the MS working group are reported in this manuscript.

Material and methods

An online questionnaire was designed using Google Forms open-access toolbox (Google.com). Questions were assembled by the members of the ESNR MS Working Group (authors J.H., T.Y., A.R., M.S.S., M.B., A.W.) and further modified/added by the ESNR subspecialty committee on Diagnostic Neuroradiology (M.W.V., A.C., A.R., A.K., L.V.D.H.).

The questionnaire featured 27 items (see supplement for details and the entire list of questions).

Results

Demographic data

A total of 428 unique (non-duplicate) entries from European institutions were received from a total of 44 countries. Countries with the most participating institutions were Italy ($n=93$, 21.7%), Spain ($n=52$, 12.1%), France ($n=49$, 11%), Germany ($n=32$, 7.2%) and Switzerland ($n=30$, 6.7%).

Among the 428 respondents, 82% ($n=349$) were neuroradiologists, 12% ($n=51$) worked as general radiologists and 4% were in training. A total of 234 (54.6%) worked in academic hospitals, 114 (26.6%) in general hospitals, 46 (10.7%) in private hospitals or clinics and 34 (7.9%) in private practice.

When we restricted the analysis to respondents who worked only in one institution ($n=407$), 213 (49.7%) worked in an academic and 194 (45.3%) in a non-academic setting. This sample excluded respondents ($n=21$, 4.9%) who worked in both settings. We used this sample to stratify several of the analyses for an academic versus non-academic setting.

Compliance with the available recommendations

Ninety-one percent of the 428 responding institutes say that they follow specific recommendations for MS imaging. The 2015 Magnetic Resonance Imaging in MS (MAGNIMS) recommendations [8, 9] are the most used (51%) followed by local guidelines (49%).

Use of MRI in MS patients

Number of MRI examinations dedicated to MS performed per week. Of the responding institutes, 13% perform less than five scans for the evaluation of MS per week, 32% five to ten scans per week, 30% ten to 20 scans per week and 25% more than 20 scans per week (Fig. 1). These proportions do not differ significantly between academic and non-academic institutions, but scan numbers were slightly higher in the academic centers.

MRI protocol duration Brain MRI examinations last more than 20 min at initial diagnosis for 81% of the responding institutes (Fig. 1). The duration is shorter at follow-up with only 57% performing brain MR examinations lasting more than 20 min. MRI protocol duration is shorter for spinal cord: MRI examinations lasting more than 20 min for 66% of institutions at initial diagnosis, 51% at follow-up.

Percentage of MRI examinations performed at 3 T A 3-T MR scan is always used in 18%, and never in 37% (Fig. 1). The use of 3 T appears slightly higher in academic centers with only 27% using always a 1.5-T MR scanner. Fifty percent of the institutes systematically use the same MR scanner for the follow-up of a given MS patient.

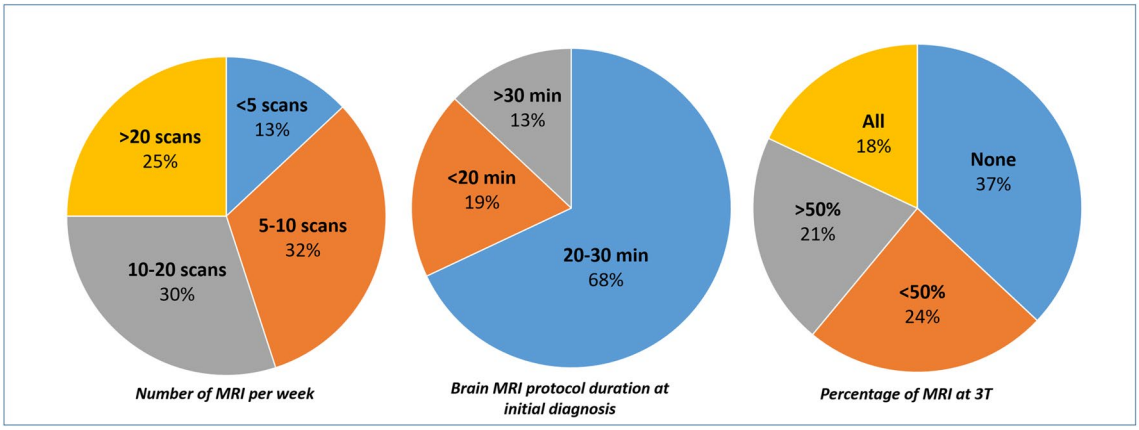

Fig. 1 Use of MRI in MS patients. Pie charts. While the systematic use of 3-T MR scanners remains rare, our survey confirmed the strong impact of MS on MRI resources

MRI protocol

Brain imaging

Standard MRI sequences Practices are rather homogeneous regarding standard MRI sequences. At the initial diagnosis, the following MRI sequences are nearly systematically performed: FLAIR (100%, of which 82% in 3D acquisition and 18% in 2D), T2-weighted (89%) and DWI (92%). Only 27% always used a proton-density sequence (Table 1).

Additional MRI sequences (PSIR, DIR, SWI) Overall, these MRI sequences are mainly used in the setting of initial diagnosis (Table 1). T2*/SWI is the most used, with 87% using it always or sometimes at initial diagnosis (68% at follow-up). Fifty-eight percent use DIR always or sometimes at initial diagnosis (50% at follow-up). Only 28% perform PSIR always or sometimes at the initial diagnosis. These proportions do not differ significantly between academic and non-academic institutions.

Optic nerve imaging An additional 2D coronal T2-weighted sequence is performed by 63% including different strategies regarding fat suppression (STIR, Fat Sat, DIXON). 17% of the institutions use 3D FLAIR or 3D DIR.

Pre-contrast T1-weighted Some institutions use several pre-contrast T1-weighted sequences since 463 responses were recorded (Fig. 2). Sixty-one percent perform a 3D acquisition in this setting. Forty-one percent perform the 3D GRE T1-weighted sequence frequently or systematically, which represents 66% of all the 3D acquisitions performed. Twenty-one percent performed 3D TSE T1, 33% 2D T1-weighted SE and 5% 2D T1-weighted GRE. TSE acquisition is more used (54%) than GRE (46%).

Use of GBCA and post-contrast T1-weighted brain imaging In line with the available recommendations, the three most frequent situations for using GBCA are (i) initial diagnosis (87%), (ii) occurrence of a new, recent, clinical episode (52%) and (iii) change of treatment (39%). Only 15% use GBCA for detecting active lesions in patients with diffuse and confluent chronic MS lesions (in whom visual detection of new T2 lesions might be difficult).

Thirty-four percent always use GBCA at follow-up and 28% in case of new lesions already visible on FLAIR/T2-weighted images (Fig. 3).

Regarding the time delay between GBCA administration and imaging, 25% do not meet the delay time of at least 5 min and only 41% use the FLAIR sequence post-contrast.

Some institutions use several post-contrast T1-weighted sequences since 538 responses were recorded (Fig. 4). A total of 67.5% performed a 3D acquisition with 40% using the 3D T1-weighted GRE sequence frequently or systematically. Twenty-seven percent use the 3D T1-weighted TSE, 29% 2D T1-weighted SE and 4%, 2D T1-weighted GRE. TSE acquisition is more used (56%) compared to GRE (44%).

Spinal cord imaging

Standard MRI sequences Over 90% of institutions always perform T2-weighted imaging in the sagittal plane, 76% STIR and only 17% PD (Table 1). Sixty-three percent always perform T2-weighted in the axial plane using a TSE acquisition and only 37% use GRE. Ninety percent use a

Table 1 Use of MRI sequences in the setting of MS. Of the standard MRI sequence, FLAIR is the only one to be systematically used. Additional MRI sequences are mainly used for brain imaging at the initial diagnosis of MS, in line with the available recommendations. A significant subset of institutions performs a single sagittal T2-weighted sequence which is not considered to be sufficient according to the available recommendations

	Use of MRI sequences in the setting of MS (% of responding institutions)		
	Systematically	*Sometimes*	*Never*
Brain Imaging			
Standard imaging: initial diagnosis			
FLAIR	100%	0%	0%
T2	89%	8%	3%
DWI	92%	6%	2%
PD	27%	18%	55%
Standard imaging: follow-up			
FLAIR	100%	0%	0%
T2	88%	7%	5%
DWI	89%	9%	2%
PD	28%	16%	56%
Additional MRI sequences: initial diagnosis			
PSIR	5%	23%	72%
DIR	23%	35%	41%
SWI/T2*	57%	30%	13%
Additional MRI sequences: follow-up			
PSIR	4%	17%	78%
DIR	22%	28%	50%
SWI/T2*	40%	28%	31%
Spinal cord imaging			
Standard MRI sequences			
T2w sagittal	93%	6%	1%
STIR sagittal	76%	17%	7%
PD sagittal	17%	14%	69%
T2w TSE axial	63%	29%	8%
T2w GRE axial	37%	40%	24%
Additional MRI sequences			
PSIR	7%	11%	82%
DIR	0%	6%	94%
DWI	4%	23%	73%

slice-thickness between 2 and 3 mm. Fifty-eight percent scan the whole spinal cord without including the lumbar spine, 17% scan the whole spine (including the lumbar spine) and 25% scan only the upper half of the spinal cord (i.e., C1 to T5).

Additional MRI sequences (PSIR, DIR, SWI) Additional MRI sequences are rarely used for spinal cord imaging. Only 27% performed DWI always or sometimes, 18% PSIR and only 5% DIR (Table 1).

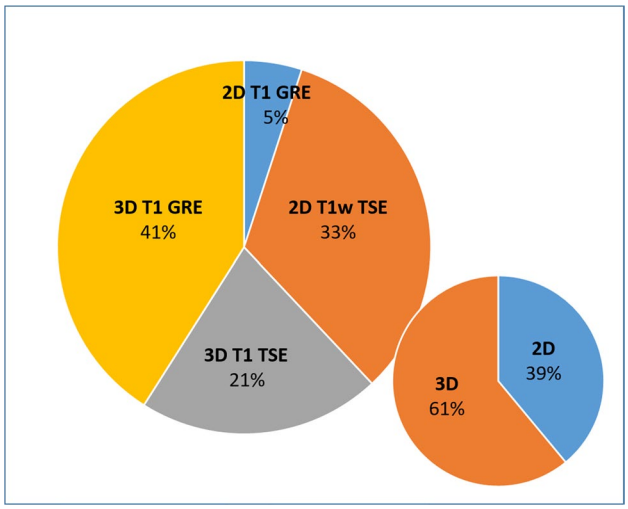

Fig. 2 Pre-contrast brain imaging. Pie charts. In MS patients, pre-contrast T1-weighted imaging is usually performed to assess atrophy which may explain the higher use of 3D GRE-based MRI sequences

Pediatric patients

Fifty-five percent of institutions take care of children. Only 40% of these follow the updated IPMSSG (International Pediatric MS Study Group) MRI criteria [3]. Less than 20% ensure a 5-year follow-up in pediatric patients having presented an ADEM, and 48% ensure a 1-year follow-up.

Use of automated tools

There is little use of automated tools for comparing MR images or to assess atrophy, with only 13% and 7% using such an approach frequently or systematically, respectively (Fig. 5). These proportions do not differ significantly between academic and non-academic institutions.

Discussion

Generalizability of results and limitations

The ESNR survey on imaging in MS had a reasonable number of responses, with a good geographical spread including Eastern Europe. We should consider however that the low response rate will have led to selection bias, likely towards an overrepresentation of those who are very active and potentially have more expertise in the field of MS. Indeed, most of the respondents were subspecialty-trained neuroradiologists and working in academic centers, seeing roughly

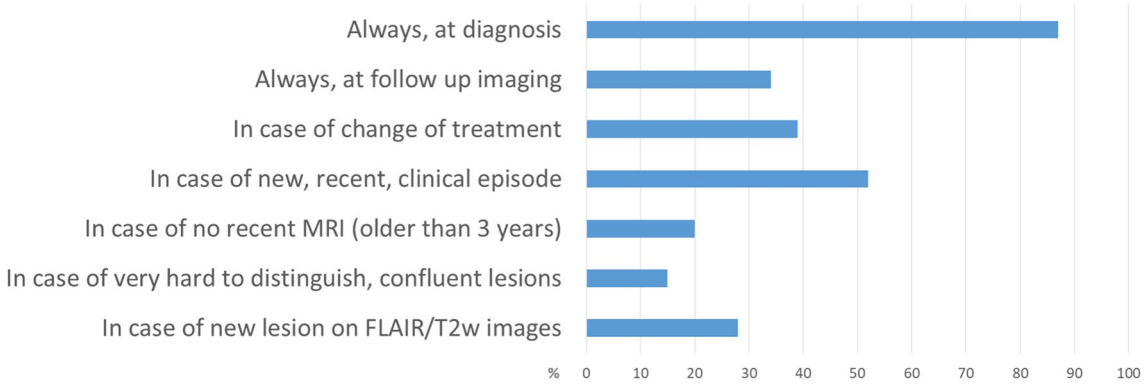

Fig. 3 GBCA use in MS patients. Our survey pointed out a clear mismatch between the current practices in Europe and the available recommendations regarding GBCA use in MS patients (mainly the follow-up strategy of MS/CIS patients)

10 to 20 scans per week for patients with MS. We stratified several results for academic versus non-academic centers and found that these did not differ, pointing towards generalizability and representativeness. Also, the response rate in this survey was slightly higher than earlier pan-European surveys conducted by the ESNR on glioma and dementia imaging [10, 11].

The reasons why some institutions follow certain recommendations and not others were not specifically evaluated for each of the items included in this survey. We assumed that it would have significantly increased the time required to complete the questionnaire, which could have been discouraging. Indeed, the purpose of this survey was not to provide a root cause analysis of the diverse practices observed among the responding institutes (which may be the objective of future studies). Rather, we aimed at assessing the current clinical practice of imaging in the evaluation of multiple sclerosis. The clinical importance of this work is significant since it will help radiologists to identify the potential mismatches between their own practices and the updated recommendations and act upon them.

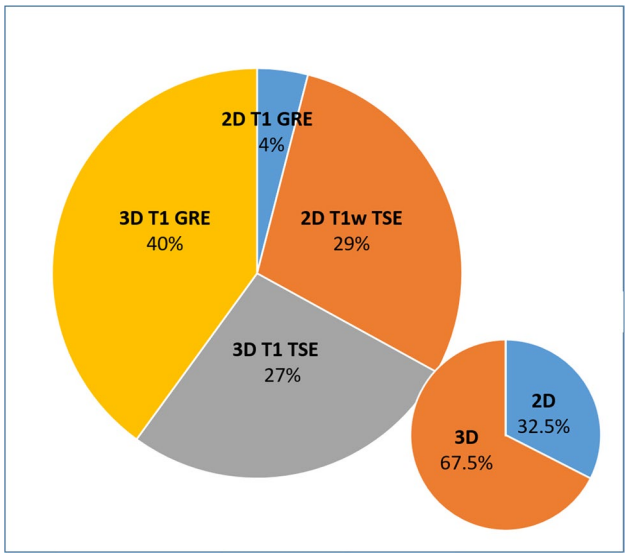

Fig. 4 Post-contrast brain imaging. Pie charts. While a significant subset of institutions still uses 2D post-contrast acquisitions, 3D T1-weighted GRE sequence is unsurprisingly the most used. Note the relative underuse of TSE-based 3D sequences

Depending on the vendors, there may be significant differences in terms of image quality or availability of MRI sequences, which may have also biased our results. As an example, the 3D heavily T1-weighted sequence phase-sensitive inversion recovery (PSIR) sequence, which was previously reported useful for the imaging of spinal cord [12] and cortical lesions [13], is still not available on all MR scanners. The ability to optimize the MRI sequences may also have influenced our results emphasizing the importance of the radiologist having a thorough understanding of MRI sequences.

Compliance with available recommendations

In adult MS patients, we observed very high reported compliance with published recommendations for diagnosis and monitoring. However, our survey revealed some mismatches between the diverse practices observed and these recommendations (particularly regarding spinal cord imaging and GBCA use, as stated above).

While a significant portion of institutions cares for children, compliance with available recommendations appears especially low in pediatric patients. Only a minority of institutions ensure an adequate follow-up of 5-year in patients with ADEM [3, 14].

Use of MRI in MS patients

Our survey confirmed the strong impact of MS on MRI resources. The longer acquisition times observed at the initial diagnosis are in-line with the recommendations [2–7].

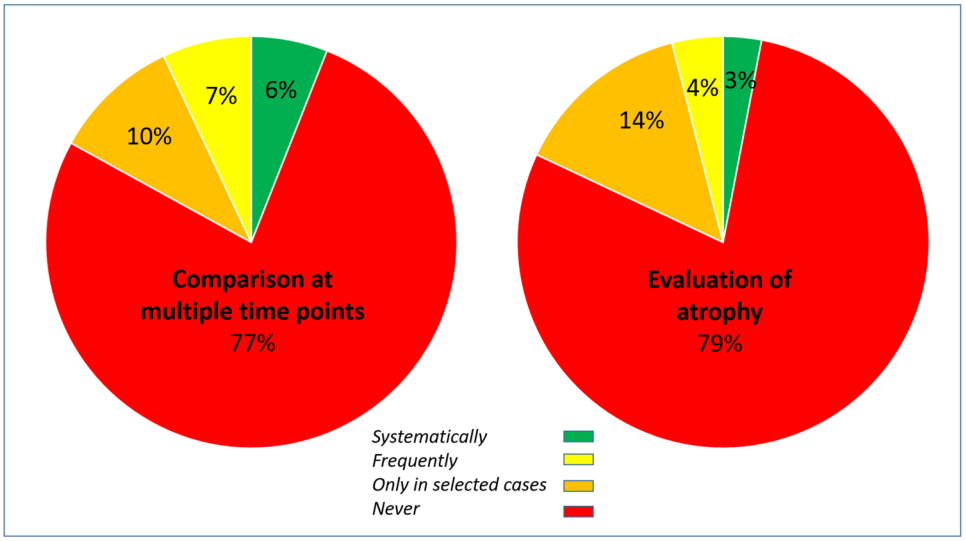

Fig. 5 Use of fully automated software. Pie charts. Our survey pointed out a very limited use of automated tools in daily routine practice

The systematic use of 3-T MRI is quite rare. Even though 3-T MR scanners provide a higher detection rate for MS lesions and shorter acquisition times, there is still no evidence that 3-T MRI leads to an earlier diagnosis of MS [15].

Identical image acquisition is strongly recommended to compare brain and spinal cord studies, also considering that image contrast/artifacts can be different from one MR scanner to another. Most of the automated software rely on data acquired with the same protocol, thus underlining the benefit of using the same MR scanner.

Since long-lasting MR examinations are performed in MS patients, reducing the scan time is a major issue. First, it may be possible to shorten the MRI protocol in selected cases (high-quality 3D FLAIR might replace T2-weighted images[2]). Some MR sequences (such as pre-contrast 3D T1-weighted and SWI) are considered optional for the diagnosis of MS and could be potentially removed. Few MS patients have lesions exclusively located below the level of the fifth thoracic vertebra [16], indeed reducing the coverage to the upper half of the cord is feasible in the absence of clinical involvement of the lower cord [2]. Acceleration techniques are also available to decrease the scan time, such as compressed-sensing, reported useful to accelerate 3D FLAIR [17] or DIR [18].

MRI protocol, brain imaging

While 3D techniques are now routinely available, some institutions still use 2D FLAIR. The value of 3D FLAIR was recently emphasized to improve diagnostic accuracy and the ability to identify new lesions [2]. Indeed, multiplanar analysis and realignment of anatomic orientation are particularly useful to compare serial MRI scans [2].

While its value in the setting of MS appears low, DWI is almost systematically used both for diagnosis and monitoring purposes. Acute demyelinating lesions can present with high signal intensity and low apparent diffusion coefficient [19]. However, restricted diffusion is not a specific marker for demyelination and DWI cannot be used as an alternative to contrast-enhanced T1-weighted imaging. On the opposite, DWI is useful to rule out the differential diagnosis and is recommended in patients at risk of developing PML [2] since this sequence may help to detect small, asymptomatic PML lesions [20, 21].

In MS patients, pre-contrast T1-weighted imaging is usually performed to assess atrophy. Since spontaneous hyperintensities are rare pre-contrast T1-weighted imaging rarely assists with the interpretation of post-contrast hyperintensities [2]. In addition, there is still insufficient evidence to recommend the routine use of brain volumetric measurements [2].

The use of 3D post-contrast imaging is recommended in MS patients [2–7]. Unsurprisingly, post-contrast 3D T1-weighted GRE is the most used. Such sequence has several advantages including high sensitivity, lack of flow-related artifacts, high spatial resolution and signal-to-noise ratio, and multiplanar analysis [22, 23]. However, enhancing lesions may be difficult to detect on heavily T1-weighted images (such as MPRAGE) due to the higher background white matter signal [25, 26]. The value of the SE acquisition was also previously reported [24]. The SE and TSE are commonly performed for 2D and 3D T1-weighted acquisitions respectively. Of note, 3D TSE/FSE sequences have the same advantages as 3D GRE but do not compromise the contrast between contrast-enhancing lesions and background. Such sequences also include a black-blood effect further improving the detection of small enhancing lesions [26, 27]. Indeed,

our survey pointed out a potential underuse of post-contrast 3D TSE sequences.

We pooled SWI and 3D T2*-weighted as the same item for clarity. SWI can identify paramagnetic rim lesions in MS patients, potentially increasing the specificity of MRI [28]. However, such a finding is still not recognized as a reliable diagnostic marker [2]. 3D T2*-weighted sequence was reported useful to detect the central vein sign [29] but is not widely available and requires specific expertise [2].

DIR may improve the detection of juxtacortical/intracortical [30], infratentorial [31], spinal cord [32] and optic nerve [33] MS lesions. It is considered in recommendations as optional [2]. Once again, image contrast and artifacts may vary according to the MR scanner used.

Optic nerve MRI has no added value in establishing a diagnosis of MS [1] and is only recommended for differential diagnosis with NMOSD and in patients with atypical clinical features [2]. The standardized protocol includes fat-suppressed T2-weighted (or STIR) and contrast-enhanced T1-weighted sequences. Of note, a small subset of institutions uses 3D FLAIR fat-suppressed or DIR sequences (some optimized 3D FLAIR/DIR sequences allow for the visualization of the optic nerves without artifacts).

GBCA use in MS patients

The recognition of gadolinium deposition in the CNS has led to specific recommendations for its use [1, 2, 34]. Our survey revealed a mismatch between the current practices in Europe and these recommendations, particularly regarding the follow-up strategy of MS/CIS patients. Indeed, the systematic use of GBCA is not recommended (i) at follow-up in clinically stable patients or, (ii) to establish MS diagnosis when the first MRI does not fulfill the criteria since the demonstration of dissemination in time can be based exclusively on the detection of new T2 lesions [2].

In addition, the time delay between GBCA administration and T1-weighted acquisition should be identical during follow-up and not shorter than 5 min (ideally 10 min) [2]. Performing the administration of GBCA before T2-weighted/FLAIR sequences is helpful to assure such a delay time [25]. Only a minority of institutions use such a cost-effective strategy.

MRI protocol, spinal cord imaging

Mismatches between practices and available recommendations were also observed for spinal cord imaging.

The spinal cord MRI protocol must include at least two of the following three sagittal sequences: T2-weighted TSE with moderately long echo times, PD-weighted echo, or STIR [2]. Some institutions perform a single sagittal T2-weighted sequence which is not considered to be sufficient (due to its limited sensitivity and because a second sequence is required to confirm lesions and exclude artifacts) [35]. The underuse of STIR may be related to longer acquisition time and difficulties encountered in optimizing this sequence.

Scanning the whole spine (including the lumbar spine) is associated with lower spatial resolution and reduced sensitivity (imaging below the level of the conus has no added value for MS diagnosis).

Axial slices are not systematically acquired which is in line with the recommendations [2]. Our survey pointed out a potential underuse of the axial T2-weighted-GRE sequence, highly sensitive at the cervical level [36, 37].

Some institutions perform DWI which is surprising considering its low added value and the difficulties of implementation. A small subset of institutions (18%) routinely perform 3D PSIR that was reported to be sensitive to detect cervical spinal cord MS lesions [38]. However, this sequence is not available on all MR scanners and requires strong expertise [2].

Image analysis

Our survey pointed out a very limited use of automated tools in the daily routine. The reasons were previously detailed in the ESNR survey on imaging of dementia including the limited availability of robust tools, lack of time to use (offline) pipelines and difficulties in the interpretation [11].

Brain volume loss in patients with MS has been shown to occur at a faster rate and atrophy has been suggested as a predictor of disability progression [39]. There is, however, not enough evidence to use this measure at an individual level [40]. Future advances in post-processing imaging are needed to facilitate the transition from clinical trials to clinical practice.

Overall, our survey therefore underlines the importance of better publicizing and applying the available recommendations in clinical routine.

Conclusion and outlook

Given the survey findings, we conclude that current practice in MS imaging is rather homogeneous across Europe, in both academic and non-academic centers. However, our survey suggests that the available recommendations are only partially followed. These mainly lie in the areas of GBCA use (mainly in terms of indication and delay-time), spinal cord imaging, underuse of specific MRI sequences and monitoring strategies (particularly in the setting of pediatrics).

Reasons for these findings may include radiologist's experience, availability of MRI sequences and differences in terms of image quality according to the vendors.

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Declarations

Guarantor The scientific guarantor of this publication is Prof Tarek Yousry.

Conflict of interest Prof A. Rovira serves/ed on scientific advisory boards for Novartis, Sanofi-Genzyme, Synthetic MR, TensorMedical, Roche, Biogen, Bristol Myers, and OLEA Medical, and has received speaker honoraria from Bayer, Sanofi-Genzyme, Merck-Serono, Teva Pharmaceutical Industries Ltd, Novartis, Roche and Biogen.
The other authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was not required for this study (ESNR online survey).

Ethical approval Institutional Review Board approval was not required due to the study design (ESNR online survey).

Methodology
- Observational
- Multicenter study

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