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MR of the Brain Using Fluid-Attenuated Inversion Recovery (FLAIR) Pulse Sequences

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PURPOSE: Results from conventional T2-weighted spin-echo sequences were compared with those obtained using fluid attenuated inversion recovery (FLAIR) pulse sequences in order to assess their relative merits in detecting disease. **METHODS:** Forty adult patients with suspected disease of the brain were examined with spin-echo sequences (TE = 20 and TE = 80), and results were compared with FLAIR sequences of several types with inversion times of 1800-3000 msec and echo times of 130-240 msec. Scans were assessed by two radiologists for lesion number, conspicuity, and extent. **RESULTS:** A total of 48 lesions or groups of lesions were recognized with both sequences. In 22 instances, more lesions were seen with FLAIR sequences, and, in the remaining 26, equal numbers were seen. In 42 lesions, conspicuity was better with FLAIR sequences, equal in five and worse in one cystic lesion. Lesion extent was better assessed in 28 of the 48 cases with FLAIR sequences and equally well seen in the remainder. **CONCLUSION:** By virtue of their long echo time and relative freedom from cerebrospinal fluid artifact FLAIR sequences provide high sensitivity to a wide range of disease. The basic sequence is easy to implement but is relatively time consuming.

Index terms: Brain, magnetic resonance; Magnetic resonance, technique.

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Although heavily T2-weighted spin-echo sequences are widely accepted as the most sensitive magnetic resonance (MR) imaging technique for examining the brain, they have important limitations. With heavy T2-weighting, the cerebrospinal fluid (CSF) signal becomes greater than that of the brain and creates artifacts both from volume averaging and fluid motion during the cardiac and respiratory cycles. These may make diagnosis of subtle lesions difficult.

By using an inversion recovery pulse sequence with an inversion time (TI) designed to null or considerably reduce the signal from CSF but allow recovery of most of the brain magnetization, it is possible to greatly reduce CSF artifact and then use long echo times to obtain very heavy T2-weighting.

To assess the value of this approach, we have compared results with conventional long repetition time (TR) and echo time (TE) spin-echo sequences to those obtained using fluid attenuated inversion recovery (FLAIR) sequences in 40 adult patients with a range of brain disease.

Subjects and Methods

Permission for this study was obtained from the Research Ethics Committee of the Royal Postgraduate Medical School.

The FLAIR pulse sequences were available in several forms:

1. The initial 180° pulse was either unselected or section selected. The unselected form was used with a multisection spin echo with a stepped TI. The section-selected form was available with the section width of the initial 180° pulse equal to that of the subsequent spin-echo data collection or with twice this value. This form had a constant TI. Useful values of TI for

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suppression of CSF were found to be in the range of about 1700-3000 msec at 1.0 T.

2. The 180° pulse was combined with single or multiple spin-echo options. The single-echo form was available as a spin echo or a field echo. The multiple spin-echo forms were available either as discrete sections with two or four echoes or as composite sections modeled on the RARE pulse sequence initially described by Hennig et al (1).

These were all operated at 1.0 T using 128 × 256 or 192 × 256 image matrices with a single excitation and 6- or 8-mm section thickness on a Picker HPQ Vista MR system. TE values of 130-240 msec were employed. The 128 × 256 variable TI form typically took 12.8 minutes for 11-17 sections and the constant TI form with TI equal to 2100 msec and TE equal to 160 msec took 13.6 minutes for 10 sections. No cardiac gating or gradient moment nulling was used.

Standard spin-echo sequences with a TR of 2500 msec (approximate) and TE of 20 and 80 msec were performed in parallel with the FLAIR sequences using two data acquisitions. In one case, a TE 160 msec scan was also obtained and compared with the TE 160 FLAIR sequence. T1-weighted images (SE 500-740/20) were also performed in selected cases with four data acquisitions. These were all obtained with a 128 × 256 matrix and 6- or 8-mm section width.

The spin-echo and FLAIR images were assessed by two independent radiologists who were blinded to the clinical diagnoses. All technically adequate studies performed since the technique was first implemented were assessed overall for lesion number, conspicuity, and size, and the results of the two radiologists were averaged. Two potential cases were excluded because of excessive motion artifact on the FLAIR and other sequences. Similar lesions (eg, periventricular lesions) were assessed as a single group and an overall assessment was then made.

Forty patients (21 male, 19 female) of mean age 42.5 years (range 16 to 65 years) were studied. Their 48 final clinical diagnoses are summarized in Table 1.

TABLE 1: Clinical diagnoses (48)

Vascular disease (17 cases)	
Peripheral infarction	3
Deep white matter	5
Periventricular	9
Infection (four cases)	
Probable cytomegalovirus	1
Herpes simplex virus (suspect or definite)	3
White matter disease (four cases)	
Probable multiple sclerosis	2
Postinfectious disease	1
Other	1
Ventricular enlargement (three cases)	
Tumors (12 cases)	
Benign	2
Primary	7
Metastases	2
Nasopharyngeal	1
Metabolic disease (two cases)	
Chronic hepatic encephalopathy	2
Miscellaneous (six cases)	

Results

For reference, a TE 160-msec FLAIR scan from a normal volunteer is included (Fig. 1). The parietal white matter and parietopontine tract normally display a high signal when a long echo time is used. Parts of the occipitothalamic radiation, as well as the corticospinal and other tracts, also display a high signal intensity. Chemical shift artifact (associated with the narrow bandwidth and long data collection (56 msec)) produced with this implementation of the FLAIR sequence is seen anteriorly in Figs. 1B and 1C. Partial volume effects from nasal mucosa are seen at the inferior aspect of the frontal lobe. Slow flowing blood in veins and sinuses may give a very high signal intensity.

Vascular Disease (19 Cases)

Nineteen patients with clinical diagnoses of cerebrovascular disease were studied. These patients were grouped into peripheral infarction, deep white matter infarction, and periventricular infarction, according to the predominant site of the lesion or lesions.

Peripheral infarction (three cases): Three cases were examined. The same number of peripheral lesions were identified but conspicuity was better with the FLAIR sequences in two cases (Fig. 2) and equal in the other one. The extent of the lesions was greater in two cases and equal in the other. Additional deep white matter lesions were present in all cases.

Deep white matter infarction (five cases): The number of lesions identified was greater with the FLAIR sequence in all five cases (Fig. 3). Conspicuity was better in four cases and lesion extent was better demonstrated with the FLAIR sequence in four cases.

Periventricular lesions (9 cases): In six cases more periventricular lesions were identified with the FLAIR sequence (Fig. 4). In the other three cases, equal numbers were seen. In all cases, the

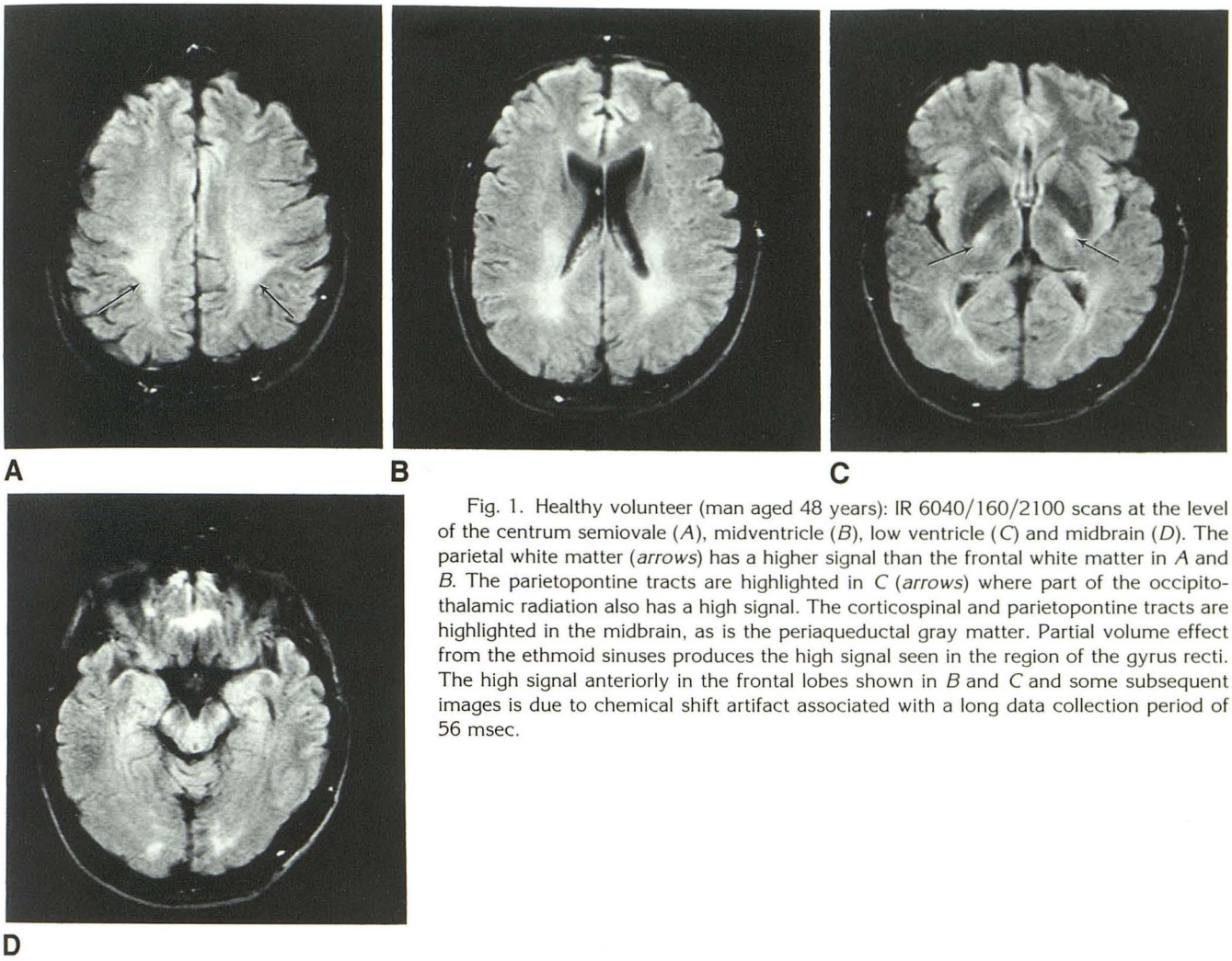


Fig. 1. Healthy volunteer (man aged 48 years): IR 6040/160/2100 scans at the level of the centrum semiovale (*A*), midventricle (*B*), low ventricle (*C*) and midbrain (*D*). The parietal white matter (*arrows*) has a higher signal than the frontal white matter in *A* and *B*. The parietopontine tracts are highlighted in *C* (*arrows*) where part of the occipitothalamic radiation also has a high signal. The corticospinal and parietopontine tracts are highlighted in the midbrain, as is the periaqueductal gray matter. Partial volume effect from the ethmoid sinuses produces the high signal seen in the region of the gyrus recti. The high signal anteriorly in the frontal lobes shown in *B* and *C* and some subsequent images is due to chemical shift artifact associated with a long data collection period of 56 msec.

conspicuity was greater with the FLAIR sequence. The lesion appeared more extensive with FLAIR sequences in six cases and equal in the others.

Infection (Four Cases)

One case of cytomegalovirus infection was recognized in a patient with chronic myeloid leukemia after bone marrow transplantation. The diagnosis was made following identification of cytomegalovirus in the urine and after response to antiviral therapy. She had mild sensory signs but a very high CSF protein (1.9 G/100 mL). Multiple lesions were seen with both the conventional spin-echo sequences and the FLAIR sequences, but the latter showed much more extensive change (Fig. 5). The effect of the 180° inversion pulse can be appreciated by comparing Figures 5B, 5C, and 5D. Increasing the echo time in a conventional spin echo from 80 msec (Fig. 5B) to 160 msec (Fig. 5C) increased lesion contrast, but the effect was largely obscured by the high level of CSF artifact. Preceding the TE 160-msec spin echo by an inversion pulse designed to suppress CSF in Figure 5D made it much easier to appreciate the increased lesion conspicuity produced by the longer echo time.

Three patients with clinically suspect or proven herpes simplex were studied. Periventricular lesions were seen in two cases. In another patient who presented with memory loss, changes in the medial temporal lobes were identified only with the FLAIR sequence (Fig. 6).

White Matter Disease (Four Cases)

A patient with a 3-year history of recurrent episodes of weakness and ataxia with some sensory loss displayed no abnormality in the centrum semiovale with conventional spin-echo pulse sequences, but three lesions were seen with the FLAIR sequence (Fig. 7). The probable diagnosis

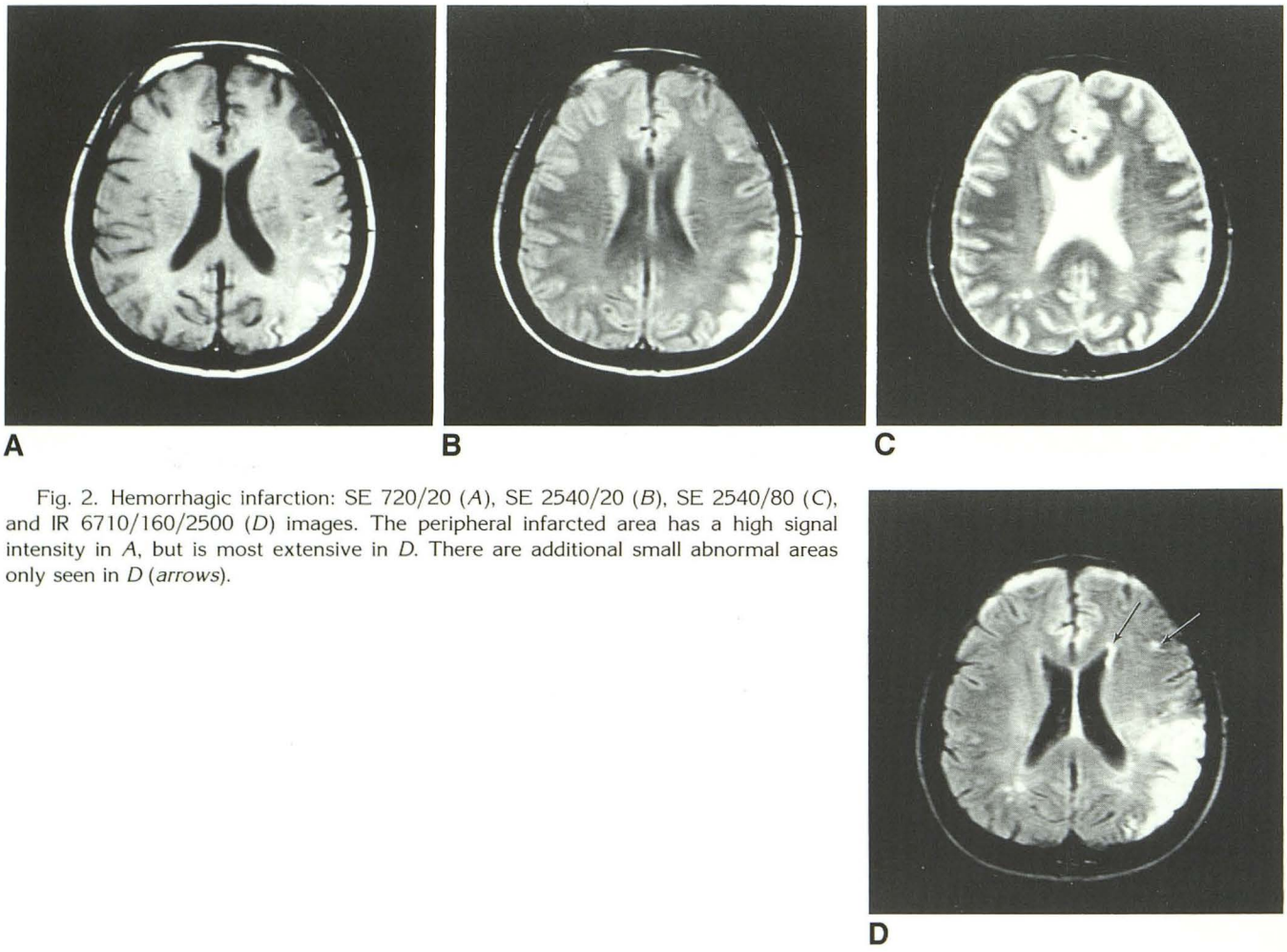


Fig. 2. Hemorrhagic infarction: SE 720/20 (*A*), SE 2540/20 (*B*), SE 2540/80 (*C*), and IR 6710/160/2500 (*D*) images. The peripheral infarcted area has a high signal intensity in *A*, but is most extensive in *D*. There are additional small abnormal areas only seen in *D* (*arrows*).

was multiple sclerosis. Additional lesions were also seen with the FLAIR sequence in one other patient with the clinical diagnosis of multiple sclerosis.

A patient with recurrent left-sided meningioma treated with surgery and radiotherapy presented with an episode of left-sided weakness that had remitted. In addition to the postoperative changes, focal lesions were seen at high ventricular level with an additional lesion shown on the FLAIR sequence. Bilateral changes were seen in the white matter of the occipital lobes at a lower level. The precise etiology of her white matter disease remains unclear at present.

Ventricular Enlargement (Three Cases)

This was identified in three patients. Periventricular changes associated with hydrocephalus were better seen with the FLAIR sequences in two of the three cases (Fig. 8) and extent of change was better seen in two of the three cases.

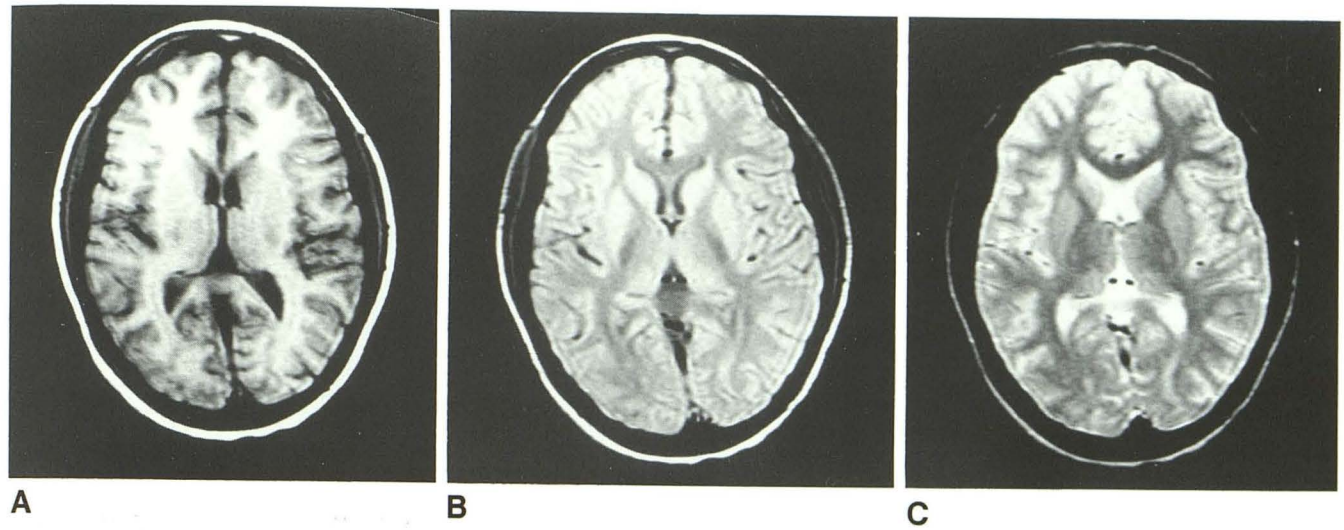
Tumors (12 Cases)

Benign (two cases): One meningioma and one chordoma were studied. The lesions were well seen with both spin-echo and FLAIR sequences, but the associated edema was better seen with the FLAIR sequence.

Primary brain tumors (seven cases): The cystic components of tumors were less well seen with some versions of the FLAIR sequence (Fig. 8) but better seen with others. The differences depended on the inversion time and CSF flow phenomena as well as the version of the FLAIR sequence that was employed.

Soft-tissue components of malignant tumors were seen with greater contrast in all cases and the signal from calcification was also lower with the FLAIR sequence than with SE 2500/20 and SE 2500/80 sequences. Overall conspicuity was greater with the FLAIR sequence in four cases. Extent was better seen in four cases.

Metastases (2 cases): Metastases were well seen with the FLAIR sequence (Fig. 9). Number,



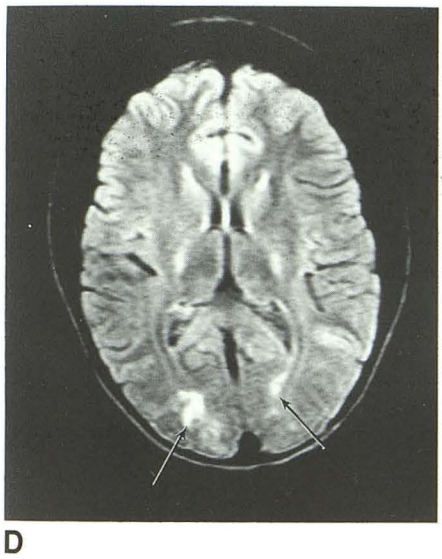


Fig. 3. Deep white matter infarction: SE 500/20 (*A*), SE 2700/20 (*B*), SE 2700/80 (*C*), and IR 6040/160/2300 (*D*) images. Areas of abnormality in both occipital lobes are best seen in *D* (*arrows*). Minimal changes are present in *B* and *D* in these areas. Abnormalities are also seen at the anterolateral angles of both lateral ventricles. The normal high signal from the parietopontine tract is seen within the posterior internal capsule.

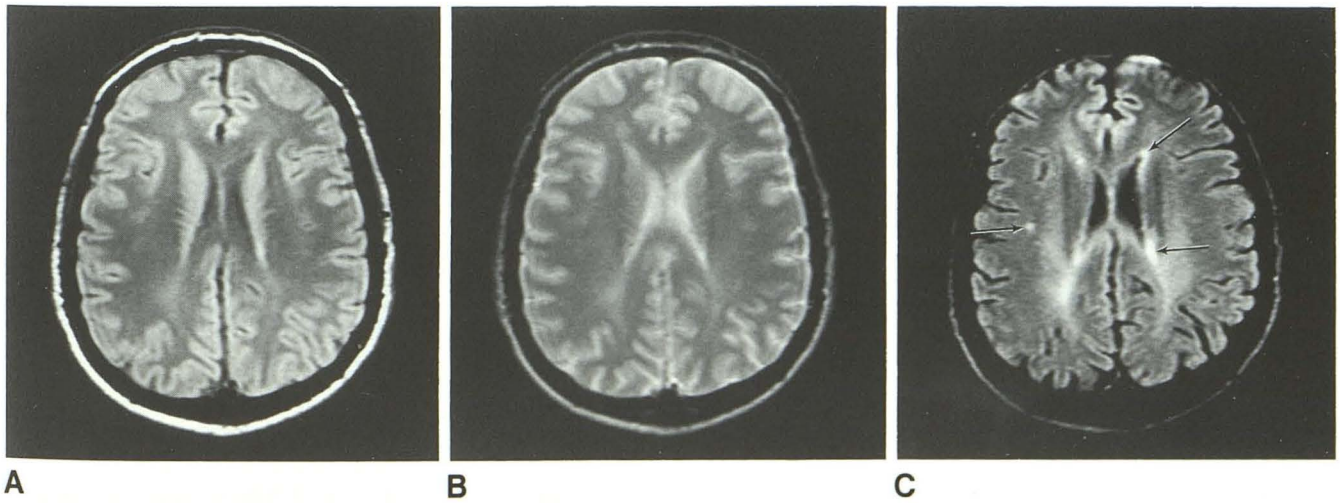


Fig. 4. Periventricular infarction: SE 2500/20 (*A*), SE 2500/80 (*B*), and IR 7070/160/3110 (*C*) images. The areas of abnormality seen in *C* (*arrows*) are either not seen or poorly seen in *A* and *B*.

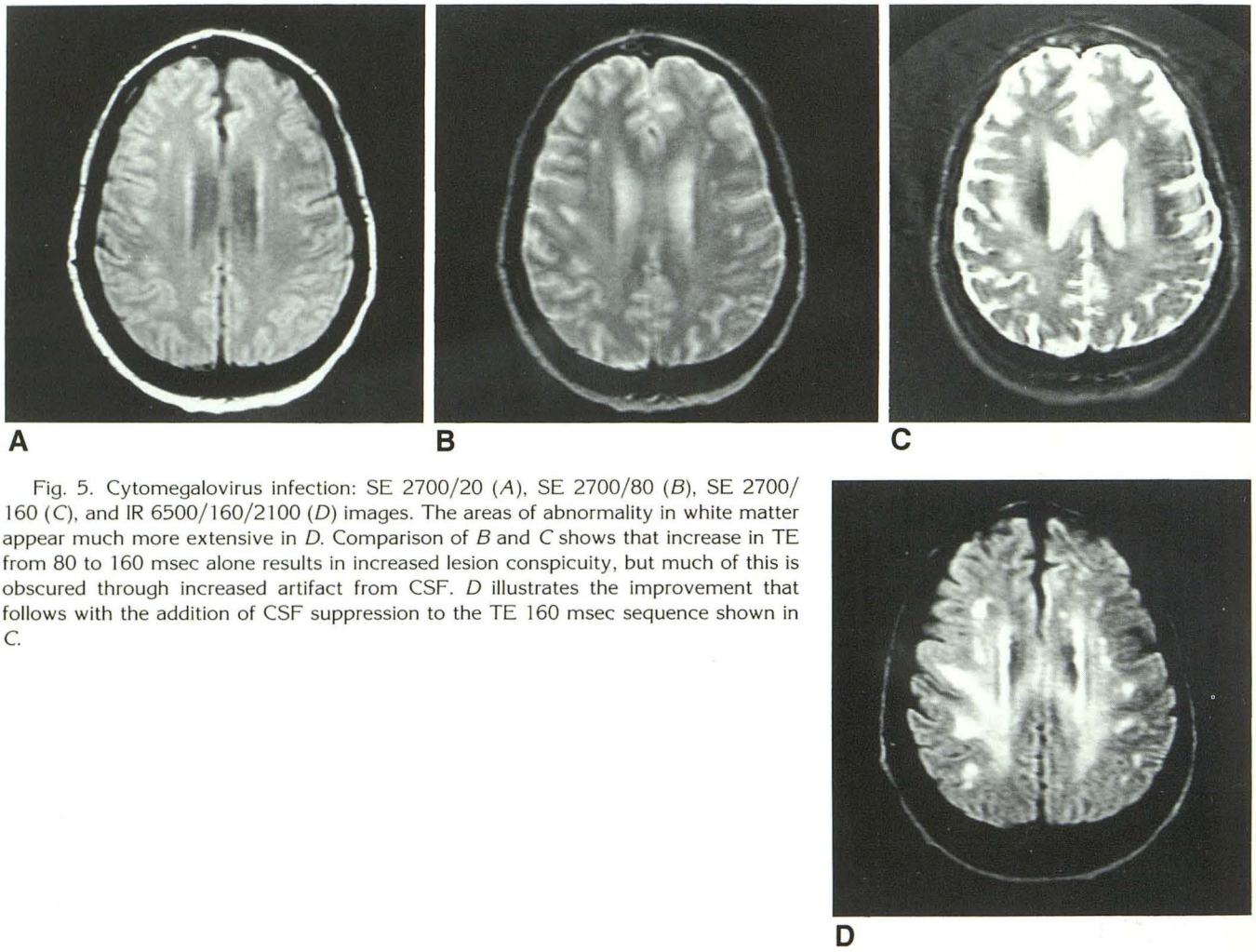


Fig. 5. Cytomegalovirus infection: SE 2700/20 (*A*), SE 2700/80 (*B*), SE 2700/160 (*C*), and IR 6500/160/2100 (*D*) images. The areas of abnormality in white matter appear much more extensive in *D*. Comparison of *B* and *C* shows that increase in TE from 80 to 160 msec alone results in increased lesion conspicuity, but much of this is obscured through increased artifact from CSF. *D* illustrates the improvement that follows with the addition of CSF suppression to the TE 160 msec sequence shown in *C*.

conspicuity, and extent were greater in both cases. In the illustrated case, the diagnosis was presumptive following a history of mental deterioration, a known breast primary tumor, bone scan and CT diagnosis of bone metastases, and a progressive downhill course following the MR scan. No brain biopsy was performed.

The patient with a chordoma displayed a low signal in the left medulla presumably due to old hemorrhage. This was best seen with the FLAIR sequence (Fig. 10).

Metabolic Disease (Two Cases)

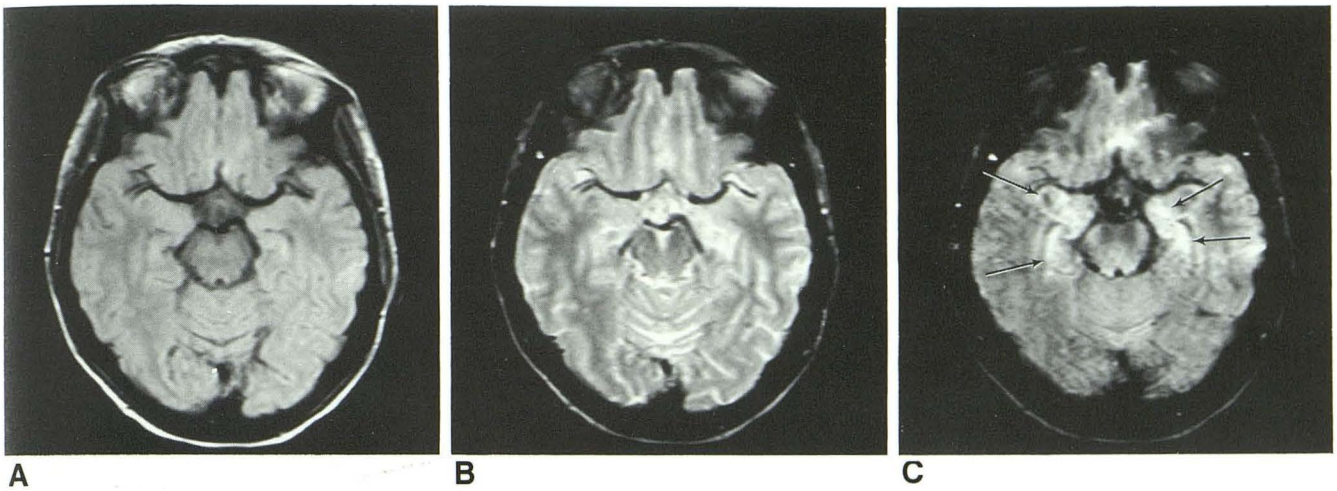
Two patients with hepatic encephalopathy were examined. In one with known vascular disease, extensive white matter changes were demonstrated. The other displayed periventricular change that was only seen on the FLAIR sequence.

Miscellaneous (Six Cases)

This group included a patient with a 10-year history of recurrent episodes of facial weakness with some sensory loss. The initial clinical diagnosis was multiple sclerosis, but this was revised to sarcoidosis. No change was seen with spin-echo sequences, but bilateral changes were seen in the region of the facial nerves, as well as in the pons with the FLAIR sequences (Fig. 11).

The category included patients with dystonia, schizophrenia, polycythemia, short-term memory loss, and suspect brain-stem encephalitis who showed no abnormality with either conventional spin-echo or FLAIR sequences.

Overall, 48 different lesions or groups of lesions were identified. More lesions were seen in 22 of these categories with the FLAIR sequence, and in the remaining 26 instances equal numbers were seen.



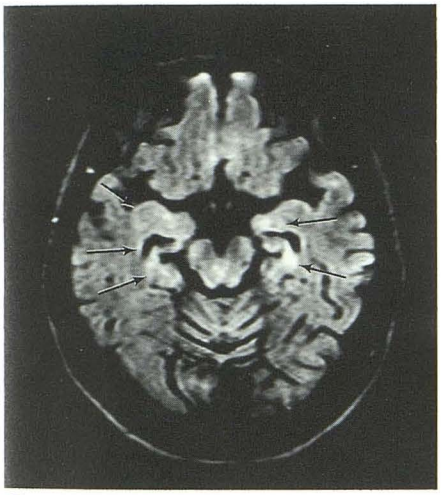


Fig. 6. Previous herpes encephalitis: SE 2500/20 (*A*), SE 2500/80 (*B*), IR 6400/160/2100 (*C*), and IR 6430/160/1730 (*D*) images. Changes are seen in the medial temporal lobes in *C* (*arrows*), as well as the anterior left temporal lobe. Similar changes are seen in the adjacent section (*D*) where the lesion contrast is reduced as a consequence of its shorter TI producing significant T1 weighting. These changes are not well demonstrated in *A* and *B*.

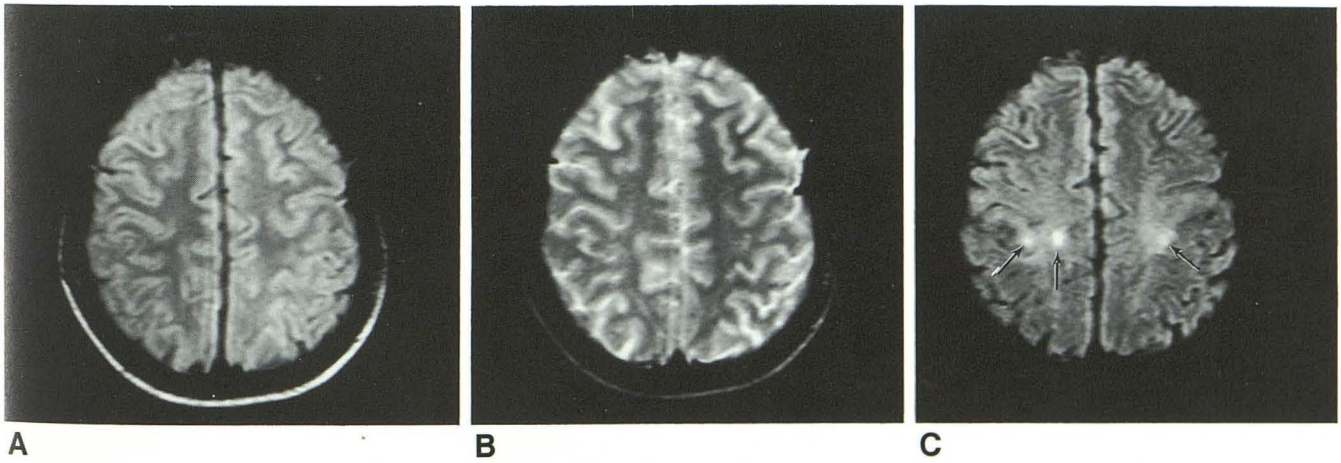


Fig. 7. Multiple sclerosis: SE 2540/20 (*A*), SE 2540/80 (*B*), and IR 6040/160/2100 (*C*) images. Lesions are seen in *C* (*arrows*) in regions where no abnormality is seen in *A* or *B*.

Conspicuity was better with the FLAIR sequence in 42 instances, equal in five, and worse in one cystic lesion (Fig. 8). Lesion extent was better seen with the FLAIR sequence in 28 of the 48 lesions or groups of lesions and equally well seen in the remainder.

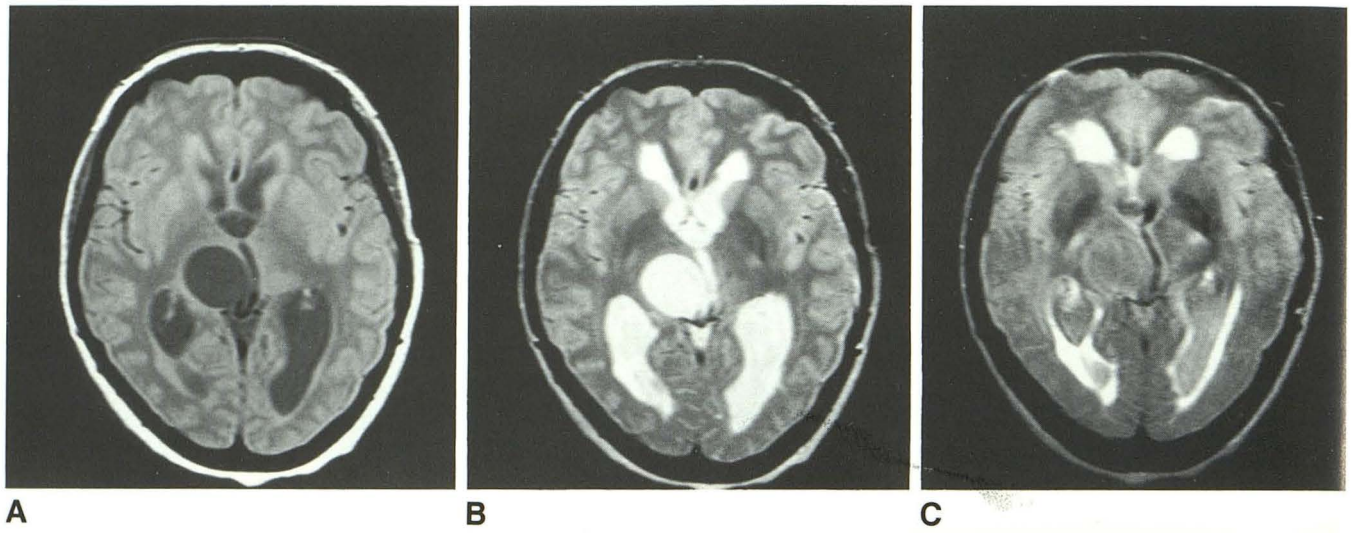
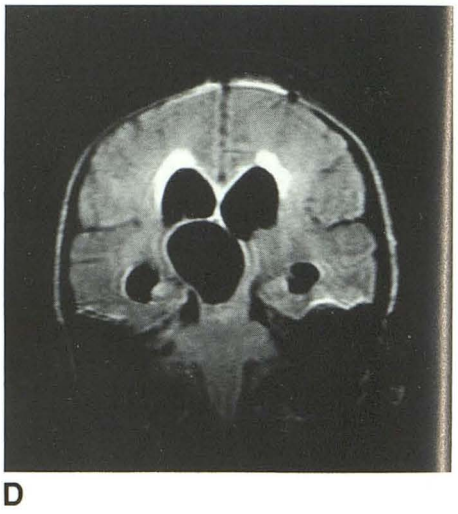


Fig. 8. Probable cystic glioma: transverse SE 2540/20 (*A*), SE 2540/80 (*B*), IR 6490/160/2100 (*C*), and coronal IR 7530/130/2760 (*D*) images. The cystic component of the tumor has a low signal in *A* and a high signal in *B*. Its signal is intermediate in *C* and very low in *D*. The periventricular edema is most obvious in *C* and *D*.



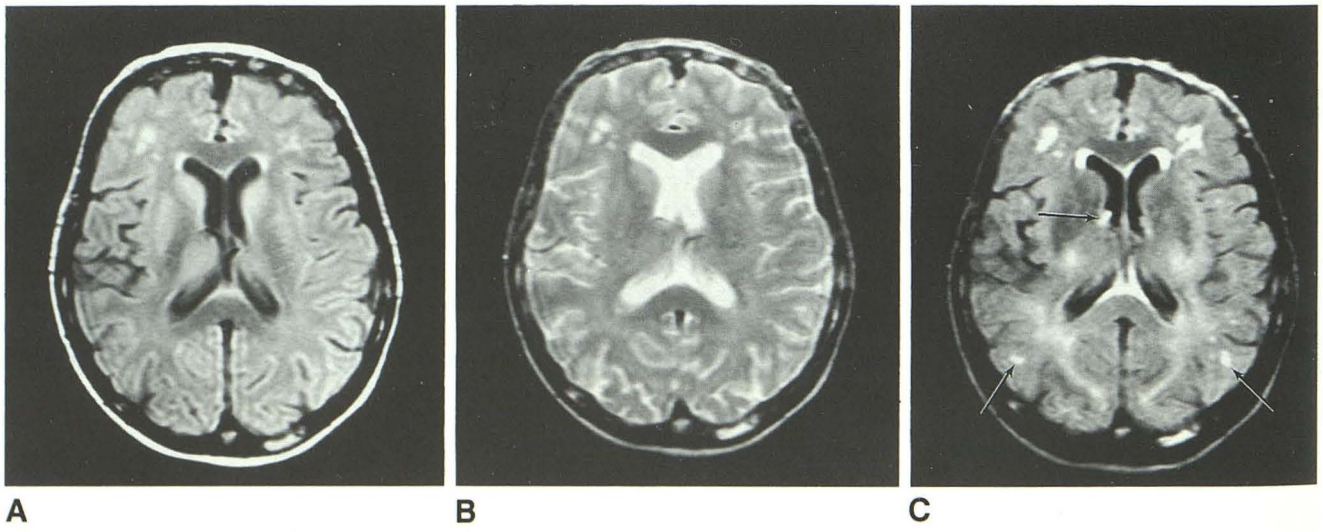


Fig. 9. Probable multiple metastases from carcinoma of the breast: SE 2500/20 (*A*), SE 2500/80 (*B*), and IR 6490/160/2100 (*C*) images. The metastases are best seen in *C*. Additional lesions not shown in *A* or *B* are indicated with *arrows* in *C*.

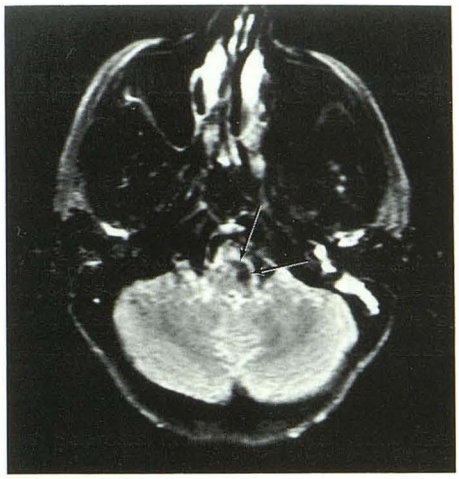


Fig. 10. Chordoma after surgery: IR 7000/160/2200 image. A dark area is seen within medulla (*arrows*). It is probably a consequence of old hemorrhage.

Lesions were identified with FLAIR sequences as the only abnormality in patients with normal spin-echo images in one patient with herpes simplex encephalitis (Fig. 6), one with probable sarcoidosis (Fig. 11), and one with chronic hepatic encephalopathy. Additional lesions were seen in patients with vascular disease, infective lesions, white matter disease, and metastases.

Discussion

FLAIR sequences display high sensitivity to a wide range of disease. The sequence is particularly useful in detecting subtle changes at the periphery of the cerebral hemispheres, around the basal cisterns, in the brain stem, at gray white matter interfaces, and in the periventricular region. These are sites where CSF artifacts and partial volume effects between gray and white matter cause problems in diagnosis with conventional T2-weighted spin-echo sequences.

Validation of the increased sensitivity shown in this study is rendered difficult by the fact that few patients have been to surgery, and, as a consequence, histologic confirmation is lacking in most cases. It is also rendered difficult because heavily T2-weighted spin-echo sequences have hitherto been regarded as the gold standard for detecting many of the changes demonstrated in this study. However, the validity of the findings with the FLAIR sequences is supported by the fact that, in each case, (except for a cyst) the abnormalities shown with the conventional spin-echo sequence were also seen with the same or higher conspicuity using the FLAIR sequence. It is also possible to correlate the different findings with the two sequences by recognizing that lesions could have been missed with conventional TE80 spin-echo sequences due to partial volume effects from CSF or gray white matter interfaces as well as the lower T2-weighting.

The signal from cystic lesions may be suppressed in the same way as CSF and present a quite different appearance than that found with conventional heavy T2-weighted spin-echo sequences. Cysts may be isointense or have a very low signal intensity as shown in Fig. 8. With versions of the FLAIR sequence employing a section-selective initial 180° pulse together with a constant value of TI, inflow of incompletely inverted CSF between the initial 180° pulse and subsequent 90° pulse may lead to increased signal from CSF. This is most evident in areas of rapid CSF flow, such as at the foramen of Monro, and can be reduced by increasing the section width of the initial 180° pulse and decreasing the value of TI, as well as by use of presaturation pulses.

It is important to note that many white matter tracts display a high signal intensity with the long TE values used in this study rather than the low signal intensity previously described with TE values of 80 msec (2). This is particularly true of the parietopontine tract, corticospinal tracts, medial lemnisci, cerebellar peduncles (except the pontine part of the middle cerebellar peduncles), the medial longitudinal fasciculi, and parts of the occipitothalamic tract.

In its simplest form, the FLAIR sequence can be implemented with an unselected 180° pulse 2000-2500 msec before a multisection spin-echo set. This provides good control of CSF flow artifact, but the TI successively increases as different levels are imaged, producing a changing appearance to the images. Also, only a limited number of sections have TIs in the appropriate range to show high lesion contrast with good CSF suppression.

The next most complex form of the FLAIR sequence employs a multisection set with a fixed inversion time. This has been implemented with 10 or 15 section sets. Improved control of CSF artifact is achieved by having a section gap equal

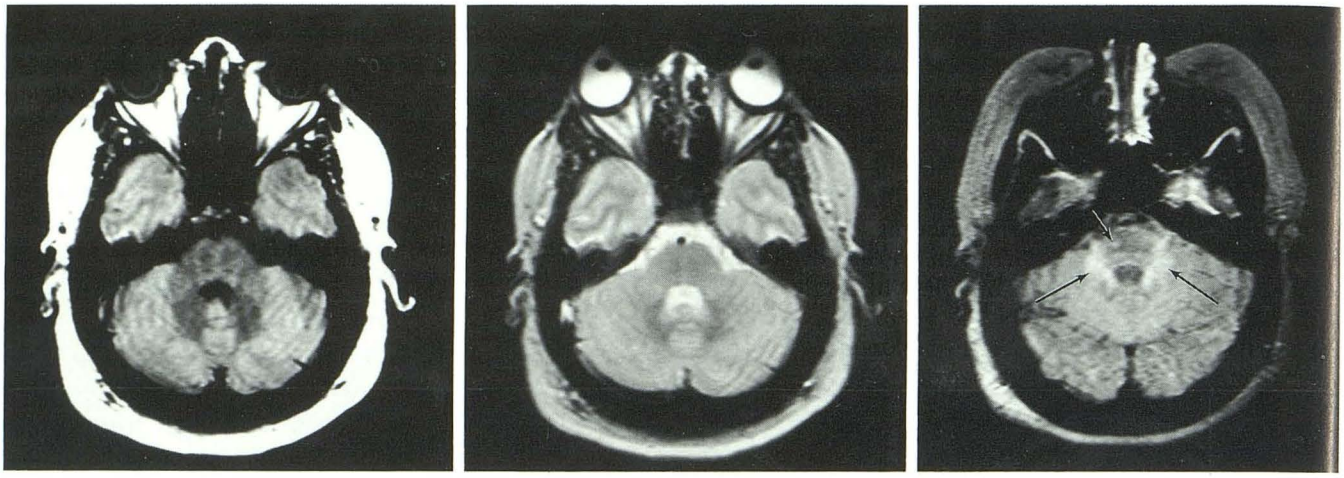


Fig. 11. Sarcoidosis: SE 2540/20 (*A*), SE 2540/80 (*B*), and IR 6040/160/2100 (*C*) images. In *C*, a lesion is seen in the pons (*small arrow*) and bilateral lesions are seen at the junction of the pons and cerebellum in the region of the facial nerves (*large arrows*). No abnormality is seen in *A* or *B*.

to the section width and making the initial section selected 180° pulse twice the width of the subsequent 90° and 180° pulses. This has been operated as an interleaved set on a routine basis.

The next most complex form of the FLAIR sequence places the 180° pulse before a multiecho spin-echo that uses several phase-encoding steps after each excitation as described with the RARE sequence (1). This has been implemented in three and four phase step versions to date (3, 4). It provides a considerable saving in time over the conventional spin-echo set at the expense of less accurate edge definition.

Although the use of an initial inversion pulse to suppress the signal from CSF has previously been used in MR imaging (5–7), its potential value in combination with a long value of TE for general imaging of the brain has not previously been appreciated. It promises to be a valuable new addition to MR, although more extensive studies will be needed to establish its role in clinical practice.

Acknowledgments

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