Fluid Attenuated Inversion Recovery (FLAIR) Imaging in Neuropsychiatric Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** To compare fluid attenuated inversion recovery (FLAIR) imaging with proton density/T2 weighted (PD/T2) imaging in neuropsychiatric systemic lupus erythematosus (NPSLE). Magnetic resonance imaging (MRI) is commonly used to evaluate NPSLE. However, the specific role of FLAIR versus conventional PD/T2 methods in NPSLE remains uncertain.

Methods. We studied 28 patients with NPSLE classified using the 1999 American College of Rheumatology Case Definitions for NPSLE. NPSLE disease activity and brain injury were estimated with the neurologic components of SLEDAI and SLICC, respectively. Axial T1, PD/T2, and FLAIR MR images were obtained at 1.5 Tesla. Lesions visible on PD/T2 and FLAIR imaging were quantitated, classified, and the lesion conspicuity was determined. Statistical comparisons were then made between imaging techniques.

Results. FLAIR detected significantly more lesions than PD/T2 ($p < 0.001$), resulting in a 5% greater diagnostic sensitivity, but infarct, leukoencephalopathy, and normal from abnormal were similar between the 2 methods ($p > 0.7$). Numbers of lesions by FLAIR correlated closely with lesions by PD/T2 ($r^2 = 0.97$, $p < 0.0001$). Conspicuity of individual lesions by FLAIR was greater than by PD/T2 in cortical, subcortical, and periventricular locations ($p < 0.01$). Both FLAIR and PD/T2 observations were similarly associated with NPSLE activity and NPSLE brain injury ($p < 0.02$).

Conclusion. FLAIR is more sensitive and demonstrates greater lesional conspicuity than conventional PD/T2 in NPSLE. Lesions on FLAIR are more obvious and less likely to be confused with nonlesional structures, thus FLAIR images have obvious advantages for both clinical care and didactic rounds. FLAIR is a reasonable addition to a NPSLE MRI examination, and will increase diagnostic sensitivity by about 5%. (J Rheumatol 2003;30:1983–9)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS NEUROPSYCHIATRIC NPSLE T2 MAGNETIC RESONANCE IMAGING FLAIR

Neuropsychiatric systemic lupus erythematosus (NPSLE) affects 14% to 95% of patients with SLE, resulting in a wide variety of neurologic and psychiatric syndromes, some associated with neuroimaging abnormalities[1-5]. Magnetic resonance imaging (MRI) is more sensitive than computed tomography for brain lesions associated with NPSLE, and currently MRI is the preferred anatomic neuroimaging modality[6-12]. Despite the obvious advantages of MRI, certain brain lesions found in NPSLE — especially foci of new onset ischemia, lesions close to cerebrospinal fluid (CSF) interfaces, and lesions with limited contrast from adjoining normal tissue — are challenging to discern on commonly used MRI sequences such as T1 weighted (spin-lattice relaxation time, T1), proton density (PD), and T2 weighted (spin-spin relaxation time, T2) sequences[5,13,14]. Further, without detailed neuroanatomic knowledge and MR experience, the nonradiologist clinician typically may have difficulty differentiating lesions with increased signal on T2 weighted images from normal structures with inherently higher signal, especially those close to cerebrospinal fluid-parenchyma interfaces.

Fluid attenuated inversion recovery (FLAIR) imaging produces a T2 weighted image, but with suppressed cerebrospinal fluid (CSF) signal that may be more sensitive for white matter lesions[13-15]. Accordingly, FLAIR might be expected to be more sensitive than PD/T2 images for detection of brain lesions in NPSLE, although preliminary results in autoimmune diseases have been disappointing[16-18]. We specifically compared FLAIR with PD/T2 in terms of diagnostic sensitivity, lesion conspicuity, and the specific relationship to NPSLE disease activity and injury.

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MATERIALS AND METHODS

Study population and research design. We studied 28 SLE subjects — 2 African Americans, 2 Native Americans (Navajo), 14 Hispanic, and 10 non-Hispanic Whites. Twenty-five controls were also studied to provide normative data. Each subject provided written informed consent for this study, which was approved by the institutional review board. The diagnosis of SLE was established in each subject using the American Rheumatism Association 1982 and American College of Rheumatology (ACR) 1997 revised criteria[19,20]. Overall SLE disease activity was determined with the SLE Disease Activity Index (SLEDAI), and SLE associated injury was measured with the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SLICC/ACR DI)[21-24].

Neuropsychiatric symptoms and findings were classified using the 1999 ACR Case Definitions for NPSLE[25,26]. The specific neurologic syndromes associated with NPSLE were defined as the categorical presence or absence of a NPSLE syndrome as defined by the ACR Case Definitions[25,26]. NPSLE activity (Neuro-SLEDAI) was defined as the sum of the specific neurologic components of SLEDAI (seizure, psychosis, organic brain syndrome, visual disturbance, cranial neuropathy, lupus headache, stroke syndrome)[21-23]. NPSLE injury (Neuro-SLICC) was defined as the sum of the specific neurologic components of SLICC/ACR DI (retinal or optic atrophy, cognitive disorder or psychosis, seizures, stroke syndrome, neuropathy, transverse myelitis)[24]. The Mini-Mental State examination (MMSE) was used to detect gross cognitive dysfunction[27].

MRI methods. MR neuroimaging studies were carried out as follows at each NPSLE episode. MRI data were acquired at 1.5 Tesla at 2 imaging sites using head coils for transmission of radiofrequency pulses and detection of signals. The imaging sequences included T1, PD/T2, and FLAIR sequences as follows: T1 weighted (TE 9 ms, TR 600 ms), PD/T2 weighted MR images (TE 30/100 ms, TR 3000 ms, field of view 24 × 24 cm; 5 mm slice thickness, 1 mm gap), FLAIR (TR 10000 ms, TE 145 ms, TI 2200 ms; 5 mm slice thickness, 0 mm gap) were obtained in the axial plane. Additional sequences, including diffusion weighted imaging, were performed as indicated. All images were interpreted by a neuroradiologist who was blinded to the NPSLE category and disease activity of the patient. In cases where there was acute leukoencephalopathy, repeat scans were performed within 10 days to determine the presence or absence of reversibility.

MRI findings by PD/T2 were categorized for both control and SLE subjects according to the following scales: cortical atrophy (0 = none, 1 = mild, 2 = moderate, 3 = severe), ventricular dilation (0 = none, 1 = mild, 2 = moderate, 3 = severe), small focal white matter lesions (0 = none, 1 = mild, 2 = moderate, 3 = severe), periventricular white matter abnormalities (0 = none, 1 = mild, 2 = moderate, 3 = severe), deep white matter abnormalities (0 = none, 1 = mild, 2 = moderate, 3 = severe), remote stroke (0 = none, 1 = one lesion, 2 = 2 lesions, 3 = 3 or more lesions), acute stroke (0 = none, 1 = one lesion, 2 = 2 lesions, 3 = 3 or more lesions), acute leukoencephalopathy (0 = none, 1 = one lesion, 2 = 2 lesions, 3 = 3 or more lesions), and gray matter edema (0 = none, 1 = mild, 2 = moderate, 3 = severe). For any category, a score of 1, 2, or 3 was considered "positive" and 0 was considered negative, and these were reported as ratios and percentages for the entire population, as in Table 3. The mean score for each category for each population was also calculated and is also noted in Table 3.

Discrete lesions for each PD/T2 and FLAIR were quantitated independently of each other. MRI findings were classified as follows: (1) normal: no focal or diffuse lesions on PD/T2 or FLAIR imaging; (2) abnormal: any focal or diffuse lesion on PD/T2 or FLAIR imaging; (3) small focal lesions: hyperintense focal lesions < 3 mm diameter on PD/T2 or FLAIR imaging not associated with local encephalomalacia; (4) remote infarcts: hyperintense lesions > 3 mm diameter on PD/T2 or FLAIR imaging associated with local encephalomalacia and typical changes on T1; (5) acute infarcts: hyperintense lesions on PD/T2 imaging associated with restricted diffusion by diffusion weighted imaging, but not associated acutely with local encephalomalacia, but which result in a chronic lesion and/or encephalomalacia on repeat imaging; and (6) acute leukoencephalopathy: hyperintense lesions with poorly defined borders, often following the gyri, but frequently extensive and occasionally involving deep white matter, but which resolve with time[5,9].

The relative conspicuity of these lesions was defined as (1) the qualitative difference in signal intensity between normal and pathological tissue on PD/T2 and FLAIR; and (2) the relative sharpness of the border between normal and pathological zones on PD/T2 and FLAIR[13-15]. For each study, the relative conspicuity of each lesion on each imaging sequence was directly compared and rated by the neuroradiologist as follows: (1) lesional conspicuity of FLAIR equivalent to that of PD/T2 (FLAIR = PD/T2), (2) lesional conspicuity of FLAIR greater than that of PD/T2 (FLAIR > PD/T2), and (3) lesional conspicuity of FLAIR less than that of PD/T2 (FLAIR < PD/T2).

Statistical analysis. Data were entered into Excel (Version 5, Microsoft, Seattle, WA, USA) and analyzed in SAS (Release 6.11, SAS/STAT Software, Cary, NC, USA). The paired t test was used to determine differences between the numbers of lesions by FLAIR and PD/T2. Differences in categorical data were determined with Fisher's exact test. Correlations between parametric data were determined with logistic regression and between nonparametric data with Spearman correlation.

RESULTS

Demographic data of the study cohorts are shown in Table 1. During the course of study the 28 SLE subjects experienced a total of 43 separate NPSLE episodes. Table 2 describes the various NPSLE syndromes that were present in this population at the time of imaging. Table 3 shows the lesions present in the SLE subjects compared to controls, with increased percentages of all forms of lesions as well as increased actual numbers of lesions in SLE subjects compared to controls. Figure 1 shows typical NPSLE lesions visible by both FLAIR and PD/T2. Table 4 summarizes the results reported from each of paired FLAIR and

Table 1. Demographics of the SLE and control cohorts.

	Patients with SLE	Controls
Total	28	25
Female, n (%)	25 (89)	22 (88)
Age, yrs, mean ± SD	37.7 ± 15.8	40.2 ± 6.7
Disease duration, yrs, mean ± SD	5.0 ± 4.7	0
SLE criteria, %		
ANA	100	0
Malar rash	59	0
Discoid lesions	7	0
Photodermatitis	59	0
Nasooral ulcers	85	5
Arthritis	91	0
Serositis	67	0
Renal disorder	26	0
Neurologic	59	0
Hematologic	70	0
Immunologic disorder	78	0
SLEDAI, mean ± SD	21.4 ± 5.7	NA
Neuro-SLEDAI, mean ± SD	12.2 ± 6.0	NA
Non-Neuro-SLEDAI, mean ± SD	9.2 ± 4.6	NA
SLICC/ACR DI, mean ± SD	4.19 ± 1.75	NA
Neuro-SLICC, mean ± SD	1.56 ± 1.25	NA
Non-Neuro-SLICC, mean ± SD	2.63 ± 2.10	NA

NA: not applicable.

Table 2. NPSLE syndromes within the SLE cohort.

NPSLE Syndrome	%
Any NPSLE symptom	100
Headache	33
Mood disorder	59
Cognitive disorder	78
Seizure disorder	41
Isolated seizures	22
Epilepsy	30
Acute confusional state	41
Anxiety disorder	44
Peripheral nervous system	41
Cerebrovascular disease	30
Cerebral infarction	15
Transient ischemic attack	12
Chronic multifocal disease	1
Hemorrhage	1
Sinus thrombosis	0
Psychosis	7
Movement disorder (chorea)	4
Demyelinating syndrome	4
Myelopathy	11
Aseptic meningitis	0
Autonomic disorder	7

PD/T2 scans in the NPSLE population. Across the entire data set, FLAIR revealed significantly more small focal lesions than did PD/T2 ($p < 0.001$), suggesting greater sensitivity. However, the discrimination of a normal from an abnormal scan, and the diagnoses of remote infarcts, acute infarcts, and acute lupus leukoencephalopathy were similar between the 2 methods ($p > 0.3$) (Table 4). Figure 2 illustrates the strong correlation between numbers of lesions by FLAIR compared with numbers of lesions determined by PD/T2 ($r^2 = 0.97$, $p < 0.0001$). Despite this linear association, on average FLAIR detected 21% more small focal lesions than PD/T2 ($p < 0.0001$, paired t test; Table 4).

Table 5 compares the relative conspicuity of individual types of lesions by FLAIR and PD/T2. Lesions were rated by the neuroradiologist as more conspicuous on FLAIR images, particularly in cortical, subcortical, and periventricular locations ($p < 0.01$).

To determine whether numbers of small focal lesions seen on FLAIR or PD/T2 images was associated with typical clinical measures in SLE, each was compared with Neuro-SLEDAI, Neuro-SLICC, and the MMSE. Numbers of lesions seen on FLAIR and PD/T2 images were each associated with Neuro-SLEDAI (FLAIR: $r = 0.3$, $p = 0.015$; PD/T2: $r = 0.35$, $p = 0.02$), and Neuro-SLICC (FLAIR: $r = 0.62$, $p = 0.0001$; PD/T2: $r = 0.62$, $p = 0.0001$). However, neither was significantly associated with the MMSE (FLAIR: $r = 0.1$, $p = 0.5$; PD/T2: $r = 0.11$, $p = 0.48$). Thus, both FLAIR and PD/T2 detected lesions that were statistically associated with NPSLE activity and NPSLE associated injury, and did so in a very similar manner. Neither method detected lesions that associated with cognitive dysfunction as measured by the MMSE.

Multivariate logistic regression revealed that the number of lesions seen on either of FLAIR or PD/T2 images had no independent value from each other for predicting the clinical measures: Neuro-SLEDAI (standard coefficient for FLAIR = 0.19, $p = 0.8$; standard coefficient for PD/T2 = –0.55, $p = 0.5$; total model $r = 0.37$, $p = 0.035$); Neuro-SLICC (standard coefficient for FLAIR = 0.41, $p = 0.56$; standard coefficient for PD/T2 = 0.15, $p = 0.8$; total model $r = 0.56$, $p = 0.0006$). Thus, neither FLAIR nor PD/T2 showed a statistically independent effect from the alternative method in terms of predicting NPSLE activity or NPSLE associated injury.

However, both NPSLE activity (Neuro-SLEDAI) and NPSLE injury (Neuro-SLICC) were independently associated with the number of lesions detected by FLAIR (Neuro-SLEDAI: standard coefficient = 0.44, $p = 0.0003$; Neuro-SLICC: standard coefficient = 0.61, $p = 0.0001$) and PD/T2 (Neuro-SLEDAI: standard coefficient = 0.43, $p = 0.0005$; Neuro-SLICC: standard coefficient = 0.61, $p = 0.0001$). This indicates that both NPSLE activity (Neuro-SLEDAI) and NPSLE associated injury (Neuro-SLICC) independently contribute to the total number of lesions seen on FLAIR (total model, $r = 0.71$, $p = 0.0001$) and PD/T2

Table 3. Comparison of MRI-visible lesions in patients with SLE compared to controls by PD/T2.

	Patients with SLE, n = 28 Ratio (%); Average Score	Controls, n = 25 Ratio (%); Average Score	p
Cortical atrophy	23/28 (82); 1.17 ± 0.76	13/25 (52), 0.64 ± 0.64	< 0.001
Ventricular dilation	17/28 (60); 0.76 ± 1.02	9/25 (36), 0.52 ± 0.77	< 0.001
Small focal white matter lesions	20/28 (71); 1.14 ± 0.95	10/25 (40), 0.56 ± 0.71	< 0.001
Periventricular white matter lesions	11/28 (39); 0.52 ± 0.87	3/25 (12), 0.12 ± 0.33	< 0.005
Deep white matter lesions	6/28 (21); 0.34 ± 0.72	3/25 (12), 0.16 ± 0.37	< 0.02
Remote stroke	7/28 (25); 0.31 ± 0.54	0/25 (0), 0.0	< 0.001
Acute stroke	5/28 (18); 0.24 ± 0.58	0/25 (0), 0.12 ± 0.33	< 0.001
Acute leukoencephalopathy	3/28 (11); 0.21 ± 0.77	0/25 (0), 0.12 ± 0.33	< 0.03
Gray matter edema	4/28 (14); 0.21 ± 0.56	0/25 (0), 0.12 ± 0.33	< 0.01
No. of small focal white matter lesions	8.91 ± 11.23	4.37 ± 5.5	< 0.01

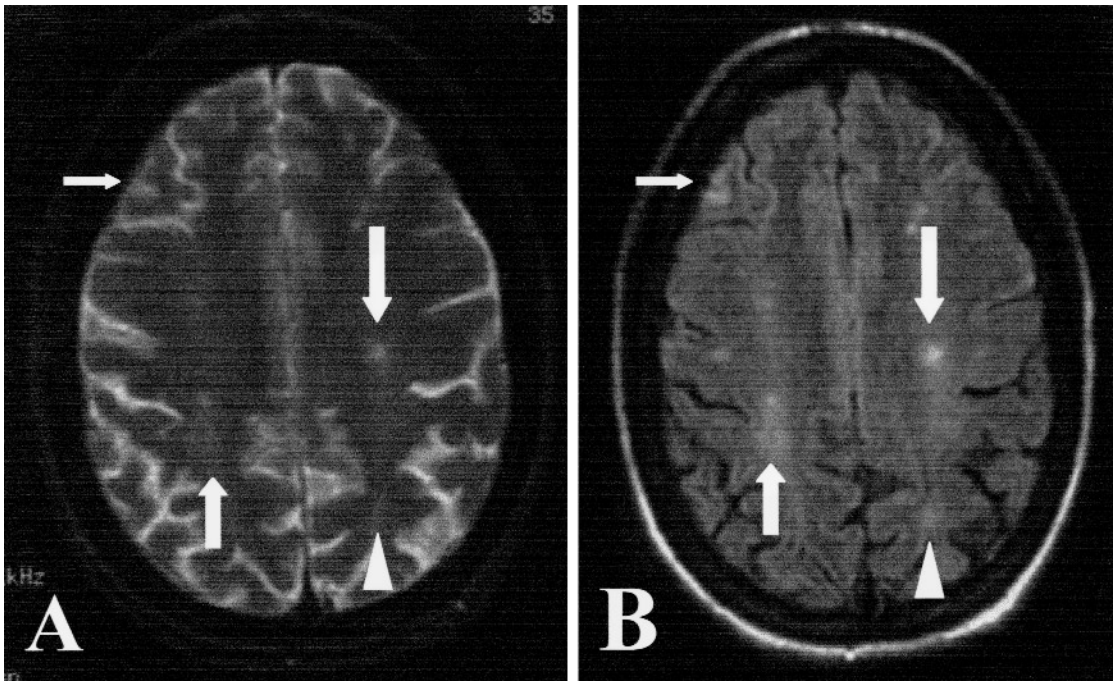

Figure 1. FLAIR and T2 in neuropsychiatric SLE. A. An axial slice showing CSF and cortical, subcortical, and deep white matter lesions by conventional T2 (TE 100 ms, TR 3000 ms). B. The same slice by FLAIR (TR 10000 ms, TE 145 ms, TI 2200 ms). Comparing A with B, the signal from CSF is markedly attenuated (darker) with FLAIR, and the lesions (areas of increased signal) have greater conspicuity on FLAIR relative to the T2 image. The focal and diffuse, ill-defined lesions (medium size arrow on both figures) are more visible on FLAIR (B) compared to T2 (A). Although the larger focal white matter lesion (large arrow on both images, representing a small infarct) is visible in the T2 image (A), the conspicuity is far better on the FLAIR image (B). Similarly, the ill-defined white matter lesions in the distal lobes (arrowhead) are barely visible on the T2 weighted image (A), but are much more obvious on the FLAIR image (B). Finally, the cortical/subcortical lesion (a reversible lesion typical of lupus acute leukoencephalopathy) in the frontal lobe (smallest arrow in both figures) is not apparent at all by T2 (A), but is obvious by FLAIR (B).

Table 4. Relative sensitivity of FLAIR and PD/T2 for detecting typical NPSLE lesions.

	FLAIR	PD/T2	p
Abnormal scans/total scans* (%)	35/43 (81)	33/43 (78)	0.60
Small focal lesions**	10.84 ± 12.6	8.91 ± 11.23	< 0.0001
Remote infarcts** (%)	16/16 (100)	15/16 (93)	0.316
Acute infarcts*** (%)	10/10 (100)	10/10 (100)	1.0
Acute leukoencephalopathy† (%)	4/4 (100)	4/4 (100)	1.0

* Total of 43 scans performed in the 28 subject cohort. ** Cross-sectional analysis of one scan each in 28 subjects. Paired Student t-test. *** Defined by FLAIR imaging and characteristic T1 weighted imaging. † Defined by FLAIR imaging, characteristic diffusion weighted imaging, and persistence of a chronic lesion and/or appearance of encephalomalacia on repeat imaging.

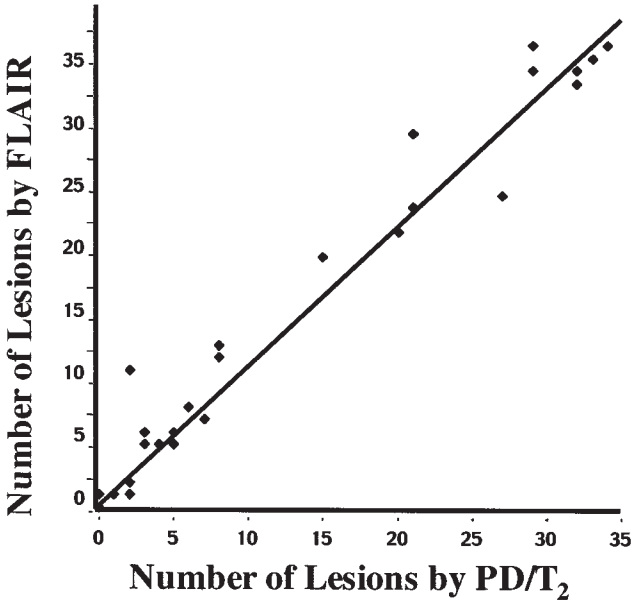

Figure 2. The close relationship between FLAIR and PD/T2 imaging for focal lesions ($r = 0.98$, $r^2 = 0.97$, $p < 0.0001$). Although the relationship is clearly linear, the slope is not unity; thus, for each point on the curve, there are more lesions by FLAIR than by PD/T2.

Table 5. Comparisons of conspicuity of lesions between FLAIR and PD/T2.

Lesion Type	Conspicuity, FLAIR > PD/T2 (%)	p
Deep white matter lesions	7/33 (21)	0.005
Cortical/subcortical lesions	24/36 (67)	< 0.0001
Paraventricular lesions	11/13 (85)	< 0.0001
Remote infarcts	1/16 (6)	0.38
Acute infarcts	2/10 (20)	0.14
Acute leukoencephalopathy	4/4 (100)	< 0.005

(total model, r = 0.70, p = 0.0001). These data indicate that lesions seen by FLAIR and PD/T2 in any individual examination could be a measure of current NPSLE activity, cumulative NPSLE associated injury, or both.

DISCUSSION

MRI is considered the method of choice to detect anatomic lesions of the brain in NPSLE[5-10]. PD/T2 imaging provides paired proton density and T2 weighted series, and is a central component of contemporary NPSLE MRI examinations. Using PD/T2 imaging, chronic lesions may be observed in 25–50% of SLE cases[28-32]. Small punctate focal lesions in white matter, especially in frontoparietal regions, are most common (15–60%), followed in prevalence by periventricular white matter changes, diffuse white matter changes, and infarct[8,9,30-37]. Recent evidence suggests that all focal lesions in NPSLE represent neuronal or vascular injury[29,31,38,39]. Lesions on PD/T2 images associated with active NPSLE include new infarct, discrete gray matter lesions, diffuse gray matter and subcortical white matter hyperintensities, and cerebral edema; however, small focal white matter lesions only correlate poorly with current neuropsychiatric signs and symptoms[8,9,13,30,31,36,40]. In this study, our SLE cohort experienced virtually all these abnormalities, as well as an increased prevalence of lesions, lesion scores, and actual lesion numbers relative to controls, confirming the increased prevalence of brain lesions in SLE noted in previous studies (Table 3).

With PD/T2 sequences, differences in signal intensity are most influenced by changes in mobile proton content (water) and in the intrinsic relaxation times (T1 and T2) of protons in that particular tissue[41-43]. The ability to recognize individual lesions on PD/T2 images depends on image contrast arising from the difference in T2 signal intensity between normal and pathological tissue and the presence of a relatively sharp border between these zones. Together, these properties describe the conspicuity of a lesion on a T2 weighted image[14,41,42]. The development of hyperintensity on T2 weighted images is thought to be caused by a focal increase of roughly 3% water relative to overall brain water content; if changes are less than this, the lesions might be less obvious by PD/T2 even though histopathological changes might be present[13,43-49]. Although PD/T2 sequences provide adequate lesion conspicuity in most instances, these sequences often fail to detect lesions with minor differences in T2, lesions that abut CSF (ventricles and subarachnoid space), and lesions close to areas of preexisting encephalomalacia[13-15]. These structures and lesions have increased free water, and thus exhibit a longer T2, obscuring adjoining lesions with similar relaxation properties[13-15,44-47].

Although fundamentally a T2 weighted method, FLAIR imaging employs the differential spin-lattice relaxation (T1) of CSF and parenchyma to null the signal from CSF[13-15,45-47]. This is accomplished by adding a 180° inversion pulse before the normal T2 weighted acquisition sequence. This inversion pulse is followed by a delay (inversion time, TI) of 2000 to 2600 ms, when the signal from ventricular and subarachnoid CSF and other free fluid-containing structures is nulled. Signals from normal parenchyma and lesions that have more efficient spin-lattice relaxation characteristics have already recovered past the null point and are then acquired by the T2 weighted sequence. When sequences are optimized, the effect is dramatic — CSF becomes hypointense (dark), while lesions become more conspicuous, particularly in areas close to tissue-fluid boundaries such as the ventricles, cortical sulci, and preexisting lesions with encephalomalacia (Figure 1). These FLAIR images have obvious advantages for the nonradiologist clinician in that CSF-containing structures have decreased signal (darkness) and are much less likely to be confused with lesions that generally have increased signal (brightness).

FLAIR has been used extensively in vascular dementia, stroke, multiple sclerosis, and other white matter diseases, and has generally been found to be more sensitive than conventional PD/T2[13-15,18,45-47,50]. Accordingly, FLAIR might have advantages for imaging in NPSLE, especially since periventricular and subcortical lesions that border CSF are common in NPSLE and have proven difficult to resolve on PD/T2 images[5,7-9,43,44]. Despite this promise, early results of FLAIR imaging in autoimmune brain disease have been disappointing[16-18]. Appenzeller, *et al* found that both FLAIR and PD/T2 revealed similar patterns of small punctate lesions in autoimmune meningoencephalitis[16]. Rovaris, *et al* directly compared FLAIR and PD/T2 using both lesion number and lesion volume quantification, and found that the 2 techniques provided similar results, although absolute lesion numbers were somewhat greater with T2 compared to FLAIR[17]. Using FLAIR, Tourbah, *et al* demonstrated some improved lesion detection in a mixed group of patients with white matter disease, especially in the paracortical areas, paraventricular regions, and internal capsule[18].

In our study of NPSLE, we observed greater lesion conspicuity with FLAIR compared to PD/T2 (Table 5). Okuda, *et al* also noted both greater qualitative and quantitative lesion conspicuity with FLAIR in patients with multiple sclerosis, but noted that FLAIR had an increased

false positive rate, that is, falsely identified normal structures as lesions[51]. Tourbah, *et al* also noted that FLAIR falsely identified normal sulci as lesions, indicating that FLAIR may have a higher false positive rate than conventional sequences[18]. However, in our study based on T1 weighted images, we did not observe an increased false positivity for lesions for the FLAIR method, although admittedly we could not quantify false positivity for lesions since autopsy and histological confirmation were not an option in this living cohort.

We compared FLAIR with PD/T2 in order to determine (1) overall diagnostic sensitivity, (2) conspicuity and diagnosis of specific lesions, (3) the relationship to overall clinical measures, and (4) whether the lesions determined by FLAIR and PD/T2 were related specifically to NPSLE activity or NPSLE associated injury. In terms of overall diagnostic sensitivity (normal versus abnormal), FLAIR and PD/T2 were very similar (Table 4), consistent with previous reports[16-18]. However, FLAIR was definitely superior in terms of conspicuity in the cortex, subcortical white matter, and periventricular areas (Figure 1, Table 5). This is similar to findings in other diseases including ischemia, stroke, and multiple sclerosis, and suggests a superiority of FLAIR in those anatomic regions in close association with CSF[13-15,18,45-47,50]. FLAIR also revealed an increased number of small focal lesions (approximately 21% more lesions) versus PD/T2 ($p < 0.0001$; Table 2). Despite this obvious increase in sensitivity for small focal lesions, FLAIR increased the overall diagnostic sensitivity (that is, final radiologic diagnosis) for NPSLE only 5%, a modest improvement (Table 2).

To determine the relationship of neuroimaging findings to typical clinical features of NPSLE, small focal lesions by FLAIR or PD/T2 were compared with the neurological components of SLEDAI, SLICC/ACR DI, and the MMSE. Numbers of lesions identified on either of FLAIR or PD/T2 were virtually equivalent in terms of predicting these clinical measures. However, these clinical measures were independently associated with the number of small focal lesions seen by either FLAIR or PD/T2, indicating that lesions by FLAIR and PD/T2 may be related to current NPSLE activity, NPSLE associated injury, or both, depending on the clinical situation. Thus, lesions revealed by either FLAIR or PD/T2 must be interpreted with caution, as they may represent either current or established injury. Neither FLAIR nor PD/T2 can definitively segregate these diagnostic possibilities.

In summary, FLAIR is superior to PD/T2 in detecting lesions typical of NPSLE, but FLAIR results in only a small improvement of 5% in overall diagnostic sensitivity. It cannot be recommended at this time to completely replace PD/T2 with FLAIR, especially in light of the sensitivity of promising quantitative T2 methods that use conventional sequences[43,44]. However, for the nonradiologist, lesions on FLAIR are more obvious and less likely to be confused with nonlesional structures, and thus FLAIR images have obvious advantages for both clinical care and didactic rounds. For the radiologist, FLAIR is a reasonable addition to an MRI examination in NPSLE, and will increase diagnostic sensitivity by about 5%.

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