# A multicentre audit on the use of MRI in the monitoring and management of people with Multiple Sclerosis

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# Contents

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# Participating centres

**England**

Nottingham University Hospital, Nottingham

National Hospital for Neurology and Neurosurgery, London

Leeds Teaching Hospitals, Leeds

Sheffield Teaching Hospitals, Sheffield

Sunderland Royal Hospital, Sunderland

Barts Health NHS Trust, London

Medway NHS Trust, Kent

Brighton and Sussex NHS Trust, Brighton

Bradford Teaching Hospitals, Bradford

Coventry University Hospital, Coventry

Salford Royal Hospital, Manchester

Mid Essex Hospitals, Essex

Great Western Hospitals NHS Trust, Swindon

Royal Stoke University Hospital, Stoke

Imperial NHS Trust, London

Queen Elizabeth Hospital, Birmingham

Addenbrooke's Hospital, Cambridge

Newcastle upon Tyne Hospital, Newcastle

University Hospitals Southampton, Southampton

**Scotland**

Western General Hospital, Edinburgh

**Wales**

University Hospital of Wales, Cardiff

Swansea Bay University Health Board, Swansea

**Northern Ireland**

Belfast City Hospital, Belfast

Causeway Hospital, Coleraine

South Eastern Trust, Dundonald

## Summary

This multicentre audit captured the use of MRI in the monitoring and management of people with MS. The aim of the audit was to compare MRI practices to MAGNIMS and the consortium of MS centres consensus guidelines. 25 MS centres across the UK collected data from local patient records to provide a heterogenous sample including people with relapsing and progressive MS.

Imaging information on 2567 individual cases was included in the analysis. The most common reasons for MRI scans were routine monitoring (44.7%), and recent clinical relapse (20.3%). The spine was imaged in addition to the brain in 1235 (48.1%) cases. There was no additional effect on DMT decisions at subsequent clinical review when the spine was imaged for routine monitoring purposes. Gadolinium sequences were obtained in 987 (38.4%) cases, 44.8% of baseline (diagnostic) scans, and 40.6% of follow-up scans, mainly when specifically requested by the clinician. In those with post-gadolinium sequences, 1 in 5 showed enhancement, and this was the only evidence of disease activity in 1 in 20 cases.

MS centres demonstrated varied scanning frequencies for people with relapsing-remitting MS with a mean inter-scan interval of 1.6 (SD1.72) years in the case of routine monitoring. In people with progressive MS, mean inter-scan intervals were significantly higher (2.6 years (SD 2.62), $p<0.001$), with the most common indication for scans being routine monitoring, regardless of DMT status (30.5%). MRI scans in people with progressive MS demonstrated less contrast enhancement compared to people with relapsing-remitting MS (12.1% vs 22.1% contrast enhanced scans) but greater lesion burden. A significant minority (8.7%) of the MRI scans were performed for PML surveillance and here there was variation in the frequency of imaging with only partial adherence to the national recommendations on imaging for PML surveillance. 25 centres provided standardised MRI protocols for imaging people with MS, showing consistency in the routine use of T2-weighted, diffusion weighted imaging (DWI) and fluid-attenuated inversion-recovery (FLAIR) sequences, but variation in the use of proton density, susceptibility weighted and T1-weighted imaging as well as 3D/volumetric sequences.

Based on these audit findings, recommendations have been provided to improve the clinical utility and practice of MRI use in the management of people with MS.

## Background

MRI has an important role in the diagnosis and management of people with multiple sclerosis (MS). MRI is used routinely in clinical practice to establish the diagnosis and disease burden and to inform prognosis for people with MS. It is also used to guide eligibility and monitor response to disease modifying treatment (DMT) by providing evidence of MS disease activity. Finally, it plays a crucial safety role in pharmacovigilance for certain DMTs.

There are no widely implemented UK national consensus guidelines on the use of MRI in the management of people with MS, but efforts have been made to begin this process. (1) NICE guidance on the management of MS in adults, briefly mentions MRI in the context of the diagnostic process. (2) The Magnetic Resonance Imaging in MS (MAGNIMS) study group published consensus recommendations on the use of MRI in the monitoring of people with MS in 2015. (3) This was followed by guidelines on the MRI criteria to be used in the diagnostic process. (4) More recently, a consortium of MS centres produced revised technical guidelines on the MRI protocols for monitoring in MS in different clinical contexts. (5)

These evidence-based guidelines have provided a comprehensive set of MRI protocols, but their application can be challenging in a clinical setting. Both personnel and equipment availability are important factors that can influence imaging protocols implemented in each centre. This is likely to lead to variation in imaging practices across the UK, but this variation has not previously been captured to identify patterns and provide meaningful recommendations.

Given the lack of information on imaging practices in MS centres cross the UK, this audit was developed to collect the relevant clinical and imaging information to compare current UK practice to published international consensus recommendations by the MAGNIMS study group and the consortium of MS centres. The audit protocol was developed in April 2020, by NHS clinicians as part of the UK MS trials and registries consortium. This consortium is a group of NHS healthcare professionals interested in improving the standard of MS studies and trials, as well as improving MS care in the UK.

## Aim

This multicentre UK audit aimed to characterise the current use of MRI in the monitoring and management of people with MS in the UK and how this compares to available international guidelines.

# Methods

Neurology services in secondary care, including MS centres around the UK were invited to participate in this audit in May 2020. Leeds Teaching Hospitals NHS Trust was the sponsor and data controller for this audit. A centre was eligible for participation if they provided clinical and radiological services for people with MS and had authorised access to clinical and radiological information on the patient sample in their centre. Participating centres were sent the audit protocol and data collection sheet along with information on registering the audit locally with their audit office. Approval from the Caldicott guardian was required in each participating centre prior to forwarding the anonymised audit collection sheet to the data controller.

## Patient Sample

Each centre was asked to audit 100 patient cases, to provide a large enough sample to identify meaningful patterns in practice in each centre, taking into account missing radiological and clinical information. Each centre reviewed the records of 100 consecutive cases of RIS, CIS or MS seen in specialist MS clinics run by neurologists and nurses from 1st September 2019. If MS clinics were separated by indication, (e.g., DMT / Relapse / Transitioning / Rehabilitation / Continence) auditors were asked to include patients attending all clinics.

## Audit dataset

Demographic data was collected for each patient including year of birth and sex. Disease specific data like MS type, current disease modifying treatment and year of diagnosis was collected. As Expanded Disability Status Scale (EDSS) data may not be routinely collected at all sites or easily determined from clinic letters, disability information was simplified to ambulation status, without aid, with aid and non-ambulant. Information on the most recent MRI scans, indications for MRI scans, scan sequences, and clinical outcomes following scans were gathered from the patient records in each centre. Individual centres also provided the MRI sequences used in scanning patient with MS for diagnostic, monitoring and relapse purposes. Scanning protocols used for patients under Progressive multifocal leukoencephalopathy (PML) surveillance was also provided. PML safety monitoring was deemed high or low risk based on the JC virus status of the patient and the duration of their treatment with natalizumab as per the stratification used in McGuigan et al. and in the physician guidelines for patients receiving Tysabri treatment. (6,7)

Data collection in participating centres took place between May and October 2020. The de-identified datasets and radiology protocol information from each centre was forwarded to the co-ordinating centre, Leeds, and analysis took place in November 2020.

# Results

38 MS centres initially expressed interest in participating in the audit and were given the audit toolkit. Of these, 25 centres provided de-identified patient data and the MRI protocols used in their centres, within the data collection period. 2572 cases were audited in total from the 25 centres. 5 cases were excluded as they were missing most of the mandatory data fields. 2567 cases were included in the analysis.

## Demographics

Of the 2567 patients included in the analysis 1814 (70.7%) were women, and 753 (29.3%) men. The mean age was 48 (SD 12.5) years, with the youngest patient 17 years, and the oldest 87 years. The distribution of ages is shown in Figure 1. The MS subtype at the time of the audit is shown in Table 1.

1540 patients were ambulant without aid (59.9%), 709 ambulant with aid (27.6%), 194 non-ambulant (7.5%), and ambulation status unknown in 124 (4.8%). The distribution of the time since patients were diagnosed with MS is shown in Figure 2. The median time since diagnosis was 9 years with the most recent confirmed diagnosis being less than a year prior to the audit and the longest duration 55 years.

The number of patients on different DMTs is shown in Figure 3. Of the 878 patients not on any DMT, 377 had RRMS (19.3% of people with RRMS), 166 had PPMS (86.9% of people with PPMS), 331 had SPMS (79.6% of people with SPMS), 3 had no diagnosis, and 1 had RIS.

**Table 1.** MS subtypes

| MS type | Number of cases (%) |
|---|---|
| Primary Progressive | 191 (7.4) |
| Relapsing-Remitting | 1956 (76.2) |
| Secondary Progressive | 416 (16.2) |
| Radiologically Isolated Syndrome (RIS) | 1 (0.0) |
| No Diagnosis | 3 (0.1) |

**Figure 1.** Distribution of patients based on age

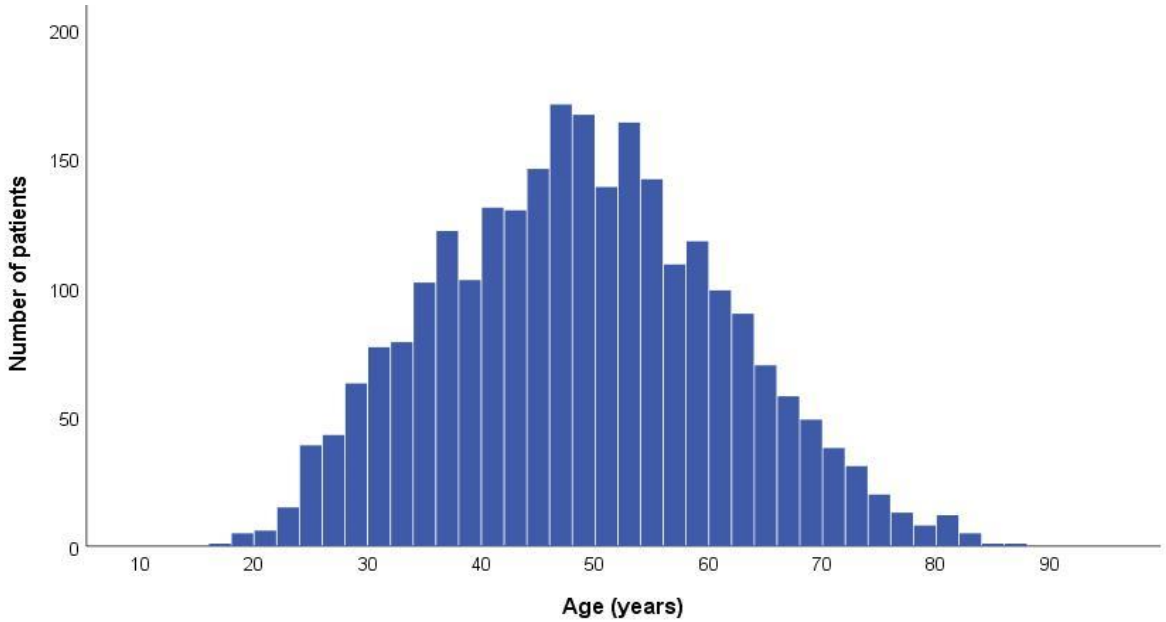



**Figure 2.** Time since diagnosis with MS

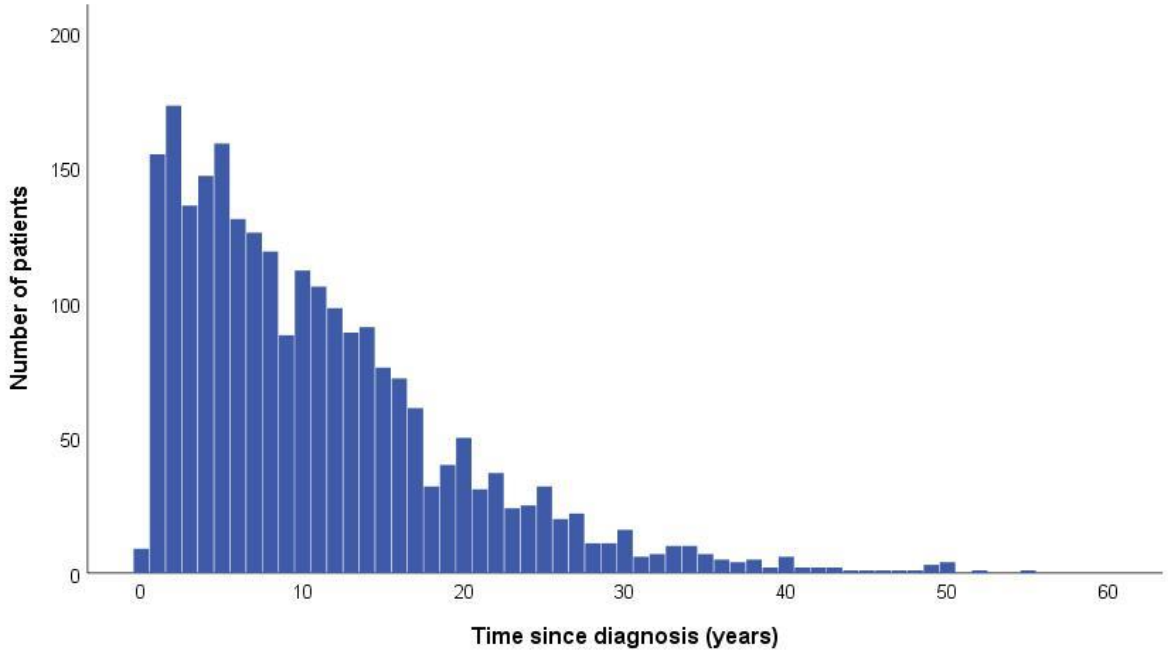
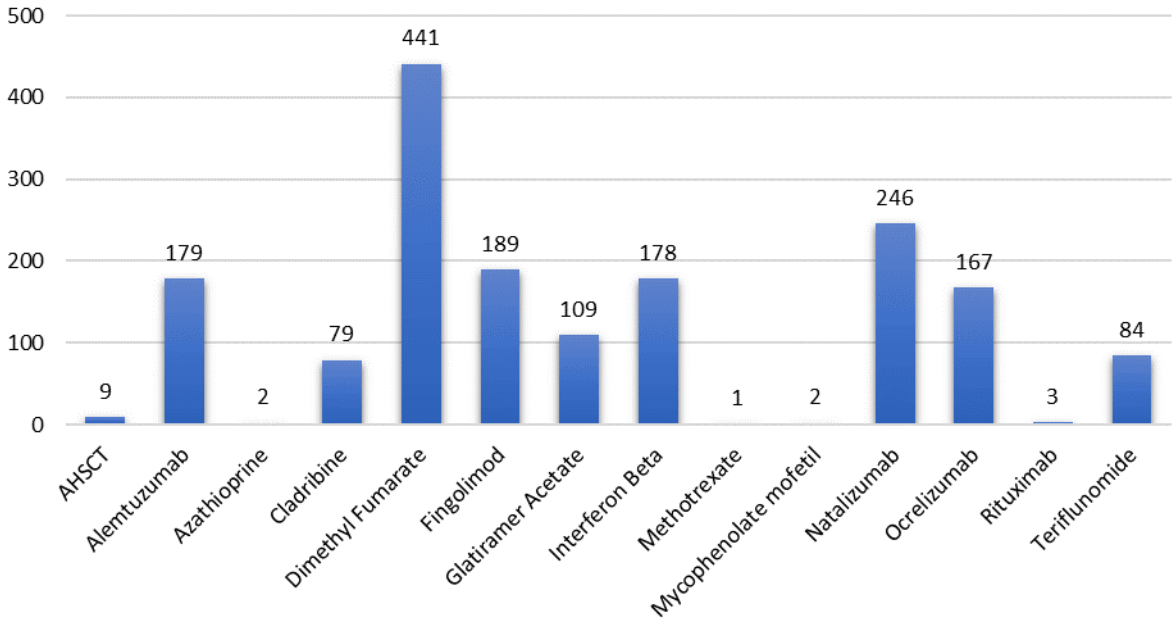


**Figure 3**. Number of cases on different disease modifying treatments




878 cases, not included in this graph were not on any disease modifying treatment. *AHSCT, autologous haematopoietic stem cell transplantation*

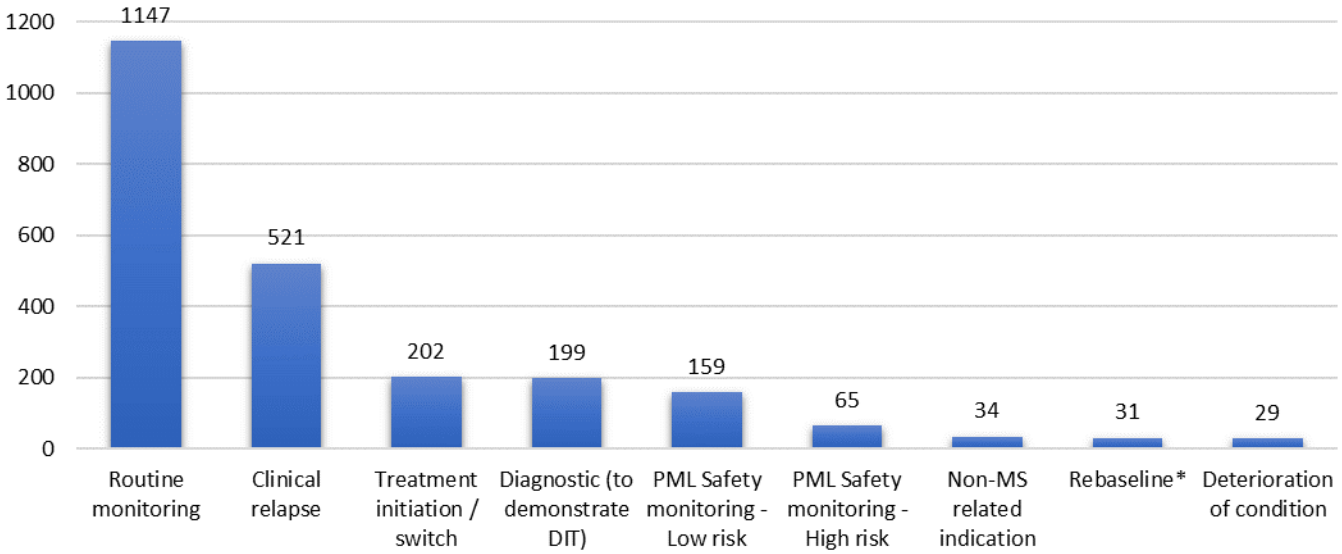
## MRI scanning indication

The indication for the most recent MRI scan in each case is shown in Figure 4. Routine monitoring accounted for most cases (44.7%). There were 34 cases (1.3%) where the reason for the MRI scan was deemed to be unrelated to that patient's MS, for example, chronic back pain, seizure, stroke, and headache. In 180 cases (7.0%), the reason for performing the MRI scan was not available, either because it was not immediately identifiable by the local auditor (including cases where the scan was imported from another centre), or not clearly indicated in the patient record. PML monitoring accounted for 224 scans (8.7%).

Figure 5 shows which region of the central nervous system was imaged based on the scan indication. Scans done for diagnostic, clinical relapse, and change of treatment purposes were more likely to include a brain and spinal protocol compared to other indications. Contrary to guideline recommendations, scans performed for routine monitoring purposes frequently included imaging of the spine. 70 (31.8%) patients who had MRI scans for PML surveillance (high or low risk), had both brain and spine imaged, which is out of keeping with current guidelines. However, it is possible that the audit failed to record clinical justification for including spinal imaging in these cases.

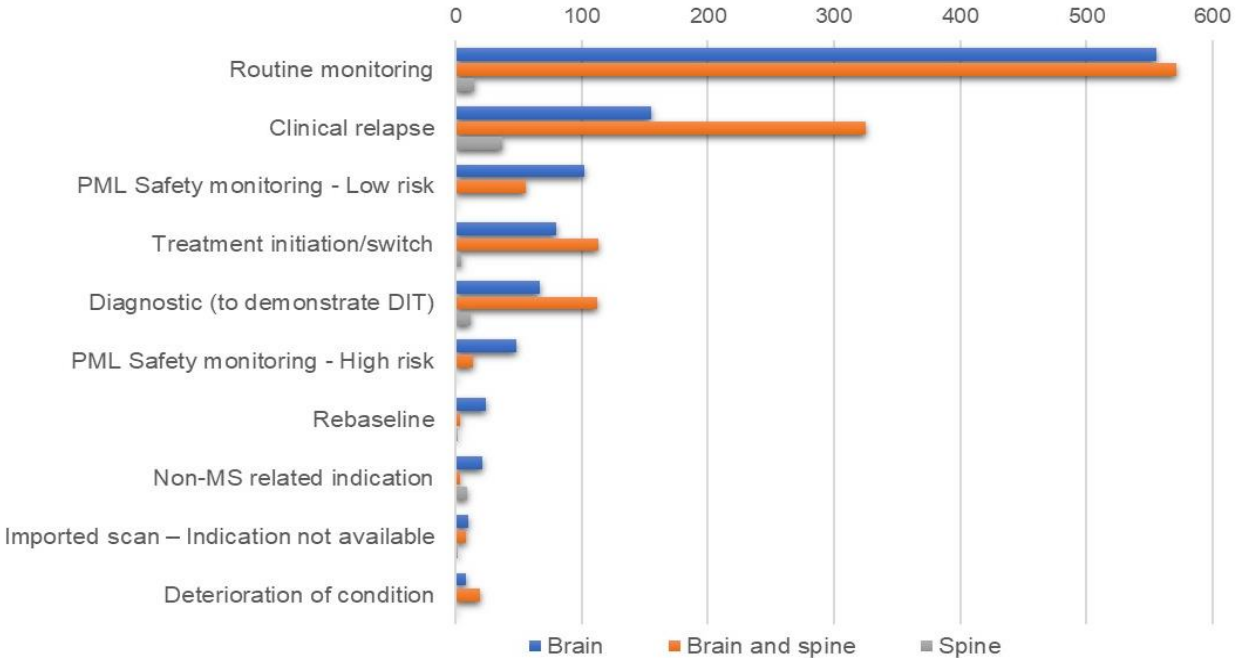
The number of new demyelinating lesions for each case is highlighted in Table 2. The number of new lesions were quantified by the radiologist in the clinical report of 1899 (89.7%) scans where a comparison scan was available. 217 (8.5%) cases had MRI scan reports where the radiologist had commented on the presence of new lesions but had not quantified these. In total, 568 out of 2116 patients (22.1%) for whom a comparison was available had new/enlarging lesions, while 1548 (60.2%) had stable scans. In 330 (12.9%) cases the radiologist commented that there was no previous MRI scan for comparison and in 121 (4.7%) cases no information on lesion count was provided, either because it was not mentioned in the scan report or it was not collected by the auditor.

**Figure 4.** Number of cases based on indication for the most recent scan




24 cases, not included in the figure, listed the scan indication as *Imported – indication not available.* 156 cases, also not included in the figure, didn't list an indication for the most recent scan. Cases were constrained to select one indication per scan. *Rebaseline scans were done after treatment was initiated compared to Treatment initiation/switch which was done prior to treatment change. *PML, Progressive multifocal leukoencephalopathy, DIT, Dissemination in time*

**Figure 5.** Number of cases with brain and spine imaging based on the scan indication




187 scans did not specify the area imaged or the indication for the scan and are not represented in the figure

**Table 2**. Number of cases based on the scan report of the number of new lesions

| Number of new lesions | Number of cases (%) |
|---|---|
| 0 | 1548 (60.3%) |
| 1 | 181 (7.1%) |
| 2 | 72 (2.8%) |
| 3 | 31 (1.2%) |
| ≥ 4 | 48 (1.9%) |
| Yes, but not quantified | 217 (8.5%) |
| Enlarging lesion(s) only | 19 (0.7%) |
| No comparison available | 330 (12.9%) |
| No information provided | 121 (4.7%) |

## Diagnostic imaging

Demonstration of radiological evidence of dissemination in time, was the reason given for the most recent MRI scan in 199 (7.8%) cases. 67 (33.7%) of these cases had imaging of the brain only while both the brain and spine were imaged in 112 (56.2%) cases, and 12 (6.0%) cases imaged the spine only. In the remaining 8 (4.0%) cases, no information was provided on which area was imaged. Of the diagnostic scans, 107 (53.8%) cases had information on the presence or absence of new lesions. There was no significant difference between brain only imaging and combined brain and spinal imaging in the identification of new lesions (50.0% vs. 52.5%, p=0.750). 81 (40.7%) scans were done with gadolinium, of which enhancing lesions were demonstrated in 22 (27.2% of those who received gadolinium) cases. Amongst these cases, there was no significant difference between enhancement when only the brain was imaged compared with brain and spinal imaging together (40.9% vs. 24.5%, p=0.239). However, with only 199 scans done for a diagnostic indication, these analyses should be interpreted with care.

## Gadolinium use

Overall, 987 (38.4%) out of 2567 audited scans included post gadolinium sequences. Table 3 shows the number of gadolinium enhancing lesions reported in these scans. This data shows that overall, 5.3 patients are administered gadolinium to detect one patient with gadolinium enhancement. When restricting this analysis to only those patients undergoing routine monitoring, 61/366 (16.7%) had enhancing lesions, so 6.0 patients are administered gadolinium to detect one patient with enhancement during routine monitoring. Figure 6 shows the scan indications for which gadolinium was used, with it being most used in the context of clinical relapse and treatment initiation/switch.

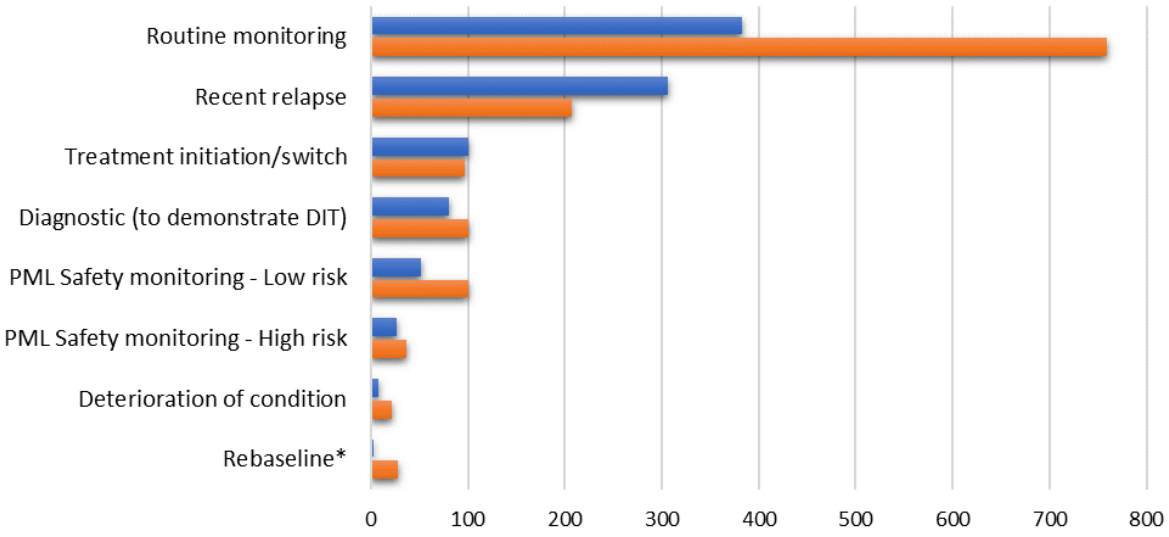
Amongst the audit sample, 825 (32.1%) cases had data on post-gadolinium images and the presence or absence of new T2 lesions. In 659 (79.9%) patients, there was no enhancement. Of the 166 cases with enhancing lesions, 122 (73.5%) were concurrently noted to have new T2 lesions, while in 44 cases (5.3% of all contrasted scans) lesion enhancement was the only evidence of disease activity. Repeating this analysis only in participants undergoing imaging for routine monitoring (n=336), 59 (17.6%) patients had enhancing lesions, and in 29 (8.6%) patients the enhancement was the only evidence of disease activity. Similarly, when restricting the analysis to scans performed due to clinical relapse (n=249), 68 (27.3%) patients had enhancing lesions, and in 7 (2.8%) patients the enhancement was the only evidence of disease activity.

**Table 3.** Number of gadolinium enhancing lesions per MRI scan

| Number of gadolinium enhancing lesions | Number of cases (%) (n=987) |
|---|---|
| 0 | 748 (76.8) |
| 1 | 74 (7.5) |
| 2 | 25 (2.5) |
| 3 | 12 (1.2) |
| ≥ 4 | 10 (1.0) |
| Yes - not quantified | 65 (6.6) |
| Unknown (no information provided) | 53 (5.4) |

186 (18.8%) scans reported some gadolinium enhancement but did not specify the number of lesions

**Figure 6.** Frequency of MRI scans done with and without gadolinium sequences based on scan indication




Only scans with information on whether gadolinium was used or not are included. *Rebaseline scans were done after treatment was initiated compared to Treatment initiation/switch which was done prior to treatment change.

## Clinical outcomes following MRI

411 (16.0%) of all cases had a change in their DMT at their next clinic review following their MRI scan, while 1908 (74.3%) had no change in treatment. 101 cases (3.9%) hadn't yet been reviewed in clinic following their MRI scan at the time of the audit. In the remaining 147 cases (5.7%) information on DMT change was not provided.

While this audit was not designed to establish causation, the presence of new lesions on MRI was significantly associated with a change in DMT at the next clinic review (48.2% vs. 7.2%, $p<0.001$). Across all imaging, when post gadolinium MRI sequences were used, there was a significantly higher chance of a subsequent DMT escalation (55.6% vs. 19.1%, $p<0.001$). However, when analysis is restricted to those undergoing MRI for routine monitoring only, results were non-significant (9.8% vs 7.5% scans with post gadolinium sequences). This reflects findings presented in Figure 6, whereby gadolinium is often used when there is ***clinical*** evidence of disease activity, which in itself will influence the DMT decision.

Imaging of the spine showed a similar influence on the outcome of DMT choices in the subsequent clinic review. When considering all scanning indications, imaging the brain and the spine together significantly increased the chance of a DMT change when compared to imaging the brain alone (22% vs. 13%, $p<0.001$). However, when restricting the cases to those who had a scan for routine monitoring, imaging the brain and spine together did not alter the rates of DMT change at the next clinic review (8.1% vs. 7.9%, $p=0.954$). This finding supports the guidelines that advise brain only imaging for routine monitoring purposes, unless there is pathology identified that localises to the spinal cord.

## Routine monitoring

Analyses restricted to routine monitoring scans, which includes DMT monitoring scans may reduce the influence of clinical activity on subsequent DMT decisions, as these patients have been defined as clinically stable. Among the 1147 cases with scans performed for routine monitoring, 1090 cases (95.0%) had data available on subsequent DMT decisions, and 998 (87.0%) had data available on both the presence of new lesions and subsequent DMT decision. Of 1090 cases undergoing routine monitoring MRI where subsequent DMT decisions were known, 87 (8.0%) had a subsequent DMT change. This suggests that around 12.5 routine monitoring scans are performed for one patient's treatment to be altered.

When routine monitoring MRI identified one new lesion, 30% of cases subsequently underwent a change in DMT; this increased to 52% of cases when 2 or more lesions were

present. When gadolinium was given in patients undergoing routine monitoring, 13.3% of those with a single gadolinium enhancing lesion had a subsequent DMT change; 38% of those with >1 gadolinium enhancing lesions had a subsequent DMT change. This difference between DMT change, being lower when contrast enhancing lesions are seen compared to the presence of new lesion can be explained by the data in this sample as more of the patients showing gadolinium enhancement in this analysis were non-ambulant and/or had progressive MS, hence a more limited DMT choice in this group.

If this analysis is restricted to only ambulant patients with RRMS (n=797), 9.2% of such patients had a subsequent DMT change, 32% when one new lesion was present, and 56% when 2 or more new lesions were present. 229 (28.7%) of these cases included post-gadolinium sequences. When one or more gadolinium enhancing lesion was present (n=32), 34% underwent subsequent DMT change

## Scanning frequency

Information was collected on the dates of the first, second and third most recent MRI scans, where available for each case. This allowed an assessment of how often patients were scanned. Table 4 shows the average scan intervals between the most recent scans based on MS subtype. People with RRMS were scanned significantly more frequently compared to people with PPMS or SPMS ($p<0.001$). Amongst progressive patients, people with PPMS were scanned significantly more frequently than people with SPMS ($p=0.001$).

The scanning interval in months between the most recent scans based on the DMT type is shown in Figure 7. Patients on high efficacy treatments, i.e., AHSCT, alemtuzumab, cladribine, natalizumab and ocrelizumab, had a significantly shorter interval been scans, on average 13.6 (SD. 11.6) months, compared to patients on lower efficacy treatments (all remaining DMTs), on average 21.1 (SD. 23.0, $p<0.001$) months. Scans done with gadolinium sequences in patients on DMT were significantly more likely to demonstrate the presence of enhancing lesions when compared to those not on treatment (22% vs. 16%, $p=0.036$). However, patients who had a scan when they were not on any DMT were significantly more likely to show new lesions compared to those on DMT (30% vs. 24%, $p=0.011$). This is likely confounded by the longer interval between scans for patients not on any treatment, leading to a perceived greater accumulation of demyelination lesions.

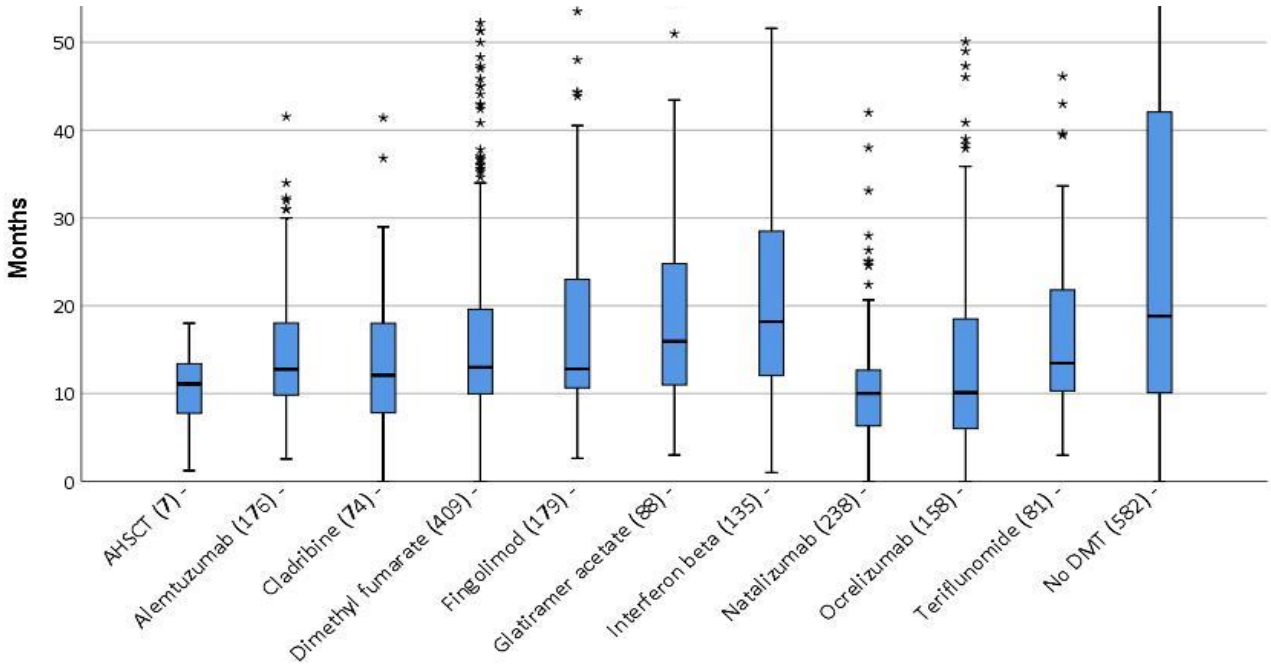
Figure 8 shows the scanning frequency in months between centres for routine monitoring of RRMS patients who are ambulant. As per guidelines, these patients should be scanned at intervals between 12 and 36 months. Given this relatively clinically homogenous sample in

Figure 8, the differences seen here are likely to represent variations in local scanning provision and practices.

**Table 4.** Average number of months between the two most recent MRI scans based on MS subtype

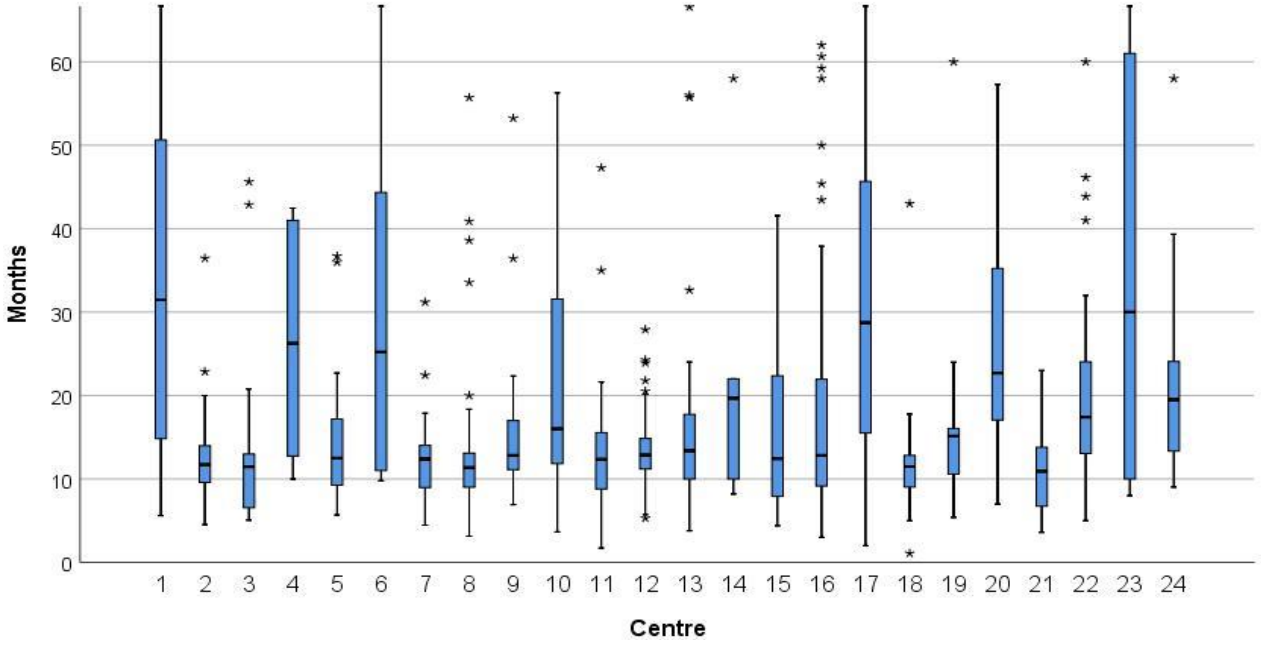
| MS Type | Mean number of months between scans (S.D.) | Number of cases |
|---|---|---|
| PPMS | 26.0 (24.6) | 124 |
| RRMS | 19.2 (21.7) | 1765 |
| SPMS | 36.1 (39.8) | 243 |
| Overall | 21.6 (25.2) | 2134 |

**Figure 7.** Boxplots showing median and interquartile ranges of the intervals between scans for MS patients based on their DMT




A limited y-axis scale is selected to represent the range of scan intervals on the graph. Several outliers have not been shown on the higher end of the scale. Number of cases on each DMT is shown in brackets. Patients on azathioprine (2), methotrexate (1), mycophenolate mofetil (2) and rituximab (2) were not included as they each had less than 5 cases. *AHSCT, autologous haematopoietic stem cell transplantation*

**Figure 8.** Boxplots showing median and interquartile ranges of the intervals between scans for routine monitoring of ambulant RRMS patients




A limited y-axis scale is selected to represent the range of scan intervals on the graph. Several outliers have not been shown on the higher end of the scale. Centre 25 had insufficient data on ambulation

## Scanning in Progressive MS

607 (23.6%) cases of the audit sample were people with a diagnosis of progressive MS; PPMS or SPMS. Incomplete scanning information was provided more frequently, and more cases did not have recorded previous scans, when compared to the RRMS group. In the progressive group, the majority of scans were done for clinical relapse (17.1%) and routine monitoring (30.5%) indications. 13.3% of cases had a diagnostic indication. Progressive MS patients were significantly less likely to see their DMT changed following an MRI scan compared to RRMS patients (7.3% vs. 20.6%, $p<0.001$). This audit was completed prior to the introduction of a licenced DMT for SPMS in the UK, but after the licencing of ocrelizumab for certain PPMS cases. Change of DMT also included stopping all DMT treatment. Therefore, the clinical utility of scanning the people with progressive MS, especially for routine monitoring will likely change in the near future. Any change in practice will likely be a significant additional cost as currently people with progressive MS are scanned less frequently. The mean scan interval in the progressive group was 32.7 (SD. 35.7) months compared to a mean of 19.2 (SD. 22.2, $p<0.001$) months in the relapsing-remitting group.

## PML surveillance

In cases where the MRI scan indication was for PML surveillance, JC virus status was grouped as negative, low titre or high titre. These were values suggested by consensus guidelines on the risk stratification for PML in MS patients receiving natalizumab. (6) Patients who were on treatment with natalizumab were grouped based on their treatment duration with the DMT being more or less than 18 months. 246 (9.6%) patients were treated with natalizumab at the time of the audit. 17 (6.9%) of these cases provide no information on treatment duration with natalizumab or JC virus serostatus. Apart from natalizumab, there were 22 (0.9%) other cases where patients had their JC virus serostatus or treatment duration recorded. These included alemtuzumab (3), cladribine (1), dimethylfumarate (1), fingolimod (7), ocrelizumab (6) or no DMT (4). These 22 cases were excluded from the PML surveillance analysis as the risk stratification tool is only relevant to patients on natalizumab. Table 5 shows the breakdown of the 229 natalizumab cases by scan interval, treatment duration and JC virus serostatus. The average scan intervals shown in the table are in keeping with consensus guidelines i.e. 6 monthly scans for patients at high risk of PML and yearly scans for those are low risk of PML on natalizumab. (6,7)

18 of 31 (58.1%) cases considered high risk for PML (high JC virus titre, treatment duration > 18months), had an average MRI scan interval of less than 6 months as recommended by consensus guidelines. 102 of 192 (53.1%) low-risk cases (JCV titre < 1.4 or negative), had an MRI scan interval of less than 12 months. 79 of 224 (35.3%) cases where the scan indication was for PML surveillance, had gadolinium administered which is not in line with current MAGNIMS guidance on PML surveillance scans which suggests a limited protocol of DWI and FLAIR sequences. Information on abnormalities detected with DWI MRI sequences was not collected as part of this audit.

**Table 5.** Distribution of cases at risk of PML, based on DMT duration and JC virus serostatus

| JC virus serostatus | DMT treatment duration | Number of cases | Average scan interval / months (S.D.) |
|---|---|---|---|
| High titre | <18 months | 7 | 5.8 (2.8) |
| | ≥18 months | 31 | 5.9 (3.3) |
| Low titre | <18 months | 18 | 12.0 (8.7) |
| | ≥18 months | 31 | 7.8 (3.3) |
| Negative | <18 months | 28 | 12.1 (10.7) |
| | ≥18 months | 114 | 12.1 (3.6) |

## MRI protocols

All centres who provided patient data in this audit also provided information on the local MR scanning protocols employed by the radiology department in their centre. There was considerable variation in the quality of data provided, with some centres providing detailed tables with scan sequences and times, whilst others provided free text information on the scan sequences used for scanning in the indications previously described. For the purposes of this audit, the scan sequences used were collected and compared to the protocols suggested by MAGNIMS and the consortium of MS centres.

The scans sequences done for diagnostic purposes are shown in Table 6 alongside the MAGNIMS and Consortium of MS centres recommended sequences. For diagnostics purposes MAGNIMS recommends axial proton-density and/or T2-FLAIR / T2-weighted sequences. 3D/volumetric FLAIR sequences are recommended as well as 2D/3D contrast-enhanced T1-weighted sequences. (8) The consortium of MS centres also recommends a 2D/3D sagittal and axial T2-FLAIR and T2-weighted sequence as well as 2D DWI. In addition, 3D inversion recovery (IR) T1 gradient echo sequences are recommended as part of the core protocol with post gadolinium T1-weighted imaging as optional. (5) Amongst the centres in this audit, Axial T2 is employed in almost all centres in addition to 2D/3D FLAIR and diffusion weight imaging (DWI) sequences. 13/25 centres use volumetric FLAIR as advised by the consortium of MS centres and MAGNIMS. With regards to gadolinium use, 18/25 centres specified that they administered gadolinium only when specifically requested by the clinician requesting the scan and a post gadolinium T1 is obtained in these circumstances. Only 3/25 centres routinely do a proton density (PD) sequence and 1/25 centres does susceptibility weight imaging (SWI). These protocols show that there is limited practice of performing T2* sequences, to look for the 'central vein sign' from a diagnostic perspective. (9) 12/25 centres routinely include the spine in the imaging protocol for diagnostic purposes, and the most frequent sequence done is a sagittal T2, with axial cuts through any areas of interest in the spine. The use of PD or short tau inversion-recovery (STIR) sequencies is very limited in the spinal protocol despite being recommended by MAGNIMS and the Consortium of MS centres.

The MRI sequences done for routine monitoring and relapse indications in people with an established diagnosis of MS are shown in Table 7. The consortium of MS centres recommends identical imaging sequences for follow-up scans as for the diagnostic scans and MAGNIMS recommends a combination of T2-FLAIR, and T2-weighted sequences. As shown in Table 7, T2-weighted and T2-FLAIR remain the most common sequences done in

centres with DWI sequences done to assess for active disease and any serious treatment-related adverse effects, such as PML. In 23/25 centres, gadolinium agents were administered only if the requesting clinician requested contrast to look for disease activity, or to assess for radiological evidence of relapse activity. Spinal imaging in addition to brain imaging for routine monitoring is not contained in any centre's protocols. However, the instances of spinal imaging for a number of indications as seen in previous sections on brain and spine imaging, provides evidence of significant variation in clinical practice.

Variation is also seen in the planes of acquisition for different sequences with coronal, sagittal and axial planes used in a number of combinations to obtain T1/T2-weighted, and T2-FLAIR sequences. 15/25 centres routinely obtain 3D/volumetric sequences for diagnostic and monitoring scans, suggesting a lack of agreement on the clinical utility of these sequences.

The MRI sequences done for PML surveillance was also collected, as shown in Table 8, and both the consortium of MS centres and MAGNIMS recommend a limited core protocol with FLAIR and DWI sequences. MAGNIMS guidelines also include a T2-weighted sequence. Scanning protocols were uniform among the majority of centres for PML surveillances with 25/25 centres routinely doing FLAIR (2D/volumetric) sequences, 21/25 centres routinely doing DWI sequences, and 19/25 centres doing T2 weight sequences. A few centres also included the option of gadolinium enhanced, PD and SWI sequences, allowing a more comprehensive assessment of disease activity in these scans as well.

Centres were asked to provide information on who reported the MRI scans performed in their centre. All centres reported a mix of scan reporting personnel with almost all scans in tertiary centres being reported by neuroradiologists internal and/or external. In the district general hospitals, scans were reported by either neuroradiologists or general radiologists, again either internal and/or external.

**Table 6.** MRI sequences done in centres for diagnostic purposes in suspected MS cases

| | Brain Sequences | | | | | | | | | | | Spine Sequences | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 3D IR-prep GE T1 | 2D T2 FLAIR | 3D/Vol T2 FLAIR | 2D Axial/Sagittal T1 | 2D Axial T2 | 3D Axial T2 | 2D Axial DWI | Pre-Gad 2D/3D Axial T1 | SWI | Post Gad 2D/3D Axial T1 | Axial 2D PD | Sagittal / Axial T2 | PD | STIR | T1-PSIR | Post Gad T1 |
| **Consortium** | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | | | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ |
| **MAGNIMS** | | ✓ | ✓ | | ✓ | | | | | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ |
| **1** | | ✓ | | | ✓ | | ✓ | ✓ | | ✓ | | ✓ | | ✓ | | ✓ |
| **2** | | | ✓ | | ✓ | | | | | | | ✓ | ✓ | ✓ | | * |
| **3** | | ✓ | | ✓ | ✓ | | ✓ | | | | | | | | | |
| **4** | | | ✓ | ✓ | ✓ | | ✓ | | | * | | ✓ | | | | |
| **5** | | | ✓ | | ✓ | | ✓ | * | | * | | ✓ | | ✓ | | * |
| **6** | ✓ | ✓ | ✓ | | ✓ | | ✓ | | | | ✓ | | | | | |
| **7** | | ✓ | | ✓ | ✓ | | ✓ | | | * | | | | | | |
| **8** | | | ✓ | ✓ | ✓ | | | * | | * | | ✓ | | ✓ | | * |
| **9** | ✓ | | | | | ✓ | | ✓ | | ✓ | | | | | | |
| **10** | | | ✓ | ✓ | ✓ | | ✓ | | | * | | | | | | |
| **11** | | | ✓ | | ✓ | | ✓ | | | * | | | | | | |
| **12** | | ✓ | | ✓ | ✓ | | ✓ | * | | * | | ✓ | | | | |
| **13** | | ✓ | | | ✓ | | ✓ | ✓ | | * | | ✓ | | ✓ | | * |
| **14** | | | ✓ | | ✓ | | ✓ | * | | * | | ✓ | | | | * |
| **15** | | ✓ | | | ✓ | | | * | | * | | ✓ | | | | * |
| **16** | | | ✓ | | ✓ | | ✓ | | | * | | | | | | |
| **17** | | | ✓ | ✓ | ✓ | | ✓ | | ✓ | | | | | | | |
| **18** | | ✓ | | | ✓ | | ✓ | * | | * | | ✓ | | | | * |
| **19** | | ✓ | | ✓ | ✓ | | ✓ | | | | | ✓ | | | | * |
| **20** | | | ✓ | | ✓ | | ✓ | * | | * | | ✓ | | ✓ | | * |
| **21** | | | ✓ | ✓ | ✓ | | ✓ | | | * | | | | | | |
| **22** | ✓ | | ✓ | | | | ✓ | | | * | ✓ | | | ✓ | | * |
| **23** | | | ✓ | ✓ | ✓ | | ✓ | | | * | | | | | | |
| **24** | ✓ | ✓ | | ✓ | ✓ | | ✓ | | | * | | ✓ | | | | * |
| **25** | | ✓ | | ✓ | ✓ | | ✓ | * | | * | ✓ | ✓ | | ✓ | | * |

*✓, scan sequences are included routinely; *, scan sequences are only included when requested by the clinician; 2D, two-dimensional; 3D, three-dimensional; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion-recovery; Gad, gadolinium; GE, gradient echo; IR, inversion recovery; PD, proton density; PSIR, phase-sensitive inversion recovery; STIR, short tau inversion-recovery; SWI, susceptibility weighted imaging; Vol, volumetric*

**Table 7.** MRI sequences done in routine monitoring and relapse indications in MS patients

| | 3D IR-prep GE T1 | 2D T2 FLAIR | 3D/Vol T2 FLAIR | 2D Axial/Sagittal T1 | 2D Axial T2 | 3D Axial T2 | 2D Axial DWI | Pre-Gad 2D/3D Axial T1 | Post Gad 2D/3D Axial T1 | Axial 2D PD |
|---|---|---|---|---|---|---|---|---|---|---|
| **Consortium** | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | |
| **MAGNIMS** | | ✓ | | | ✓ | | | | ✓ | |
| **1** | | ✓ | | | ✓ | | ✓ | ✓ | * | |
| **2** | | | ✓ | | ✓ | | | | | |
| **3** | | ✓ | | ✓ | ✓ | | | | ✓ | |
| **4** | | | ✓ | ✓ | ✓ | | ✓ | | * | |
| **5** | | | ✓ | | ✓ | | ✓ | * | * | |
| **6** | | ✓ | ✓ | | ✓ | | ✓ | * | * | ✓ |
| **7** | | ✓ | | ✓ | ✓ | | ✓ | | * | |
| **8** | | | ✓ | | ✓ | | ✓ | * | * | |
| **9** | | | ✓ | | | ✓ | | * | * | |
| **10** | | | ✓ | ✓ | ✓ | | ✓ | | * | |
| **11** | | | ✓ | | ✓ | | ✓ | | * | |
| **12** | | ✓ | | ✓ | ✓ | | ✓ | | * | |
| **13** | | | ✓ | | ✓ | | ✓ | * | * | |
| **14** | | | ✓ | | ✓ | | | * | * | |
| **15** | | ✓ | | | ✓ | | | * | * | |
| **16** | | | ✓ | | ✓ | | ✓ | | * | |
| **17** | | | ✓ | | | ✓ | ✓ | | * | |
| **18** | | ✓ | | | ✓ | | ✓ | * | * | |
| **19** | | ✓ | | | ✓ | | ✓ | | * | |
| **20** | | | ✓ | | ✓ | | ✓ | * | * | |
| **21** | | | ✓ | | ✓ | | ✓ | | * | |
| **22** | ✓ | | ✓ | | | | ✓ | | * | ✓ |
| **23** | | | ✓ | ✓ | ✓ | | ✓ | | * | |
| **24** | ✓ | ✓ | | | ✓ | | | | * | |
| **25** | | ✓ | | | ✓ | | ✓ | * | * | ✓ |

*✓, scan sequences are included routinely; *, scan sequences are only included when requested by the clinician; 2D, two-dimensional; 3D, three-dimensional; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion-recovery; Gad, gadolinium; GE, gradient echo; IR, inversion recovery; PD, proton density; Vol, volumetric*

**Table 8.** MRI sequences done for PML surveillance in MS patients

| | 3D IR-prep GE T1 | 2D T2 FLAIR | 3D/Vol T2 FLAIR | 2D Axial/Sagittal T1 | 2D Axial T2 | 2D Axial DWI | Pre-Gad 2D/3D Axial T1 | SWI | Post Gad 2D/3D Axial T1 | Axial 2D PD |
|---|---|---|---|---|---|---|---|---|---|---|
| **Consortium** | | ✓ | ✓ | | | ✓ | | | | |
| **MAGNIMS** | | ✓ | ✓ | | ✓ | ✓ | | | | |
| **1** | | ✓ | | | ✓ | ✓ | ✓ | | * | |
| **2** | | | ✓ | | ✓ | ✓ | | | | |
| **3** | | ✓ | | ✓ | ✓ | ✓ | | | | |
| **4** | | | ✓ | | | ✓ | | | | |
| **5** | | | ✓ | | | ✓ | | ✓ | | |
| **6** | | ✓ | ✓ | | ✓ | ✓ | | | | |
| **7** | | ✓ | | | | ✓ | | ✓ | | |
| **8** | | | ✓ | | ✓ | ✓ | | | | |
| **9** | | | ✓ | | | ✓ | | | | |
| **10** | | ✓ | | | ✓ | ✓ | | | | |
| **11** | | | ✓ | | ✓ | ✓ | | | * | |
| **12** | | ✓ | | ✓ | ✓ | | | | | |
| **13** | | ✓ | | | ✓ | ✓ | | | | |
| **14** | | ✓ | | | ✓ | | * | | * | |
| **15** | | ✓ | | | ✓ | | * | | * | |
| **16** | | | ✓ | | ✓ | ✓ | | | | |
| **17** | | ✓ | | ✓ | ✓ | ✓ | | ✓ | | |
| **18** | | ✓ | | | ✓ | ✓ | | | | |
| **19** | | ✓ | | | ✓ | ✓ | | | | |
| **20** | | | ✓ | | ✓ | ✓ | | | | |
| **21** | | | ✓ | ✓ | ✓ | ✓ | | | * | |
| **22** | | | ✓ | | | ✓ | | | | |
| **23** | | | ✓ | | | ✓ | | | | |
| **24** | ✓ | ✓ | | | ✓ | | | | | |
| **25** | | ✓ | | | ✓ | ✓ | | | | ✓ |

*✓, scan sequences are included routinely; *****, scan sequences are only included when requested by the clinician; 2D, two-dimensional; 3D, three-dimensional; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion-recovery; Gad, gadolinium; GE, gradient echo; IR, inversion recovery; PD, proton density; SWI, susceptibility weighted imaging; Vol, volumetric*

## Recommendations

The following recommendations are based on the findings from this audit and some of them reflect the consensus guidelines already provided by MAGNIMS and the consortium of MS centres.

- Spinal imaging should not be included in addition to brain imaging when scanning people with an established diagnosis of MS for routine monitoring purposes. Inclusion of spinal imaging didn't show any additional effect on DMT change at subsequent clinic review.
- Contrast enhancement sequences should only be used in select clinical circumstances (e.g., for diagnostic purposes and when linked to DMT eligibility criteria) and not routinely when scanning people with MS for monitoring purposes.
- Imaging for routine monitoring in people with progressive MS is less frequently associated with a subsequent DMT change, due to the limited treatment options in this cohort, and should be considered on a case by case basis. This may change in the near future due to the recent introduction of new DMTs for active SPMS and PPMS.
- Scanning intervals for routine monitoring of RRMS patients on DMTs should be brought in line with recommendations (i.e., between 12 and 36 months for patients on DMTs), trying to limit the variation in intervals seen amongst centres.
- PML surveillance scanning intervals should be better adhered to with those patients in the high-risk group requiring more frequent scans; this audit shows that almost all centres failed to meet this criteria completely.
- MRI protocols for diagnostic purposes should include spinal sequences as a routine, which increases the detection rate of demyelinating lesions.
- Centres demonstrated significant heterogeneity in MRI protocols, and should review their diagnostic protocols in line with current recommendations on the use of 3D sequences as well as consider the use of new techniques like the central vein sign (T2*/FLAIR*/SWI) in diagnostic scans.
- MRI sequences for PML surveillance should only include T2/FLAIR and DWI sequences in line with current international recommendations to improve scan utility
- Centres should develop a standard form of reporting for MRI scans for people with MS, whether it be quantifying the number of demyelinating and/or gadolinium enhancing lesions seen on T1/T2 weight imaging. This will allow for a more comprehensive comparison of disease burden across time.

- Procedures for easy acquisition of historical MRI scans of people with MS who have moved hospitals/regions should be put in place, which will allow improved clinical utility of new MRI scans.

## Conclusion

This national audit attempted to capture the use of MRI in the monitoring and management of people with MS. Scanning practices follow the consensus guidelines in the majority of centres, but there is significant variation amongst centres, on the scanning protocols and frequency. Local equipment and scanner availability inevitably contribute to this variation, but the use of contrast enhancement and spinal imaging are examples of scanning practices that may be inefficient, and should be brought in line to adhere more strictly to international consensus recommendations. In addition, emerging evidence should guide local MRI protocols to reduce scanning cost, whilst improving clinical utility. A subsequent re-audit of scanning practices should reassess these areas following local interventions, as well as reviewing any changes in practice brought about by new DMTs for progressive MS.

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