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Gray-matter-specific MR imaging improves the detection of epileptogenic zones in focal cortical dysplasia: A new sequence called fluid and white matter suppression (FLAWS)

Xin Chen[a,b,1], Tianyi Qian[b,c,1], Tobias Kober[d,e,f], Guojun Zhang[g], Zhiwei Ren[g], Tao Yu[g], Yueshan Piao[h], Nan Chen[a,b,*], Kuncheng Li[a,b]

[a] Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing, PR China
[b] Beijing Key Laboratory of Magnetic Resonance Imaging and Brain Informatics, Beijing, PR China
[c] MR Collaborations NE Asia, Siemens Healthcare, Beijing, PR China
[d] Advanced Clinical Imaging Technology, Siemens Healthcare HC CEMEA SUI DI PI, Lausanne, Switzerland
[e] Department of Radiology, University Hospital (CHUV), Lausanne, Switzerland
[f] LTS5, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland
[g] Department of Functional Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing, PR China
[h] Department of Pathology, Xuanwu Hospital, Capital Medical University, Beijing, PR China

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ABSTRACT

Objectives: To evaluate the diagnostic value and characteristic features of FCD epileptogenic zones using a novel sequence called fluid and white matter suppression (FLAWS).

Materials and methods: Thirty-nine patients with pathologically confirmed FCD and good surgery outcomes (class I or II, according to the Engel Epilepsy Surgery Outcome Scale) were retrospectively included in the study. All the patients underwent a preoperative whole-brain MRI examination that included conventional sequences (T2WI, T1WI, two-dimensional (2D) axial, coronal fluid-attenuated inversion recovery [FLAIR]) and FLAWS. An additional 3D-FLAIR MRI sequence was performed in 17 patients. To evaluate the sensitivity and specificity of FLAWS and investigate the cause of false-positives, 36 healthy volunteers were recruited as normal controls. Two radiologists evaluated all the image data. The detection rates of the FCD epileptogenic zone on different sequences were compared based on five criteria: abnormal cortical morphology (thickening, thinning, or abnormally deep sulcus); abnormal cortical signal intensity; blurred gray-white matter junction; abnormal signal intensity of the subcortical white matter, and the transmantle sign. The sensitivity and specificity of FLAWS for detecting the FCD lesions were calculated with the reviewers blinded to all the clinical information, i.e. to the patient identity and the location of the resected regions. To explore how many features were sufficient for the diagnosis of the epileptogenic zones, the frequency of each criterion in the resected regions and their combinations were assessed on FLAWS, according to the results of the assessment when the reviewers were aware of the location of the resected regions. Based on the findings of the 17 patients with an additional 3D-FLAIR scan when the reviewers were aware of the location of the resected regions, quantitative analysis of the regions of interest was used to compare the tissue contrast among 2D-axial FLAIR, 3D-FLAIR, and the FLAWS sequence. Visualization score analysis was used to evaluate the visualization of the five features on conventional, 3D-FLAIR, and FLAWS images. Finally, to explore the reason for false-positive results, a further evaluation of the whole brain FLAWS images was conducted for all the subjects.

Results: The sensitivity and specificity for detecting the FCD lesions on the FLAWS sequence were 71.9% and 71.1%, respectively. When the reviewers were blinded to the location of the resected regions, the detection rate of the FLAWS sequence was significantly higher than that of the conventional sequences ($P = 0.00$). In the 17 patients who underwent an additional 3D FLAIR scan, no statistically significant difference was found between the FLAWS and the 3D-FLAIR ($P = 0.25$). All the patients had at least two imaging features, one of which was "the blurred junction of the gray-white matter." The transmantle sign, which is widely believed to be a specific feature of FCD type II, could also be observed in type I on the FLAWS sequence. The relative tissue contrast of FLAWS was higher than that of the 2D-FLAIR with respect to lesion/white matter (WM), deep gray matter (GM)/

* Corresponding author at: No. 45 Chang-Chun St., Xicheng District, Beijing 100053, PR China.
E-mail address: chenzen8057@sina.com (N. Chen).
[1] The first two authors contributed equally to this work.

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WM, and cortex/WM ($P = 0.00$ for all three measures) and higher than that of the 3D-FLAIR with respect to the lesion/WM ($P = 0.01$). The visualization score analysis showed that the visualization of FLAWS was more enhanced than that of the conventional and 3D-FLAIR images with respect to the blurred junction ($P = 0.00$ for both comparisons) and the abnormal signal intensity of the subcortical white matter ($P = 0.01$ for both comparisons). The thin-threadlike signal and individual FCD features outside the epileptogenic regions were considered the primary cause of the false-positive results of FLAWS.

Conclusions: FLAWS can help in the detection of FCD epileptogenic zones. It is recommended that epileptogenic zone on FLAWS be diagnosed based on a combination of two features, one of which should be the "blurred junction of the gray-white matter" in types I and II. In type III, the combination of "the blurred junction of the gray-white matter" with "abnormal signal intensity of subcortical white matter" is recommended.

1. Introduction

Focal cortical dysplasia (FCD) is an underlying cause of seizures in some patients. A complete resection of the epileptogenic zone is critical for eliminating these seizures (Oluigbo et al., 2015; Rowland et al., 2012). As a non-invasive imaging method with multi-contrasts, magnetic resonance imaging (MRI) plays an important role in pre-operative epileptogenic zone localization. However, approximately 22–38% of FCD patients have negative findings on conventional MRI (Kim et al., 2011; Lerner et al., 2009). As the effectiveness of identifying the epileptogenic zones largely depends on the hardware (e.g., field strength) and software (e.g., MR sequences and post-processing methods) of MRI, as well as the experience of the reader and the MR methods (Duncan et al., 2016), improvements in these factors are needed.

In recent years, several new sequences, such as three-dimensional fluid-attenuated inversion recovery (3D FLAIR) (Saini et al., 2010; Tschampa et al., 2015) and 3D double inversion recovery (3D-DIR) (Soares et al., 2016; Wong-Kisiel et al., 2016), have been used to improve the contrast of the cortex. However, the application of these sequences is limited due to several reasons. First, most studies currently show the superiority of the new sequence through measuring quantitative parameters, such as rating the visual score or measuring the signal-to-noise ratio or tissue contrast, on different types of images. Consequently, they only choose visible lesions on the images. Because the primary objective of applying novel sequences in epilepsy is to improve the detection of epileptogenic zones (defined as cortical areas responsible for seizure generation) that cannot be identified using conventional MRI, it is necessary to recruit patients with negative findings on conventional MRI and with good surgery outcomes. Second, although it is widely believed that five typical MRI features can help to visually identify FCD on conventional sequences (Bernasconi et al., 2011), including abnormalities of the cortex (abnormal cortical morphology, signal increase on T2WI) and the subcortical white matter (blurred junction of the gray-white matter, T2 signal increase, and transmantle sign), there is only one study for type II FCD (Mellerio et al., 2012), that has clearly stated how many features are sufficient for the diagnosis of epileptogenic zones on MRI. Third, it may be difficult to identify lesions from false-positive results caused by the techniques themselves, which have too high a sensitivity and a low specificity (Duncan et al., 2016; Woermann and Vezina, 2013).

In this study, we applied in FCD a new sequence known as fluid and white matter suppression (FLAWS) (Tanner et al., 2012). This sequence provides three different high spatial resolution anatomical images in one scan. First, FLAWS acquires two sets of 3D high spatial resolution images at two different inversion times (TI): TI1, which suppresses the white-matter (WM) signal (WM-nulled image), and TI2, which suppresses the cerebrospinal fluid (CSF) signal (CSF-nulled image). Subsequently, a set of synthetic minimum FLAWS-contrast images is calculated based on the two previously mentioned sets of images, and this suppresses both the WM and CSF signals (gray-matter-specific). Because FCD is caused by localized cortical disruptions of neuronal proliferation and organization (Prayson et al., 2002; Taylor et al., 1971), the gray matter-specific images have the potential to improve the visualization of the FCD epileptogenic zones. To our knowledge, there is to date no published research on the application of FLAWS in FCD. The purpose of this study was to explore whether the FLAWS sequence could help in the detection of FCD epileptogenic zones and to facilitate the application of FLAWS in clinical practice.

2. Methods and materials

Thirty-nine patients with pathologically-confirmed FCD were recruited from our Xuanwu Hospital between October 2014 and July 2017 and retrospectively included in this study. Each patient had a preoperative MRI examination including conventional and FLAWS scans. Their surgical outcomes were categorized as class I or II, according to the Engel Epilepsy Surgery Outcome Scale (Engel, 1993), which were defined as good surgery outcomes. An additional pre-operative 3D-FLAIR scan was performed on 17 patients. This study was approved by the Ethics Committee of Xuanwu hospital. Written informed consent was obtained from each participant.

To evaluate the sensitivity and specificity of FLAWS and investigate the cause of any misdiagnoses, healthy volunteers were recruited as normal controls.

Table 1
Scan parameters for the FLAWS, 3D-FLAIR, and conventional sequences.

	FLAWS	3D-FLAIR	2D-FLAIR	2D-FLAIR	T1WI	T2WI	DWI
TR/TE (ms)	5000/2.88	6000/395	8500/85	8500/88	160/3.05	3800/93	5500/90
TI (ms)	TI1/TI2 409/1100	2100	2371.5	2439			
Flip angle (degree)	FA1/FA2 5/5	T2 var	150	150	70	150	90
Matrix	256 × 256	256 × 256	256 × 180	256 × 256	256 × 205	256 × 256	136 × 136
Slices thickness (mm)	1.0	1.0	3.0	3.0	3.0	3.0	3.0
BW (Hz/px)	310	781	287	201	360	219	1598
Orientation	Sagittal	Sagittal	Axial	Coronal	Axial	Axial	Axial
FOV (mm)	256	250	240	230	240	240	240
iPAT	2	2	2	2	2	2	2
Scan time (sec)	657	422	114	104	38	36	40

2D, two-dimensional; 3D, three-dimensional; BW, band width; DWI, diffusion weighted imaging; FLAIR, fluid-attenuated inversion recovery; FLAWS, fluid and white matter suppression; WM, white matter; FOV, field of view; TE, echo time; TI, inversion time; TR, repetition time.