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# Adult Cerebrovascular Disease: Role of Modified Rapid Fluid-Attenuated Inversion-Recovery Sequences

Julia A. Alexander, Scott Sheppard, Patricia C. Davis, and Paul Salverda

**PURPOSE:** To compare a rapid fluid-attenuated inversion-recovery (FLAIR) sequence with T1-weighted, fast spin-echo proton density-weighted, and T2-weighted images in the evaluation of cerebrovascular disease. **METHODS:** All patients underwent standard T1-, proton density-, and T2-weighted fast spin-echo and fast FLAIR MR imaging at 1.5 T. Images were compared for lesion size, location, and conspicuity. **RESULTS:** Forty-five infarctions were identified on T2-weighted and fast FLAIR sequences. Lesion size was comparable on the proton density-weighted, fast T2-weighted, and fast FLAIR sequences, although lesion conspicuity was superior on the fast FLAIR images in 43 (96%) of the lesions. Associated periventricular and pontine hyperintensities were more extensive on the fast FLAIR images. **CONCLUSION:** Our modified fast FLAIR technique provided improved conspicuity of infarctions and white matter disease as compared with T1-, proton density-, and T2-weighted spin-echo images, and a reduced scan time compared with conventional FLAIR sequences in patients with cerebrovascular disease.

**Index terms:** Brain, infarction; Brain, magnetic resonance; Magnetic resonance, comparative studies

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As originally conceived, fluid-attenuated inversion-recovery (FLAIR) pulse sequences used a conventional inversion-recovery sequence with a long echo time in order to achieve T2-weighting, with inversion time chosen specifically to null the signal intensity of cerebrospinal fluid (CSF) (1–3). Advantages of FLAIR imaging include improved contrast between the signal intensity of a variety of diseases that prolong brain T2 relaxation and the suppressed signal intensity of the adjacent ventricular or subarachnoid space CSF (1, 4). The major disadvantage of conventional FLAIR sequences is

a very long acquisition time, on the order of 12.8 to 13.6 minutes for 10 axial plane sections (1).

Recently, pulse sequences have been proposed in which FLAIR-like sequences are coupled with fast spin-echo techniques in order to reduce scanning times (5–8) (J. A. den Boer, P. Salverda, T. R. Peters, R. L. Prevo, “Multislice Turbo-FLAIR in Brain Studies of Multiple Sclerosis,” presented at the annual meeting of the Society for Magnetic Resonance in Medicine, New York, NY, August 1993). In our study, the clinical utility of an optimized fast FLAIR pulse sequence was compared prospectively with findings on T1-weighted, proton density-weighted, and T2-weighted magnetic resonance (MR) images in 26 patients with suspected cerebrovascular disease.

## Subjects and Methods

Twenty-six patients with suspected cerebrovascular disease were identified prospectively from a population of 400 patients who underwent brain MR imaging at our hospital. The group included 11 men and 15 women, 30 to 87

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years old, who were referred for MR imaging. Five patients had known infarction, 10 were thought to have infarction, and 11 had transient ischemic attack(s).

All patients had MR imaging at 1.5 T as follows: sagittal T1-weighted scout location sequences; axial T1-weighted spin-echo (500/15/2 [repetition time/echo time/excitations]) sequences with an acquisition time of 3 minutes 42 seconds; proton density-weighted and T2-weighted fast spin-echo (3500/22 and 3500/120) sequences with an echo train length of 12, a half-Fourier acquisition factor of 0.625, and an acquisition time of 2 minutes 6 seconds; and fast FLAIR (8000/120) sequences with an inversion time of 1900 and echo train length of 20. Seriously ill or claustrophobic patients were studied with shorter fast FLAIR sequences using one signal measurement (acquisition time of 2 minutes 8 seconds), whereas more stable and cooperative patients were studied with two signal measurements (acquisition time of 4 minutes 16 seconds). All sequences were obtained with identical scan resolution and geometry (192 × 256 matrix, 220 field of view, and 23 5-mm sections with a 1-mm section gap).

The three significant modifications that were used in our optimized fast FLAIR sequence were based on the work of den Boer et al ("Multislice Turbo-FLAIR") and modified by Rydberg et al (3). These modifications include an acquisition of several lines in k-space per repetition time, analogous to rapid acquisition with relaxation enhancement (RARE) sequences and other fast spin-echo sequences, with improved scan time efficiency; a long inversion delay (1900 milliseconds), allowing interleaving of inversion pulses and echo trains from several sections to maximize the number of sections obtained per repetition time; and a doubling of the inversion section width such that the inversion pulse encoded a 10-mm section, and the 90° excitation pulse encoded a 5-mm imaging section (1, 5). The result of these adaptations was a two-package acquisition with imaging of odd sections first, followed by even sections in the second package.

To explore the possibility that differences in brain contrast on our modified fast FLAIR sequence, as compared with those of conventional FLAIR imaging, were the result of an off-resonance magnetization transfer effect of multi-section fast FLAIR imaging (7), a healthy volunteer was scanned repeatedly with fast FLAIR sequences with variable intersection gaps ranging from 5 to 20 mm with all other parameters held constant. Uncorrected region-of-interest measurements of signal intensity from the pons were obtained and compared.

Two neuroradiologists compared the T1-weighted, fast proton density-weighted, fast T2-weighted, and fast FLAIR images from each subject and rated the findings by consensus for lesion presence, size (maximum lesion diameter), conspicuity, and location. The reviewers were blinded to the patients' medical history and results of prior imaging studies. Patients' charts were reviewed retrospectively to determine presenting signs and symptoms and to estimate the chronicity of cerebral infarctions.

Region-of-interest measurements of signal intensity from the pons with a variable intersection gap in a healthy volunteer

Intersection Gap, mm	Mean Signal Intensity	Standard Deviation
5	521	72
7	585	75
10	627	73
15	657	82
20	742	84

## Results

Region-of-interest measurements of signal intensity obtained from the pons with fast FLAIR sequences with variable intersection scan intervals obtained from a healthy volunteer are charted in the Table.

Forty-five cerebral infarctions were identified on MR images of the 26 patients with clinical evidence of cerebrovascular disease. Twenty-five were lacunar infarctions ranging in size from 0.3 to 1.2 cm, and 20 were cortical and subcortical lesions (2.0 to 10.4 cm).

For lacunar infarctions, lesion size was comparable in seven (28%) of 25 cases, and slightly larger (1 to 3 mm) in eight cases (32%) on fast proton density-weighted and fast T2-weighted studies compared with fast FLAIR images. In 10 cases (40%), lesion size was larger on fast FLAIR images. Lesion conspicuity was rated superior on fast FLAIR images compared with both the proton density-weighted and T2-weighted images in 24 (96%) of the 25 cases. Twelve lacunae were hypointense on T1-weighted images and thus were probably chronic lesions. On fast FLAIR images, 18 lacunae were hypointense centrally with a thin peripheral rim of hyperintensity (Fig 1), one was entirely hypointense without a peripheral rim of hyperintensity, and six clinically acute lacunar infarctions were hyperintense on both fast T2-weighted and fast FLAIR sequences.

A comparison of the 20 cortical and subcortical infarctions between the fast FLAIR and the T2-weighted sequences confirmed comparable lesion size and superior lesion conspicuity on the fast FLAIR images in 16 (80%) of the cases (Fig 2). Although four acute infarctions were initially thought to be larger on the fast T2-weighted images, the improved demarcation of these lesions from adjacent brain tissue on the fast FLAIR sequences suggests that the lesion

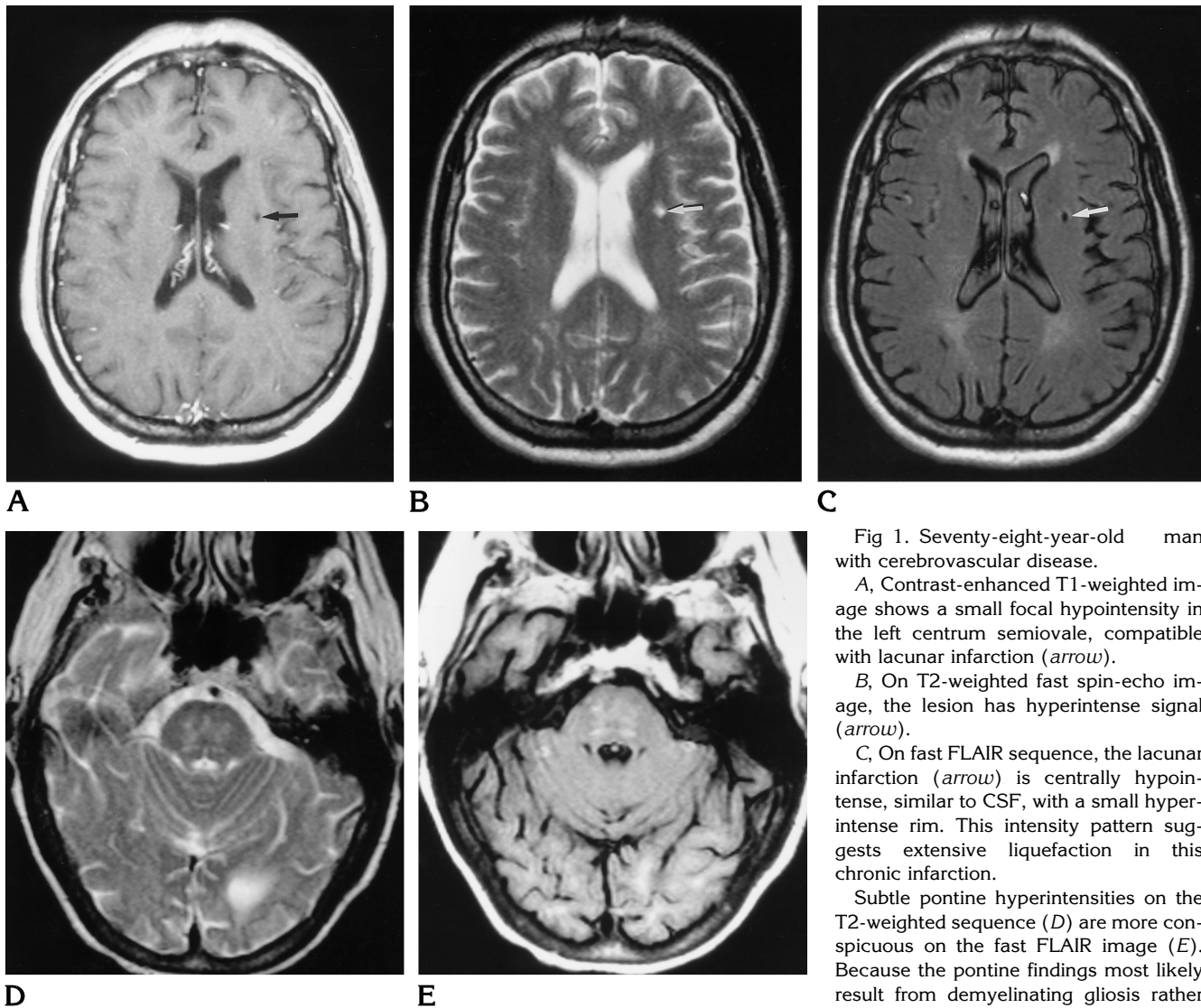


Fig 1. Seventy-eight-year-old man with cerebrovascular disease.

A, Contrast-enhanced T1-weighted image shows a small focal hypointensity in the left centrum semiovale, compatible with lacunar infarction (arrow).

B, On T2-weighted fast spin-echo image, the lesion has hyperintense signal (arrow).

C, On fast FLAIR sequence, the lacunar infarction (arrow) is centrally hypointense, similar to CSF, with a small hyperintense rim. This intensity pattern suggests extensive liquefaction in this chronic infarction.

Subtle pontine hyperintensities on the T2-weighted sequence (D) are more conspicuous on the fast FLAIR image (E). Because the pontine findings most likely result from demyelinating gliosis rather than from frank infarction with liquefaction, these areas appear hyperintense on fast FLAIR sequences.

size was overestimated on the T2-weighted images.

One infarction contained foci of hyperintensity on T1-weighted images, suggesting the presence of subacute hemorrhage, necrosis, or dystrophic calcification (Fig 3). No signal loss suggestive of hemorrhage was apparent in this case on fast FLAIR or T2-weighted fast spin-echo sequences.

Periventricular white matter ( $n = 17$ ) and pontine/brain stem hyperintensities ( $n = 16$ ) associated with aging and/or hypertension were seen better on fast FLAIR images than on T2-weighted images in all cases (Fig 1D and E). Likewise, periventricular white matter changes

were larger and were distinguished better from surrounding CSF and brain parenchyma on fast FLAIR images than on proton density-weighted and T2-weighted sequences in all cases (Fig 4).

Incomplete nulling of CSF signal due to CSF inflow effects has been reported to result in imaging artifacts on FLAIR and similar sequences (1). As expected, we encountered similar CSF flow-related artifacts with our modified fast FLAIR sequence. These artifacts were relatively minor in extent and predictable in location, and did not hinder visibility of parenchymal disease (Fig 2E). The most striking CSF artifacts occurred at the foramen of Monro and in the ad-

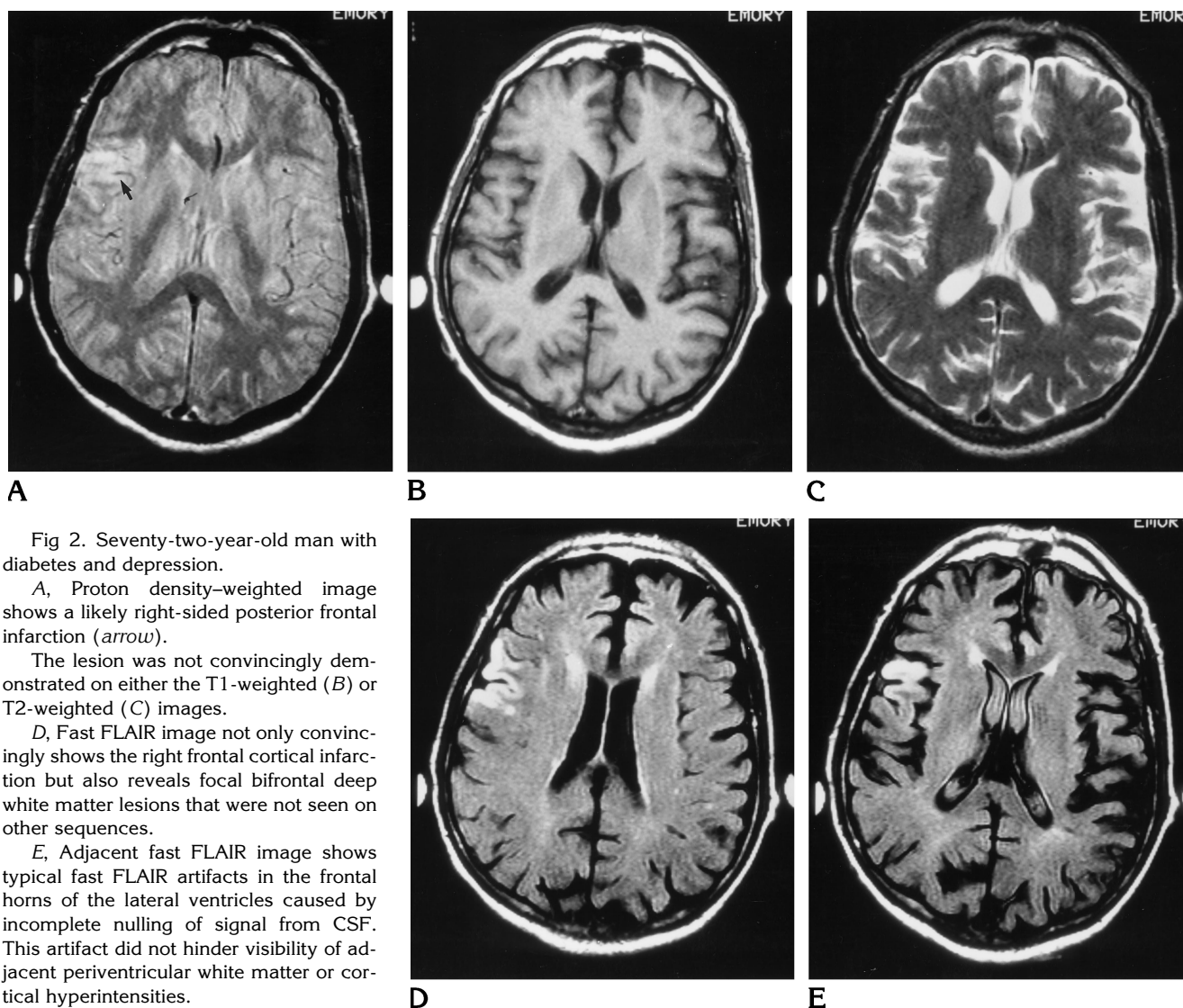


Fig 2. Seventy-two-year-old man with diabetes and depression.

A, Proton density-weighted image shows a likely right-sided posterior frontal infarction (arrow).

The lesion was not convincingly demonstrated on either the T1-weighted (B) or T2-weighted (C) images.

D, Fast FLAIR image not only convincingly shows the right frontal cortical infarction but also reveals focal bifrontal deep white matter lesions that were not seen on other sequences.

E, Adjacent fast FLAIR image shows typical fast FLAIR artifacts in the frontal horns of the lateral ventricles caused by incomplete nulling of signal from CSF. This artifact did not hinder visibility of adjacent periventricular white matter or cortical hyperintensities.

adjacent frontal horns of the lateral ventricles, with moderate CSF artifacts in the posterior fossa.

In contrast to the imaging findings of other reported conventional FLAIR techniques (1), normal findings with our fast FLAIR protocol included a very small continuous periventricular line of hyperintensity and focal hyperintensity of the periaqueductal gray matter and hypothalamus (K. Nixon, J. Webber, J. Hoffman, et al, "Normal MR Appearance of Adult Brain with the FLAT TIRE [Fluid Attenuated Turbo Inversion Recovery] Sequence," presented at the annual meeting of the American Society of Neuroradiology, Nashville, Tenn, May 1994). Normal mature white matter appeared mildly hypointense to isointense relative to gray matter. Although the brain stem white matter pathways have been reported to appear hyperintense on con-

ventional FLAIR sequences (2), no other normal brain regions appeared hyperintense on the fast FLAIR sequences in our study.

## Discussion

FLAIR sequences have demonstrated improved sensitivity in showing brain parenchymal lesions, particularly those located in the brain stem, immediate periventricular white matter, and superficial cortical and subcortical brain (6-8)(den Boer et al, "Multislice Turbo-FLAIR"). In part, this improvement is the result of nulling of CSF signal resulting in reduced CSF flow and partial volume artifacts (2). In addition, FLAIR sequences use a longer echo time than is normally used for spin-echo T2-weighted sequences. The primary disadvantage

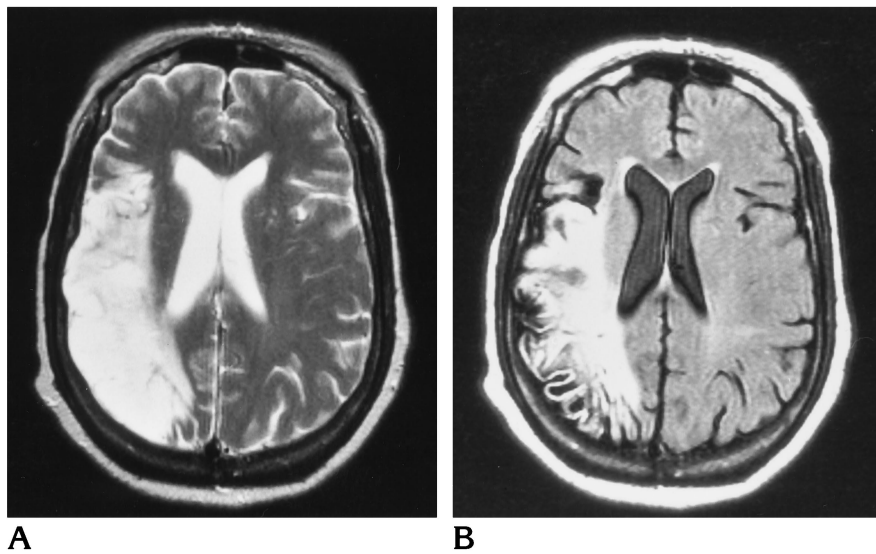


Fig 3. Fifty-six-year-old woman with prior infarction.

A, On T2-weighted fast spin-echo image, the borders of this chronic infarction were indistinguishable from the hyperintense signal of the adjacent subarachnoid spaces.

B, The lesion morphology is seen better on this fast FLAIR image. The small hypointense regions may represent liquefaction within this chronic infarction.

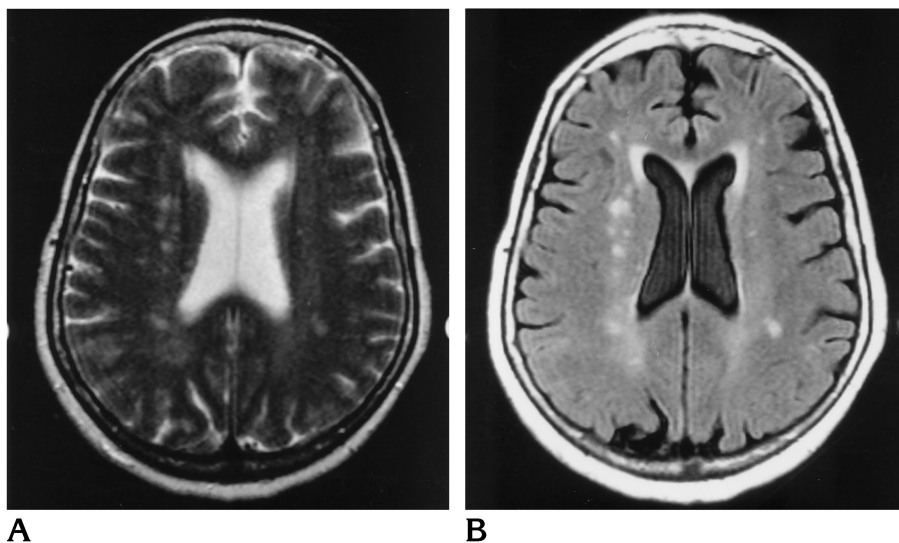


Fig 4. Sixty-three-year-old woman with hypertension.

A, T2-weighted axial image shows subtle areas of periventricular white matter hyperintensity.

B, These foci are more conspicuous and more extensive on fast FLAIR image.

of FLAIR sequences has been the lengthy scanning time required for acquisition of relatively few and thick sections with a limited imaging matrix. For example, the FLAIR sequence described by De Coene and coworkers required 12.8 to 13.6 minutes for imaging 10 to 17 sections with a thickness of 6 to 8 mm and a  $128 \times 192$  imaging matrix (1).

Several investigators report obtaining a faster FLAIR sequence by using multiple echoes per repetition time, based on RARE and fast spin-echo sequences described by Hennig and colleagues (5). Parameters for the faster sequences described by Rydberg et al (3) are an acquisition time of 5 minutes 8 seconds, a repetition time of 11 seconds, an inversion time of

2600 milliseconds, and an echo train length of 16. Our modified fast FLAIR pulse sequence accomplished a further reduction in scanning times to between 2 minutes 8 seconds and 4 minutes 16 seconds by using a repetition time of 8 seconds, an inversion time of 1900 milliseconds, and an echo train length of 20. Because one of the trade-offs of these changes is a reduction in the available time for echo sampling (5), our sequence used a larger sampling bandwidth with a consequent reduction in the signal-to-noise ratio. A comparison of sampling bandwidth on our scanner using protocols with an echo train length of 16 or 21 resulted in a  $T_{acq}$  (time of acquisition, which is sampling time per pixel expressed in units of 1 per band-

width per pixel) of 5.1 and 4.5 milliseconds, respectively. Because the signal-to-noise ratio is proportional to the square root of the sampling bandwidth, the signal-to-noise difference with this change in bandwidth is 0.93, or 7%  $[(T_{acq1}/T_{acq2})^{1/2}]$ .

Although conventional FLAIR sequences offer exquisite detail in images of white matter pathways (4), these white matter tracts did not appear as discrete entities or have high signal intensity on previously reported fast FLAIR sequences or on our modified fast FLAIR sequence (3). Although the selection of an inversion time of 1900 milliseconds for this protocol contributes to this finding, our experience is that a longer inversion time of 2200 milliseconds results in only marginally improved visibility of white matter tracts. The region-of-interest measurements from the pons of a healthy volunteer (Table) demonstrate an increase in signal intensity with increasing intersection intervals. This finding suggests that the lack of brain stem and white matter tract hyperintensity on fast FLAIR sequences also results from an off-resonance magnetization transfer contrast effect occurring in closely spaced multisection sequences, similar to that reported by Constable et al (6). White matter pathways are known to be influenced by magnetization transfer contrast effects; hence, the selective alteration in contrast of myelinated tissues. Another possible factor is J-coupling, which results in signal loss in multiple spin systems, such as lipids in myelinated white matter (9). This lack of white matter tract detail is a significant disadvantage of fast FLAIR sequences. If deemed clinically essential, delineation of white matter tracts using a fast FLAIR technique could be achieved by using a single-section sequence at the level of concern with a short echo spacing and long echo train. Although use of a larger intersection gap might result in fast FLAIR images that are more like those of conventional FLAIR sequences, the infeasibility of studying a patient with a 20-mm or greater intersection gap is a limiting factor.

In our study, the overall lesion morphology was better defined on fast FLAIR images than on proton density-weighted and T2-weighted fast spin-echo images. In particular, infarcted tissue and adjacent CSF were often similar in intensity on T2-weighted images with result-

ing difficulty in gauging lesion size, although admittedly in most cases this limitation could be overcome by using the available proton density-weighted images. On fast FLAIR images, the nulling of CSF signal provided ready demarcation between CSF and infarction. One interesting observation was the mixed low and high signal intensity encountered on fast FLAIR images in chronic infarctions. Presumably, portions of very old infarctions may be so liquefied or gliotic that their signal intensity matches that of CSF and is thus nulled on fast FLAIR sequences. However, these older lesions would also be visible as hypointense foci on T1-weighted sequences.

Although a recent study found improved detection of subarachnoid hemorrhage using FLAIR sequences (10), few reports describe the appearance of intraparenchymal hemorrhage on FLAIR or fast FLAIR sequences. In our study, the only infarction identified that may have contained blood products was similar in intensity on both fast FLAIR and fast T2-weighted spin-echo sequences.

In summary, we demonstrated improved conspicuity of lacunar and cortical/subcortical infarcts and of pontine and periventricular hyperintensities associated with cerebrovascular disease by using a modified fast FLAIR sequence as compared with fast spin-echo imaging. The advantages of the fast FLAIR sequence modifications used in this study included a further reduction in imaging time compared with other fast FLAIR pulse sequences. With further experience, fast FLAIR might serve as a replacement for proton density-weighted and T2-weighted fast spin-echo imaging of brain parenchymal lesions in patients with cerebrovascular disease.

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