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Magnetic Resonance Imaging of Multiple Sclerosis: A Study of Pulse-Technique Efficacy

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Forty-two patients with the clinical diagnosis of multiple sclerosis were examined by proton magnetic resonance imaging (MRI) at 0.5 T. An extensive protocol was used to facilitate a comparison of the efficacy of different pulse techniques. Results were also compared in 39 cases with high-resolution x-ray computed tomography (CT). MRI revealed characteristic abnormalities in each case, whereas CT was positive in only 15 of 33 patients. Milder grades 1 and 2 disease were usually undetected by CT, and in all cases, the abnormalities noted on MRI were much more extensive than on CT. Cerebral abnormalities were best shown with the T2-weighted spin-echo sequence (TE/TR = 120/1000); brainstem lesions were best defined on the inversion-recovery sequence (TE/TI/TR = 30/400/1250). Increasing TE to 120 msec and TR to 2000 msec heightened the contrast between normal and abnormal white matter. However, the signal intensity of cerebrospinal fluid with this pulse technique obscured some abnormalities.

The diagnosis of multiple sclerosis continues to be a clinical challenge [1, 2]. The lack of an objective means of assessment further complicates the evaluation of treatment regimens. Evoked potentials, cerebrospinal fluid (CSF) analysis, and computed tomography (CT) are currently used for diagnosis, but all lack sensitivity and/or specificity. Furthermore, postmortem examinations demonstrate many more lesions than those suggested by clinical means [3]. Two previous investigations [4, 5] have established the sensitivity of magnetic resonance imaging (MRI) for detecting cerebral abnormalities in multiple sclerosis. However, both reports were limited by the small numbers of patients and the variety of pulse techniques used.

In our series, seven different MR scan techniques were used to evaluate the relative efficacy of T1- and T2-weighted images. Findings were correlated with the patients' clinical histories, laboratory data, and CT examinations.

Subjects and Methods

Patients

Forty-two patients (16 men and 26 women) with a clinical diagnosis of multiple sclerosis were studied. In each case, multiple neurologic events separated by both anatomic site and time had been observed. The age range of patients was 26–66 years, and the duration of disease varied from 1 month to 30 years. The three patients over age 55 all had greater than a 10-year history of multiple sclerosis. Oligoclonal bands were present in the cerebrospinal fluid in eight of 21 cases tested.

CT

High-resolution GE CT/T 8800 scans were performed with and without intravenous contrast enhancement (300 ml of a 30% meglumine iohalamate solution as a continuous drip) in 38 of the 42 patients. Of these examinations, 33 were done within 2 weeks of the MR scan. The CT scanner was operated at 120 kVp with contiguous 10-mm sections obtained from the base of the skull to the vertex. The CT scans were examined for focal areas of low attenuation

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and abnormal contrast enhancement, ventricular enlargement, and cortical atrophy.

MR

A Technicare 0.5-T superconducting magnetic resonance imager with a 28-cm-ID radiofrequency coil was used. Data were acquired using a 256×128 pixel matrix, with interpolation along the y axis to yield a 256×256 matrix and a pixel size of 2.2×2.2 mm. The slice thickness was 1 cm. The protocol for MRI required 2 hr per patient and consisted of three anisotropic volume studies of the brain, each with 32 contiguous transverse sections and four identical level transverse sections through the body of the lateral ventricles.

Two spin-echo (SE) volume techniques were used. The 30 msec TE and 250 msec TR is primarily proton density and T1-weighted with a very slight T2 contribution; the 120 msec TE and 1000 msec TR is primarily T2-weighted. The third volume technique was a T1-weighted inversion-recovery (IR) sequence with 30 msec TE, 400 msec T1, and 1250 msec TR. The scan times for these three volume techniques were 10, 37, and 47 min, respectively. Motion artifact was minimized by the use of adhesive tape and Velcro straps to restrain the head.

Each of the single sections was obtained at the same level with four spin-echo techniques, TE/TR (in msec) being 30/500, 60/1000, 120/1000, and 120/2000. Axial sections were obtained to facilitate comparison with CT, but the angles of the MR sections did not duplicate the CT due to limitations imposed by the smaller internal diameter of the MR head coil. Of the 42 patients, 37 had complete examinations. Five other examinations were limited in scope due either to technical problems or the patients' medical conditions. Five patients were studied twice at intervals ranging from 3 to 14 weeks.

This complex and lengthy imaging protocol was used for three reasons. First, the acquisition of three volume studies allowed a direct comparison of the three pulse sequences, lesion for lesion, throughout the entire brain. Second, these scans permitted a thorough assessment of the extent of intracranial involvement. Third, the four identical-level spin-echo sections allowed a more complete comparison of the utility of different pulse techniques.

Disease severity on MRI was graded on a scale of 1–4 by the size, number, and definition of lesions. Grade 1 disease involvement was limited to the periatral and supraventricular regions. Supraventricular lesions, when present, were poorly defined. Grade 2 was defined by the identification of disease involvement in an additional anatomic region, usually the periventricular white matter. The supraventricular lesions were larger than those of grade 1, measuring more than 0.25 cm in diameter, and well separated from the ventricular system. The addition of well-defined frontal horn involvement, supraventricular lesions greater than 0.5 cm in diameter, and white matter lesions in the frontal, parietal, occipital, temporal, or capsular regions constituted grade 3 disease. The presence of brainstem lesions with grade 3 supratentorial white matter changes constituted grade 4. Without brainstem changes, white matter involvement distant from the periventricular, supraventricular, and capsular lesions was required for diagnosis of grade 4 disease.

Each volume study was analyzed for lesions by anatomic location. Areas of artifact, noise, or significant mottle were excluded. The efficacy of a particular MR scan technique was defined as the percentage of lesions detected by one method, at a given anatomic level, when compared with the method demonstrating the maximum number of lesions. Asymmetry of involvement and confluence of lesions were also assessed. The four 2D spin-echo techniques were rated by diagnostic value in each case.

Calculated T1 and spin-density images were also acquired in a limited number of patients. Two images, SE 30/1250 and IR 30/400/

TABLE 1: Comparative Efficacy of CT/MRI in Recognition of Multiple Sclerosis

Disease Severity by MRI	No. Cases	CT Positive*
Grade 1	11	0
Grade 2	9	5
Grade 3	8	6
Grade 4	5	4
Total	33	15

* Criteria for diagnosis by CT included focal areas of low attenuation and abnormal areas of contrast enhancement.

1250, were obtained in sequence, minimizing potential errors arising from instrument fluctuations. T1 values were calculated by fitting the two observed points to a single exponential curve and obtaining the time constant for the curve. Mobile proton density was computed from the upper limit of this curve defined by the observed T1 calculation. A slight T2 dependence is introduced in this calculation by T2 dephasing due to the finite time (30 msec) spent generating the spin echo.

Results

Clearly defined abnormalities of both high and low signal intensity were detected in each case of multiple sclerosis scanned by magnetic resonance. Of the 33 CT examinations, only 15 (45%) showed discrete areas of low attenuation or abnormal areas of enhancement. Less specific findings of ventricular enlargement and cortical atrophy were seen equally well on MRI and CT. Detection of disease by CT increased with severity as judged by MRI (table 1). No MRI grade 1 cases, the least severe disease involvement, had positive findings on CT, as compared with 80% of grade 4 cases.

The distribution of lesions in multiple sclerosis, as assessed by MRI, correlated well with autopsy data in the literature [1], showing a predilection for symmetrical, periventricular involvement (table 2). Lesions contiguous with the frontal and occipital horns, as well as along the bodies and atria of the lateral ventricles, were most common. Supraventricular white matter was also frequently involved (84%) (fig. 1). Brainstem lesions were not uncommon (30% of patients had an area of abnormality in the pons). Cerebellar lesions were seen least frequently, with a total of four lesions detected in three patients. Lesions were typically confluent around the frontal and occipital horns and atria on all the MR techniques used. In the white matter not immediately adjacent to the ventricles, lesions tended to be more discrete and often circular. Abnormalities noted in the brainstem were either circular or bar-shaped.

The variation in appearance of abnormalities with different pulse sequences is illustrated in figure 2, with an example of the four routinely obtained 2D sections. In a T1-weighted image (TE/TR = 30/500), the lesions appeared as discrete areas of low signal intensity (black) contrasting with the surrounding higher-intensity white matter. As TE and TR were lengthened, the T2 contribution to signal intensity became progressively greater. Abnormalities on these latter scans

TABLE 2: Efficacy of MR Scan Technique and Distribution of Lesions

Location	Efficacy (%)			Abundance*
	SE 30/250	SE 120/1000	IR 30/400/1250	
Periventricular:				
Frontal	79	100	86	97
Body	48	100	72	86
Atrial	59	100	51	100
Occipital	33	100	24	92
Temporal	0	100	13	32
White matter:				
Supraventricular	66	100	98	84
Frontal	32	100	61	46
Parietal	6	100	33	46
Occipital	0	100	60	11
Temporal	0	100	8	19
External capsule	17	100	67	11
Internal capsule	38	88	100	43
Corona radiata	48	86	100	30
Brainstem:				
Mesencephalon	31	63	100	22
Pons	13	25	100	30
Medulla	0	0	100	5
Cerebellum	25	100	50	8

Note.—Data from 37 studies.

* Percentage of patients with lesions in the given anatomic region.

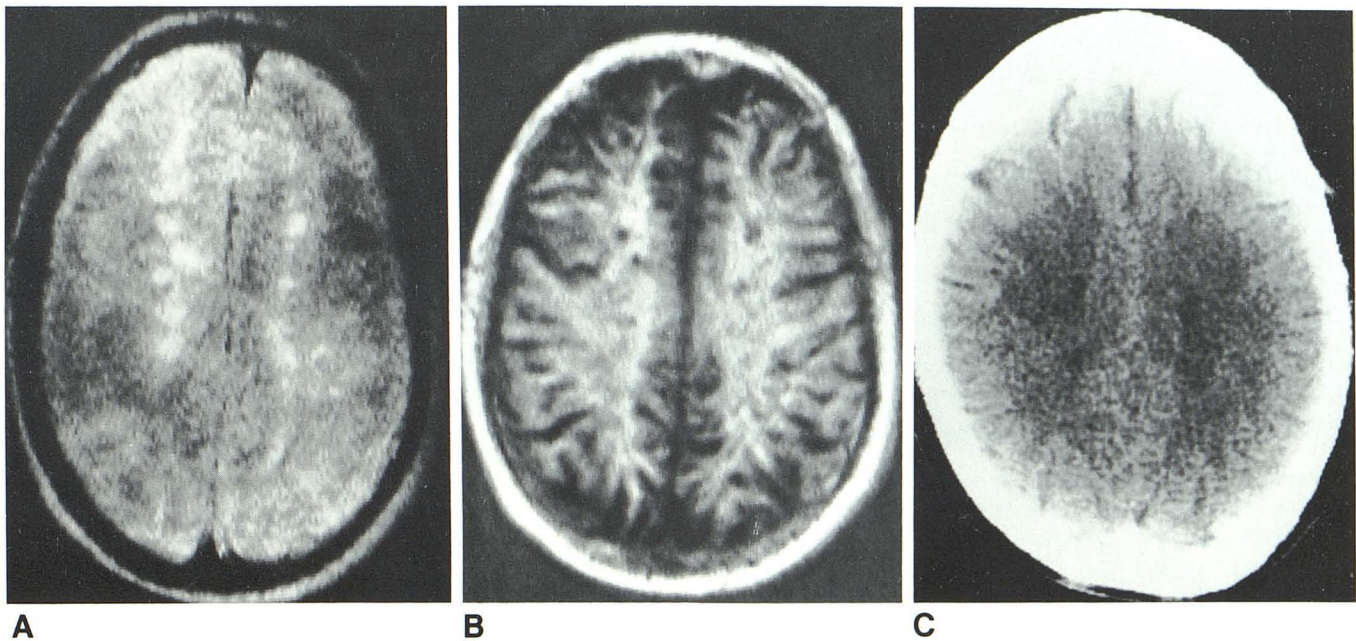


Fig. 1.—Supraventricular white matter lesions of multiple sclerosis seen by two different anisotropic volume MR techniques. A, SE 120/1000. Lesions are seen as areas of high signal intensity (white). B, IR 30/400/1250. Lesions are

seen as areas of low signal intensity (black). Although severity of disease was grade 3 by MRI, CT in this patient was normal (C).

were then noted as areas of high signal intensity (white) compared with the darker normal surrounding white matter. A wide range of T1 and T2 values of abnormal areas was encountered (fig. 3). An intermediate echo time (TE) and repetition time (TR), for example 60 msec TE and 1000 msec TR (fig. 3A) may show lesions of both high and low signal

intensity. Of the four 2D spin-echo techniques (survey of 32 cases, table 3), the SE 120/1000 technique proved to be most valuable, consistently showing the largest number and greatest extent of multiple sclerosis lesions. Of note, however, is that no one technique was superior in all cases. Increasing the TR to 2000 msec improved the signal-to-noise ratio and

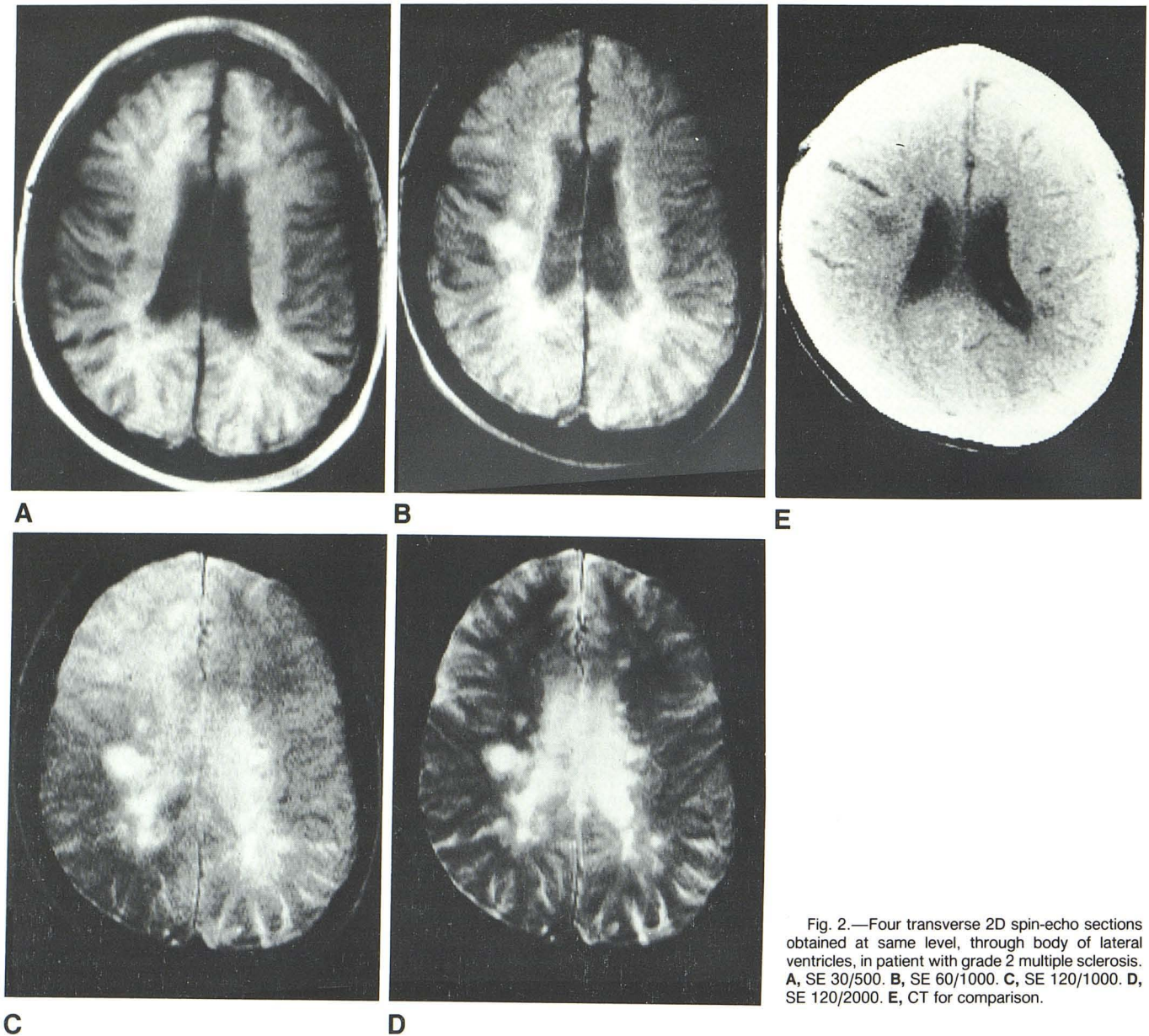


Fig. 2.—Four transverse 2D spin-echo sections obtained at same level, through body of lateral ventricles, in patient with grade 2 multiple sclerosis. A, SE 30/500. B, SE 60/1000. C, SE 120/1000. D, SE 120/2000. E, CT for comparison.

increased the T2 dependence of the image, resulting in better definition of lesions and identification of smaller lesions, with higher contrast between abnormal and normal white matter, as noted on a previous investigation [7]. With this sequence, however, the higher signal intensity of CSF obscured some periventricular lesions. With SE 60/1000, some lesions became isointense.

In a comparison of the three different anisotropic volume techniques (table 2), the T2-weighted study (SE 120/1000) was generally superior for detection of lesions in the cerebral hemispheres, with the exception of those in the internal capsule and corona radiata. These lesions and those in the cervical cord, medulla, and pons were best seen with the T1-weighted inversion-recovery technique (IR 30/400/1250). The

short spin-echo sequence (SE 30/250) was most time-efficient and demonstrated a large number of lesions well. However, the contrast between normal and abnormal white matter was relatively low, preventing the detection of many lesions.

In the cerebral hemisphere, the inversion-recovery technique was not as efficacious, as some lesions at the normal gray-white matter junction were lost, while others were difficult to distinguish from partial-volume effects of the cortical sulci. Lesions in the internal capsule (fig. 4) and corona radiata, two areas unaffected by the previous considerations, were indeed best seen by the inversion-recovery technique. In general, lesion margins were more distinct on inversion-recovery scans than on T2-weighted sequences (table 4).

Lesions adjacent to the frontal horns were consistently well

Fig. 3.—Comparison of appearance and detectability of supraventricular lesions with two different spin-echo (2D) techniques. **A**, SE 60/1000. **B**, SE 120/2000. Range of T1 and T2 values demonstrated by lesions is evident, with abnormal areas of high signal intensity in **B** corresponding to regions of both high and low signal intensity in **A**.

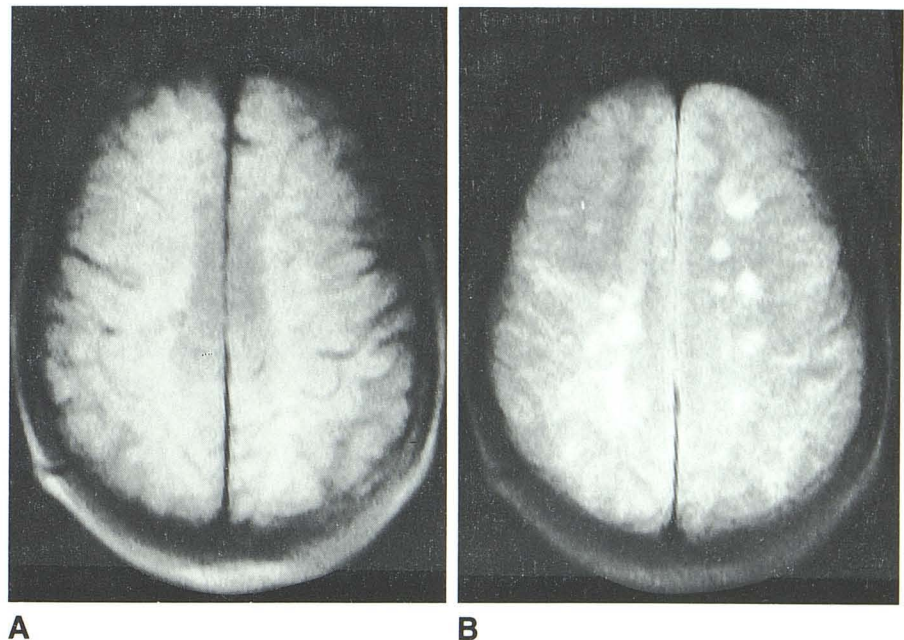


TABLE 3: Rating of MR SE Techniques by Diagnostic Value

TE/TR (msec)	Rating*
30/500	4.0
60/1000	2.3
120/1000	1.4
120/2000	2.1

* Comparison of 2D transverse sections obtained at level of body of lateral ventricle (32 cases), scale of 1-4 with 1 being most diagnostic.

identified by inversion-recovery technique with proper windowing of the image. However, lesions adjacent to the body of the lateral ventricles were often difficult to identify due to the poor contrast with adjacent CSF (both areas manifesting a low signal intensity on inversion-recovery technique). Thus, the presence of these lesions often created an appearance of irregularity in the margins of the lateral ventricles, a "lumpy-bumpy" pattern that could be identified readily as abnormal (recognition of this pattern was not included in the calculations of table 2).

Cerebellar lesions were noted in only three patients (fig. 5). Because of the small group size, the results concerning efficacy of scan technique in this region were not statistically significant. However, T2-weighted techniques did seem to be superior in the diagnosis of cerebellar plaques, as these lesions were difficult to differentiate from CSF spaces with the inversion-recovery technique. Brainstem lesions, as noted previously, were best identified with the inversion-recovery technique (fig. 6). Distinct areas of high signal intensity, resembling lesions, were noted in a few patients on inversion-recovery scans. In one patient (fig. 7), rings of high signal intensity were seen surrounding otherwise typical low-signal-intensity plaques.

No definite abnormalities were noted in the optic nerves in any of the 42 cases. This may reflect poor definition due to

either eye motion during the long scan times or the 1-cm section thickness. Sagittal and coronal sections (fig. 8) were obtained in a small number of patients, illustrating the appearance of disease in other planes. Figure 9 illustrates the use of more recently introduced scan techniques in the examination of a patient with multiple sclerosis.

In the five patients studied twice (with the interval between examinations varying from 3 to 14 weeks), no overall change in grade of disease involvement was noted (fig. 10). Differences were observed, however, in the appearance of individual lesions, with the regression of some abnormalities and progression of others.

The MR scans were also examined for asymmetry of disease involvement, considering lesions in the first six categories of table 2. Of the 42 examinations, 22 (52%) showed unilateral predominance of lesions, seven with marked asymmetry.

Little correlation was noted between disease severity, as graded on MRI, and duration of disease. Recently diagnosed (< 6 months) cases of multiple sclerosis were equally distributed among the four grades of disease severity. Three of five grade 4 cases had a history of the disease for greater than 20 years. There was, however, a statistical difference in age of the patient population when comparing disease grades 1 and 4 (37 ± 10 years compared with 48 ± 8 years, respectively; $p < 0.025$). A more extensive comparison and evaluation of disease severity on MRI as compared with patient disability is in progress.

Discussion

The signal intensity observed in MRI of solid tissues depends on three factors: proton density (ρ), T1, and T2. A large contrast scale exists because of the difference in T1 and T2 between gray and white matter and the changes that

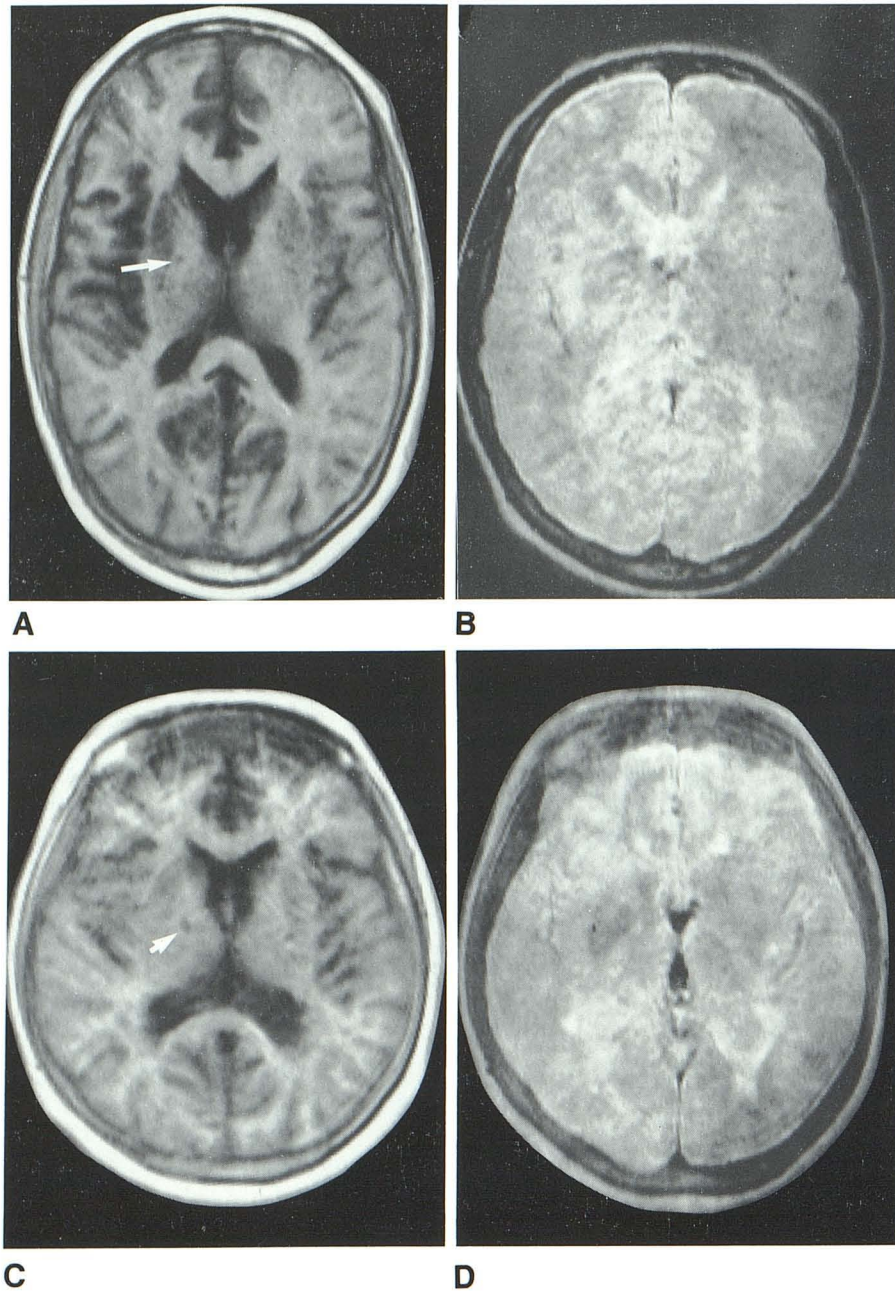


Fig. 4.—Internal capsule lesions (arrows) in two patients seen on images from anisotropic 3D volume data acquisitions. These lesions are better identified on IR 30/400/1250 (A and C) than on SE 120/1000 (B and D).

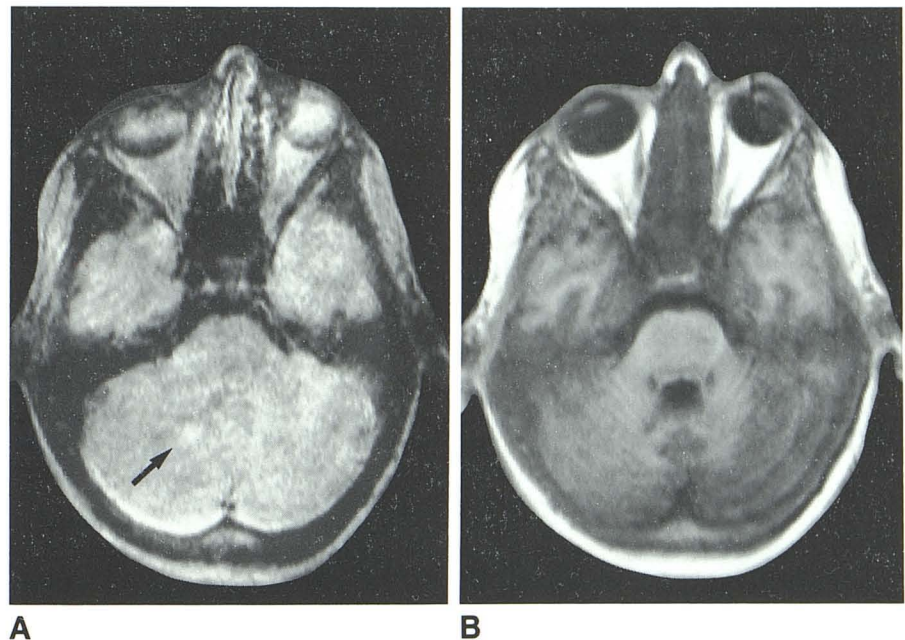
TABLE 4: Ability by Scan Technique to Identify Discrete Lesions

Scan Technique	Confluent Lesions (no. cases)*	Discrete Lesions (no. lesions)†
SE 120/2000:		
Left	21	35
Right	24	25
IR 30/400/1250:		
Left	8	87
Right	6	89

Note.—Data from 34 cases, supraventricular region.
 * Number of cases in which lesions were confluent over supraventricular area.
 † Number of discrete lesions counted.

occur in these relaxation times with certain disease processes. The value of magnetic resonance in the diagnosis of neurologic disease derives from this high level of contrast, the lack of bone artifact, specific changes noted with pathologic conditions, the flexibility in imaging technique and plane selection, and the lack of known biologic hazard [6]. The contribution of T1 to image intensity is enhanced on an inversion-recovery type of pulse technique, although only a narrow range of T1 differences is emphasized. Here, lesions attributed to multiple sclerosis are seen as discrete areas of low signal intensity (black), in contrast to the high signal intensity (white) of normal surrounding white matter. T2 dif-

Fig. 5.—Cerebellar lesion (arrow). A, SE 120/1000. B, IR 30/400/1250.



ferences are emphasized in spin-echo images with 60+ msec TE and 1000+ msec TR. This produces an image in which the white matter has a lower signal intensity than gray matter (a reversal of that seen with inversion recovery), and in which the lesions of multiple sclerosis are seen as areas of high signal intensity. Changes relatively specific for multiple sclerosis on MRI include the abundance of discrete lesions, the anatomic distribution of plaques, the asymmetry of disease involvement, and the presence of a "lumpy-bumpy" pattern adjacent to the lateral ventricles. Previous investigators have demonstrated the relative insensitivity of CT in the detection of multiple sclerosis, even with high-dose contrast enhancement and thin sections [8–10]. The marked superiority of MRI was immediately apparent with its introduction [4, 5], lesions being seen on a scale not previously possible, except at autopsy.

From the 42 cases examined, the efficacy of different scan techniques in detection of abnormalities was established. A T2-weighted spin-echo sequence (SE 120/1000) proved superior in the cerebral hemispheres and cerebellum, with two exceptions: the corona radiata and the internal capsule. Lesions in these areas, as well as those in the brainstem, were best identified on inversion-recovery technique (IR 30/400/1250). This result may be due in part to the low signal-to-noise ratio of the T2-weighted images that were used. Increasing TR to 1500 or 2000 msec, while maintaining TE at 120 msec, should improve the ability to detect brainstem lesions on T2-weighted images. Further, acquisition of adjacent (contiguous) sections, from the base of the skull to the vertex, should be mandatory for the MR imaging technique used to avoid missing small lesions between nonadjacent sections.

The ability to increase contrast between normal and abnor-

mal white matter by prolonging both TE and TR was demonstrated, confirming previous work [7]. Although smaller lesions could then be identified and the areas of abnormality often appeared more discrete, the use of very long TE and TR resulted in obscuration of periventricular lesions by the high signal intensity of CSF. The optimum technique in the cerebral hemispheres (of the four evaluated) proved to be SE 120/1000.

As noted previously, no one sequence was superior in all cases. This variability relates, in part, to the range of T1 and T2 values [5] that the abnormalities of multiple sclerosis exhibit. This range of abnormal relaxation times was confirmed through visual inspection of images (e.g., figs. 3 and 9), although not computed from the data. These differences in image characteristics may correlate with the pathologic variations in demyelination, gliosis, axonal loss, and edema demonstrated in plaques at autopsy [5, 11, 12]. Although techniques for the acquisition of calculated T1 and T2 images exist [13], the application of these in the diagnosis of multiple sclerosis is uncertain due to the long scan time and relatively poor resolution. Spin-density images may find use in the evaluation of the water content of multiple sclerosis plaques. However, more extensive use and experience with calculated T1 and T2 images may allow improved characterization of disease, particularly the age and severity of lesions. The use of multiecho techniques allows the acquisition of MR sections differing in T2 weight simultaneously, thereby facilitating identification of tissue pathology and reducing significantly the overall examination time.

Several cautionary notes must be added to these conclusions. The correspondence between lesions at autopsy and on MRI has not been confirmed pathologically, so no statements can be made concerning the absolute specificity and

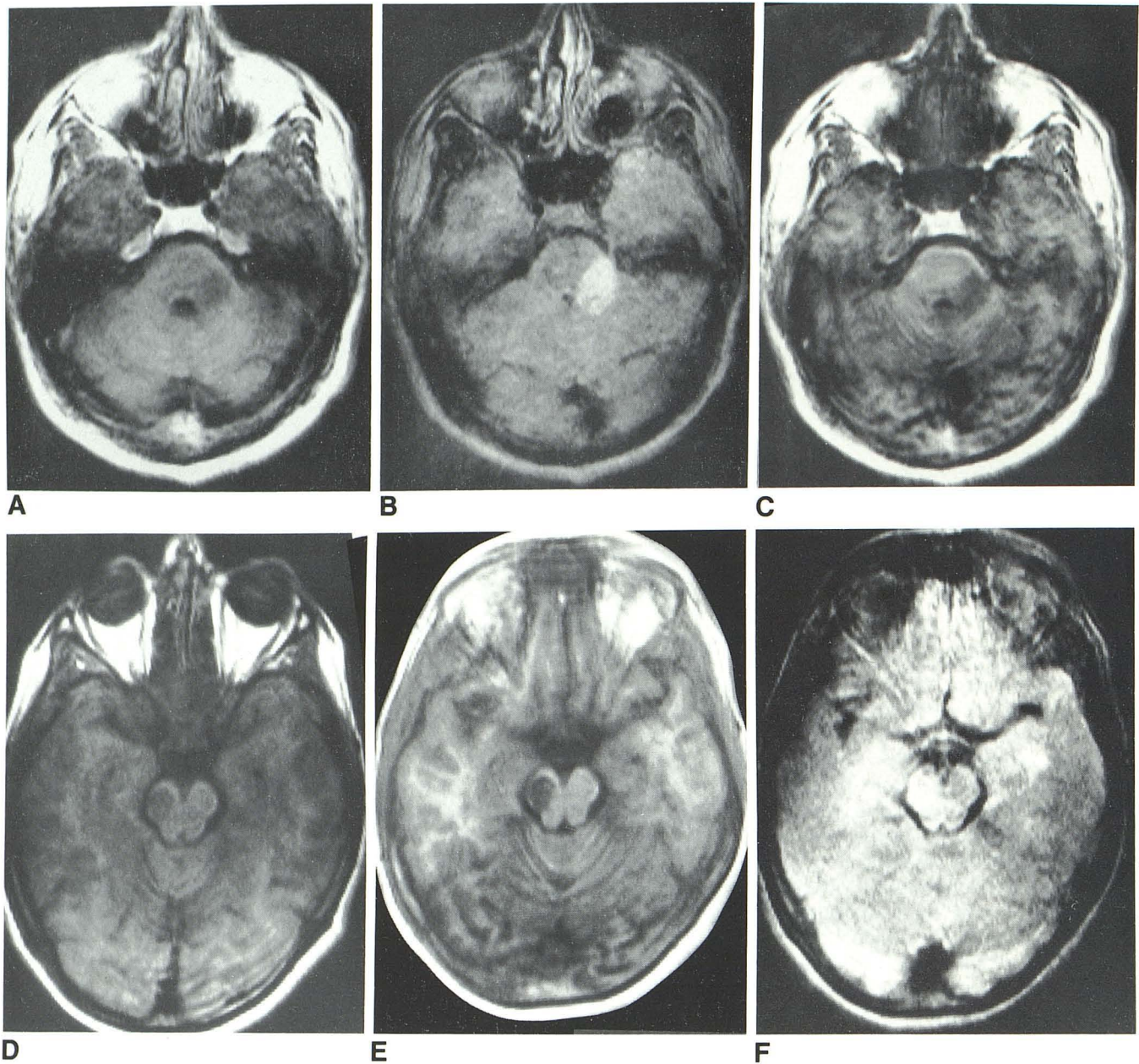


Fig. 6.—Two patients with brainstem lesions. Region of abnormality in left cerebellar peduncle seen on three 3D volume techniques: A, SE 30/250. B, SE 120/1000. C, IR 30/400/1250. Round, well circumscribed lesion of multiple

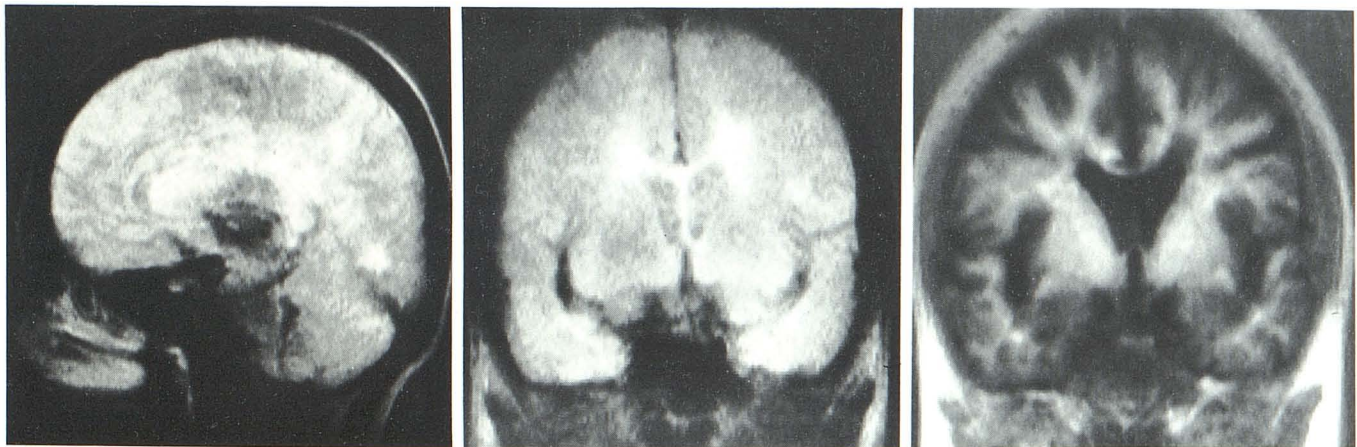
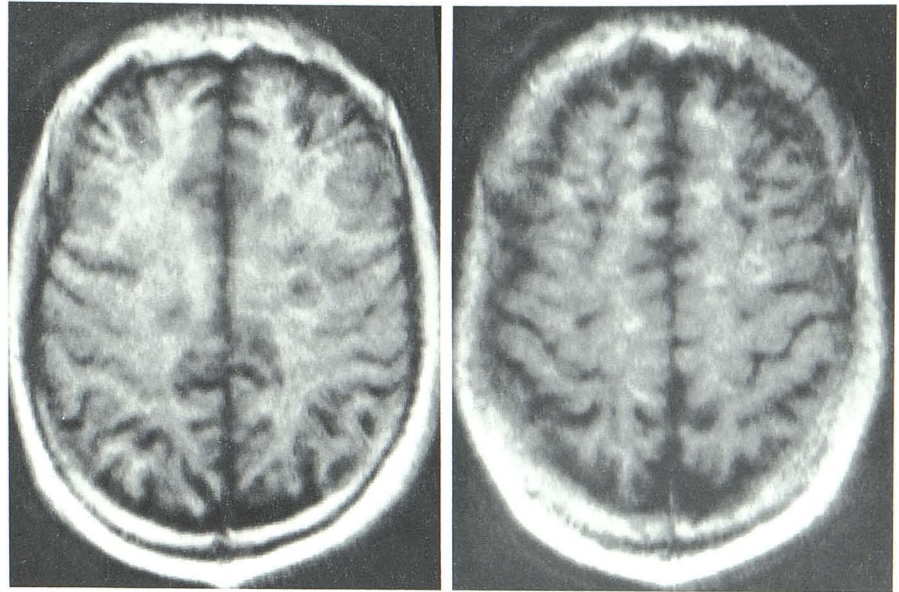
sclerosis in mesencephalon. Although lesion is well seen on two T1-weighted 3D anisotropic volume techniques, SE 30/250 (D) and IR 30/400/1250 (E), it is poorly seen on T2-weighted study, SE 120/1000 (F).

sensitivity of the technique. Multiple sclerosis on MRI must be distinguished from deep white matter infarcts that appear in the elderly in a similar pattern [14]. However, these occur in a clinically distinct group of patients [15, 16] and present a significantly more diffuse pattern both on CT and MRI. The spinal cord, a common site of lesions, has yet to be imaged with sufficient detail to enable the diagnosis of lesions due to multiple sclerosis. Finally, some of the findings presented are specific to the field strength used (0.5 T). Increasing the field strength causes a prolongation of T1, inducing smaller changes in T2 as well. The impact of changes in field strength

on the efficacy of imaging techniques is yet to be established. The observation of "white" (high signal intensity) lesions on inversion-recovery images probably results from a shortening of T1 in such areas of pathology and may relate to the stage of disease evolution. The patient presented in figure 7 was acutely symptomatic, with two enhancing lesions noted on CT corresponding to abnormalities on MRI.

The implications for the future are many. Diagnosis of abnormalities by CT can be improved significantly with the present experience in distribution and abundance of multiple sclerosis lesions on MRI. A retrospective review of the CT

Fig. 7.—Rings of high signal intensity surround more typical lesions of low signal intensity on two scans from 3D IR 30/400/1250. Although previously undescribed, areas of high signal intensity (in contrast to those of low signal intensity), presumed also to represent pathologic changes, were noted in a minority of patients (5%) on inversion-recovery scans.



A

B

C

Fig. 8.—Sagittal (A) and coronal (B and C) sections from two patients with multiple sclerosis. A, SE 120/2000. B, SE 120/1000. C, IR 30/450/1500.

examinations showed significantly more lesions than previously recognized. Newly available multiecho techniques (fig. 9) should be relevant because of the wide range of abnormal T1 and T2 values and the present lack of a single superior scan technique. New multislice techniques will significantly reduce scan times while increasing resolution, compared with the current anisotropic volume techniques. The use of thinner, 5-mm sections also should improve the sensitivity of MRI, avoiding the loss of lesions due to partial-volume averaging. Paramagnetic intravenous contrast agents [17, 18] may further increase the diagnostic ability of MRI. In vivo proton

chemical shift imaging [19] may become important in the evaluation of a disease process such as multiple sclerosis, which causes significant changes both in lipid and water content.

MRI seems to be the method of choice at present for the diagnosis and evaluation of multiple sclerosis. Care must be exercised in selection of the appropriate scan technique for the region of interest. Our limited experience with the temporal change in appearance of the disease (five patients) suggests that evolution of the disease process is being observed. Present experience with temporal change in the disease is

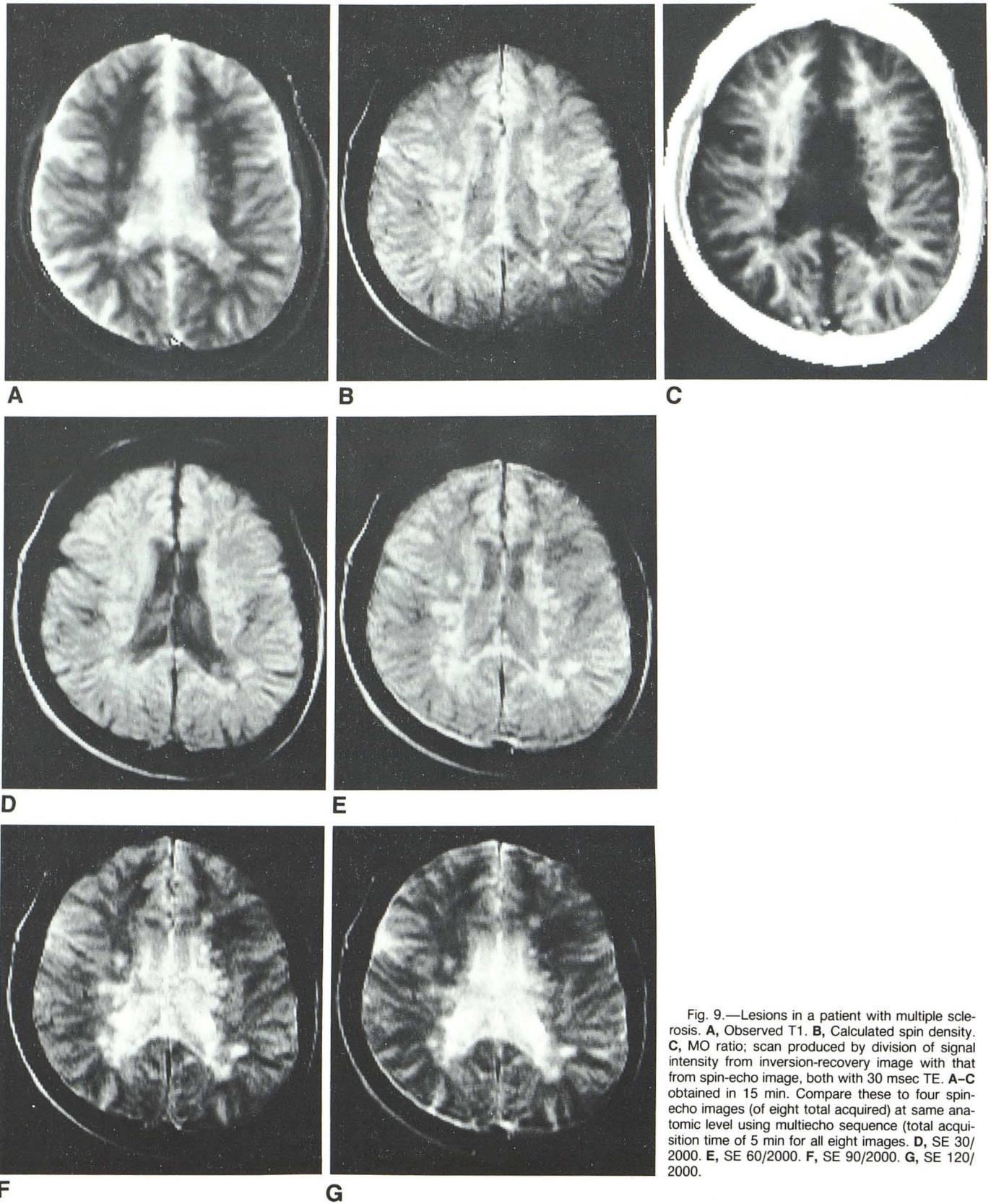
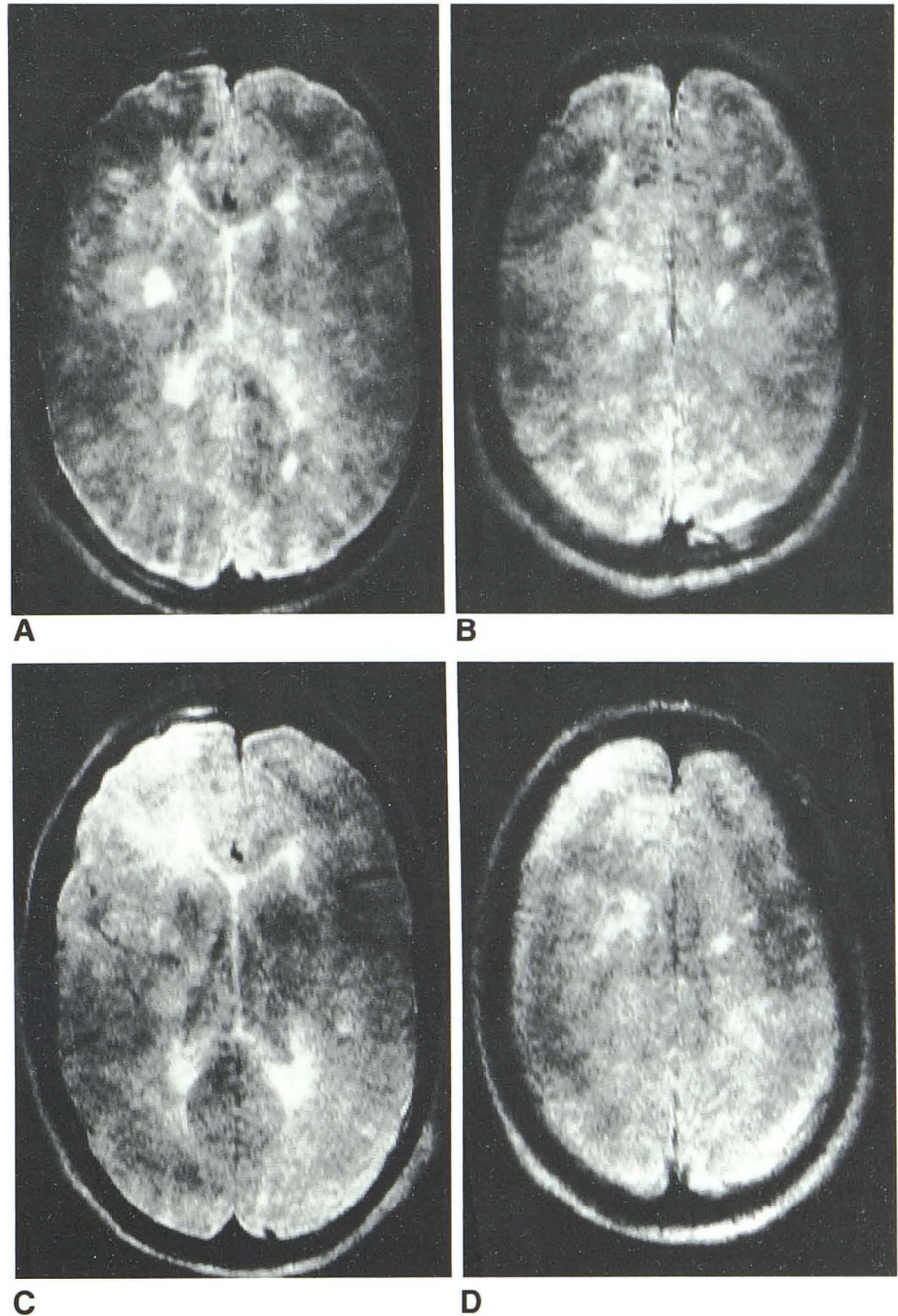


Fig. 9.—Lesions in a patient with multiple sclerosis. **A**, Observed T1. **B**, Calculated spin density. **C**, MO ratio; scan produced by division of signal intensity from inversion-recovery image with that from spin-echo image, both with 30 msec TE. **A–C** obtained in 15 min. Compare these to four spin-echo images (of eight total acquired) at same anatomic level using multiecho sequence (total acquisition time of 5 min for all eight images. **D**, SE 30/2000. **E**, SE 60/2000. **F**, SE 90/2000. **G**, SE 120/2000.

too limited to permit a comparison of relaxation rates and age of involved areas. The significance of these findings and the

application of MRI in the evaluation of therapeutic measures await further clinical trials.

Fig. 10.—Changes in peri- and supraventricular lesions of multiple sclerosis over time on 3D volume SE 120/1000 images. **C** and **D** obtained 3 months after **A** and **B**.



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