Comparison of Multiple Sclerosis Lesions at 1.5 and 3.0 Tesla

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Objective: To evaluate the relative sensitivity of MR scanning for multiple sclerosis (MS) at 1.5 Tesla (T) and 3.0 T using identical acquisition conditions, as is typical of multicenter clinical trials.

Methods: Twenty-five subjects with MS were scanned at 1.5 T and 3.0 T using fast spin echo, and T_1-weighted SPGR with and without gadolinium contrast injections. Image data, blinded to field strength, were analyzed using automated segmentation and lesion counting.

Results: Relative to scanning at 1.5 T, the 3.0 T scans showed a 21% increase in the number of detected contrast enhancing lesions, a 30% increase in enhancing lesion volume and a 10% increase in total lesion volume.

Discussion: The improved detection ability using high-field MR imaging is prominent even when sequence parameters are optimized around the midfield units. Multicenter trials using both 1.5 T and 3.0 T instruments may be affected by these sensitivity differences.

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Magnetic resonance imaging (MRI) plays an increasingly important role in the management and understanding of multiple sclerosis (MS). Serial contrast-enhanced MRI studies are now used to monitor acute disease activity and to determine total lesion load with proton density (PD) or T_2 lesion volume measurements. These MRI measures of MS disease activity have not only advanced our understanding of the pathophysiology of MS but are now used routinely to evaluate the efficacy of new treatments.[1,2] The quest to determine lesion loads in an accurate and reproducible way has identified several factors that can affect the number and volume of MS lesions that can be identified on serial MRI scans. These include the choice of pulse sequence,[3–5] slice thickness,[6,7] spatial resolution,[7] repositioning errors,[8] segmenting algorithms,[9,10] differences among scanners of different types,[11] and magnetic field strengths.[12]

As MRI field strength is increased, the effects on image quality are manifold. The MR signal strength increases linearly, but practical tradeoffs, such as minimization of chemical shift artifacts through increased receiver bandwidth result in less than linear gains in signal-to-noise ratio (SNR).[13] Contrast varies as a strong function of field strength as tissue relaxation properties change,[14] and at higher field strengths additional problems of signal intensity uniformity arise and can be problematic in automated segmentation.[15] When, as is typical of multicenter trials, an attempt is made to normalize the sensitivity across performance sites through the use of identical MR sequence acquisition parameters, the relative performance of the different field strengths may yet introduce important differences in lesion detection.

The effect of magnetic field strength on MRI has been approached from different perspectives. Initial studies compared the qualitative differences between MRI scans performed at different field strengths to determine if the use of

higher field magnets might translate into improved diagnostic accuracy. In studies of multiple sclerosis,[12,16] knee injuries[17–19] and various central nervous system disorders[20] there were no differences in the ability of experienced radiologists to diagnose these disorders despite variations in magnet field strength. However, radiologists consistently rated the higher field scans (usually 1.5 versus 0.5 T) as being of superior quality and easier to interpret.[21]

MRI scan information plays a central role in the newest diagnostic criteria for multiple sclerosis, especially in patients who have early forms of the disease.[22] In addition, early treatment may lead to better long term outcomes.[23,24] While the ability to make the diagnosis of MS in advanced cases may not be affected very much by magnet field strength differences, increased sensitivity to the appearance of new lesions may lead to the earlier identification and treatment of high risk patients and subsequently better patient outcomes.

Previous comparisons of MS lesions at different field strengths have favored the higher field system. Comparing MS patient scanned sequentially on a low field "open" scanner at 0.23 T and a 1.5 T scanner, larger numbers of lesions were identified on the 1.5 T scans. This included T_1 lesions (+30%), T_2 lesions (+31%), and enhancing lesions (+60%). The scanning protocols were similar but not identical and the high-field scans were done at 2 NEX.[25] Keeping scanning times and signal to noise similar, Keiper et al.[16] were able to produce higher-resolution T_2-weighted scans on a 4 T system compared with a 1.5 T system. White matter lesion counts were 45% higher on the 4 T scans and the tissue heterogeneity within lesions was better appreciated.

Although the qualitative differences in scan appearance may not impact the ability to diagnose MS, especially when field strengths of at least 0.5 T are used, quantitative differences appear to be quite large. Clearly, if optimized, higher-field scanners are capable of producing superior images of higher resolution and tissue contrast compared with scans done at similar imaging times on the lower field scanner. Increased postcontrast lesion numbers are caused in large part by the augmented effect of field strength on T_1 contrast of brain with gadolinium when magnetic field strength is higher that 2.3 T.[26] However, to date no study has examined the effect of field strength on quantitative measures of MS lesions when imaging parameters and matrix sizes are the same and when no attempt has been made to exploit the advantages of the higher field. This has important implications in the setting of a multicenter clinical trial using MRI measures as primary or secondary outcome measures when imaging parameters are fixed across sites.

The purpose of this study was to determine the effect of scanner field strength on the measurement of multiple sclerosis lesion counts. Identical patient positioning techniques and pulse sequences were used as in a typical multicenter clinical trial. In addition, the data were normalized and analyzed in a standard fashion to determine what effect higher field strength would have on MRI measures of MS, namely number and volume of enhancing lesions and white matter lesion volumes.

MATERIALS AND METHODS

Informed consent was obtained from all subjects. Twenty-five subjects with clinically definite multiple sclerosis were enrolled in the study. Expanded disability status scale (EDSS)[27] rating and clinical information were obtained by a neurologist. Scans were performed during 2 sessions separated by 1 to 3 days on both 1.5 and 3.0 T GE Signa imaging systems (GE Medical Systems, Milwaukee, WI). Scanning order was randomized. The first scan was performed on the 1.5 T in 15 of the 25 subjects. For the first 5 subjects studied, variable T_2-weighted pulse sequences were used. The T_2 lesion data from these subjects was not included in the analysis. Identical pulse sequences for the dual echo fast spin echo (FSE) scans as described below were obtained in the last twenty subjects. The T_1-weighted scans were identical for all 25 subjects studied. Subjects received identical doses of contrast during each scanning session. Positioning was done in the same way for each scan. A series of scout images were obtained to identify the true sagittal plane. Axial images were then obtained on a plane parallel to the anterior and posterior limbs of the corpus callosum. FSE images were obtained using the following pulse sequence: 3-mm slices, no gap, field of view (FOV) 22, matrix 256 × 256, TR 4500/TE 17/85. This was followed by a T_1-weighted 3D volume scan before and after the administration of Gadolinium (Omniscan) at a dose of 0.1 mm/kg: SPGR, sagittal 1.2 mm, FOV 24, matrix 256 × 256, IR prepped 400 milliseconds.

All scan data were transferred digitally to a Silicon Graphics workstation for image analysis. The proton density weighted scans were used for analysis of white matter lesions. First the skull and meninges were stripped using an automated algorithm.[28] A registration target was created using the automated image registration method previously described.[29,30] Scans from each individual were then registered to the target and resliced. Scan intensity values were normalized using a custom software package that performed a z-transformation on the stripped, resliced data. The volume of PD lesions was determined using a semi-automated local thresholding technique (DISPLAY- Montreal Neurologic Institute). The same threshold value was used for every PD weighted scan to minimize bias. Enhancing lesion number and volume were determined in a similar fashion using the same semi-automated technique. All measurements were performed in random order by the same individual who was blind to the identity of the subject and the scanner used. Statistics were performed using student's *t* test for paired and unpaired samples. Reported *P* values reported are 2-tailed.

RESULTS

Clinical Characteristics

A total of 25 patients were studied. All subjects except for one were women. The mean age was 43 years (range 28 to 50 years). Mean disease duration was 18 years (range 6 to 33 years) and the mean EDSS score was 4.0 (range 1.0 to 6.5). The 25 patients could be divided into 2 groups according to disease type. There were 12 secondary progressive (SP) cases and 13 relapsing remitting (RR) cases. The mean EDSS score for the SP patients was 6.1 whereas the mean EDSS for the RR patients was 2.2; this difference was statistically significant ($P < 0.00005$). All patients were off all immunosuppressive therapy at the time of study. None had received copolymer 1 or interferon β for at least 6 months or steroids for at least 3 months before the study. Subjects tolerated the scanning procedure well. There were no adverse reactions to the contrast injections reported. During the 1.5 T scan 1 subject (subject 7) developed a hematoma during the contrast injection and received a suboptimal dose of gadolinium. This subject had no evidence of enhancing lesions on either scan.

Lesion Data: Gadolinium-Enhancing Lesions

At 1.5-T field strength a total of 23 enhancing lesions were detected in 4 of the 24 patients studied (16% positive). On the 3.0 T scans, 28 lesions were detected in 6 patients (25% positive) representing a 21% increase in the number of enhancing lesions detected at the higher field strength. In one patient, 2 enhancing lesions were detected on 3.0 T whereas none were seen at 1.5 T. In another patient, a retrospective look at the 1.5 T revealed a slight bit of enhancement that was not evident on the initial analysis (Fig. 1).

TABLE 1. Gadolinium-Enhancing Lesion Data

	1.5 T		3.0 T	
Subject	Number	Volume (mm^3)	Number	Volume (mm^3)
1	13	1768.8	14	2480.0
5	0	0	2	39.9
6	1	2.1	1	2.1
17	2	67.5	2	144.5
19	0	0	1	17.9
22	7	253.1	8	369.1
Totals	23	2091.5	28	3053.5

The total mean enhancing lesion volumes was higher at 3.0 T compared with 1.5 T (3053 mm^3 versus 2091 mm^3), representing a 54% increase. When only the lesions seen on each of the scanners was quantified the difference was 30% higher on the 3.0T scans (Table 1).

Lesion Data: Proton Density Lesions

The mean PD lesion volume in the twenty patients who had identical pulse sequences used at each field strength was also higher on the 3.0T scans (11.6 cm^3 versus 10.66 cm^3) representing a 10.7% increase in total lesion volume compared with the 1.5T scans. The average percentage difference on an individual basis was 12.3% higher on 3.0 T (range −16.8 to 42.6% of 3.0 T volume). Proton density lesion volume was higher on the 3.0 T scan in 16 of the 20 patients studied (Table 2). Overall, however, the total lesion volumes obtained on both scanners for the same individual were highly correlated ($r = 0.99$).

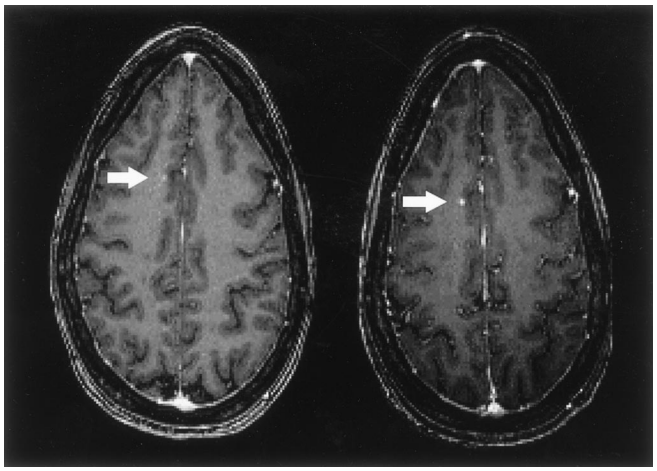

FIGURE 1. T_1-weighted images after contrast of a single MS patient, from the 1.5 T (left) and 3.0 T (right) scanners. The figure demonstrates the greater contrast effect evident at the higher field. A single enhancing lesion that was initially missed on the 1.5 T scan is clearly seen on the 3.0 T scan (arrows).

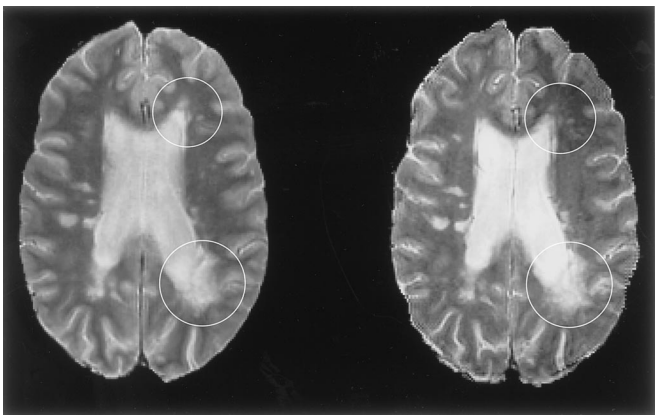

FIGURE 2. Proton density-weighted images of a single MS patient obtained on the 1.5 T (left) and 3.0 T (right) scanners. At the higher field, the ventricular/lesion boundary is more apparent and lesion detail is more pronounced (see circled areas).

TABLE 2. White Matter Lesion Volumes (in cm^3)

Subject Number	1.5 T	3.0 T	Percentage Difference
6	2.45	2.97	17.51
7	2.6	3.08	15.58
8	10.94	10.9	−0.37
9	11.49	13.23	13.15
10	9.49	9.35	−1.50
11	18.63	20.5	9.12
12	27.61	27.05	−2.07
13	10.63	11.89	10.60
14	0.39	0.66	40.91
15	14.64	16.78	12.75
16	0.82	1.16	29.31
17	16.74	19.44	13.89
18	17.66	18.86	6.36
19	4.58	3.92	−16.84
20	2.99	3.09	3.24
21	0.97	1.69	42.60
22	30.66	32.66	6.12
23	5.2	6.34	17.98
24	12	13.14	8.68
25	12.67	15.8	19.81
Mean	10.66	11.63*	12.34
Median	10.79	11.40	11.68

*Paired t-test, $P = 0.0006$

There were no regional differences in lesion detection between the 2 field strengths noted. The scans from the 3.0 T produced images with better tissue resolution especially at the ventricular/brain interface making lesion identification and segmentation easier on the 3.0 T images (Fig. 2).

DISCUSSION

MRI scans of multiple sclerosis patients, performed on both 1.5 and 3.0 T field strengths using the same pulse sequences with the same image resolution, yielded greater numbers of gadolinium enhancing lesions and larger volumes of enhancement as well as greater white matter lesion volumes from the higher field scanner. The number of gadolinium-enhancing lesions detected on the 3.0 T scans was increased by 21% in comparison to the 1.5 T scans. In addition, 2 subjects who did not have evidence of enhancement on the 1.5 T scan were found to have enhancing lesions on the higher field scans. The volume of enhancement was also increased on average by 30% at 3.0 T. In many clinical trials of new MS treatments, enhancing lesion numbers and volumes are the primary outcome measures of efficacy.[31,32] In addition, inclusion criteria and treatment group stratification are frequently based on the presence or absence of enhancing lesions. The greater sensitivity of the higher field scanner can lead to higher relative lesions counts, but could also result in the inclusion of subjects into a clinical trial who have disease characteristics that differ from those at other centers using lower field strength scanners.

The volume of white matter lesions was also on average 10% higher on the 3.0 T proton density-weighted scans compared with the 1.5 T scans, although the values obtained on each scanner were highly correlated ($r = 0.99$). The greater volume on 3.0 T scans was seen after normalizing the data and using a standard segmentation approach and without specifically exploiting the greater signal to noise of the 3.0 T scanner. The degree of this increased sensitivity will likely vary depending on the specific pulse sequences chosen and the segmentation algorithm used. Other MR techniques, such as magnetization transfer, diffusion-weighted imaging, and spectroscopy, indicate that the "normal-appearing" white matter in MS patients is in fact very abnormal when compared with controls.[33–37] In advanced MS, when lesion loads are high, and white matter lesions become more confluent, it is difficult to determine the exact boundaries of abnormality. The higher signal from the 3.0 T studies made it easier to segment these areas as seen in Figure 2. Monitoring changes in these ill-defined areas may be critical in determining the efficacy of newer MS treatment strategies such as neuroprotection and precursor cell transplants. This general finding is particularly noteworthy, inasmuch as the 3.0 T images typically display strong intensity inhomogeneities.[38]

In this study, the biggest impact of the higher field strength was on the post contrast scans. This is expected as the T_1 of brain tissue increases with field strength. In addition, it should be noted that the SPGR scans performed in this study have been shown to have less sensitivity to gadolinium.[39,40] The magnitude of this effect may be differ with other pulse sequences such as 2D spin echo techniques that are more commonly used in clinical trials of MS.

In summary, compared with a 1.5-T strength scanner, 3.0 T scans are more sensitive at detecting both gadolinium enhancing lesions and white matter lesions even when the scanning protocols have not been optimized for the higher field. Ideally, prior to data acquisition in a multicenter clinical trial, scan data should be normalized across scanners with regard to contrast to noise measures. Adjustments to the scanning protocols will depend in part on the data processing approach to be used. The greater field inhomogenieties at higher fields may require more extensive preprocessing of this data. Segmentation algorithms may need modification to adjust for the greater sensitivity of the higher field scanners. The use of magnets of varying field strengths in multicenter clinical trials of multiple sclerosis will add another level of variability to the study results, and should be approached with caution. Future studies should examine the differences between mid and high field scanner strengths in newer MR

techniques such as magnetization transfer, diffusion imaging and spectroscopy which may provide better markers for disease progression and disability in multiple sclerosis and will likely be used as outcome measures in subsequent clinical trials.

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