




# The Role of the Three-Dimensional Edge-Enhancing Gradient Echo Sequence at 3T MRI in the Detection of Focal Cortical Dysplasia: A Technical Case Report and Literature Review

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## Abstract

**Introduction** Focal cortical dysplasia (FCD) is a most common cause of intractable focal epilepsy in children. Surgery is considered as a radical option for such patients with the prerequisite of lesion detection. Magnetic resonance imaging (MRI) plays a significant role in detection of FCDs in epilepsy patients; however, the detection of FCDs even in epilepsy dedicated MRI sequence shows relatively low positive rate. Last year, Middlebrooks et al introduced the novel three-dimensional Edge-Enhancing Gradient Echo (3D-EDGE) MRI sequence and using this sequence successfully identified five cases of FCDs which indicates its potential role in those epilepsy patients who may have FCDs.

**Case Presentation** We present a 14-year-old, right-handed, male patient who has suffered from drug-resistant epilepsy over the past 3 years. It was unable to localize the lesion of the seizure, even using the series of epilepsy dedicated MRI sequences. Inspired by the previous report, the lesion of the seizure was successfully targeted by 3D-EDGE sequence. Combined with intraoperative navigation and precisely removed the lesion. He was uneventfully recovered with no signs of cerebral dysfunction and no seizure recurrence 8 months after surgery.

**Conclusion** The 3D-EDGE sequences show a higher sensitivity for FCD detection in epilepsy patients compared with a series of epilepsy-dedicated MRI protocols. We confirmed that the study by Middlebrooks et al is of great clinical value. If the findings on routine MRI sequences or even epilepsy-dedicated MRI sequences were reported as

## Keywords

- 3D-EDGE
- focal cortical dysplasia
- drug-resistant epilepsy
- MRI sequences

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negative, however, the semiology, video-electroencephalography, and fluorodeoxyglucose–positron emission tomography results suggest a local abnormality, and the results are concordant with each other, a 3D-EDGE sequence may be a good option.

## Introduction

Focal cortical dysplasia (FCD) is a localized cerebral cortical malformation frequently associated with medically intractable epilepsy in children.<sup>1,2</sup> Epilepsy surgery is a well-established option for remediating patients with drug-resistant epilepsy, and accurately locating epileptogenic focus is the key to successful surgical resection.<sup>3</sup> The majority of patients with cryptogenic epilepsy have FCDs that, even with epilepsy-specific magnetic resonance imaging (MRI) protocols, are difficult to detect.<sup>4–7</sup> Last year, Middlebrooks et al<sup>8</sup> introduced a novel three-dimensional Edge-Enhancing Gradient Echo (3D-EDGE) MRI sequence and successfully identified five cases of FCD, indicating a potential role for this technique in detecting FCDs.

In this report, we used the new 3D-EDGE MRI sequence to successfully detect a drug-resistant epilepsy patient who was reported as negative on epilepsy dedicated MRI sequences and discussed the clinical value of the 3D-EDGE sequence.

## Case Presentation

Our patient was a 14-year-old, right-handed boy with no notable prior medical history and no family history of epilepsy. When he was 11 years of age, he experienced the onset of myoclonic jerks which affected his right arm and right leg without disturbing consciousness, occurred four to five times per day, and lasted approximately 20 seconds each time. Two months later, the myoclonic jerks evolved into secondarily generalized tonic-clonic (GTC) seizures. After the first GTC seizure, he was started on 500-mg bd levetiracetam and 600-mg bd oxcarbazepine. Over the next 3 years, the frequency of his myoclonic jerks gradually increased to 10–15 times per day and was refractory to different combination treatments of levetiracetam, valproate, and oxcarbazepine. Due to no obvious abnormal lesions were found on epilepsy-dedicated MRI sequences, a stereotactic EEG (SEEG) was planned at another hospital to locate the epileptic focus. However, his parents refused the SEEG procedure for financial reasons.

## Methods

The patient was examined by MRI, fluorodeoxyglucose–positron emission tomography (FDG-PET; interictally), and video-electroencephalography (V-EEG) monitoring (ictally and interictally). MRI scanning was performed on a 3-Tesla (3T) Siemens Skyra (Siemens Healthineers AG, Erlangen, Germany) with an eight-channel head coil. The standard protocols included a 3D T1-MPRAGE, two-dimensional (2D) T2-transmissible spongiform encephalopathies (TSE), 3D T2-fluid-attenuated inversion recovery (FLAIR), 3D T1-magnetization-prepared 2 rapid acquisition gradient echo (MP2RAGE), double inversion recovery (DIR), as well as the novel 3D-EDGE se-

quence. All the sequences were scanned at the same time and we obtained the following images as shown in ►Fig. 1.

According to the method of literature, the mean signal intensity of the “transmantle sign” and the mean signal intensity of the normal contralateral white matter (WM) was calculated, and we compared the contrast ratio of 3D-EDGE (mean signal intensity of transmantle)/3D-EDGE (mean signal intensity of contralateral WM) to FLAIR (mean signal intensity of transmantle)/FLAIR (mean signal intensity of contralateral WM) and all other sequences. The key parameters that we adjusted for the novel 3D-EDGE sequence included: inversion time (TI) = 445 ms with a flip angle of 8 degrees, repetition time (TR) = 2,000 ms, echo time (TE) = 2.12 ms, isotropic resolution of 1 mm × 1 mm × 1 mm, receiver bandwidth = 270 Hz/Px, echo spacing = 6.40 ms, turbo factor = 154, generalized autocalibration partially parallel acquisition (GRAPPA) = 2, and slice partial Fourier = 7/8. The resultant acquisition time was 5:20 minute.

## Results

Of the six MRI sequences used, abnormalities were found only on the 3D-EDGE imaging. This sequence showed a 2-cm subcortical hypointensity that combined with a transmantle sign that originated from the bottom of a left lateral paracentral lobule and terminated toward the upper wall of the left lateral ventricle ependymal surface, features typical of a type-IIb FCD (►Fig. 1F–F2). The contrast ratio for the transmantle sign was greater on the 3D-EDGE images compared with MPRAGE (78 vs. 1%), FLAIR (78 vs. 5%), MP2RAGE (78 vs. 1%), and DIR (78 vs. 10%). Combined with the cases provided in literature and our case, contrast ratio of lesions in six patients on 3D-EDGE sequence was compared with the typical sequences of epilepsy, FLAIR, and MP2RAGE. 3D-EDGE sequence shows the highest contrast ratio (►Supplementary Fig. S1, available in the online version).

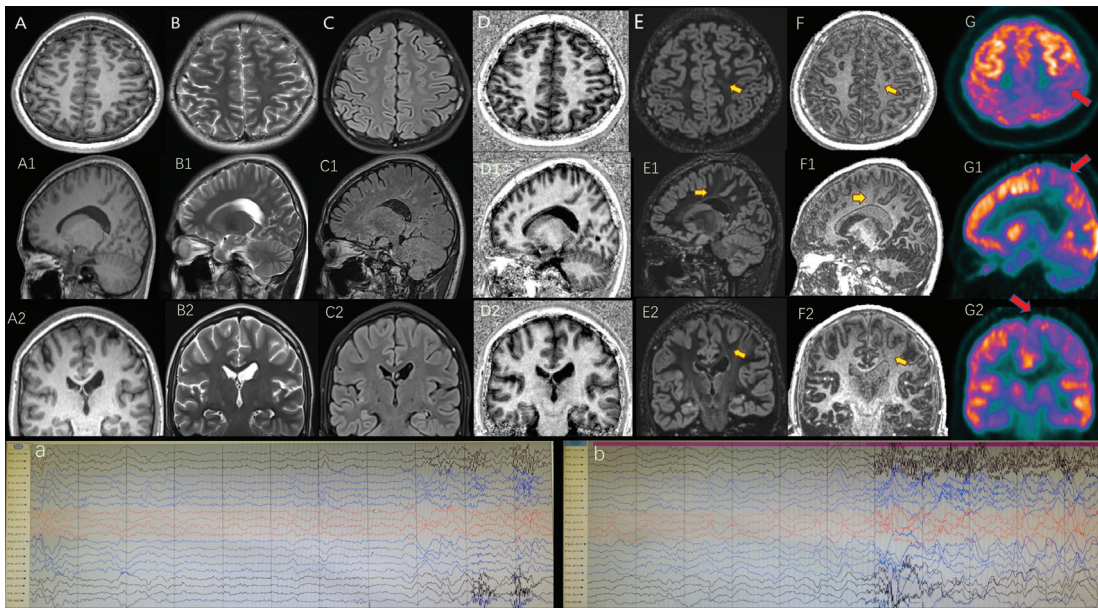
The FDG-PET study showed regional glucose hypometabolism bilaterally in the paracentral lobule, lobulus parietalis superior, precentral gyrus, and postcentral gyrus which was thought to be reflective of interictal metabolic changes (►Fig. 1G–G2).

The V-EEG showed interictal slow-wave activity, intermittent spike-waves, and sharp waves predominantly in the left central-parietal area (►Fig. 1a). Ictal abnormal EEG changes are associated with myoclonic jerks (►Fig. 1b).

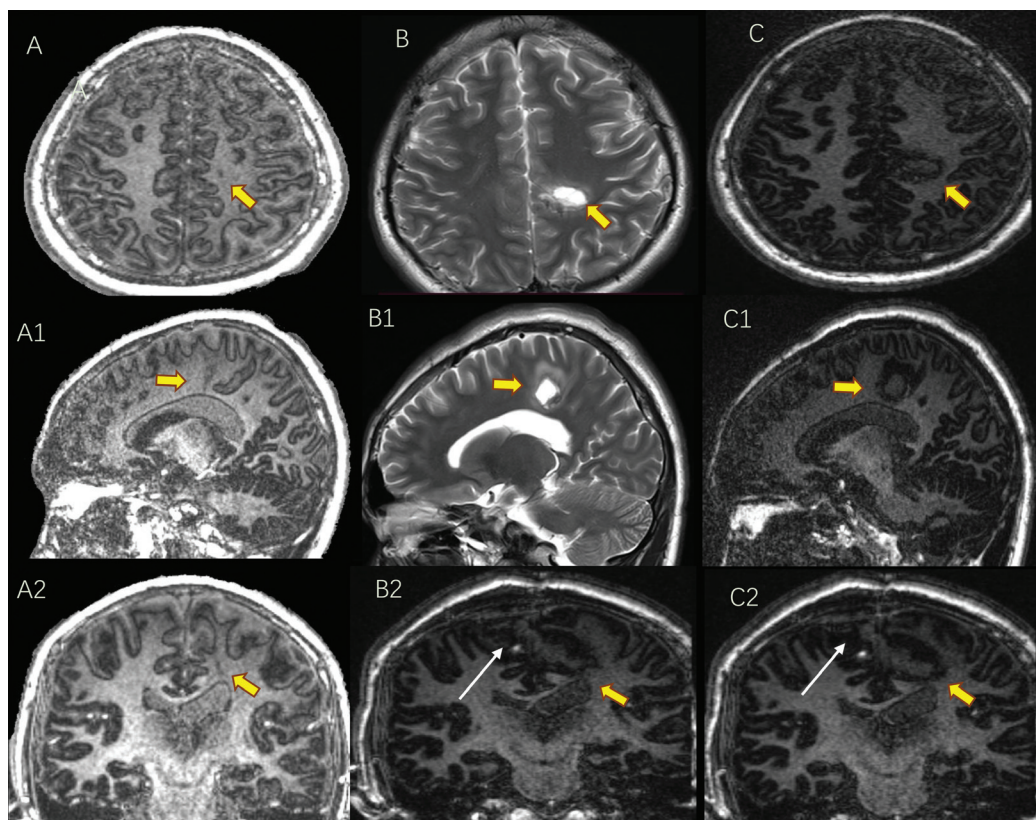
## Discussion

All FCD subtypes may exhibit some degree of abnormal gray matter-WM (GM-WM) border boundaries.<sup>1</sup> The pathology of type-I FCDs, such as cortical dyslamination and presence of ectopic neurons in the underlying WM will affect normal T1 values in GM-WM boundary tissues,<sup>9</sup> manifest primarily by





**Fig. 1** Comparison between different MRI sequences (A–A2) transverse, sagittal, and coronal views of MPRAGE, (B–B2) T2-TSE, (C–C2) T2-FLAIR, (D–D2) MP2RAGE, (E–E2) DIR, (F–F2) 3D-EDGE imaging. Subcortical hypointense with a transmantle sign is seen only at the 3D-EDGE sequence (arrows in F–F2). Based on the lesions found on 3D-EDGE sequence imaging, reviewed the other MRI sequences carefully, and DIR sequence indicates that there is a subtle fuzzy abnormal signal at the same level of lesions (arrows in E–E2). On the FDG-PET, there was extensive hypometabolism in the left parietal lobe area (arrows in G). (a), interictal EEG. Note spike waves over the left central-parietal area. (b) Ictal EEG associated with myoclonic jerks. 3D-EDGE, three-dimensional edge-enhancing gradient echo; EEG, electroencephalography; FDG-PET, fluorodeoxyglucose–positron emission tomography; FLAIR, fluid-attenuated inversion recovery; MPRAGE, magnetization-prepared rapid acquisition gradient echo MRI, magnetic resonance imaging; MP2RAGE, magnetization-prepared 2 rapid acquisition gradient echo; TSE, transmissible spongiform encephalopathies.



**Fig. 2** We choose the right parietal interhemispheric approach to reach the lesion (white arrow B2, C2). (A–A2) 3D-EDGE transverse, sagittal and coronal view of the lesion. Postoperative MRI images showed complete resection of the lesion. (B–B1) Postoperative T2-TSE images transverse, sagittal view. (C–C2, B2) Postoperative 3D-EDGE imaging the same level of lesion transverse, sagittal, and coronal view. 3D-EDGE, three-dimensional edge-enhancing gradient echo; MRI, magnetic resonance imaging; TSE, transmissible spongiform encephalopathies.

subtle widening, or blurring of the GM-WM junction and smearing of the underlying WM on T1-weighted image (WI) MRI sequences. Compared with type-I FCDs pathological changes, the type II FCDs pathology, such as abnormal neuronal and glial proliferation in the cortex and radial extensions of abnormal neurons in underlying hypomyelinated WM, can create more pronounced alterations in cortical or subcortical signal and easier to detection on MRI, those manifests on MRI with GM thickening and T2 prolongation in the cortex and a transmantle sign in the WM. Thus, in the FCDs detection, to identify those subtle abnormalities, routine MRI sequences were used which have higher GM-WM contrast to maximizing the contrast between GM and WM.<sup>10</sup> However, while the abnormality is too subtle to create pronounced MR signal alternations, there are no obvious contrast between the FCDs and surrounding tissues that will not be detected on MRI (►Fig. 1A–D). Achiriloaie et al<sup>11</sup> reported that conventional MRI sequences that shows to be negative at the early stage might change and lesions may appear after years, especially whom has high seizure frequency. But it generally takes a long time. 3D-EDGE does not depend on conventional T1 or T2 contrast. With an appropriate TI, on the 3D-EDGE sequences, GM and WM signals cancel each other and leads to nulling of MR signal in voxel at the GM–WM boundary and in voxels containing FCD and WM, such voxel of nulling signals easy to identify. Additionally, the signal cancellation area includes the FCDs and the part of normal GM or WM. To a certain degree, it can magnify and shows the lesion of FCDs. Therefore, it has greater sensitivity for minor changes in T1 relaxation and microarchitectural abnormalities present in the normal GM-WM boundary and in the WM.<sup>8</sup> Middlebrooks et al used the 3D-EDGE sequence to clearly identify five FCD cases (two transmantle signs and three in subcortical regions) which were not obvious on FLAIR or MP2RAGE. Our case is unique: we compared 3D-EDGE findings with those of five typical MRI sequences and found an obvious abnormality only using the 3D-EDGE sequence. Additionally, the contrast ratio is much higher than the contrast ratio on the five typical MRI sequences. We firmly believe that many FCDs like this case are missed by the conventional MRI.

Another potential advantage of 3D-EDGE lies in defining the full extent of the FCD. This is essential for complete resection of the lesion. If this patient undergoes SEEG to locate the epileptogenic foci, the convexity gyrus used to implant the SEEG electrode may be mistaken for the target of surgical resection because the epileptic discharge involves a range that is wider than the extent of structural abnormalities.

Because the configuration of our MRI machine (Siemens 3.0T Skyra used 8-channel coil) was different compared with the one that Middlebrooks et al used (Siemens 3.0T Vida used 64-channel coil), we could not adjust the parameters to precisely match the parameters provided in the literature. Thus, our image signal-to-noise ratio (SNR) was not as good as literature (►Fig. 1F–F2).

Postoperative MRI images showed that part of the paracentral lobule and the bottom with transmantle were precisely resected (►Fig. 2). Clinical symptoms disappeared after the surgical operation, and there was no brain dysfunction. The

patient also did not experience a seizure recurrence over an 8-month follow-up. This is the first report of a patient that underwent surgical treatment with 3D-EDGE MRI sequence imaging and achieved a good surgical outcome.

## Conclusion

3D-EDGE sequences show a higher sensitivity for FCD detection in epilepsy patients compared with a series of epilepsy-dedicated MRI protocols. We confirmed that the study by Middlebrooks et al is of great clinical value. If the findings on routine MRI sequences or even epilepsy-dedicated MRI sequences were reported as negative; however the semiology, V-EEG, and FDG-PET results suggest a local abnormality, and the results are concordant with each other, a 3D-EDGE sequence maybe a good option.

### Consent for Publication

Written consent was obtained from the patient's guardian for publication.

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### Conflict of interest

None declared.

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