

Comparison of T2-Weighted and Fluid-Attenuated Inversion-Recovery Fast Spin-Echo MR Sequences in Intracerebral AIDS-Associated Disease

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PURPOSE: To compare the value of fast fluid-attenuated inversion-recovery (FLAIR) with T2-weighted fast spin-echo MR imaging in the detection of acquired immunodeficiency virus (AIDS)-related lesions of the brain. **METHODS:** Forty-four human immunodeficiency virus (HIV)-positive patients were examined with both sequences on either a 1.0-T or a 1.5-T MR system. The number, size, location, and conspicuity of the lesions were evaluated by two independent observers. Contrast ratios between lesions and normal brain/cerebrospinal fluid were determined, and contrast-to-noise ratios were calculated. **RESULTS:** FLAIR was found to be superior to T2-weighted fast spin-echo in detection of small lesions and of lesions located in cortical/subcortical regions and deep white matter. The two techniques were equal in delineation of lesions larger than 2 cm and for lesions located in the basal ganglia and posterior fossa. In 24 patients, more lesions were detected with the FLAIR fast spin-echo technique. Lesion/cerebrospinal fluid contrast ratios and contrast-to-noise ratios were significantly higher for the FLAIR fast spin-echo sequences than for the T2-weighted fast spin-echo sequences. **CONCLUSION:** FLAIR allows early detection of small lesions in subcortical and cortical locations, especially in HIV encephalitis. Because of its improved lesion detection rate and greater overall lesion conspicuity, we believe FLAIR is useful in the evaluation of subtle changes in the brains of AIDS patients with central nervous system disease, and could even replace the T2-weighted fast spin-echo technique.

Index terms: Acquired immunodeficiency syndrome (AIDS); Brain, magnetic resonance; Magnetic resonance, comparative studies

AJNR Am J Neuroradiol 18:1601–1609, October 1997

T2-weighted magnetic resonance (MR) imaging is crucial for the assessment of central nervous system (CNS) disease. Because of its improved quality and shorter acquisition time, the T2-weighted fast spin-echo technique has widely replaced conventional T2-weighted spin-echo sequences (1). Recently, fluid-attenuated inversion-recovery (FLAIR) sequences, which

use this fast spin-echo technique, have been introduced for brain imaging and have been reported to improve diagnostic accuracy (2–14). In general, these studies have exhibited improved delineation of lesions, particularly in regions of the brain where cerebrospinal fluid (CSF) partial volume effects interfere with high-signal-intensity lesions.

CNS lesions in patients who are positive for the human immunodeficiency virus (HIV) might be difficult to detect, particularly in early stages of the disease, and FLAIR sequences have the potential to improve imaging assessment in these patients. Typically, T1- and T2-weighted sequences are used for the assessment of CNS lesions in patients with acquired immunodeficiency syndrome (AIDS) (15–17). These sequences, however, are reportedly not sensitive enough to detect some AIDS-associated CNS

Received November 18, 1996; accepted after revision March 16, 1997.

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AJNR 18:1601–1609, Oct 1997 0195-6108/97/1809–1601

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abnormalities, and more sensitive techniques are needed. This is particularly true for the lesions in HIV encephalitis, which might be missed on T2-weighted images and are usually not visible on T1-weighted images (16, 17).

The purpose of this study was to evaluate the diagnostic efficacy of FLAIR sequences in assessing AIDS-associated CNS disease as compared with T2-weighted fast spin-echo images.

Patients and Methods

Patients

We studied 44 consecutive HIV-positive patients (33 men and 11 women; 26 to 64 years old; mean age, 39 years) who were referred for MR imaging because of neurologic symptoms. The final diagnosis was confirmed by biopsy samples in one case, by autopsy in 12 patients, and on the basis of clinical presentation, laboratory data, and imaging findings in the other 31 patients. Pathologic conditions included HIV encephalitis (n = 14), toxoplasma encephalitis (n = 5), cytomegalovirus encephalitis (n = 3), primary cerebral lymphoma (n = 6), progressive multifocal leukoencephalopathy (n = 1), intracerebral hemorrhage (n = 1), infarct (n = 1), CNS tuberculosis (n = 1), and *Staphylococcus aureus* infection (cerebral abscesses) (n = 1). In 11 cases, MR imaging revealed no signal abnormalities, laboratory findings were normal, and clinical symptoms resolved spontaneously within 2 weeks.

MR Technique

The MR examinations were performed on either a 1.0-T (n = 21) or a 1.5-T (n = 23) system with a circularly polarized head coil. Axial T1-weighted spin-echo images, T2-weighted fast spin-echo images, and FLAIR fast spin-echo images were obtained; the T1-weighted sequence was repeated after intravenous administration of contrast material in a standard dose of 0.1 mmol/kg body weight. We used a section thickness of 6 mm, an intersection gap of 1 mm, a field of view of 230 mm with a 75% rectangular field of view, and an image matrix of 205 × 256 pixels. Sequence parameters for the T1-weighted spin-echo sequences at 1.0 T (1.5 T) were as follows: 550(488)/10(15)/2 (repetition time [TR]/echo time [TE]/excitations). For the T2-weighted fast spin-echo sequences, parameters included a TR of 20 (20) for the first echo and 3000 (3452) for the second echo, an effective TE of 120 (130), an echo train length of 18 (24), and four excitations. For the FLAIR sequences, parameters included an inversion-recovery time of 2100 (2600), a TR of 7000 (9000), an effective TE of 140 (150), an echo train length of 16 (18), and four excitations.

Subjective (Qualitative) Image Assessment

The FLAIR and T2-weighted fast spin-echo (second echo) images were evaluated side by side by two experi-

enced neuroradiologists, independently. The proton density-weighted images were not evaluated in the study. Signal abnormalities seen on either of the two sequences and for which artifacts could be excluded as the cause were regarded as lesions. The lesions were categorized according to size (group A = < 5 mm, group B = 5 to 20 mm, and group C = > 20 mm in diameter) and location (cortical/subcortical, deep white matter, basal ganglia, and posterior fossa). They were then further classified as being not visible, barely visible, clearly visible, or strikingly visible on both the FLAIR fast spin-echo and T2-weighted fast spin-echo sequences. Lesion conspicuity was compared between the two sequences by using Wilcoxon's signed rank test ($P < .05$) and between the two readers by using weighted κ statistics (18).

Objective (Quantitative) Image Assessment

For objective image assessment, contrast ratios and contrast-to-noise ratios (CNRs) of lesions to normal adjacent white matter and CSF, respectively, were determined as follows: signal intensities of individual types of tissue were assessed by region-of-interest measurements, with the regions of interest placed identically on both FLAIR fast spin-echo and T2-weighted fast spin-echo images. Signal intensities were related to each other by calculating the contrast ratio:

$$CR_{\text{tissue}^{1,2}} = \frac{S_{\text{tissue}^1} - S_{\text{tissue}^2}}{S_{\text{tissue}^1} + S_{\text{tissue}^2}}$$

where CR = contrast ratio and S = signal intensity. In addition, signal differences were related to the image noise as assessed with the standard deviation (SD) of background air measured in areas free of ghost artifacts (SD_{air}) by determining the CNR:

$$CNR_{\text{tissue}^{1,2}} = \frac{S_{\text{tissue}^1} - S_{\text{tissue}^2}}{SD_{\text{air}}}$$

Contrast ratios and CNRs of the T2-weighted fast spin-echo and FLAIR fast spin-echo sequences were compared by using a paired one-tailed t test ($P < .05$).

Results

Subjective Image Assessment

Lesion Detection.—A total of 175 lesions were found on either T2-weighted fast spin-echo or FLAIR fast spin-echo images in the brains of 33 of the 44 HIV-positive patients. In 11 patients, neither sequence revealed any abnormalities. In these patients, laboratory findings were normal and follow-up MR examinations showed no abnormalities. In 24 of the 33 patients with brain lesions, more lesions were depicted by the FLAIR fast spin-echo technique. A total of 147 lesions were detected on T2-weighted fast spin-echo images, whereas 28 additional lesions

TABLE 1: Lesion conspicuity (mean value \pm SD) according to size and location for two MR imaging sequences

Lesion Conspicuity	T2-Weighted FSE	FLAIR FSE	P
Lesion size, mm			
<5	1.76 \pm 0.80	2.71 \pm 0.52	<.0001
5–20	2.27 \pm 0.67	2.85 \pm 0.40	<.0001
>20	2.41 \pm 0.80	2.81 \pm 0.52	NS
Lesion location			
Cortical/subcortical	1.32 \pm 0.95	2.81 \pm 0.40	<.0001
Deep white matter	1.65 \pm 1.01	2.75 \pm 0.52	<.0001
Basal ganglia	2.50 \pm 0.73	2.70 \pm 0.60	NS
Posterior fossa	2.13 \pm 1.19	2.60 \pm 0.74	NS

Note.—FSE indicates fast spin-echo; FLAIR, fast fluid-attenuated inversion recovery; and NS, not significant.

were found on the FLAIR fast spin-echo images. None of the lesions found on the T2-weighted fast spin-echo sequences was missed on the FLAIR.

Lesion Size.—Of 175 lesions, 70 were smaller than 5 mm in diameter (group A), 68 were between 5 mm and 2 cm in diameter (group B), and 37 were more than 2 cm in diameter (group C). Of the 28 lesions found only on the FLAIR fast spin-echo images, 20 were classified as group A (< 5 mm) and eight were categorized as group B (5 to 20 mm). Lesions larger than 20 mm were always detected with both sequences.

Lesion Location.—Of the 147 lesions found on both sequences, 39 were located in the cortical/subcortical region, 65 were in the deep white matter, 30 were in the basal ganglia, and 13 were in the posterior fossa. Of the 28 lesions detected only on FLAIR images, 14 were in a cortical or subcortical location, 12 were found in the deep white matter, and two were detected in the posterior fossa.

Lesion Conspicuity.—For overall lesion conspicuity, FLAIR fast spin-echo was considered superior to T2-weighted fast spin-echo by both reviewers (Table 1). Our analysis revealed significantly ($P < .0001$) superior detectability of small lesions (groups A and B) (Figs 1 and 2) by FLAIR fast spin-echo. The two techniques were found to be equal in the detection of lesions larger than 2 cm in diameter.

With respect to lesion location, FLAIR proved significantly superior to T2-weighted fast spin-echo in the detection of lesions in the cortical/subcortical region and deep white matter ($P < .0001$) (Table 1 and Figs 1 and 2). The sequences were equally capable in the detection of lesions located in the basal ganglia and posterior fossa (Figs 3 and 4).

Interobserver Variability.—The κ score for interobserver reproducibility of the classification of lesion conspicuity was .61 for the T2-weighted fast spin-echo sequence (good reproducibility) and .76 (excellent reproducibility) for the FLAIR sequence.

Imaging Features of Different Entities.—In patients with HIV encephalitis, two imaging patterns were observed: the first was focal abnormalities of high signal intensity (detected in 10 patients; Fig 2) and the second was diffuse moderate to high signal intensity changes in the white matter (noted in five patients; Fig 5). Of the focal high-intensity signal abnormalities, nine lesions were identified only on FLAIR images. The diffuse type of white matter abnormalities was seen on images obtained with both techniques, but both readers agreed that the detection and distinct delineation of those abnormalities were improved on the FLAIR images (Fig 5).

In five patients with cerebral toxoplasmosis, the sequences were equal in the detection of large lesions. Small lesions located at the gray-white matter junction or in the posterior fossa were delineated better on the FLAIR images. Furthermore, six small lesions (groups A and B) were detected only on FLAIR images. Four of those were located in the cortical/subcortical region, one was in the posterior fossa, and another was in the deep white matter.

In three patients, a cytomegalovirus infection of the brain was found at autopsy. In one case, patchy areas of hyperintensity were detected periventricularly, adjacent to the third ventricle. On FLAIR fast spin-echo images, visibility of signal abnormality was improved owing to high contrast relative to low CSF signal intensity. In another patient, hyperintense lesions were located in the periventricular white matter of the left parietal and right frontal lobes, associated with diffuse white matter changes. Both reviewers agreed that the conspicuity was superior with FLAIR in this case as well.

FLAIR was superior to T2-weighted fast spin-echo in delineation of abscesses due to tuberculosis or *S aureus* infection. Although the number of detected lesions was equal, FLAIR images provided better distinction between lesions and perifocal edema and better definition of the abnormality in the cortical locations (Fig 6).

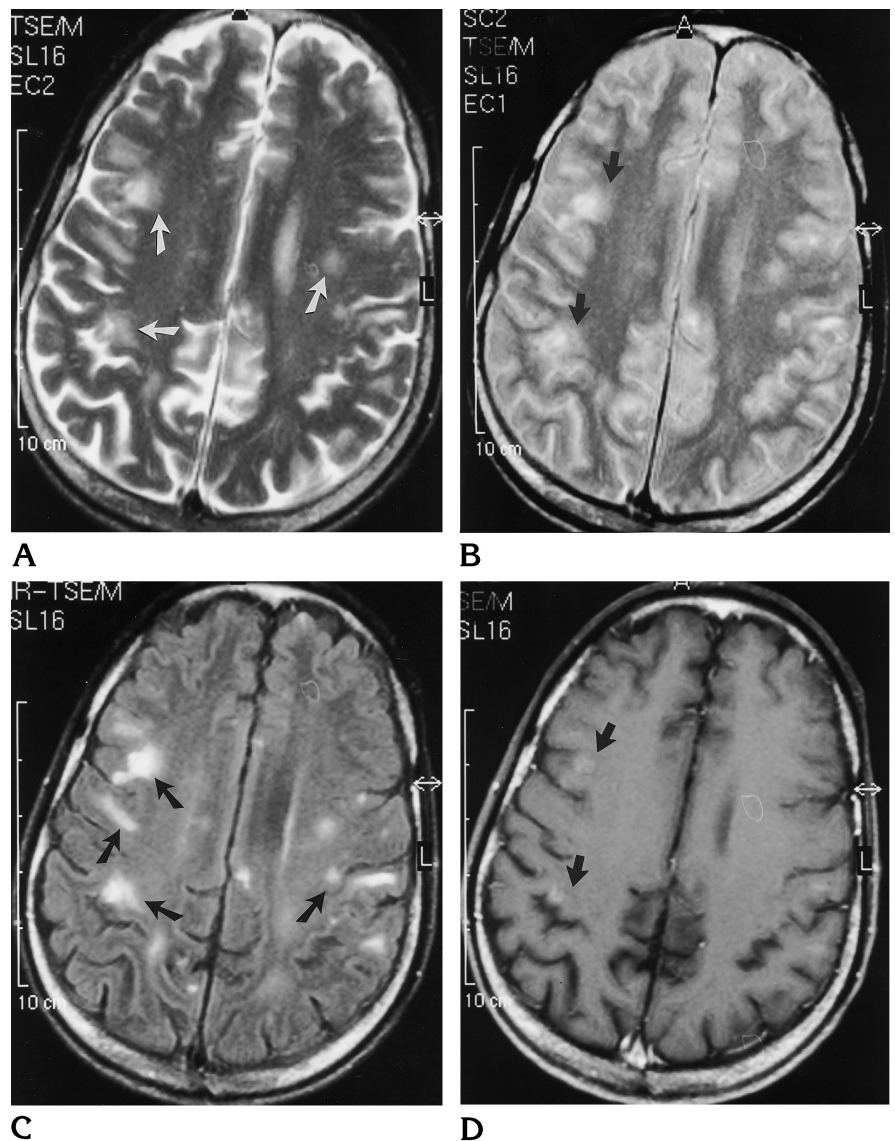
In six patients with primary cerebral lymphoma, no significant difference in lesion detec-

Fig 1. Cerebral toxoplasmosis in a patient with AIDS.

A and B, Depiction of multiple hyperintense lesions (*arrows*) and differentiation from CSF is difficult on axial T2-weighted fast spin-echo (3452/120/4) (A) and proton density-weighted (3452/23/4) (B) MR images.

C, On axial FLAIR fast spin-echo (7000/150/4; inversion time, 2100) MR image, the detection of all lesions, particularly in the subcortical region (*arrows*) of the parietal lobes, is improved relative to A and B.

D, Contrast-enhanced axial T1-weighted (550/20/1) MR image shows only a faint enhancement of some of the lesions in the subcortical regions (*arrows*). Most of the lesions do not show enhancement.



tion between the two sequences was observed. The majority of lesions were larger than 20 mm in diameter, and were easily detected with both techniques. Smaller lesions located in cortical or subcortical regions of the brain were again depicted better with the FLAIR technique (Fig 7). Differentiation of vasogenic edema from the mass itself was more obvious on FLAIR images.

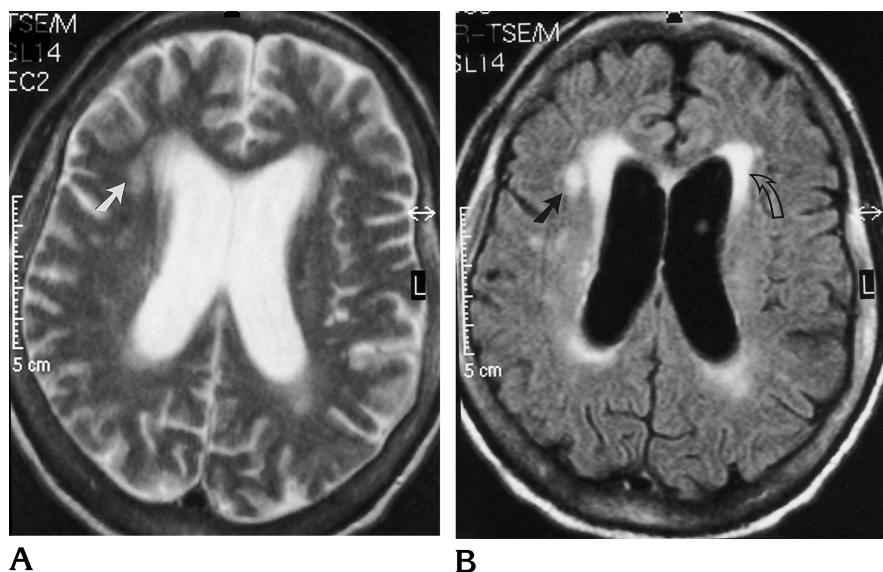
In the one patient with cerebral infarction, two lesions were detected in the right frontal lobe and right parietal lobe, respectively. Conspicuity of lesions was again better with the FLAIR sequence.

In the one patient with progressive multifocal leukoencephalopathy, in whom the diagnosis was made by autopsy, the same number of lesions was detected on both sequences; how-

ever, conspicuity was superior on images obtained with the FLAIR technique (Fig 8).

Objective Image Assessment

The contrast ratio and CNR of lesion to background and lesion to CSF were obtained for both FLAIR and T2-weighted fast spin-echo images. Quantitative analysis of lesion to background (normal adjacent white matter) showed no significant differences in contrast ratio and CNR ratio between the techniques (18.68 ± 10.39 for FLAIR fast spin-echo versus 17.83 ± 12.18 for T2-weighted fast spin-echo). Conversely, FLAIR images provided a much higher contrast ratio of lesion to CSF (-34.64 ± 20.16 for T2-weighted fast spin-echo versus 35.34 ± 13.38 for FLAIR) ($P < .0001$) (Table 2).



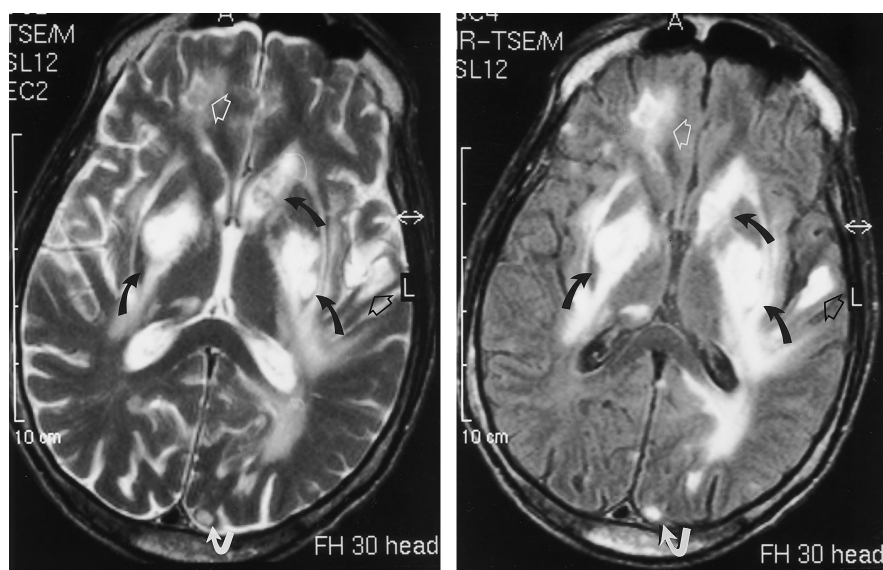
A

B

Fig 2. Autopsy-proved HIV encephalitis in an AIDS patient with dementia.

A, Axial T2-weighted fast spin-echo (3452/120/4) MR image at the level of the lateral ventricles shows hyperintensities (arrow) in the deep white matter.

B, On FLAIR fast spin-echo (7000/150/4; inversion time, 2100) MR image, these lesions (solid arrow) as well as periventricular hyperintense abnormalities (open arrow) are clearly visible.



A

B

Fig 3. Autopsy-proved cerebral toxoplasmosis in an AIDS patient. Multiple hyperintense lesions in both basal ganglia regions (solid black arrows) are well demarcated on both T2-weighted fast spin-echo (3752/120/4) (A) and FLAIR fast spin-echo (7000/150/4; inversion time, 2100) (B) MR images. Note additional lesion in the white matter of the right frontal lobe (open white arrow), which also is clearly visible with both techniques. Small lesions located in the cortical regions of the right frontal and left occipital lobe (curved white arrow), as well as the lesion in the left superior temporal gyrus (open black arrow), can be seen to better advantage on the FLAIR image.

Discussion

Like T2-weighted images, FLAIR fast spin-echo images provide contrast because most lesions display a high signal intensity; however, unlike T2-weighted images, the high CSF signal is suppressed. Our results revealed an improved lesion conspicuity of CNS lesions in HIV-positive patients on FLAIR fast spin-echo images. Regardless of the pathogenesis of the lesions, the FLAIR sequence proved to be particularly helpful in the detection of small lesions located adjacent to CSF spaces, such as those in periventricular or cortical/subcortical regions. These findings are in accord with observations

about CNS lesions in a variety of other pathologic conditions (2, 4, 5, 7, 8), and may be attributed to suppression of the CSF signal, which can obscure high-intensity lesions adjacent to CSF on T2-weighted images. Conversely, CSF collections can also be misinterpreted as lesions, because of partial volume artifacts. Thus, on FLAIR images, even small lesions adjacent to CSF can be diagnosed quite easily and confidently, whereas detection might be difficult on T2-weighted images. The subjective results are also in agreement with the objective quantitative image assessment. As in previous investigations comparing FLAIR and

Fig 4. B-cell lymphoma of the brain in a patient with (autopsy-proved) AIDS. The delineation and conspicuity of the high-signal-intensity lesions in the bilateral posterior fossa (*arrows*) are equal on both T2-weighted fast spin-echo (3752/120/4) (A) and FLAIR fast spin-echo (7000/150/4; inversion time, 2100) (B) MR images.

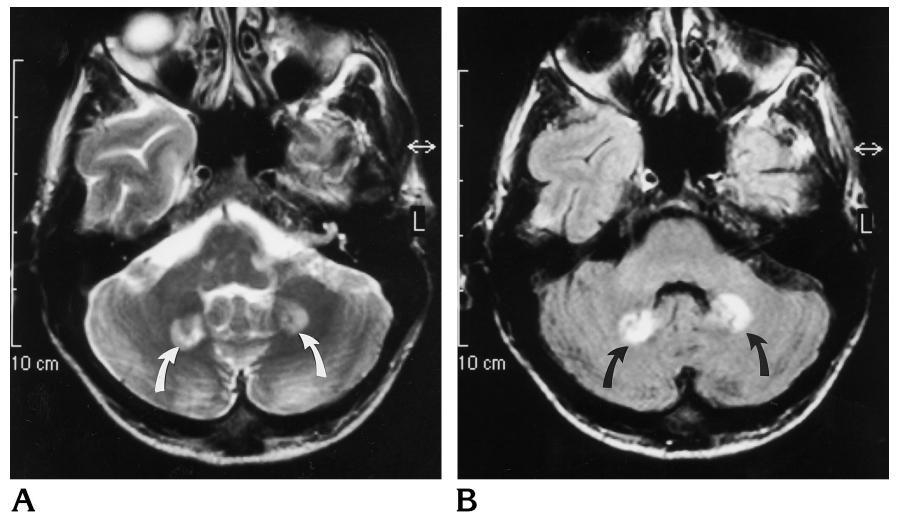
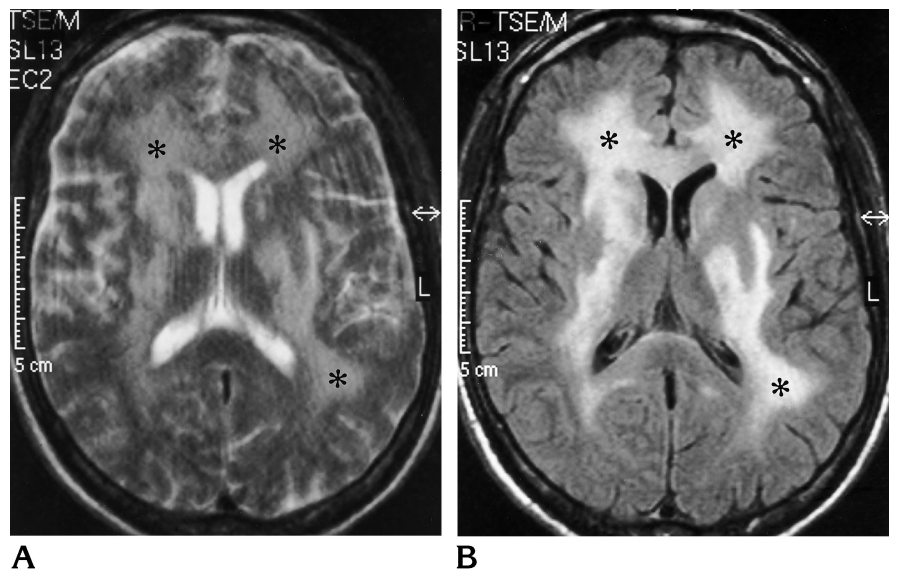


Fig 5. Autopsy-proved HIV encephalitis in a 35-year-old patient with AIDS. Diffuse white matter changes (*asterisks*) can be seen on both T2-weighted fast spin-echo (3452/120/4) (A) and FLAIR fast spin-echo (7000/150/4; inversion time, 2100) (B) MR sequences. The conspicuity is, however, slightly better in B.



T2-weighted fast spin-echo sequences (5, 6), lesion-to-background contrast ratios and CNRs were similar for both sequences without statistical significance, but lesion-to-CSF contrast ratios and CNRs were significantly higher for FLAIR than for T2-weighted fast spin-echo images. These higher lesion-to-CSF contrast ratios and CNRs are the result of the CSF signal suppression caused by the FLAIR technique. This increase in lesion-to-CSF contrast is the major factor contributing to the detection of lesions adjacent to CSF. Nonetheless, lesion-to-background contrast is not affected negatively by the FLAIR technique, and lesions surrounded by normal white matter can be delineated as well as on T2-weighted fast spin-echo images.

Because HIV encephalitis is the most com-

mon AIDS-associated CNS disease, small lesions are typically found in early stages of the disease. Early lesions of HIV encephalitis are small and focal and lack edema or mass effect, which might create problems in their detection, particularly on T2-weighted fast spin-echo images. Pathologically, microglial nodules are the hallmarks of HIV-infected brains (19). Direct infection of the brain with neurotropic HIV may also present as diffuse white matter abnormalities, but in the early stages, white matter lesions are typically small and focal (20–22). A review of MR images of 365 AIDS patients showed that 31% had white matter signal abnormalities (20). The presence of focal white matter hyperintensities can be due to the normal aging process or to other causes, such as hypertension or vascu-

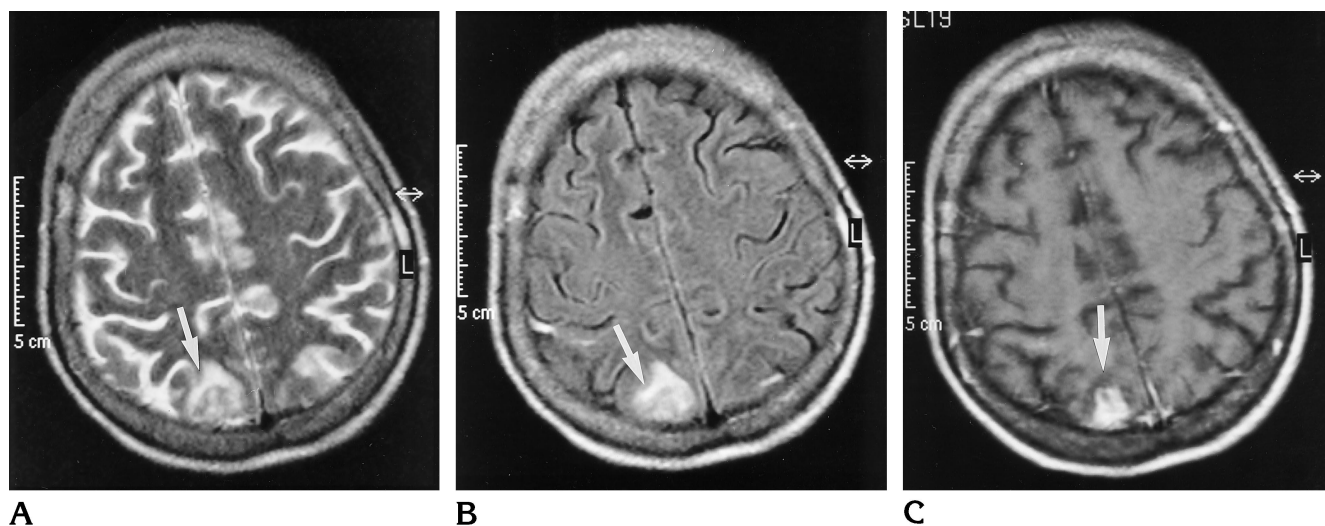


Fig 6. Autopsy-proved cerebral tuberculosis in a patient with AIDS.

A, Axial T2-weighted fast spin-echo (3752/120/4) MR image shows a hyperintense cortical lesion in the right parietal lobe (*arrow*).

B, On FLAIR fast spin-echo (7000/150/4; inversion time, 2100) MR image, the lesion is more conspicuous (*arrow*), with improved differentiation of the lesion from perifocal edema.

C, Contrast-enhanced axial T1-weighted spin-echo (550/20/1) MR image at the same level shows intense enhancement of the lesion (*arrow*).

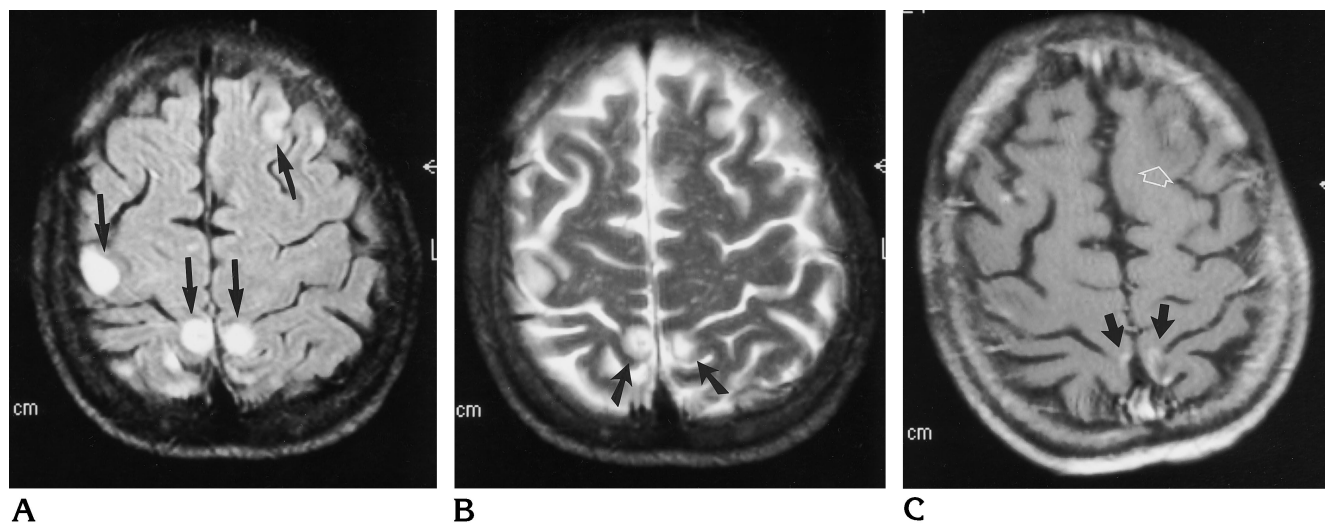


Fig 7. Multicentric cerebral non-Hodgkin lymphoma in a patient with (autopsy-proved) AIDS.

A and B, Cortical lesions (*arrows*) are seen more convincingly on FLAIR fast spin-echo (6000/120/4; inversion time, 2050) axial MR image (A) than on T2-weighted fast spin-echo (2877/120/4) axial MR image (B).

C, Contrast-enhanced T1-weighted axial MR image (550/20/1) shows faint peripheral enhancement of the bilateral parietal lesions (*solid black arrows*). The lesions in the left frontal lobe (*open white arrow*) are not enhanced.

lar disease. In the majority of AIDS patients, who are usually young, HIV encephalitis is a common cause of small white matter lesions.

Previously published studies indicate that conventional T2-weighted MR sequences are relatively insensitive in the detection of brain abnormalities and direct neural damage caused by HIV (17, 21, 22). In a study by Chrysikopoulos et al (17), in which computed tomographic

and MR imaging findings were correlated with histopathologic findings in HIV encephalitis, cortical microglial nodules seen at autopsy were not detected on MR images. Their data show that even when positive, MR imaging was grossly inadequate in demonstrating the true extent of parenchymal disease in all instances. Similarly, Grafe et al (23), in a postmortem MR study, reported that T2-weighted MR sequences

Fig 8. Progressive multifocal leukoencephalopathy in a patient with (biopsy-proved) AIDS. Extensive white matter abnormalities (*asterisk*) in the left hemisphere, with involvement of the corpus callosum (*arrow*), are well seen on T2-weighted fast spin-echo (3752/120/4) (A) and FLAIR fast spin-echo (7000/150/4; inversion time, 2100) (B) MR images.

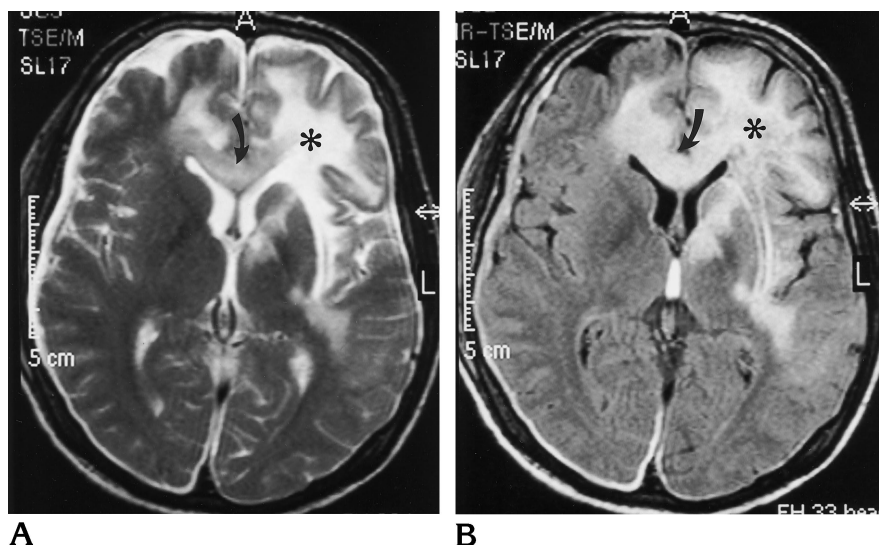


TABLE 2: Contrast ratio (CR) and contrast-to-noise ratio (CNR) of central nervous system lesions

	T2-Weighted FSE	FLAIR FSE	P
Lesion to Background			
CR \pm SD	0.23 \pm 0.12	0.24 \pm 0.10	NS
CNR \pm SD	17.83 \pm 12.18	18.68 \pm 10.39	NS
Lesion to Cerebrospinal Fluid			
CR \pm SD	-0.28 \pm 0.16	0.59 \pm 0.17	<.0001
CNR \pm SD	-34.64 \pm 20.16	35.34 \pm 13.38	<.0001

Note.—FSE indicates fast spin-echo; FLAIR, fluid-attenuated inversion recovery; and NS, not significant.

failed to show the vast majority of microglial nodules in HIV encephalitis. Less commonly, small white matter lesions and gray matter involvement can also be found in progressive multifocal leukoencephalopathy and cytomegalovirus infection. In addition, lesions that tend to have a periventricular distribution are also seen better on FLAIR than on T2-weighted sequences. Although FLAIR fast spin-echo imaging does not seem to improve the specificity of brain MR imaging in HIV-positive patients, it clearly improves the sensitivity for detecting small lesions. Since small lesions often are the first abnormalities detected, FLAIR fast spin-echo imaging might also lead to earlier and therefore more effective therapy. New antiviral therapies have been introduced in the treatment of HIV infection of the CNS, so the ability of FLAIR to show more lesions could be useful in therapeutic trials in which follow-up studies are needed to monitor the disease. Detection of more lesions earlier might also facilitate the establishment of more specific lesion patterns, but this remains subject to further investigation.

Larger brain lesions in HIV-positive patients

are more commonly found in lymphoma and toxoplasmosis but also in more advanced cases of HIV encephalitis and progressive multifocal leukoencephalopathy (15, 24). Toxoplasmosis and lymphoma lesions are often associated with a prominent inflammatory response and mass effect. These larger lesions are readily detected with both FLAIR and T2-weighted fast spin-echo techniques, but the demarcation of peritumoral edema was more easily assessed on the FLAIR fast spin-echo images. Thus, in patients with larger lesions of the brain, FLAIR images are not a necessity, but they may help to delineate tumor from surrounding edema.

The lack of pathologic correlation might represent a limitation to this study, because it was not our goal to characterize the different lesion patterns of the various entities affecting the brains of HIV-positive patients. Rather, our primary goal was to evaluate the efficacy of the FLAIR sequence in detecting lesions. Although it is known that multisection FLAIR sequences with section-selective inversion pulses are prone to some types of artifacts, such as CSF pulsation artifacts, they are easily recognizable

and discriminable from pathologic lesions (2–13, 25–29). Previous investigations have shown that small hyperintense lesions of the brain on FLAIR images represent pathologic conditions, even when they cannot be delineated on T2-weighted fast spin-echo images. Thus, T2-weighted fast spin-echo images should no longer serve as the standard of reference in the MR detection of brain lesions. On the basis of our results, we strongly recommend the incorporation of FLAIR fast spin-echo sequences into the routine MR evaluation of AIDS patients with neurologic disorders.

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