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# Surgical treatment of pediatric intractable frontal lobe epilepsy due to malformation of cortical development

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## Abstract

**Background:** Malformation of cortical development (MCD) is a common cause of intractable epilepsy in children. In this study, the effectiveness of frontal lobe epilepsy (FLE) surgery in children with intractable epilepsy due to MCD was assessed and its prognostic factors were studied.

**Methods:** Seventy-six patients with intractable FLE who received epilepsy surgery between January 2016 and March 2018 in Peking University First Hospital were recruited in this study. All the resected brain tissues were demonstrated to be MCD. All patients were followed up for at least 3 years. The clinical data and prognosis were analyzed retrospectively. Univariate and multivariate analyses were performed to investigate the correlations between clinical variables and prognostic outcome (Engel classification).

**Results:** Sixty (78.9%) patients had Engel class I postoperative outcome. The mean age at surgery was  $6.00 \pm 4.24$  years. Sixty-six patients (86.8%) had daily seizures, 40.2% of the patients had epileptic spasm, and 33% of the patients had extensive interictal EEG abnormalities, which, however, could not provide any helpful information for localizing epileptogenic zones. About 29% of the patients had normal MRI findings even by experienced radiologists, and 26% of the patients had epileptogenic lesion involving adjacent lobes. There was a significant correlation between acute postoperative seizure (APOS) and prognosis ( $P < 0.05$ ): APOS predicted poor prognosis. There was a significant correlation between pathology and prognosis ( $P < 0.05$ ): FCD IA and FCD IIB were correlated with a good outcome. Both variables with a significance level of  $P < 0.05$  during univariate analysis, including pathology and APOS, were included in multivariate analysis, which were significant independent predictors of prognosis.

**Conclusions:** The clinical manifestations of pediatric intractable FLE due to MCD are more complicated than those in adults. Multidisciplinary presurgical evaluation in pediatric epilepsy is mandatory. The surgical outcome of pediatric FLE due to MCD could reach a seizure-free rate of 78.9% with the follow-up of at least 3 years. The post-operative pathology and APOS may be related to the prognosis of surgery in this group of pediatric patients.

**Keywords:** Surgery, Intractable frontal epilepsy, Children, Malformation of cortical development

## Background

Surgical treatment of drug-resistant epilepsy has been recognized as the most effective treatment among all others. The pediatric epilepsy surgery committee was formed by the International League Against Epilepsy (ILAE) in 1998 to formulate guidelines and recommendations for epilepsy surgery in

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childhood [1]. In the last two decades, pediatric epilepsy surgery has gradually developed and been accepted worldwide [2, 3]. For intractable epilepsy, surgical treatment can effectively terminate seizure occurrence, provide children with opportunities for cognitive and motor development, and improve their quality of life [4–6]. According to the ILAE's statistics, the incidence of refractory epilepsy which firstly occurred under 1 year of age is about 46%, and about 60% under 2 years. Malformation of cortical development (MCD) is the most common pathological cause for pediatric epilepsy, while hippocampal sclerosis is the most common pathology in adult intractable epilepsy [7]. Focal cortical dysplasia (FCD), a dominating subtype of MCD, is responsible for most of the medically refractory epilepsies in pediatric patients with MCD [8].

In the literature, with regard to the location of epileptogenic zone, the frontal lobe epilepsy (FLE) is the second most common surgically treatable epilepsy, only next to the temporal lobe epilepsy, and accounts for 6%–30% of all surgical cases [9–11]. However, the incidence of intractable frontal epilepsy is much higher in children than in adults [12–14], probably due to the high incidence of MCD, especially in very young children. More recent studies have demonstrated the absolutely improved seizure outcome compared to the past [15], but the surgical treatment of intractable epilepsy in young children with exclusive MCD has not been studied extensively. Here we present data of 76 children with frontal intractable epilepsy due to MCD in the Pediatric Epilepsy Center, who received epilepsy surgery in the past several years. The clinical data, surgical outcome and its prognostic factors were analyzed retrospectively.

## Material and methods

### Patient selection

Seventy-six patients (51 males and 25 females) with intractable FLE who received epilepsy surgery between January 2016 and March 2018 in Peking University First Hospital were recruited in this study. Only cases with main resection and epileptic lesion located within the frontal lobe were included and all the resected brain tissues were demonstrated to have MCD pathology, accounting for 87.4% (76/87) of total frontal surgeries performed during this period. All the children were followed up for more than 3 years. The clinical characteristics were collected, including gender, age at surgery, etiology, surgical side, semiology, seizure frequency, preoperative EEG characteristics, preoperative brain magnetic resonance imaging (MRI), PET-MRI fusion, surgical resection extension, pathology and postoperative recurrence time. The

postoperative seizure outcome was classified according to Engel's classification.

### Presurgical evaluation

Presurgical evaluation included detailed medical history and physical examination, preoperative scalp video electroencephalogram (VEEG), brain MRI (3.0 T) of specific pediatric epileptic sequences, and fluorodeoxyglucose positron emission tomography (FDG-PET) examination. Functional magnetic resonance imaging (fMRI) examination was performed for surgical candidates whose epileptogenic zone was supposed to be in or adjacent to the eloquent cortex.

Semiology of each seizure was categorized into the following: (1) focal seizure; (2) infantile spasms; (3) focal + spasms; and (4) multiple types of seizures. Four patients had other types of seizures including atypical absence, hyperactivity, myoclonic, and secondary tonic-clonic seizure, thus were excluded in final statistical analysis.

Seizure frequency was classified as follows: (1) cluster; (2) more than 10 times per day; (3) less than 10 times per day; (4) several times per week; (5) several times per month; and (6) several times over months.

VEEG monitoring was performed for all children to catch at least 3–5 habitual seizures using NIHON KOH-DEN 32-channel VEEG-1200-C system, with recording electrodes placed according to the international 10–20 system. Surface electromyography (EMG) of bilateral deltoid muscle and bilateral quadriceps femoris was simultaneously recorded. Interictal EEG abnormalities were categorized as: (1) focal; (2) generalized + focal; (3) multi-focal; (4) multi-focal + generalized; and (5) hypsarrhythmia.

Brain MRI scanning was performed using a Philips Achieva 3.0 T TX magnetic resonance scanner and a 32-channel head coil. Children under 5 years and unable to stay awake and undertake MRI examination were sedated by oral administration of 10% chloral hydrate (0.3 ml/kg–0.5 ml/kg, maximum total volume not exceeding 10 ml). Scanning sequence included T1WI, T2WI, T2 FLAIR and DWI. MCD in MRI structure always showed grey matter thickening, blurring grey-white matter junction and abnormal signal in white matter and et cetera. We defined the positive MRI results according to the reports from radiologists. Sino software, a neurosurgical robot navigation and positioning system from the Sinovision company, was used for three-dimensional reconstruction of the skull and brain, and the surgical resection plan was defined according to the results of multidisciplinary consultations.

PET-CT scanning was performed using the Philips Gemini GXL PET-CT scanner. PET results were

determined as negative or positive according to the following criteria: (1) positive: a lesion site with visible hypometabolism in the frontal lobe; (2) negative: cortical area with completely normal metabolism and symmetrical distribution.

The PET images were fused with 3D T1WI sequence with software SPM8 (Institute of Neurology, University College of London, UK) using MATLAB 7.9 (The Math-Works Inc., USA).

A preoperative multidisciplinary conference was conducted by Pediatric Epilepsy Center, Peking University First Hospital. The final diagnosis and treatment including surgical planning were determined by the conference.

**Surgery and pathology classifications**

Surgery was carried out under general anesthesia, and the intraoperative electrocorticogram was done for every patient by monitoring the cortex using grid electrodes. Somatosensory-evoked potential and compound muscle action potential were monitored continuously during resections in children with lesions involving or adjacent to the central cortex. Resection extension involved the following: (1) mesial side (superior frontal gyrus); (2) dorsal and inferior side (including the medial frontal gyrus and inferior frontal gyrus); (3) total frontal lobe (the resection included greater than 75% of the frontal lobe with the anterior central gyrus retained); (4) partial frontal lobe + other part of the cerebral lobe; and (5) total frontal lobe + other part of the cerebral lobe.

Pathology of brain tissues was classified according to the report by Palmini [8]: (1) FCD Ia; (2) FCD Ib; (3) FCD IIa; (4) FCD IIb (including one case of tuber sclerosis); and (5) other MCD subtypes. Three cases had disconnection surgeries, without pathological results.

**Postoperative outcome**

Follow-up was conducted at 3, 6, 12 months and once in the coming years after surgery. Acute postoperative seizure (APOS) was defined as a seizure occurring within the first post-operative month. Seizure prognosis was graded according to Engel classification: class I (free of seizures) and class II-IV (seizures still occur at different degrees).

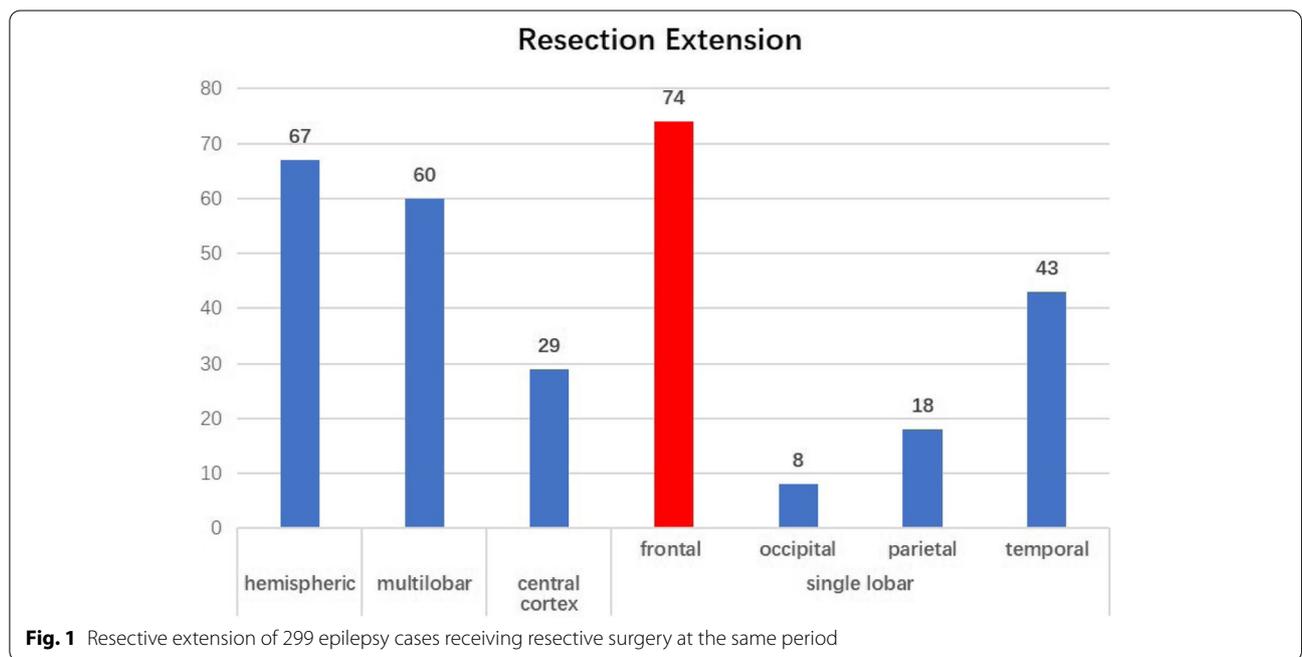
**Statistical analysis**

Data were analyzed with *t* test and chi-square test to compare between different groups for univariate analyses. *P* < 0.05 was considered as statistically significant. Variables with a significance level of < 0.05 on initial univariate analysis were then tested in a multivariate logistic regression analysis. All statistical analyses were made using the SPSS 20.0 (IBM, USA) software.

**Results**

**Clinical data**

From January 2016 to March 2018, a total of 299 patients received resective surgery for epilepsy, and the details of resection extension are shown in Fig. 1. Of these 299 patients, 86 (28.8%) had FLE, and 10 of them were not



MCD patients. A total of 76 FLE patients due to MCD were recruited in this study. Their age at surgery ranged 1.10 to 19.12 years, with an average of  $6.00 \pm 4.24$  years. The age at seizure onset was 0.01–12.00 years, with an average of  $2.52 \pm 2.89$  years. The duration of epilepsy was 0.37–14.24 years, with an average of  $3.49 \pm 2.82$  years. In addition, 18 patients were under 3 years, accounting for 23.7% in our cohort; 86.8% of the patients had daily seizures, with over half having > 10 seizures per day. Six children had multiple seizure types, among whom 5 had epileptic spasms. A total of 29 (40.2%) children had epileptic spasm. Only 6 patients had APOS (Table 1).

Fifty-four (71.1%) cases underwent large resection (total frontal lobe or more than single lobe) and in plus-frontal resection cases, there were 7 referring to insular lobes, 3 parietal lobes and 2 temporal lobes. Intraoperative monitoring of evoked potentials was performed for nearly half of the patients. FCD IIb was the most common pathological type (Table 2).

Further, 71.1% of lesions could be observed through MRI, and PET-CT showed hypermetabolism or hypometabolism in cerebrum in 100% of the patients (Table 3).

It was more visually intuitive for PET-MRI combination to localize the exact lesions.

The different surgical resection extensions were significantly correlated with pathological results ( $P=0.020$ ). Surgical resection in most patients with MCD pathology extended beyond the frontal lobe (Table 4).

In addition, according to the presurgical MRI reports, it was difficult to identify the pathological subtypes of frontal cortical dysplasia (Table 5).

**Surgical outcome and prognostic factors**

All the patients were followed up for at least 3 years, with an average of  $4.88 \pm 0.59$  years. At the last follow-up, 60 patients (78.9%) were completely free of seizures. There were no significant effects of gender, age at surgery, age at onset, course of disease, and follow-up time on prognosis. There were 8 patients having APOS within 30 days after surgery. Three patients with APOS finally had a good prognosis, although the other 5 continued to suffer seizures till the last follow-up. APOS significantly increased the postoperative seizure recurrence rate in children with FLE ( $P<0.05$ ) (Table 1). Nine patients

**Table 1** Clinical characteristics of patients

		ENGEL		P value
		I	II-IV	
Gender (%)				0.659
Male	51 (67.2)	41	10	
Female	25 (32.8)	19	6	
Age at surgery (years) (SD)	$6.00 \pm 4.24$	$6.03 \pm 4.24$	$6.00 \pm 4.21$	0.827
Age at seizure onset (years) (SD)	$2.52 \pm 2.89$	$3.50 \pm 2.84$	$2.52 \pm 2.87$	0.823
Seizure exposure time (years) (SD)	$3.49 \pm 2.82$	$3.50 \pm 2.84$	$3.49 \pm 2.80$	0.482
Follow-up time (years) (SD)	$4.88 \pm 0.59$	$4.86 \pm 0.55$	$4.88 \pm 0.59$	0.001
Seizure frequency (%)				0.562
Cluster	3 (3.9)	1	2	
Each day > 10	30 (39.4)	24	6	
Each day < 10	36 (47.4)	29	7	
Weekly	5 (6.6)	4	1	
Monthly	1 (1.3)	1	0	
Once every few months	1 (1.3)	1	0	
Semiology (%)	total (n = 72)			0.338
Focal	42 (55.3)	33	9	
Multiple types	6 (7.9)	6	0	
Spasm	18 (23.7)	13	5	
Spasm + focal	6 (7.9)	5	1	
Spasm (%)	total (n = 72)			0.951
Yes	29 (40.3)	23	6	
No	43 (59.7)	37	10	
Acute postoperative seizure (%)				0.002
Yes	8	3	5	
No	68	57	11	

**Table 2** Surgical data and pathology

	Total (n = 76)	ENGEL		P
		I	II-IV	
Side (%)				0.744
Left	36 (47.4)	29	7	
Right	40 (52.5)	31	9	
Extensive resection (%)				0.410
Internal side	10 (13.2)	7	3	
Dorsal and external side	12 (15.8)	11	1	
Total frontal lobe	34 (44.8)	28	6	
Partial frontal lobe + other lobes	10 (13.2)	8	2	
Total frontal lobe + other cerebral lobes	10 (13.2)	6	4	
Intraoperative SSEP and CMAP (%)				0.657
Yes	39 (51.3)	30	9	
No	37 (48.7)	30	7	
Invasive monitoring (%)				1
Yes	9 (11.8)	8	1	
No	67 (88.2)	60	7	
Pathology (%)	total (n = 73)			0.033
FCD Ia	4 (5.5)	4	0	
FCD Ib	9 (12.3)	5	4	
FCD IIa	13 (17.8)	11	2	
FCD IIb	27 (37.0)	25	2	
Other MCD subtypes	20 (27.4)	13	7	

**Table 3** Presurgical radiological data and scalp EEG

	Total (n = 76)	ENGEL classification		P
		I	II-IV	
MRI (%)				0.935
Positive	54 (71.1)	42	12	
Negative	22 (28.9)	18	4	
Inter-ictal EEG (%)				0.801
Multi-focal	6 (7.9)	5	1	
Multi-focal + generalized	12 (15.8)	9	3	
Hypsarrythmia	4 (5.3)	3	1	
Focal	51 (67.1)	40	11	
Focal + generalized	3 (3.9)	3	0	

underwent repeated surgery, including one receiving palliative vagus nerve stimulation and 8 receiving curative enlargement resection or hemispherotomy, with 6/8 (75%) seizure-free rate.

There was no significant difference in surgical outcome between patients with surgery on the left side (n = 36) and those on the right side (n = 40). There was no significant correlation between surgical resection

extension and surgical prognosis. Children with spasms (n = 6, 20.7%) did not have higher seizure occurrence rate than those without spasms (n = 10, 23.3%) (Table 2).

The recurrence rate after extensive (frontal lobectomy or multilobar) resection (28.6%) was not significantly higher than that with focal (medial, dorsal and lateral) resection (22.2%). A total of 39 children received intraoperative evoked potential (SSEP and CMEP) monitoring. Eight patients underwent subdural electrode implantation before surgery, and one patient underwent stereotactic electroencephalography (SEEG). There was a significant relationship between the pathological type of MCD and prognosis (P < 0.05). All patients with FCD Ia pathologies were seizure-free after surgery. The seizure outcomes of FCD Ib and other MCD subtypes were less favorable, with 55.6% and 65% being free of seizures, respectively (Table 2).

In this study, 21 patients with frontal cortical dysplasia had negative MRI findings preoperatively, while all cases had positive PET-CT findings preoperatively. However, positive MRI finding did not improve the surgical outcome. In addition, there was no significant difference in seizure outcome between patients having

**Table 4** Resection extension and pathology

Resection extension	Pathology (%)					Total
	IA	IB	IIA	IIB	Other MCDs	
Internal side	1 (25)	1 (11.1)	3 (23.1)	7 (25.9)	0	12
Dorsal and external side	0	1 (11.1)	4 (30.8)	5 (18.5)	0	10
Total frontal lobe	3 (75)	5 (55.6)	3 (23.1)	8 (29.6)	12 (60)	31
Partial frontal lobe + other lobes	0	1 (11.1)	2 (15.4)	5 (18.5)	2 (10)	10
Total frontal lobe + other cerebral lobes	0	1 (11.1)	1 (7.7)	2 (7.4)	6 (30)	10
Total	4	9	13	27	20	73

**Table 5** Pathology and MRI

Pathology	MRI		Total
	Positive	Negative	
Ia	2	2	4
Ib	6	3	9
IIa	9	4	13
IIb	19	8	27
Other MCD subtypes	16	4	20
Total	52	21	73

extensive interictal EEG abnormalities and those with focal EEG abnormalities (Table 3).

Variables with a significance level of  $P < 0.05$ , including APOS and follow-up time, were included in multivariate analysis, and both were shown to be significant independent predictors of prognosis (Table 6).

**Discussion**

The purpose of this study was to explore the clinical characteristics of FLE children with MCD pathology who received surgery, and to investigate the effectiveness of surgical treatment and its prognostic factors. MCD is the most common pathological type in children with intractable epilepsy surgery, accounting for about 40% of all etiologies [7]. In this study, among the 299 patients who underwent resective epilepsy surgery in our pediatric epilepsy center, 193 cases were proved to be MCDs, accounting for 64.5% of all. The percentage of MCD was much higher than that reported in the literature,

probably due to the following reasons. First, technique developments in pre-surgical evaluation including high-resolution 3.0 T MRI and PEC-CT have made MCD lesions much easier to be localized during neuroimaging, and the three-dimensional reconstructions of the brain using the Sino software can exhibit the spatial extension of lesions more exactly. Second, with increased practice of presurgical evaluation, more and more pediatric neurologists are realizing that MCD is one of the most epileptogenic lesions of all congenital lesions, therefore these patients could be easily referred to the surgery unit. Although MCD can occur in various cerebral lobes of the brain, it occurs more often in the temporal lobe and frontal lobe [16]. The data from our center showed that, in patients with single lobe resection, 74 (52%) patients had frontal lobe epilepsy, while 43 (30%) patients had temporal lobe epilepsy. This could be caused by the developmental nature of pediatric epilepsy patients, especially those at a very young age [14, 17].

The clinical manifestations of FLE with MCD pathology in childhood are very different from those in adults. The frontal lobe is a large region, accounting for 55% of the total brain, and contains important functional cortex including those related with motor and language. Extratemporal lobe epilepsy (ETLE) including FLE is more commonly seen in children. Our study demonstrated the clinical severity of epilepsy and great difficulty in presurgical evaluation for children with intractable epilepsy due to MCD. The seizure usually started at a very young age (average age of  $2.52 \pm 2.89$  years). Nearly 90% of our patients had daily

**Table 6** Logistic regression analysis between variables ( $P < 0.2$ ) and prognosis

Parameter	B	SE	Wald	D.f	Sig	Exp (B)
Follow-up time (years)	1.089	0.493	4.879	1	0.027	2.972
APOS	-2.531	0.594	18.156	1	0.000	0.080
Constant	-4.841	2.416	4.015	1	0.045	0.008

B Beta (regression coefficient), SE Standard Error, D.f. Degree of Freedom, Sig. Significance, Exp (B) Exponential B

seizures, with more than half having over 10 seizures per day. There was usually a long seizure exposure time before surgery. These surgical candidates were usually referred to our center very late, suggesting a need for improved dissemination of guidelines and new knowledge on medical care of this area. There are still gaps in knowledge on epilepsy surgery among many healthcare professionals in epilepsy [18].

Our data also showed great difficulty in presurgical evaluation for children with intractable FLE with MCD pathology; 40.2% of the patients had epileptic spasm, which is a very special seizure type usually recognized as generalized seizure, and 33% of the patients had extensive interictal EEG abnormalities, which, did not provide any helpful information for localizing the epileptogenic zone at all. About 29% of the patients were reported to be normal in MRI even by experienced radiologists. Nearly half of the patients had epileptogenic lesions beyond the frontal lobe. In conclusion, compared with adult patients with FLE, it is more complicated in pediatric FLE patients to localize the epileptogenic zone.

There have been few reports on surgery for FLE in children, and only a few have studied the postoperative cognitive and neuropsychological outcomes of FLE surgery in children [19–21]. Neither have the prognostic factors for FLE surgery been studied in children. The prognosis of FLE surgery is worse than that of temporal lobe epilepsy surgery and the percent of seizure freedom ranges from 13% to 80% [15]. FLE surgery is difficult to perform, because the quick propagation of seizure leads to obscure localization of epileptogenic foci and the functional cortex may be injured during surgery. The MRI negative rate in MCD is higher than that in tumor, cerebral hemorrhage, and other causes, while on the other hand, MCD in FLE is often extensive and involves adjacent lobes. Both factors could lead to difficulties in delineating epileptogenic boundaries.

Although the presence of a lesion on MRI has been associated with a better surgical outcome, patients without MRI lesions can also have good outcome. FCD I usually has non-specific changes in MRI [22, 23], but its metabolic abnormalities are often obvious in PET-CT. Although most MRI examinations of FCD type II patients produce positive results, 33% of FCD type II patients showed very subtle abnormality on MRI, which are often recognized to be MRI-negative [24]. The most common MRI features of FCD II are focal cortical thickening, increased T2WI and FLAIR signals, unclear gray-white matter boundary and transmantle sign (abnormal linear or wedge signals extending from the lateral ventricle to the cortex surface) [22, 23, 25, 26]. In our study, no significant differences between pathological types and MRI-positive rate were found. However, the

positive rate of PET-CT was significantly higher than that of MRI, which greatly improved the detection rate of epileptic lesions. The hypometabolic regions found by  $^{18}\text{F}$ -FDG PET are generally more extensive than the epileptic regions, which indicates that both the epileptic region and the projection region are affected by epileptic seizures [27]. In this study, the detection rate of PET-CT reached 96.1%. Usually, the final resection range is less than the area with abnormal metabolism. Due to the non-specific property, the surgical extension cannot be completely defined according to the results of PET-CT. We therefore employed Sino software which was exclusively designed for co-registration of various presurgical modalities to make surgical plans for resection. Every surgical plan in this study was made by Sino, which is also a practical tool in pediatric epilepsy surgery to delineate the exact resective region. For children with epileptic lesions that are difficult to localize, SEEG or subdural electrode implantation can be used to find the lesion location. In this study, the only one child with SEEG had a good prognosis, but one patient still had a poor prognosis following subdural electrode implantation.

Our study showed a significant correlation between pathological type and prognosis. All the patients with FCD IIB and FCD Ia were seizures free after the surgery. FCD IIB is usually correlated with favorable seizure outcomes because the lesion can often be localized easily on MRI. Patients with FCD Ia are usually not considered to be good surgical candidates because of the unclear appearance of lesions on MRI and that the pathological lesions are wide spread in nature. In this study, the 100% seizure-free rate in the very small sample of FCD Ia patients is incomparable to other groups. On the other hand, FCD IB and other MCD subtypes had less prognosis because of their widely distributed abnormalities and unclear boundaries to normal cortex. The pathological results of other MCD subtypes often indicate a wider resection range, either total frontal lobe or multi-lobes. One study of 143 cases of cortical dysplasia who were followed up for 10 years reported a 63% seizure-free rate [28]. The seizure-free rate of FCD IIB was higher (92.6%) and there was no significant difference between MRI-positive and -negative patients [24].

APOS is often considered as a factor for poor prognosis after epilepsy surgery [29]. Tigarán et al. [30] investigated for the first time the relationship between APOS and FLE surgery, but found no significant relationship. In contrast, here we found that the prognosis of children with APOS was significantly worse than that of children without APOS. This phenomenon may be due to the relatively small sample size in the study by Tigarán et al.

As to APOS, cautions should be made to differentiate real APOS from post-operative seizures induced by the edema of adjacent cortex, especially the motor cortex which could be easily affected by edema to cause focal seizures. The key is to distinguish whether APOS is similar to the habitual seizures before the surgery.

## Conclusions

In this study, 76 children with intractable FLE due to MCD were followed up for at least 3 years. Our results showed that frontal lobe MCD accounts for a large proportion in children with refractory epilepsy, and surgical treatment is of great significance. The clinical characteristics of intractable epilepsy children due to frontal lobe MCD are very different from those of adults, which deserves further investigations. For surgical treatment, it would be very helpful to improve presurgical evaluation and long-term surgical outcome by focusing on the correlated factors, although no independent prognostic factors are discovered here. The MCD pathology and the presence of APOS are related to the prognosis of children with FLE.

## Abbreviations

APOS: Acute postoperative seizure; CMAP: Compound muscle active potential; EMG: Electromyography; ETL, extratemporal lobe epilepsy; FCD: Focal cortical dysplasia; MRI: Magnetic resonance imaging; FLE: Frontal lobe epilepsy; fMRI: Functional magnetic resonance imaging; MCD: Malformation cortical development; SEEG: Stereotactic electroencephalogram; SSEP: Somatosensory evoked potential; VEEG: Video electroencephalogram.

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## Authors' contributions

Lixin Cai designed the study and revised the paper; Hao Yu and Qiang Lv drafted the paper, analysed and interpreted the data, and submitted the paper; Shuang Wang, Taoyun Ji, Wen Wang, Dongming Wang and Ruofan Wang analysed and interpreted the data; Yuwu Jiang, Lixin Cai, Qingzhu Liu, and Xiaoyan Liu collected the patients. The author(s) read and approved the final manuscript.

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## Availability of data and materials

The datasets of the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of Peking University (2015[870]). Patients' caregivers gave written informed consent.

### Consent for publication

Not applicable.

## Competing interests

Author Yuwu Jiang and Xiaoyan Liu are the members of the Editorial Board for *Acta Epileptologica*, who were not involved in the journal's review of, or decisions related to this manuscript.

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## References

- Cross JH, Jayakar P, Nordli D, Delalande O, Duchowny M, Wieser HG, et al. Proposed criteria for referral and evaluation of children for epilepsy surgery: recommendations of the subcommission for pediatric epilepsy surgery. *Epilepsia*. 2006;47(6):952–9.
- Duchowny M, Jayakar P, Resnick T, Harvey AS, Alvarez L, Dean P, et al. Epilepsy surgery in the first three years of life. *Epilepsia*. 1998;39(7):737–43.
- Duchowny M. Recent advances in candidate selection for pediatric epilepsy surgery. *Semin Pediatr Neurol*. 2000;7(3):178–86.
- Langfitt JT, Holloway RG, McDermott MP, Messing S, Sarosky K, Berg AT, et al. Health care costs decline after successful epilepsy surgery. *Neurology*. 2007;68(16):1290–8.
- Silfvénus H. Cost and cost-effectiveness of epilepsy surgery. *Epilepsia*. 1999;40(Suppl 8):32–9.
- Widjaja E, Li B, Schinkel CD, Puchalski Ritchie L, Weaver J, Snead OC, et al. Cost-effectiveness of pediatric epilepsy surgery compared to medical treatment in children with intractable epilepsy. *Epilepsy Res*. 2011;94(1–2):61–8.
- Harvey AS, Cross JH, Shinnar S, Mathern GW. Defining the spectrum of international practice in pediatric epilepsy surgery patients. *Epilepsia*. 2008;49(1):146–55.
- Palmini A. Revisiting the classification of focal cortical dysplasias. *Epilepsia*. 2011;52(1):188–90.
- Salanova V, Quesney LF, Rasmussen T, Andermann F, Olivier A. Reevaluation of surgical failures and the role of reoperation in 39 patients with frontal lobe epilepsy. *Epilepsia*. 1994;35(1):70–80.
- Tellez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. *Brain*. 2005;128(Pt 5):1188–98.
- Laskowitz DT, Sperling MR, French JA, O'Connor MF. The syndrome of frontal lobe epilepsy: characteristics and surgical management. *Neurology*. 1995;45(4):780–7.
- Cahan LD, Sutherland W, McCullough MA, Rausch R, Engel J Jr, Crandall PH. Review of the 20-year UCLA experience with surgery for epilepsy. *Cleve Clin Q*. 1984;51(2):313–8.
- Prats AR, Morrison G, Wolf AL. Focal cortical resections for the treatment of extratemporal epilepsy in children. *Neurosurg Clin N Am*. 1995;6(3):533–40.
- Pomata HB, Gonzalez R, Bartuluchi M, Petre CA, Ciraolo C, Caraballo R, et al. Extratemporal epilepsy in children: candidate selection and surgical treatment. *Childs Nerv Syst*. 2000;16(12):842–50.
- Jeha LE, Najm I, Bingaman W, Dinner D, Widdess-Walsh P, Luders H. Surgical outcome and prognostic factors of frontal lobe epilepsy surgery. *Brain*. 2007;130(Pt 2):574–84.
- Sisodiya SM. Surgery for malformations of cortical development causing epilepsy. *Brain*. 2000;123(Pt 6):1075–91.
- Siegel AM, Cascino GD, Meyer FB, Marsh WR, Scheithauer BW, Shalhough FW. Surgical outcome and predictive factors in adult patients with intractable epilepsy and focal cortical dysplasia. *Acta Neurol Scand*. 2006;113(2):65–71.
- Erba G, Moja L, Beghi E, Messina P, Pupillo E. Barriers toward epilepsy surgery: A survey among practicing neurologists. *Epilepsia*. 2012;53(1):35–43.
- Chieffo D, Lettori D, Contaldo I, Perrino F, Graziano A, Palermo C, et al. Surgery of children with frontal lobe lesional epilepsy: neuropsychological study. *Brain Dev*. 2011;33(4):310–5.

20. Lendt M, Gleissner U, Helmstaedter C, Sassen R, Clusmann H, Elger CE. Neuropsychological outcome in children after frontal lobe epilepsy surgery. *Epilepsy Behav.* 2002;3(1):51–9.
21. Braakman HM, Vaessen MJ, Jansen JF, Debeij-van Hall MH, de Louw A, Hofman PA, et al. Frontal lobe connectivity and cognitive impairment in pediatric frontal lobe epilepsy. *Epilepsia.* 2013;54(3):446–54.
22. Colombo N, Tassi L, Galli C, Citterio A, Lo Russo G, Scialfa G, et al. Focal cortical dysplasias: MR imaging, histopathologic, and clinical correlations in surgically treated patients with epilepsy. *AJNR Am J Neuroradiol.* 2003;24(4):724–33.
23. Krsek P, Pieper T, Karlmeier A, Hildebrandt M, Kolodziejczyk D, Winkler P, et al. Different presurgical characteristics and seizure outcomes in children with focal cortical dysplasia type I or II. *Epilepsia.* 2009;50(1):125–37.
24. Chassoux F, Landre E, Mellerio C, Turak B, Mann MW, Daumas-Duport C, et al. Type II focal cortical dysplasia: electroclinical phenotype and surgical outcome related to imaging. *Epilepsia.* 2012;53(2):349–58.
25. Colombo N, Tassi L, Deleo F, Citterio A, Bramero M, Mai R, et al. Focal cortical dysplasia type IIa and IIb: MRI aspects in 118 cases proven by histopathology. *Neuroradiology.* 2012;54(10):1065–77.
26. Widdess-Walsh P, Diehl B, Najm I. Neuroimaging of focal cortical dysplasia. *J Neuroimaging.* 2006;16(3):185–96.
27. Rathore C, Dickson JC, Teotonio R, Ell P, Duncan JS. The utility of 18F-fluorodeoxyglucose PET (FDG PET) in epilepsy surgery. *Epilepsy Res.* 2014;108(8):1306–14.
28. Chang EF, Wang DD, Barkovich AJ, Tihan T, Auguste KI, Sullivan JE, et al. Barbaro, predictors of seizure freedom after surgery for malformations of cortical development. *Ann Neurol.* 2011;70(1):151–62.
29. Greiner HM, Horn PS, Arya R, Holland K, Turner M, Alsaïdi MH, et al. Acute postoperative seizures and long-term outcome following pediatric epilepsy surgery. *Seizure.* 2014;23(6):483–6.
30. Tigarán S, Cascino GD, McClelland RL, So EL, Richard MW. Acute postoperative seizures after frontal lobe cortical resection for intractable partial epilepsy. *Epilepsia.* 2003;44(6):831–5.

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