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Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) Combined with Positron Emission Tomography-Computed Tomography (PET-CT) and Video-Electroencephalography (VEEG) Have Excellent Diagnostic Value in Preoperative Localization of Epileptic Foci in Children with Epilepsy

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Background: To investigate the effect that dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has on surgical decision making relative to video-electroencephalography (VEEG) and positron emission tomography-computed tomography (PET-CT), and if the differences in these variables translates to differences in surgical outcomes.

Material/Methods: A total of 166 children with epilepsy undergoing preoperative DCE-MRI, VEEG, and PET-CT examinations, surgical resection of epileptic foci, and intraoperative electrocorticography (ECoG) monitoring were enrolled. All children were followed up for 12 months and grouped by Engles prognostic classification for epilepsy. Based on intraoperative ECoG as gold standard, the diagnostic values of DCE-MRI, VEEG, PET-CT, DCE-MRI combined with VEEG, DCE-MRI combined with PET-CT, and combined application of DCE-MRI, VEEG, and PET-CT in preoperative localization for epileptic foci were evaluated.

Results: The sensitivity of DCE-MRI, VEEG, and PET-CT was 59.64%, 76.51%, and 93.98%, respectively; the accuracy of DCE-MRI, VEEG, PET-CT, DCE-MRI combined with VEEG, and DCE-MRI combined with PET-CT was 57.58%, 67.72%, 91.03%, 91.23%, and 96.49%, respectively. Localization accuracy rate of the combination of DCE-MRI, VEEG, and PET-CT was 98.25% (56/57), which was higher than that of DCE-MRI combined with VEEG and of DCE-MRI combined with PET-CT. No statistical difference was found in the accuracy rate of localization between these three combined techniques. During the 12-month follow-up, children were grouped into Engles grade I (n=106), II (n=31), III (n=21), and IV (n=8) according to postoperative conditions.

Conclusions: All DCE-MRI combined with VEEG, DCE-MRI combined with PET-CT, and DCE-MRI combined with VEEG and PET-CT examinations have excellent accuracy in preoperative localization of epileptic foci and present excellent postoperative efficiency, suggesting that these combined imaging methods are suitable for serving as the reference basis in preoperative localization of epileptic foci in children with epilepsy.

MeSH Keywords: **Electroencephalography • Epilepsy • Magnetic Resonance Imaging**

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Background

Epilepsy is a group of neurological diseases characterized by epileptic seizures that are the result of excessive and abnormal cortical nerve cell activity in the brain [1]. About 1% of people worldwide (65 million) have epilepsy, and nearly 80% of cases occur in developing countries [2]. In 2013 epilepsy resulted in 116,000 deaths, up from 112,000 deaths in 1990 [3]. The most common type (60%) of seizures are convulsive; of these, one-third begin as generalized seizures from the start, affecting both hemispheres of the brain; two-thirds begin as partial seizures (which affect one hemisphere of the brain), which may then progress to generalized seizures; and the remaining 40% of seizures are non-convulsive, which present as a decreased level of consciousness and usually last about 10 seconds [4]. Additionally, automatisms may occur, which are non-consciously generated activities, mostly simple repetitive movements like smacking of the lips or more complex activities such as attempts to pick up something [5]. Furthermore, epilepsy is a common disease in children, and seizures are uncontrollable with medication in 20–30% of children with epilepsy, which may affect the development of their intelligence [6]. Generally, the symptoms in children with epilepsy are closely related to focus location, such as epileptic foci in the motor area resulting in limb spasm [7]. Therefore, an effective and accurate preoperative localization technique for epileptic foci is of vital significance in the treatment of epilepsy.

Children with intractable epilepsy pose a diagnostic and therapeutic challenge and should be considered for early epilepsy surgery, in that successful resection of epileptic foci may contribute to better social, psychological, and cognitive development [8]. The most important aspect of preoperative evaluation is to identify a discrete epileptogenic region, which can be resected without causing an unacceptable loss of neurologic function and which will lead to complete seizure control [9]. However, in two-thirds of patients with focal epilepsy, there are no identifiable brain lesions on conventional magnetic resonance imaging (MRI), and it is sometimes difficult to identify the source of epileptic discharges with scalp electroencephalography (EEG) [10,11]. When the location of the epileptic focus remains unclear, other diagnostic tests can be performed such as ^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET), which is useful for the detection of high-grade malignant brain tumors but is less effective in the diagnosis of low-grade tumors [12]. An accurate noninvasive and high-spatial-resolution method to localize epileptic foci thus remains a major challenge.

In the present study, we compared the preoperative localization results of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), video-electroencephalography (VEEG), positron emission tomography-computed tomography (PET-CT),

DCE-MRI combined with VEEG, DCE-MRI combined with PET-CT, and combined application of DCE-MRI, VEEG, and PET-CT for epileptic foci in a group of children undergoing surgery with the postoperative outcomes, to provide potential information on surgical efficacy.

Material and Methods

Ethics statement

This study was approved by the ethics committee of Linyi People's Hospital. Informed consent was obtained from the children's family members. All the procedures in this study were in compliance with the Declaration of Helsinki [13].

Patients

A total of 166 children (95 boys and 71 girls; average age, 8.9 ± 2.7 years) diagnosed with epilepsy in Linyi People's Hospital between June 2009 and September 2012 were included in this study. The inclusion criteria included the following: (1) the course of epilepsy not less than 3 months, with unsatisfactory pharmacotherapeutic efficacy or progressive cognitive dysfunction; (2) detailed preoperative evaluation results of skulls, including MRI examination, VEEG examination, and PET-CT electroencephalograms; (3) diagnosis of epilepsy definitely confirmed by epilepsy specialists; (4) normal examination of the nervous system; (5) complete case data provided with approval from patients or their family members; and (6) parents of children had strong requirements for an operation after understanding the operative risk and prognosis. The exclusion criteria were (1) clinical symptoms or medical history not conforming to the diagnostic criteria for epilepsy; (2) symptoms of epilepsy seriously affecting work, learning, and life; (3) postoperative significant neurological impairment; and (4) poor compliance, or failure to cooperate during examinations and treatments.

DCE-MRI examination

All DCE-MRI examinations were performed on a 3.0 T superconducting MRI scanner (Magnetom TrioTim, Siemens, Erlangen, Germany) using a 32-channel phased-array coil [maximum gradient field strength, 40 mT/m; maximum gradient conversion rate: 200 mT/(m·s)]. T2-weighted imaging (T2WI) sequence applied in the detection of whole lesions at DCE-MRI scanning was single-shot spin-echo echo-planar imaging (SS-EPI) sequence [repetition time (TR)=2,000 ms, echo time (TE)=27 ms, flip angle=90°, matrix=128×128, number of excitations (NEX)=1, continuous phase=24, time resolution=2 s, scan time=48 s]. A three-dimensional (3D) gradient-echo sequence (VIBRANT 3D) and fat suppression were used in T1WI DCE-MRI scanning with

scanning parameters as follows: TR=4.5, TE=2.1, flip angle=10°, matrix=384×256, NEX=1, field-of-view (FOV)=34 cm, slice thickness=1.2 mm, gap between slice=0 mm, continuous phase=7, acquisition time for each phase=58 s, total scan time=286 s. Before injection with contrast agent for enhanced scanning, BIVRANT Mask scanning was conducted. MRI contrast agent [0.1 mmol/kg Magnevist solution (GD-DTPA)] was injected at a rate of 2.5 mL/s using a bolus injection method, followed by a washing tube with 20-25 mL of isotonic saline solution.

VEEG examination

VEEG monitoring was performed on a Stellate VEEG machine (Stellate Inc., Canada) for 2, 12, and 24 h. A total of 21-lead EEG signals including FP1, FP2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, FZ, CZ, PZ, PG1, and PG2 were recorded. During the last 15 min of the monitoring, sphenoidal electrode examination was conducted by using a domestic 3-inch needle vertically penetrating 4~5 cm from the beginning of the mandibular notch of the zygomatic arch. After monitoring, retrospective analysis was conducted by multiple combined lead methods, and comparisons were performed with video data on the same screen for the synchronous analysis of records during the seizure period second by second. Principles of judgment interpretation were as follows: repeated emergence of epileptiform discharges (spike wave, sharp wave, slow spike wave, paroxysmal rhythmic δ wave, and polymorphic δ activity) could facilitate localization or lateralization diagnosis, and amplitude peak in T7/T5 and T3/T4 was determined to be temporal lobe discharge. Bilateral independent epileptiform discharges with discharge in one side 90% larger than that in the opposite side was considered as a guarantee for unilateral localization diagnosis; otherwise, lateralization diagnosis was not made.

¹⁸F-FDG PET-CT

After 6-h fasting for reducing glucose uptake, patients underwent PET-CT examination and intravenous injection of ¹⁸F-FDG. Brain imaging was performed 30 min later, and the metabolic process and distribution situation of ¹⁸F-FDG were monitored in brain tissue; meanwhile, a CT Tomoscan scan was conducted for reconstructed images. Appearance of continuous high or low metabolic zones in two levels was considered as abnormal, and when the relative intensity of radioactivity was reduced or increased by 15% in bilateral corresponding zones, this was regarded as indicating a metabolic abnormality. The localization diagnosis for epileptic foci was performed in terms of brain function and imageology. The Discovery 16 CT and MINITrace Cyclotron produced by GE Corp. (USA) were used. ¹⁸F-FDG PET-CT was performed using a Tracerlab FXFN synthesizer from GE Medical Systems (USA), with a radiochemical purity of FDG >95%. According to scan plan, multilayer CT

scanning was initially conducted with parameters as follows: voltage, 120 kV; electric current, 180 mA; 3D model reconstruction, FORE-interactive reconstruction; axial field-of-view (FOV), 25 cm; emission scanning acquisition, 25 min; thickness, 3.75 mm; matrix, 128×128; scanning range, entire head. A total of 40 cross-sectional images were obtained, and image fusion was performed through an Xeleris and AW4.3 workstation.

Operative treatment and intraoperative electrocorticography (ECoG) monitoring and positioning

ECoG results and pathological results were regarded as the gold standard. ECoG imaging and DCE-MRI, VEEG, and PET-CT were compared during interictal seizures with respect to the sensitiveness of preoperative localization for pathogenic foci and diagnostic consistency. Ataractics were forbidden prior to operation. Patients underwent conventional craniotomy, and the dura mater was cut open to observe abnormal structure and color change in the brain surface. ECoG was traced on the exposed cortical surface, and comprehensive and careful tracing was performed for the projection of epileptic foci on the brain surface, which was followed by a recording within 5 min. Furthermore, epileptic waves (spike wave or sharp wave) were searched to determine the boundaries of the epileptic foci, brain function area, preoperative suspected epileptic foci, and the extent of primary surgical resection. After lesion resection, ECoG monitoring was conducted for paradoxical discharge from the cerebral cortex, and the operation was ended when abnormal EEG results were obviously reduced or disappeared. Conventional pathological examination was prior to lesion resection.

Postoperative treatments

All patients were treated with an intravenous injection of sodium valproate and an intramuscular injection of luminal within 3 d postoperatively and were orally administrated Tegretol (an anti-epileptic drug, 200 mg) twice per day postoperatively. Patients were carefully observed for epileptic seizures after the operation, and the drug dosage and anti-epilepsy treatment were adjusted in a timely manner according to clinical symptoms. The dosage of drug was also adjusted based on its concentration in blood. Drug administration was maintained for at least 2 years, and periodic review for liver and kidney function was required. For 3~6 months postoperatively, MRI review and scalp VEEG were conducted.

Follow-up results

All patients were followed up for 12 months and classified according to postoperative condition and Engles prognostic classification for epilepsy [14] into grade I (epileptic seizure disappeared completely or only presymptoms were presented, n=106),

Table 1. Clinical manifestations in children with epilepsy (N=166).

Clinical seizure types	No.
SPS	63
Autonomic nervous seizure	7
Nervous seizure	6
Motor seizure	37
Somatic sensation or special sense seizure	13
CPS	31
Only disturbance of consciousness	11
Disturbance of consciousness combined with automatism	20
sGTCS	67
SPS → sGTCS	18
CPS → sGTCS	43
SPS → CPS → sGTCS	6
GTCS	5

SPS – simple partial seizure; CPS – complex partial seizure; sGTCS – secondary generalized tonic-clonic seizure; GTCS – generalized tonic-clonic seizure.

grade II (epileptic seizure did not occur more than 2 times per year, n=31), grade III (seizure rate was reduced by more than 75%, n=21), and grade IV (seizure rate was reduced by less than 75%, n=8). Sensory aphasia occurred in 2 patients on the second postoperative day, and 1 week after enhanced dehydration and neurotrophic treatment, all symptoms were improved. Among the patients who received no intraoperative wake-up, decreased muscle strength of the contralateral limb occurred in 1 patient on the postoperative fifth day, and urinary incontinence and spiritual dimming occurred in 1 patient within 1 week postoperatively. Both patients were treated with dehydration and neurotrophic drug, and subsequently symptoms were relieved; review after 3 months revealed that all symptoms had disappeared. No permanent limb nerve dysfunction was found.

Statistical analysis

Data were processed by the SPSS 21.0 statistical software package. $P < 0.05$ was considered as a statistically significant difference. Univariate analysis for enumeration data was performed by using the χ^2 test, and correlations between all preoperative examinations and operation results were analyzed, with continuous calibration χ^2 test conducted when the case number was not more than 5. Multivariate analysis was conducted by analysis of variance, and logistic regression analysis was performed for various factors influencing the effect of the operation. Engel classification was applied in a postoperative evaluation with patients in grades I, II, and III as the effective group and patients in grade IV as the non-effective group. The positive rate and accuracy rate of each examination before the operation were counted for each group.

Results

Clinical manifestations and intraoperative lesion localization

Seizure symptoms of all 166 children included (1) simple partial seizures (SPS, n=63), autonomic nervous seizures mainly characterized by palpitation and flushing (n=7), nervous seizures mainly characterized by fear (n=6), motor seizures (n=37) that consisted of single limb rigidity (n=21), posture rigidity (n=5), and unilateral or bilateral limb clonus (n=11), and somatic sensation or special sense seizures manifested as numbness of the limbs, gastrointestinal discomfort, and so forth (n=13); (2) complex partial seizures (CPS, n=31) including only disturbance of consciousness (n=11) and hand automatism, speech automatism, and oropharynx automatism (n=20); (3) secondary generalized tonic-clonic seizures (sGTCS, n=67), among which there were 18 children with generalized seizures that developed from SPS, 43 children with generalized seizures that developed from CPS, and 6 children with CPS and sGTCS that developed from SPS; and (4) generalized tonic-clonic seizures (GTCS, n=5), as seen in Table 1.

All patients underwent surgical treatment and intraoperative ECoG examination with spike-wave, sharp-wave, or slow spike-wave complex detected. Among them were 76 children with epileptic discharge initiated in focal lesions, 85 children with extensive initiation, and 5 others with uncertain initial position of discharge. All patients received epileptic foci or/and epileptogenic foci resection under ECoG monitoring.

Table 2. Results of focus location detected by using DCE-MRI.

Detected abnormalities	DCE-MRI positive foci			
	Number of detected foci (left)	Accurate account (%)	Number of detected foci (right)	Accurate account (%)
Softening lesion formation	22	14 (63.64%)	24	15 (20.83%)
Frontal subarachnoid cyst	5	2 (40.00%)	3	2 (66.67%)
Calcification foci	7	3 (42.86%)	2	2 (100.00%)
Glioma	2	1 (50.00%)	3	1 (33.33%)
Central hippocampal sclerosis and atrophy	17	8 (47.06%)	11	6 (54.55%)
Brain atrophy	1	1 (100.00%)	2	2 (100.00%)
Total		57/99 (57.58%)		

DCE-MRI – dynamic contrast-enhanced magnetic resonance imaging.

Table 3. Results of focus location detected by using VEEG.

	During interictal seizures (n=114)	During seizure period (n=13)	P
Discharge types			
Unilateral discharge	97	10	0.430
Bilateral discharge	17	3	0.430
Focus location			
Temporal lobe	64	5	0.253
Frontal lobe	11	2	0.623
Temporal frontal lobe	20	4	0.267
Parietal lobe	4	1	0.423
Other locations	15	1	1.000

VEEG – video-electroencephalography.

Localization value of DCE-MRI

DCE-MRI imaging of 166 children with epilepsy showed abnormalities in brain development, cerebral softening, central hippocampal sclerosis and atrophy, increased signal intensity, loss of internal structural detail, etc. Among them, 99 children had abnormalities on DCE-MRI examination and a positive detection rate of 59.64%. In the left occipital lobe, 23 showed softening lesion formation, 5 displayed a frontal subarachnoid cyst, 7 presented calcification foci in the parietal lobe, 2 had frontal glioma, 17 showed central hippocampal sclerosis and atrophy, and 1 had left brain atrophy; while in the right occipital lobe, 24 showed softening lesion formation, 3 displayed a frontal subarachnoid cyst, 2 presented calcification foci in the frontal lobe and parietal lobe, 3 had frontal glioma,

11 showed central hippocampal sclerosis and atrophy, and 2 had right brain atrophy (Table 2). In the 99 children, foci in 57 were in line with the results of intraoperative lesion localization by ECoG, showing a localization accuracy rate of 57.58%.

Localization results of VEEG

All 166 patients received VEEG examination with a mean duration of 24 h, and results showed that epileptiform discharges were recorded during interictal seizures in 114 patients, epileptiform discharges during the seizure period and interictal seizures in 13 patients, and no typical epileptic discharges in 39 patients. Among those 114 patients with epileptiform discharges during interictal seizures, the VEEG results demonstrated (Table 3) mainly unilateral discharge and a few bilateral

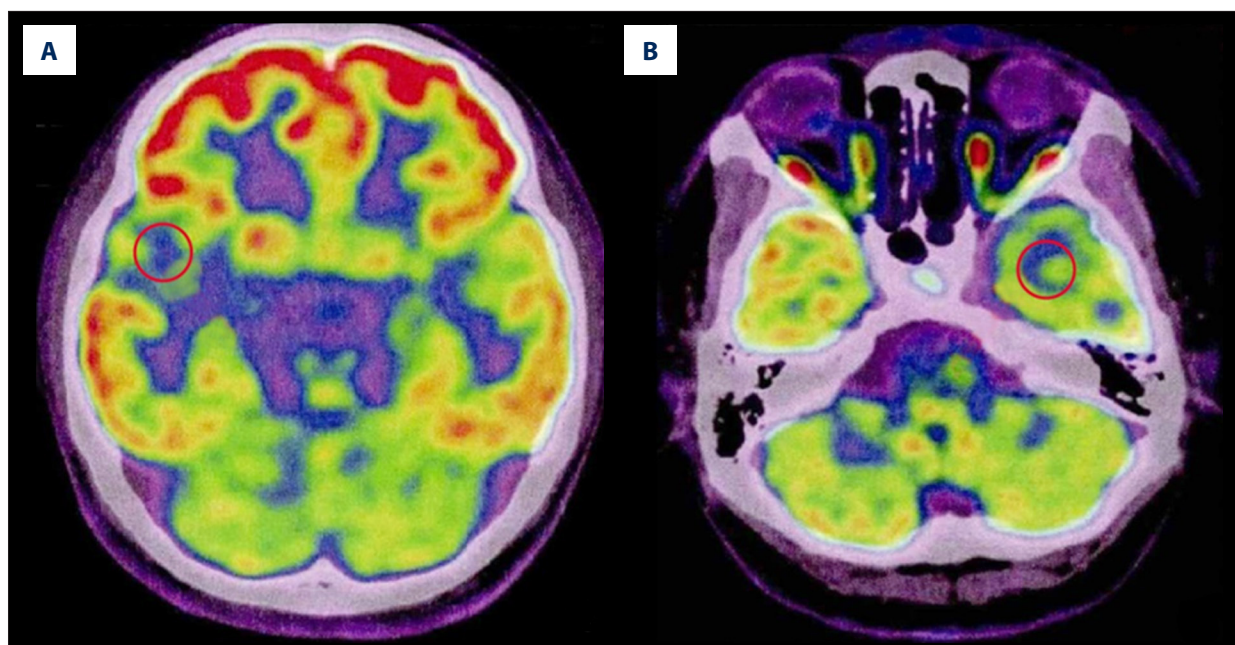


Figure 1. (A) PET-CT imaging showed metabolic reduction in the lateral cortex of the anterior temporal lobe (right), indicating epileptic focus. (B) PET-CT imaging showed metabolic reduction in the medial cortex, basal surface, and partial lateral cortex of the anterior temporal lobe (left), indicating epileptic focus. PET-CT, positron emission tomography-computed tomography.

discharges in 97 patients, and mainly bilateral discharge in only 17 patients; 64 patients had foci located in the temporal lobe, 11 had foci in the frontal lobe, 20 had foci in the temporal frontal lobe, 4 had foci in the parietal lobe, and 15 had foci in the other positions. Among those 13 patients with epileptiform discharges during the seizure period, the VEEG results revealed that a total of 43 seizures occurred with a mean frequency of 3 seizures per patient; 10 patients mainly showed unilateral discharge and only 3 patients mainly presented bilateral discharge; 5 patients had foci located in the temporal lobe, 2 had foci in the frontal lobe, 4 had foci in the temporal frontal lobe, 1 had foci in the parietal lobe, and 1 had foci in the other positions.

Localization results of PET-CT

PET-CT imaging of children with epilepsy mainly showed cerebral metabolic reduction during interictal seizures or cerebral metabolic increase during the seizure period (Figure 1). As shown in Table 1, 156 out of 166 patients had positive PET-CT imaging, 10 showed no obvious abnormalities, and detection sensitivity for foci reached 93.98% (156/166). Among the positive cases, 149 patients displayed cerebral metabolic reduction during interictal seizures, with 49 patients (32.89%) showing metabolic reduction in the temporal lobe, 44 (29.53%) in the frontal lobe, 21 (14.09%) in the temporal frontal lobe, 7 (4.70%) in the insular area, 16 (10.74%) in the parietal lobe, and 12 (8.05%) in the other positions; while 7 patients (5.37%) displayed cerebral metabolic increase during the seizure period,

with 3 patients (42.86%) showing metabolic increase in the temporal lobe, 2 (28.97%) in the frontal lobe, 1 (14.29%) in the temporal frontal lobe, and 1 (14.29%) in the parietal lobe. No statistical difference was found in the focus location between children with metabolic reduction during interictal seizures and children with metabolic increase during the seizure period (all $P > 0.05$) (Table 4).

Diagnostic value of DCE-MRI/VEEG/PET-CT in preoperative localization for epileptic foci

All 166 patients who underwent the operation received intraoperative ECoG monitoring, which was compared with DCE-MRI/VEEG/PET-CT and the monitoring results of integrated application (Table 5). Preoperative foci were detected as positive by DCE-MRI in 99 children with epilepsy, and intraoperative ECoG findings on 57 children were in line with preoperative localization by DCE-MRI, with an obvious abnormal intracranial signal detected; therefore, the accuracy rate of DCE-MRI preoperative localization was 57.58%. With preoperative VEEG, positive foci were detected in 127 children, 86 of whom had results consistent with intraoperative ECoG monitoring, contributing to an accuracy rate of VEEG preoperative localization of 67.72%. With PET-CT, positive foci were detected in 156 children, with 142 children having results consistent with intraoperative ECoG monitoring, which showed that the accuracy rate of PET-CT preoperative localization was 91.03%.

Table 4. Results of focus location detected by using PET-CT.

Focus location	Cerebral metabolic reduction during interictal seizures	Cerebral metabolic increase during seizure period	P
Temporal lobe	49 (32.89%)	3 (42.86%)	0.687
Frontal lobe	44 (29.53%)	2 (28.97%)	1.000
Temporal frontal lobe	21 (14.09%)	1 (14.29%)	1.000
Insular area	7 (4.70%)	0 (0.00%)	1.000
Parietal lobe	16 (10.74%)	1 (14.29%)	0.562
Other locations	12 (8.05%)	0 (0.00%)	1.000

PET-CT – positron emission tomography-computed tomography.

Table 5. Sensitivity and diagnostic accuracy of each imaging technology for preoperative epileptic focus localization.

Detection method	Positive		Negative		Accurately localized foci	
	No.	%	No.	%	No.	%
DEC-MRI	99	59.64%	67	40.36%	57	57.58%
VEEG	127	76.51%	39	23.49%	86	67.72%
PET-CT	156	93.98%	10	6.02%	142	91.03%
P	<0.001		<0.001		<0.001	

DCE-MRI – dynamic contrast-enhanced magnetic resonance imaging; VEEG – video-electroencephalography; PET-CT – positron emission tomography-computed tomography.

Table 6. Diagnostic value of DCE-MRI combined with VEEG and PET-CT techniques in preoperative epileptic focus localization.

Combined imaging techniques	Accurately localized foci by DCE-MRI (N=57)	
	Accurate account	Accurate rate
VEEG	52	91.23%
PET-CT	55	96.49%
VEEG and PET-CT	56	98.25%
P	0.182	

DCE-MRI – dynamic contrast-enhanced magnetic resonance imaging; VEEG – video-electroencephalography; PET-CT – positron emission tomography-computed tomography.

Diagnostic value of DCE-MRI/VEEG, DCE-MRI/PET-CT, and DCE-MRI/VEEG/PET-CT in preoperative localization for epileptic foci

DCE-MRI combined with other imaging techniques significantly improved localization accuracy. To be more specific, 57 out of 99 children with positive detection on DCE-MRI examination had foci that were accurately localized, and among them, 52 children had DCE-MRI localization results consistent with VEEG positive detection. Therefore, the accuracy rate of localization in DCE-MRI combined with VEEG was 91.23% (52/57). In addition, 55 children had DCE-MRI localization results consistent

with PET-CT positive detection, and the accuracy rate of localization with DCE-MRI combined with PET-CT was 96.49% (55/57); 56 children had DCE-MRI localization results consistent with VEEG and PET-CT detection. Localization accuracy rate of the combination of DCE-MRI, VEEG, and PET-CT was 98.25% (56/57), which was higher than that of DCE-MRI combined with VEEG and of DCE-MRI combined with PET-CT. No statistical difference was found in the accuracy rate of localization between these three combined techniques ($P=0.182$). The accuracy rate of localization with these three combined techniques was far higher than that of DCE-MRI, DCE-MRI and PET-CT alone (Table 6).

Table 7. Postoperative therapeutic effects of DCE-MRI combined with VEEG and PET-CT techniques in epileptic focus localization.

DCE-MRI combined with other imaging methods	No.	Engles prognostic classification				Effective rate
		Grade I	Grade II	Grade III	Grade IV	
VEEG						
Consistent	52	41 (78.85%)	9 (17.31%)	2 (3.85%)	0 (0.00%)	100.00%
Inconsistent	5	0 (0.00%)	1 (20.00%)	2 (40.00%)	2 (40.00%)	60.00%
PET-CT						
Consistent	55	43 (78.18%)	11 (20.00%)	1 (1.82%)	0 (0.00%)	100.00%
Inconsistent	2	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (50.00%)	50.00%
VEEG and PET-CT						
Consistent	56	43 (76.79%)	11 (19.64%)	2 (3.57%)	0 (0.00%)	100.00%
Inconsistent	1	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00)	0.00%

DCE-MRI – dynamic contrast-enhanced magnetic resonance imaging; VEEG – video-electroencephalography; PET-CT – positron emission tomography-computed tomography.

Observation of postoperative therapeutic effects

All children received operative treatment, postoperative long-term VEEG monitoring, and 12-month follow-up. According to postoperative conditions, all children were grouped with Engles prognostic classification for epilepsy into grade I (epileptic seizure disappeared completely or only presymptoms were presented), grade II (epileptic seizure did not occur more than 2 times per year), grade III (seizure rate was reduced by more than 75%), and grade IV (seizure rate was reduced by less than 75%). Among the 57 children with accurate foci localization by DCE-MRI, 52 of them had consistent foci localization in DCE-MRI combined with VEEG, with 41 children in postoperative Engles grade I, 9 in postoperative Engles grade II, and 2 in postoperative Engles grade III, showing an effective group (grades I, II and III) that accounted for 100% of the children. Among the 5 children with inconsistent foci localization in DCE-MRI combined with VEEG, 1 child was classified into postoperative Engles grade I, 2 into postoperative Engles grade III, and 2 into postoperative Engles grade IV, indicating an effective group (grades I, II, and III) that accounted for 60% of the children. Among the 55 children with consistent foci localization in DCE-MRI combined with PET-CT, 43 children were classified into postoperative Engles grade I, 11 into postoperative Engles grade II, and 1 into postoperative Engles grade III, indicating an effective group (grades I, II, and III) that accounted for 100% of the children. Among the 2 children with inconsistent foci localization in DCE-MRI combined with PET-CT, 1 child was classified into postoperative Engles grade II and 1 into postoperative Engles grade IV, revealing an effective group (grade I, II and III) that accounted for 50% of the children. Among the 56 children with consistent foci localization using DCE-MRI combined with PET-CT and VEEG, 43

children were classified into postoperative Engles grade I, 11 children into postoperative Engles grade II, and 2 children into postoperative Engles grade III, indicating an effective group (grades I, II, and III) that accounted for 100% of the children. In addition, 1 child with inconsistent foci localization in DCE-MRI combined with PET-CT and VEEG was classified into postoperative Engles grade IV. Postoperative therapeutic effects in foci localized consistently by DCE-MRI combined with VEEG, DCE-MRI combined with PET-CT, and DCE-MRI combined with PET-CT and VEEG were superior to those in foci localized inconsistently (Table 7).

Discussion

The purpose of this study was to investigate the effect that DCE-MRI has on surgical decision making relative to VEEG and PET-CT, and if the differences in these variables translate to differences in surgical outcomes. It was found that the accuracy of DCE-MRI combined with VEEG and of DCE-MRI combined with PET-CT was evidently higher than that of DCE-MRI, VEEG, and PET-CT alone, suggesting that combined diagnostic methods are far superior to a single method for the localization of epileptic foci. Currently, most patients with epilepsy are recommended to receive PET examination and routine ¹⁸F-FDG metabolic imaging to preoperatively localize foci, while our study proved that application of DCE-MRI combined with PET-CT is of excellent accuracy (and is superior to DCE-MRI combined with VEEG) [15]. Aaron et al. found that MRI combined with FDG-PET had a trend toward the most influence on surgical candidacy [16]. Rubi et al. also demonstrated that PET/MRI coregistration is an imaging variant that is accurate in detecting the epileptogenic zone in pediatric nonlesional patients [17].

In addition, preoperative localization with both DCE-MRI combined with VEEG and DCE-MRI combined with PET-CT was demonstrated to have excellent postoperative efficiency according to Engles prognostic classification for epilepsy.

PET-CT is the most advanced imaging equipment that is capable of organically combining tissue and cell metabolism imaging provided by PET, molecular imaging conducted based on macromolecules, proteins, and nucleic acids, and imaging reflecting anatomic structure and blood flow perfusion provided by CT [8]. This imaging equipment is mainly used in cases of conventional MRI and EEG negative detection or localization contradiction, especially in inconsistent localization between intracranial electrode and VEEG and MRI, and is characterized by higher sensitivity than VEEG and DCE-MRI, which was evidenced in our study [15]. Statistical analysis revealed that PET-CT detected abnormal brain function in 156 children, among whom 94.63% displayed cerebral metabolic reduction during interictal seizures and 5.37% displayed cerebral metabolic increase during the seizure period. During the seizure period, epileptic foci present neuronal hyperactivity, and a considerable number of neuronal cells repeatedly participate in polarization, which causes increased energy consumption, leading to significantly increased local blood flow and glucose metabolism; therefore, PET-CT imaging showed cerebral metabolic increase [18]. Similarly, during interictal seizures, glucose transporter-1 dysfunction that results in the inability of glucose to pass through the blood-brain barrier and be uptaken by neurons and glial cells, combined with abnormal function of neurons in the tissue adjacent to the epileptic zone and the inhibition of hyperpolarization, contributes to cerebral metabolic reduction on PET-CT imaging [18–20].

Compared with CT, DCE-MRI has numerous advantages, including higher resolution, ability to exclude the interference of bone on the imaging, clear display of minimal abnormal lesions in the brain, capability of primary localization of epileptic foci from the aspect of morphology, and ability to detect abnormal structures in the brain such as intracranial space-occupying structures, cerebral softening, inflammation, brain atrophy, etc. [21]. Thus, as a major means of detection in preoperative evaluation of epilepsy, it has been widely used for the preoperative evaluation of epileptic foci localization, providing clear and intuitive anatomical images for the diagnosis

and surgery of intractable epilepsy [11]. Moreover, Zajac et al. reported that neuroimaging by MRI is particularly important in younger children with a longer course of epilepsy and an abnormal neurological examination, and for detection of migration and hippocampal changes [22]. However, it lacks of high specificity and has a low sensitivity for primary epilepsy without obvious structural changes [23]. In our study, the positive rate of DCE-MRI detection was 59.64%, and in cases of negative DCE-MRI detection or DCE-MRI localization results inconsistent with the gold standard (ECoG monitoring), PET-CT or DCE-MRI combined with PET-CT was required.

Although VEEG has a vital role in epilepsy diagnosis and epileptic foci localization, VEEG has several limitations as a basic localization detection method in children with epilepsy. Firstly, epileptic foci contributing to epilepsy formation may not exist in the abnormal discharge area; thus, VEEG alone for clear localization is insufficient. Secondly, because of interference by some negative factors such as the number of electrodes, lead method, skull, and scalp, VEEG always is unable to offer the exact location and range of the epileptic foci, resulting in low sensitivity and specificity in epileptic foci localization [24]. Intracranial electrode implantation can exclude the above-mentioned interferences to some extent; however, it is an invasive detection method that may lead to intracranial infection and hematoma [25]. Therefore, DCE-MRI is suggested for imaging localization inconsistent with VEEG localization to ensure the location of epileptic foci in general; intracranial electrode implantation is required when noninvasive detection fails to further localize epileptic foci.

Conclusions

In conclusion, both DCE-MRI combined with VEEG and DCE-MRI combined with PET-CT have excellent accuracy in preoperative localization of epileptic foci, and present excellent postoperative efficiency, suggesting that these combined imaging methods are suitable for serving as a reference basis in preoperative localization of epileptic foci in children with epilepsy.

Competing interests

We declare that we have no conflicts of interest.

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