Magnetic resonance imaging: serial observations in multiple sclerosis.

M A Johnson, D K Li, D J Bryant and J A Payne

AJNR Am J Neuroradiol 1984, 5 (5) 495-499
http://www.ajnr.org/content/5/5/495

Magnetic Resonance Imaging: Serial Observations in Multiple Sclerosis

M. A. Johnson[1]
D. K. B. Li[2]
D. J. Bryant[3]
J. A. Payne[3]

Three patients with four or more follow-up magnetic resonance imaging (MRI) examinations over a 15–22 month period are described to illustrate the differing patterns of follow-up seen with MRI in multiple sclerosis (MS). These cases illustrate patterns of remission, exacerbation and remission, and rapid progression. The value of MRI in the follow-up of MS is discussed.

Magnetic resonance imaging (MRI) has been shown to be a very sensitive method of detecting lesions in multiple sclerosis (MS) [1–3]. We illustrate the use of MRI in follow-up by presenting three patients with clinically definite MS examined on four or more occasions each over a 15–22 month period.

Subjects and Methods

Three patients with four or more follow-up studies are described; each had a different clinical pattern of MS. Their clinical histories are presented in detail to correlate with MRI findings. The MRI scanner and basic pulse sequences used in this study have been described [3, 4]. The principal pulse sequences used during the study are listed in table 1 and described according to American College of Radiology nomenclature [5]. Examination times were 60–150 min depending on the number of slices scanned. Up to 15 individual slices were obtained at each examination. Present slice thickness is 10 mm.

All examinations conformed to the guidelines for clinical MRI established by the National Radiological Protection Board [6]. The examinations were performed with the permission of the Ethics Committee of the Royal Postgraduate Medical School, and informed consent was obtained from each patient. No preparation or exogenous contrast agents were required, and no adverse effects were noted during or after the MRI examination.

Case Reports

Case 1

A 25-year-old man had acute left hemiplegia that progressed over 1 week and subsequently recovered completely. During the acute phase, he developed reflex and postural changes of an upper motor neuron lesion. Auditory- and visual-evoked potentials were normal. Lumbar puncture revealed slight increase in the number of lymphocytes (6/mm^3) as well as oligoclonal banding in the cerebrospinal fluid (CSF).

Initial computed tomography (CT) with and without contrast enhancement revealed a low-attenuation, nonenhancing lesion in the right supra- and periventricular region. An MRI inversion-recovery (IR) scan demonstrated a large lesion with long T1 in the corresponding location (fig. 1A). A smaller lesion with long T1 was also noted in the posterior limb of the right internal capsule.

Follow-up examinations 2 months later when the clinical symptoms had completely resolved revealed the right periventricular lesion to be smaller on CT and MRI scans (fig. 1B). The third follow-up MRI scan (17 months after the initial scan) included both IR and spin-echo (SE) pulse sequences and showed further diminution of the right periventricular lesion, with long

Received January 4, 1984; accepted after revision March 29, 1984.

M. A. Johnson is a Medical Research Fellow of the Alberta Heritage Foundation.

[1] Department of Diagnostic Radiology, NMR Unit, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Rd., London W12 0HS, England. Address reprint requests to M. A. Johnson.

[2] Department of Diagnostic Radiology, University of British Columbia, Vancouver V6T 2B5, British Columbia, Canada.

[3] Hirst Research Laboratory, Wembley, London HA9 7PR, England.

AJNR 5:495–499, September/October 1984
0195-6108/84/0505-0495

T2 as well as long T1 (figs. 1C and 1D). The long T1 lesion in the internal capsule was smaller, but more easily identified because of improved image quality. A rim of long T2 surrounding the lateral vertricles was noted. Final IR and SE scans 22 months after initial presentation were unchanged, apart from improved image quality (figs. 1E and 1F). The patient remained clinically well with no new symptoms.

Case 2

A 49-year-old woman had right leg cramps and unsteadiness of gait. Physical findings included positive jaw jerk, exaggerated deep tendon reflexes, bilateral leg spasticity, bilateral ankle clonus, and extensor plantar responses. Lumbar puncture revealed an elevated CSF level of immunoglobulin G (IgG) (24% of total protein), suggestive of MS. A tentative diagnosis of spastic paraparesis from MS was made, and treatment with dantrolene sodium was begun to relieve the leg spasms. Three years later, she developed tingling of the left face, left side of the body, and left hand, with subsequent loss of power in her hand and shoulder and loss of sensation in her hand. A high cervical relapse of MS involving the lowest sensory trigeminal fibers was diagnosed. This resolved, leaving residual paresthesia of the left hand.

The patient was well, apart from continuing leg spasms, for another 21 months until she developed numbness of the right face and slurred speech. CT revealed two contrast-enhancing lesions adjacent to the left lateral ventricle, suggesting acute MS lesions. Initial IR and SE scans demonstrated multiple lesions with long T1 and long T2; the largest of these lesions corresponded to the contrast-enhancing lesions on CT (figs. 2A and 2B). At least six more lesions were identified on MRI. On repeat IR and SE scans 10 days later, the two largest lesions were enlarged, while the rest of the lesions were unchanged.

The acute symptoms resolved over 12 days, leaving leg spasms as well as minimal ataxia. Repeat CT 6 months after the initial scan revealed reduction in size and degree of contrast enhancement of the left periventricular lesions. Corresponding IR and SE scans revealed diminution of the previously noted lesions (figs. 2C and 2D).

Subsequently, the patient was clinically stable with occasional minor relapses. A 1 year follow-up MRI scan was unchanged, allowing for differences in positioning and improved image quality. An MRI scan 14 months after initial scanning revealed enlargement of several right periventricular lesions, especially one lesion at the posterior horn (figs. 2E and 2F).

TABLE 1: **MRI Pulse Sequences**

MRI Pulse Sequence	Time Interval (msec)		
	Repetition	Inversion	Echo
Inversion-recovery	1400	400	...
	1400	400	44
	1500	500	44
Spin-echo	544	...	44
	1080	...	80
	1580	...	80

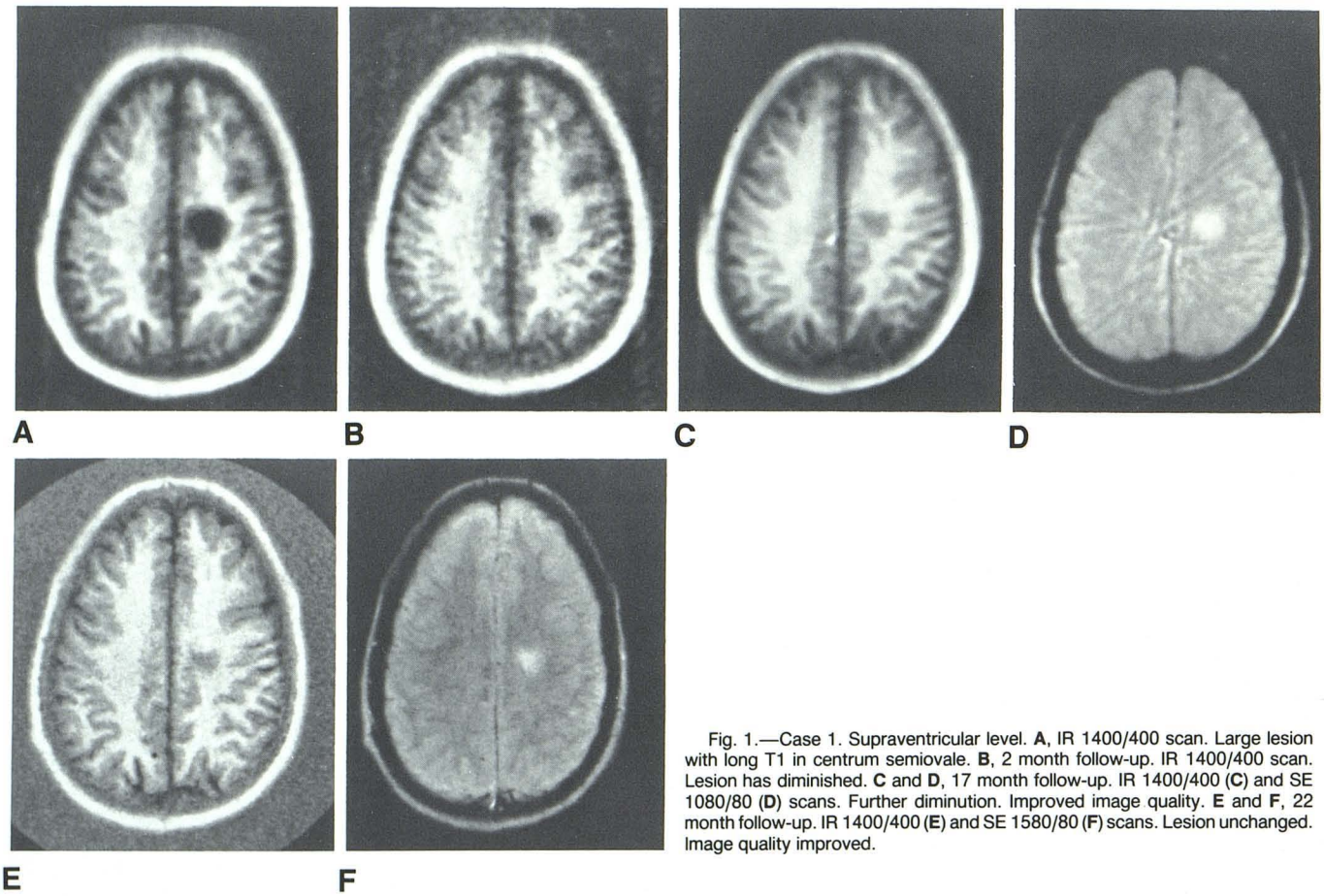

Fig. 1.—Case 1. Supraventricular level. **A**, IR 1400/400 scan. Large lesion with long T1 in centrum semiovale. **B**, 2 month follow-up. IR 1400/400 scan. Lesion has diminished. **C** and **D**, 17 month follow-up. IR 1400/400 (**C**) and SE 1080/80 (**D**) scans. Further diminution. Improved image quality. **E** and **F**, 22 month follow-up. IR 1400/400 (**E**) and SE 1580/80 (**F**) scans. Lesion unchanged. Image quality improved.

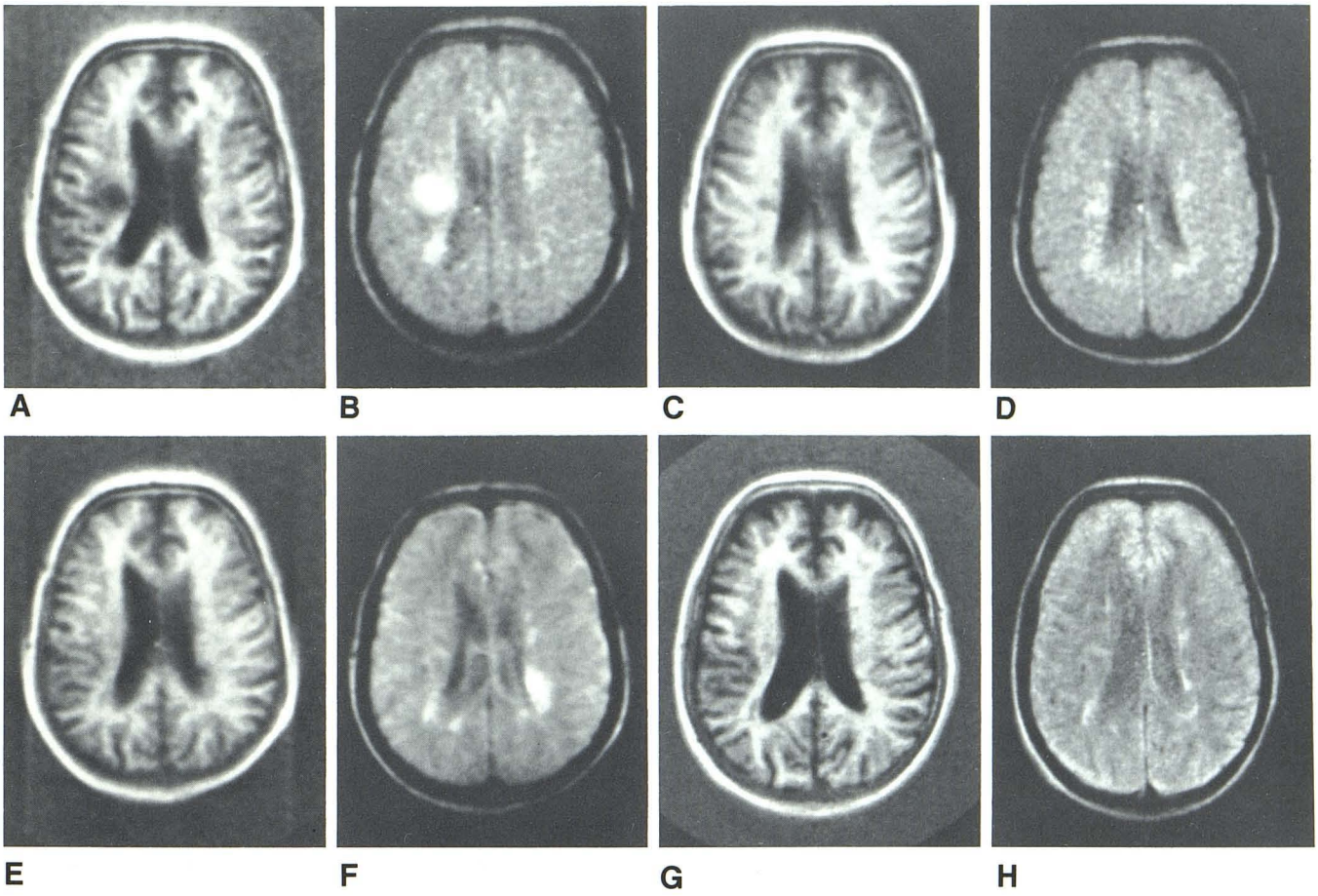

Fig. 2.—Case 2. **A** and **B**, Initial IR 1400/400 (**A**) and SE 1080/80 (**B**) scans. Multiple long T1 (**A**) and long T2 (**B**) lesions in periventricular white matter. **C** and **D**, 6 month follow-up. IR 1400/400 (**C**) and SE 1080/80 (**D**) scans. Diminution of lesions. **E** and **F**, 14 month follow-up. IR 1400/400 (**E**) and SE 1080/80 (**F**) scans. Increased size of lesions. **G** and **H**, 17 month follow-up. IR 1400/400/44 (**G**) and SE 1580/80 (**H**) scans. Diminution of lesions. Improved image quality.

Final IR and SE scans 17 months after initial scanning revealed the previously noted lesions to be smaller (figs. 2G and 2H). Fewer levels were scanned, however, due to technical difficulties.

Case 3

A 36-year-old woman had had five attacks of paresthesia and numbness involving the extremities. During one of these attacks, vertigo and diplopia on right horizontal conjugate gaze was noted. Physical examination revealed decreased light touch in the right hand with poor fine movements. Lumbar puncture showed the presence of 15 lymphocytes and elevated IgG at 20% of the total protein (normal, less than 12%) in the CSF. A tentative clinical diagnosis of MS was made.

Over the next 5 years the patient experienced numerous relapses and demonstrated signs of retrobulbar neuritis as well as upper motor neuron and cerebellar involvement. Treatment during this period included several doses of Synacthen.

The patient's first CT and MRI scans were obtained during a clinical relapse when she noted vertigo, right hand paresthesia, internuclear ophthalmoplegia on gaze to the left, and dysconjugate eye movements. CT demonstrated four low-attenuation lesions, including a single lesion in the centrum semiovale and a lesion adjacent to the posterior horn of the lateral ventricle bilaterally.

Initial IR and SE scans clearly demonstrated at least 16 lesions with long T1 and long T2 in the periventricular white matter, the centrum semiovale, and the brainstem, consistent with plaques of MS (figs. 3A and 3B).

Treatment with azathioprine was begun but discontinued 2 weeks later because of allergy. Another relapse with development of retrobulbar neuritis occurred 8 months later. IR and SE scans demonstrated enlargement of several periventricular lesions as well as new lesions (figs. 3C and 3D). Repeat CT scans 1 month later when the patient continued to have retrobulbar neuritis demonstrated a left periventricular lesion not seen on the previous CT scan but seen on the original MRI scan. Repeat MRI 1 month after the previous scan was unchanged.

Treatment with Synacthen and prednisolone at intervals over the next 6 months was attempted, but several relapses occurred. Fifteen months after initial MRI, slurring of speech, gait unsteadiness, and left limb weakness occurred. Left cerebellar incoordination was found, and the speech slurring was believed to be cerebellar in origin also. Tone was reduced on the left. MRI revealed large new lesions in the

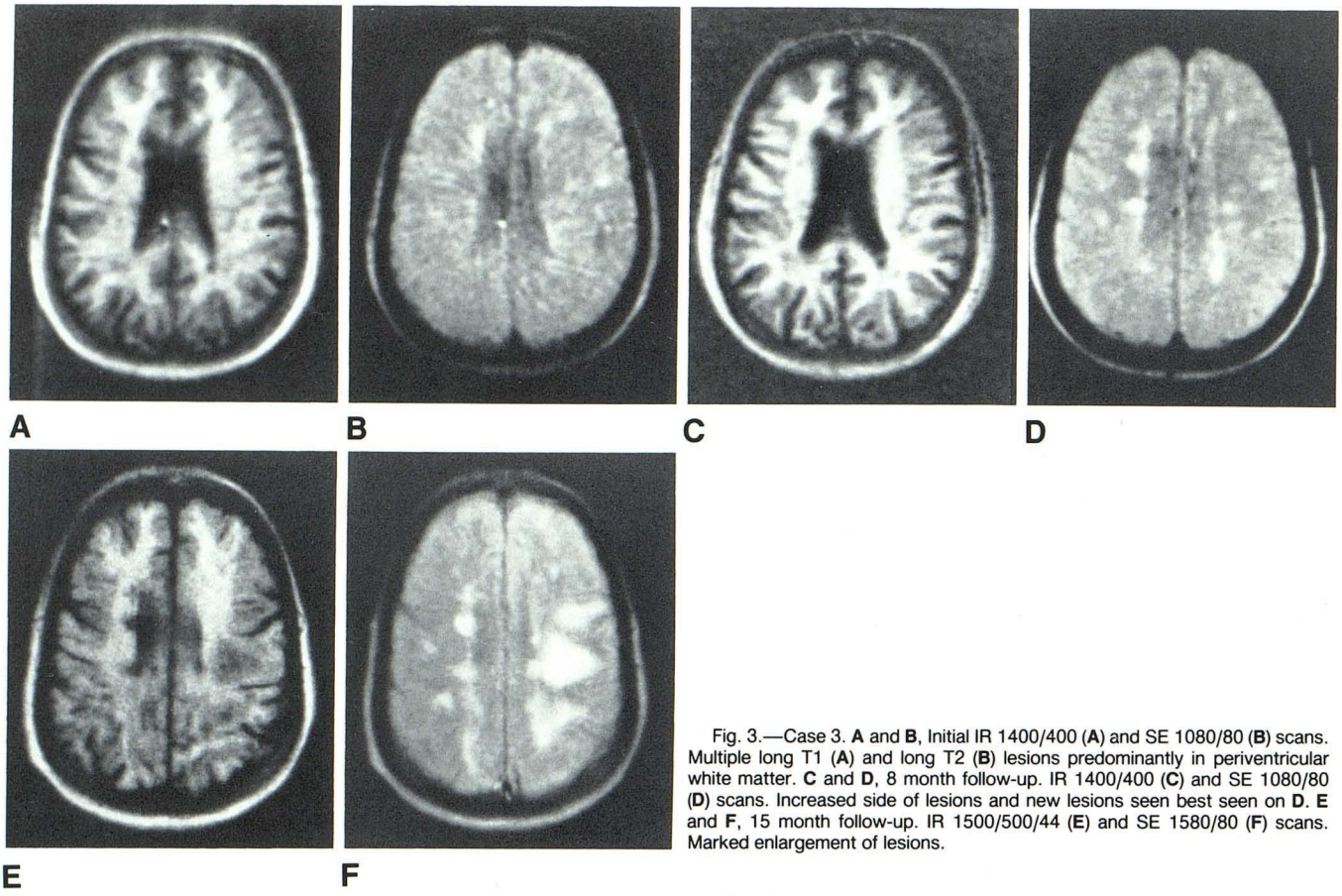

Fig. 3.—Case 3. **A** and **B**, Initial IR 1400/400 (**A**) and SE 1080/80 (**B**) scans. Multiple long T1 (**A**) and long T2 (**B**) lesions predominantly in periventricular white matter. **C** and **D**, 8 month follow-up. IR 1400/400 (**C**) and SE 1080/80 (**D**) scans. Increased side of lesions and new lesions seen best seen on **D**. **E** and **F**, 15 month follow-up. IR 1500/500/44 (**E**) and SE 1580/80 (**F**) scans. Marked enlargement of lesions.

right centrum semiovale as well as adjacent to the posterior horns of the lateral ventricles (figs. 3E and 3F). The patient was incapacitated and was transferred to a chronic care facility.

Discussion

Each of the three patients demonstrated a different clinical pattern of MS. Case 1 suffered one acute episode that gradually resolved with no relapse. MRI initially demonstrated two lesions that diminished on scans at 2 and 19 months and were static on a scan at 22 months.

Case 2 demonstrated a more chronic course with occasional exacerbations. Her first MRI scan revealed multiple lesions, two of which corresponded to contrast-enhancing lesions on CT. The lesions diminished on scans at 6 months and 1 year, but several lesions were larger on a scan at 14 months. Follow-up scans 2 months later showed a diminution of these lesions.

Case 3 suffered a chronic progressive course despite treatment resulting in incapacitation. Multiple MS lesions were identified initially on MRI scans. Repeat scan at 8 months during a clinical relapse demonstrated new lesions as well as enlargement of several previously noted lesions. MRI scans at 9 months were unchanged, but at 15 months, during another relapse, several large, new lesions were present.

As expected, these serial follow-up examinations reveal decreasing size, but not disappearance, of lesions after acute episodes. During relapses, new lesions appear and existing lesions become larger.

Problems exist in accurate interpretation of serial examinations. Slice selection and angulation may not be exactly comparable. Equipment improvements may result in different slice profiles and thicknesses along with improvements in image quality and resolution. The technique of image reconstruction may alter lesion detectability. Projection-reconstruction techniques produce better signal-to-noise ratios than do two-dimensional Fourier transformation techniques [7].

New pulse sequences may improve lesion detectability. For example, our initial studies on MS did not include any SE images, since initial studies with SE sequences failed to demonstrate pathology in a few cases. Further studies with SE sequences using a longer time for spin-spin relaxation showed SE images to be very sensitive in detecting abnormalities.

Multislice capability [8, 9] is necessary if a complete multisequence study of the brain, the optimal examination for MS, is to be completed in a reasonable period of time. Three-dimensional volume acquisition of data and reconstruction would facilitate accurate comparison between a series of follow-up examinations on the same patient [10]

Despite these difficulties, follow-up examinations are important in assessment of the natural history of MS, acute exacerbations, and assessment of healing after treatment.

Although the MRI findings in MS are well defined [1–3, 8, 11–13], the exact histologic and biochemical changes that produce these abnormalities are uncertain. Follow-up MRI studies will demonstrate the natural history of the lesions and can be compared and correlated with histochemical changes in pathologic specimens [14, 15] as well as with corresponding abnormalities of high-dose contrast-enhanced delayed CT scans. These contrast-enhancing lesions indicate regions of blood-brain barrier disruption, and there is evidence to suggest that they correlate with more acute MS lesions [16]. Serial examinations provide a measure of activity and quiescence of the disease process and an indication of the severity and extent of lesions. Buonanno et al. [17] suggested that determination of T1 values of MS lesions may provide a quantitative method of characterization of activity of individual MS lesions, although quantification was not attempted in our study pending validation studies of the accuracy of T1 and T2 measurements.

It is necessary to be able to document in vivo arrest and/or healing and remyelination of specifically identified lesions if the effectiveness of therapeutic regimens is to be monitored [18], since clinical signs and symptoms do not correlate with the extent and activity of lesions seen at necropsy [19]. Therapeutic trials in MS have been hampered by the lack of a good laboratory indicator of disease activity, the placebo effect, the extremely variable clinical course of the disease, and the lack of knowledge of the etiology of MS [18, 20]. Because it is sensitive, has no known hazards, and does not require exogenous contrast agents, MRI appears to be an ideal method for monitoring disease activity in treated and untreated MS patients.

REFERENCES

1. Young IR, Hall AS, Pallis CA, Legg NJ, Bydder GM, Steiner RE. Nuclear magnetic resonance imaging of the brain in multiple sclerosis. *Lancet* **1981**;2:1063–1066
2. Bydder GM, Steiner RE, Young IR, et al. Clinical NMR imaging of the brain: 140 cases. *AJNR* **1982**;3:459–480, *AJR* **1982**;139:215–236
3. Bailes DR, Young IR, Thomas DJ, Straughan K, Bydder GM, Steiner RE. NMR imaging of the brain using spin-echo sequences. *Clin Radiol* **1982**;33:335–414
4. Young IR, Burl M, Clarke GJ, et al. Magnetic resonance properties of hydrogen: imaging of the posterior fossa. *AJNR* **1981**;2:487–493, *AJR* **1981**;137:895–901
5. American College of Radiology. *Glossary of NMR terms*. Chicago: American College of Radiology, **1983**
6. National Radiological Protection Board. *Exposure to nuclear magnetic resonance clinical imaging*. Harwell, Oxon, England: National Radiological Protection Board, **1980**
7. King KF. *Signal to noise ratios in nuclear magnetic resonance imaging* (thesis). Madison, WI: University of Wisconsin, **1983**
8. Crooks LE, Mills CM, Davis PL, et al. Visualization of cerebral and vascular abnormalities by NMR imaging: the effects of imaging parameters on contrast. *Radiology* **1982**;144:843–852
9. Crooks L, Arakawa M, Hoenninger J, et al. Nuclear magnetic resonance whole-body imager operating at 3.5 kGauss. *Radiology* **1982**;143:169–174
10. Buonanno FS, Pykett IL, Brady TJ, et al. Clinical relevance of two different nuclear magnetic resonance (NMR) approaches to imaging of a low grade astrocytoma. *J. Comput Assist Tomogr* **1982**;6:529–535
11. Young IR, Randell CP, Kaplan PW, James A, Bydder GM, Steiner RE. NMR imaging in white matter disease of the brain using spin-echo sequences. *J Comput Assist Tomogr* **1983**;7:290–294
12. Buonanno FS, Pykett IL, Vielma J, et al. In: Witcofski RL, Karstaedt N, Partain CL, eds. *NMR imaging*. Winston-Salem, NC: Bowman Gray School of Medicine, **1982**:147–157
13. Brant-Zawadzki M, Davis PL, Crooks LE, et al. NMR demonstration of cerebral abnormalities: comparison with CT. *AJNR* **1983**;4:117–124, *AJR* **1983**;140:847–854
14. Lumsden CE. The neuropathology of multiple sclerosis. In: Vinkin PJ, Bruyn GW, eds. *Handbook of clinical neurology*, vol 9. Amsterdam: North Holland, **1970**:217–309
15. Bernstrom J, Barron KD. Chemical pathology of multiple sclerosis. In: Vinken PJ, Bruyn GW, eds. *Handbook of clinical neurology*, vol 9. Amsterdam: North Holland, **1970**:310–319
16. Lebow S, Anderson DC, Mastri A, Larson D. Acute multiple sclerosis with contrast-enhancing plaques. *Arch Neurol* **1978**;35:435–439
17. Buonanno FS, Brady TJ, Pykett IL, et al. NMR imaging in patients with multiple sclerosis: potential of in-vivo lesion characterization using T_1 NMR imaging (abstr). *Neurology* (NY) **1982**;32:163
18. McFarlin DE, McFarland HF. Multiple sclerosis. *N Engl J Med* **1982**;307:1246–1251
19. McDonald WI, Halliday AM. *Diagnosis and classification of multiple sclerosis. Br Med Bull* **1977**;33:4–8
20. McFarlin DE. Treatment of multiple sclerosis. *N Engl J Med* **1983**;308:215–217