MR Identification of White Matter Abnormalities in Multiple Sclerosis: A Comparison between 1.5 T and 4 T

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BACKGROUND AND PURPOSE: **Although MR spectroscopy and functional MR imaging of the brain have been successful at 4 T, conventional fast spin-echo imaging of the brain at 4 T has not been adequately evaluated. The purpose of this study was to compare the detection of white matter abnormalities in multiple sclerosis (MS) at 1.5 T and 4 T.**

METHODS: **Fifteen patients with clinically definite MS were imaged at both 1.5 T and 4 T within a 1-week period. Comparison was made between fast spin-echo long-TR images at both field strengths. Pulse sequences were tailored to maximize resolution and signal-to-noise ratio in clinically relevant imaging times (< 7 min). Four interpreters independently reviewed the images obtained at both field strengths in separate sessions and evaluated them for lesion identification, size, characterization, and subjective resolution. Differences in interpretations at 1.5 T and 4 T were subsequently recorded.**

RESULTS: **Images obtained at 4 T showed a mean of 88 more lesions as compared with images obtained at 1.5 T. All the lesions measured less than 5 mm and were typically aligned along perivascular spaces. Twenty-five consensually identified lesions on 4-T images were not seen at all on 1.5-T images. Moreover, 4-T images showed 56 additional consensually identified lesions, which were indistinct and seen only in retrospect on 1.5-T images. These lesions were frequently (n = 48) identified in large confluent areas of white matter signal intensity abnormality at 1.5 T. All observers also agreed that 4-T images subjectively enhanced the perception of normal perivascular spaces and small perivascular lesions.**

CONCLUSION: **MR imaging at 4 T can depict white matter abnormalities in MS patients not detectable at 1.5 T through higher resolution with comparable signal-to-noise ratio and imaging times.**

The diagnosis of definite multiple sclerosis (MS) by clinical means alone can be difficult and requires dissemination of clinical symptoms and findings in time and space (1, 2). This documentation is frequently impossible, particularly in the early stages of the disease. Historically, paraclinical tests such as evoked potentials and CSF analysis have been used as supplementary diagnostic tools in the documentation of objective clinical abnormalities in patients with suspected disease (3–6). The reported sensitivities

and predictive values of these tests in the diagnosis of MS have varied and have been disappointing (7, 8).

The emergence of MR imaging made possible the early documentation of white matter lesions in patients with MS (9–11). This technique has quickly become the most sensitive of the paraclinical tests and is used widely in this regard (7, 8, 12). Although it has proved to be a relatively sensitive diagnostic tool, MR imaging has lacked specificity (13), which has prompted investigation into appropriate MR imaging criteria for the specific diagnosis of MS (14–16). These criteria have concentrated on the enhanced identification, characterization, and localization of lesions for diagnosis.

High-field MR imaging has provided a potential method for acquiring high-resolution images in conventional imaging times. Theoretically, with the increase in signal-to-noise ratios (S/N) at higher field strengths, a trade-off between thinner sections and higher-resolution matrices may enhance the detection

of white matter lesions in MS. The purpose of this study was to determine whether conventional imaging contrast is possible at 4 T and to compare the relative identification and characterization of lesions on images obtained at field strengths of 1.5 T and 4 T.

Methods

Fifteen patients (nine women and six men; 24 to 51 years old) with clinically definite MS were imaged at 1.5 T and 4 T within a 1-week period. No patient had symptoms or signs of active disease, and none were receiving medical therapy at the time of imaging. All patients had previously documented white matter lesions on prior MR imaging studies.

To confirm higher S/N at 4 T, objective S/N measurements were obtained in 10 healthy control subjects in six white matter locations on 1.5-T and 4-T images acquired with identical imaging parameters. The parameters used were as follows: 5000/85/1 (TR/TE_{eff}/excitations), echo train length of 8, matrix of 512 × 256, receiver bandwidth of 32 kHz, and a field of view of 20 cm. S/N ratio was calculated by using the equation 8 mm² ROI of white matter/8 mm² ROI of background.

Comparative imaging at 1.5 T and 4 T was standardized for appropriate clinical imaging times (< 7 min per sequence). Sequences were accordingly maximized for S/N and maximum resolution under this time constraint. All imaging was performed on GE Signa magnets with a gradient strength of 10 mT/m. Axial fast spin-echo dual-echo imaging with a standardized 22-cm field of view (FOV) and 3-mm interleaved sections was carried out at both field strengths. The imaging protocol at 1.5 T was 2500/80/1, an echo train length of 8, a matrix of 256 × 192, and a receiver bandwidth of 16 kHz. The imaging protocol at 4 T was 4000–5000/85/1, an echo train length of 8, a matrix of 512 × 256, and a receiver bandwidth of 32 kHz. Total imaging time was 6 minutes 35 seconds at 1.5 T and 5 minutes 47 seconds at 4 T.

Four neuroradiologists who were aware of the patients' diagnoses of clinically definite MS independently evaluated the images obtained at 1.5 T and 4 T. The images were presented without annotation and in random order to each observer. The 1.5-T images were presented at least 3 weeks apart from the 4-T images. White matter lesions were defined as foci of abnormally increased signal intensity on long-TR images that were not directly attributable to other disease processes and did not correspond to normal structures, such as perivascular spaces or adjacent CSF. Interpreters were asked to identify the number, size, location, and internal characteristics of white matter lesions as well as to give a subjective appraisal of image quality in terms of resolution, S/N, and ability to perceive the normal perivascular spaces.

A comparison between findings at 1.5 T and 4 T was then performed by one of the observers after all the studies were evaluated. Special attention was given to relative lesion detectability, characterization, and location between 1.5-T and 4-T images. To ensure that differences in lesion detectability at 1.5 T and 4 T were not simply due to chance, statistical analysis using a two-tailed, paired t-test with the patient as the unit of analysis was performed. In addition, subsequent to the initial blinded interpretations, all four observers independently compared the 1.5-T and 4-T images in each patient directly to evaluate relative characterization of the lesions visible at both field strengths. Interpreters were asked to comment on the differences in internal signal characteristics and margins of these lesions at 1.5 T and 4 T.

Results

T2 contrast was possible at 4 T with the use of TR times of at least 4 to 5 seconds, thereby minimizing partial saturation of spins in tissues with longer T1 values at a higher field strength. Given the differences in T1 relaxation at 1.5 T and 4 T, similar T2 contrast was obtained with the higher TR values at 4 T and lower TR values at 1.5 T in this study. As expected, differences in TE had little effect on image contrast, since T2 relaxation is not as significantly dependent on field strength. Images obtained at 4 T showed an objective, confirmed increase in S/N for white matter as compared with those obtained with identical imaging parameters at 1.5 T. The mean S/N value at 4 T was 55.3 ± 7.4 compared with 21.2 ± 5.9 at 1.5 T. The increase in S/N at 4 T permitted the use of a higher-resolution matrix and larger receiver bandwidth to produce images with S/N and imaging times similar to those of the lower-resolution 1.5-T images. Conversely, imaging at 1.5 T necessarily required a lower-resolution matrix and lower receiver bandwidth to produce comparable S/N at similar imaging times. Mean calculated white matter S/N measurements with the imaging protocol used in the comparison analysis in this study at 1.5 T was 47.9 ± 7.8.

All four interpreters agreed that subjective S/N and resolution were superior at 4 T for each patient. Specifically, they agreed that the normal perivascular spaces were seen with distinct advantage on the 4-T images as compared with the 1.5-T images (Fig 1).
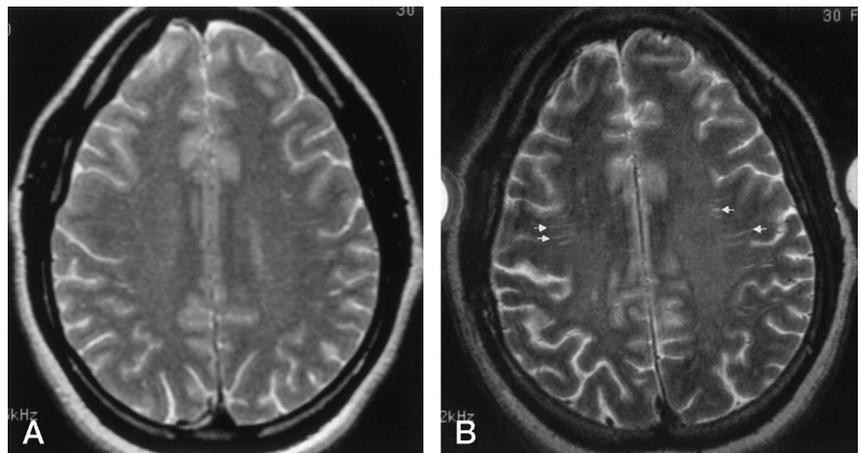

Fig 1. *A* and *B*, Axial fast spin-echo (2500/80/1) 1.5-T image (*A*) and (4000/85/1) 4-T image (*B*) show the superior spatial resolution of the 4-T image, which depicts the normal perivascular spaces with exquisite detail (*arrows*).

Lesion detectability was also uniformly superior for all four interpreters at 4 T as compared with the 1.5-T images (see Table). A mean of 88 more lesions were seen at 4 T than at 1.5 T. This difference between mean number of lesions seen in each patient at 1.5 T and 4 T was statistically significant ($P = .0001$). Eighty-one of the lesions seen at 4 T but not at 1.5 T were identified by all observers. Of these 81 consensually identified lesions, 25 were not seen at all on 1.5-T images (Fig 2). These lesions measured between 1 and 5 mm and were typically seen as focal oblong regions of T2 prolongation oriented along the axis of deep transmedullary vessels (Fig 3).

The remaining 56 consensually identified lesions on 4-T images were seen only in retrospect on the 1.5-T images. Forty-eight of these 56 lesions were within indistinct areas of confluent increased signal intensity on 1.5-T images (Fig 4). The remainder were located in the subependymal white matter and difficult to differentiate from adjacent CSF in the lateral ventricles at 1.5 T. Lesions measuring 5 mm or more were seen equally well at 1.5 T and 4 T. However, 43 consensually identified lesions measuring 5 mm or

more were characterized better subjectively in terms of their margins and internal signal characteristics at 4 T. In no case was a lesion of any size seen at 1.5 T but not at 4 T.

Discussion

Since the introduction of recent technological advances in gradients and software for lower-field magnets (< 1 T), the debate concerning the relative benefits of low- versus high-field MR imaging has been rekindled (17). Proponents of low-field imaging assert equal lesion detection at all field strengths with lower cost and potentially wider dissemination of instrumentation (18). Proponents of high-field imaging ($\geq$ 1.5 T) maintain the added benefits of increased S/N at high field strengths, which permit faster imaging times, higher-resolution matrices, thinner sections, and/or higher contrast (19, 20). Although it is probably true that imaging quality at low field strengths may potentially be equal, the imaging times required to produce the equivalent S/N and image quality as a high-field magnet are frequently prohibitive. This is particularly important when considering the possible negative effects on image quality in debilitated patients who cannot remain motionless for long periods of time.

Higher-field imaging ($\geq$ 3.0 T) has proved to be possible in the CNS and musculoskeletal tissues (21–23). With the use of appropriate imaging parameters, T1, spin density, and T2 contrast are possible and can potentially be used to evaluate intracranial disease (24). However, little has actually been written about the application of higher-field magnets to the study of clinical disease. In fact, most of the contemporary literature on 4-T imaging of the CNS involves functional and spectroscopic imaging, not conventional spin-echo imaging (25–30). Nonetheless, given the tremendous theoretical advantages of the higher S/N at 4 T, conventional high-field imaging has true potential.

In the case of MS, a fast, high-resolution imaging technique that could identify the smallest of perivascular lesions would be helpful in the initial diagnosis of white matter disease. This is particularly true in the

Comparison of mean number of multiple sclerosis lesions at 1.5 T and 4 T

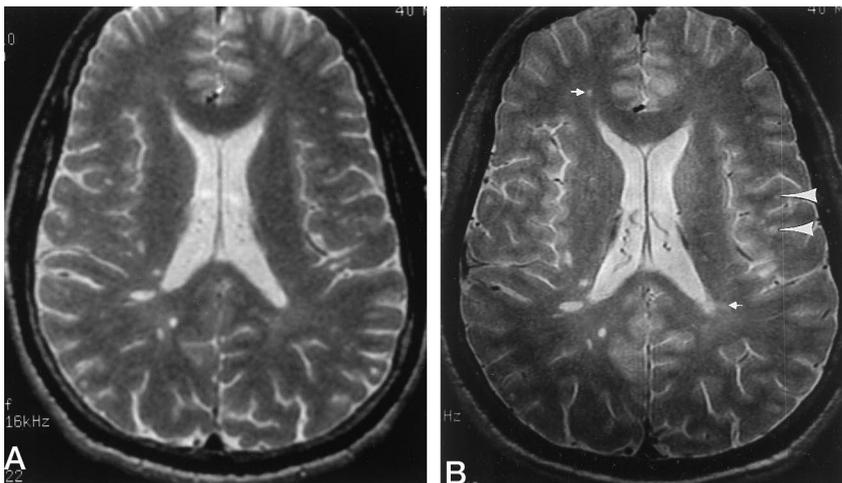| Patient	1.5 T	4 T (% change)
1	15	23 (53)
2	5	8 (60)
3	22	27 (23)
4	14	19 (36)
5	8	13 (63)
6	15	23 (53)
7	10	16 (60)
8	16	21 (31)
9	31	39 (26)
10	3	6 (50)
11	27	34 (26)
12	8	12 (50)
13	22	28 (27)
14	8	14 (43)
15	11	20 (81)
Total	215	303 (45)

Fig 2. *A* and *B*, Axial fast spin-echo (2500/80/1) 1.5-T image (*A*) and (4000/85/1) 4-T image (*B*) in a patient with known MS. The 4-T image shows a small right frontal periventricular and left peritrigonal lesion (*arrows*) not seen on the 1.5-T image. Additional lesions (*arrowheads*) in the subcortical white matter of the left temporal lobe are also seen better on the 4-T image as compared with the 1.5-T image.

FIG 3. *A* and *B*, Axial fast spin-echo (2500/80/1) 1.5-T image (*A*) and (4000/85/1) 4-T image (*B*) in an MS patient with moderate periventricular disease. The 4-T image shows multiple small lesions aligned along the visible perivascular spaces in the bilateral periventricular white matter (*arrows*). These lesions are either not seen or are indistinct on the 1.5-T image.
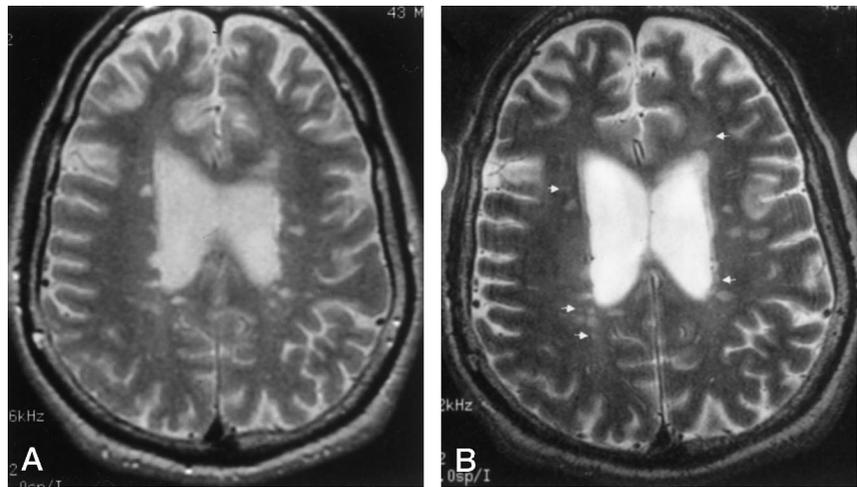

FIG 4. *A* and *B*, Axial fast spin-echo (2500/80/1) 1.5-T image (*A*) and (5000/85/1) 4-T image (*B*) in a patient with advanced MS. Areas of hazy high signal intensity at 1.5 T (*arrows, A*) are seen to be composed of multiple smaller linear lesions oriented along the perivascular spaces at 4 T (*arrows, B*). In addition, the margins and internal architecture of the larger lesions are better defined at 4 T (*arrowheads*).
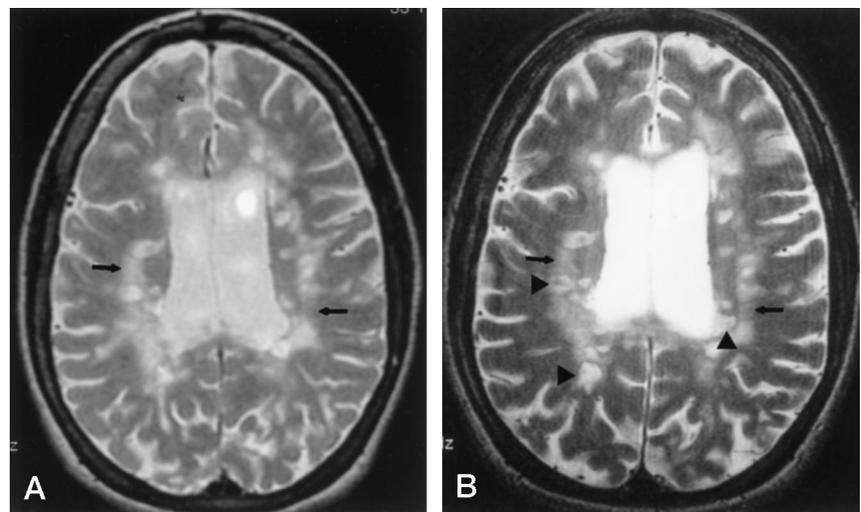
early stages of disease when documentation of the dissemination of symptoms and signs in time and space is frequently extremely difficult. Several groups have attempted to establish MR imaging criteria for MS at 1.5 T (14–16). These criteria focus on the identification of a threshold number (three to five), size (> 3 to 5 mm), and location (periventricular and infratentorial regions, which convey higher specificity for MS) of lesions as the ideal combination for providing clinically reasonable sensitivity and specificity in the initial diagnosis of MS.

Considering these criteria, improved detection and characterization of white matter lesions become critical in contributing to the earlier diagnosis of MS. The fast, high-resolution 4-T technique used in this study produced superior identification and characterization of MS lesions and may potentially be used as an effective paraclinical tool for the early diagnosis of MS. This would also allow earlier institution of therapy and appropriate long-term follow-up for these patients. Moreover, as further longitudinal studies are performed at 4 T, new diagnostic MR criteria may also be established to improve the accuracy of MR imaging in the diagnosis of MS.

The 4-T images also provided excellent anatomic detail of the perivascular spaces. Smaller lesions were seen oriented along the deep medullary perivascular spaces potentially representing the earliest radiologic correlates of Dawson's fingers and perivenous demyelination (31, 32). In addition, areas of hazy increased signal intensity frequently seen in MS patients at 1.5 T were seen to be composed of multiple smaller and more complex lesions at 4 T. The increased internal complexity of these lesions may represent different stages of inflammation, demyelination, and gliosis in the individual lesion. Thus, the high-quality, high-resolution 4-T images may potentially provide insight into the pathologic progression of disease from the smallest of perivascular lesions to larger, more complex plaques.

The presence of white matter lesions seen at 4 T but not at 1.5 T may also explain abnormalities noted with MR spectroscopy, calculated relaxation times, and magnetization transfer imaging in normal-appearing white matter at 1.5 T (33–36). Moreover, as techniques at higher field strengths evolve, high-resolution fast spin-echo imaging, MR spectroscopy, and magnetization transfer imaging may all potentially be performed in one imaging session and provide the highest sensitivity for the identification of white mat-

ter abnormalities in MS patients. Debilitated MS patients can easily tolerate the short imaging times at 4 T, thereby minimizing motion artifacts frequently encountered with high-resolution techniques at 1.5 T, which require prohibitive imaging times to approximate the S/N at 4 T.

Conclusion

High-resolution imaging of white matter abnormalities in MS patients is not only possible at 4 T but is superior to 1.5 T imaging in terms of lesion detection. It clearly reveals lesions within normal-appearing white matter at 1.5 T and may contribute to a more accurate assessment of total lesion load. MR imaging at 4 T may provide insight into the pathologic progression of disease in MS patients and, along with clinical data, potentially allow the earlier diagnosis of MS as these MR criteria become better defined. Future prospective studies evaluating the use of high-resolution 4-T imaging in patients with suspected but not documented MS are required to further evaluate its potential as a paraclinical test and as an aid in monitoring the effects of medical therapy on early lesions.

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