



Research paper

High density electric source imaging in childhood-onset epilepsy due to focal cortical dysplasia



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ABSTRACT

Objective: The goal of this study was to investigate the diagnostic utility of electric source imaging (ESI) in the presurgical evaluation of children with focal cortical dysplasia (FCD) and to compare it with other imaging techniques.

Methods: Twenty patients with epilepsy onset before 18 years, surgically treated focal epilepsy with a minimal follow-up of 2 years, and histologically proven FCD were retrospectively selected. All patients underwent MRI, positron emission tomography (PET), and 16 patients also had ictal single-photon emission computed tomography (iSPECT). ESI, using EEG with 64 electrodes or more (HD-ESI), was performed in all 20 patients. We determined sensitivity, specificity and accuracy of ESI, and compared its yield to that of other imaging techniques.

Results: Twelve patients were seizure-free post-operatively (60%). Among all patients, highest localization accuracy (80%) was obtained with ESI, followed by PET and iSPECT (75%). When results from ESI and SPECT were concordant 100% of patients achieved Engel I outcome. If ESI and PET showed concordant localization, 90% of patients achieved postoperative seizure freedom.

Conclusions: Our findings demonstrate that HD-ESI allows accurate localization of the epileptogenic zone in patients with FCD.

Significance: In combination with other imaging modalities, ESI helps with planning a more accurate surgery and therefore, the chances of postoperative seizure control are higher. Since it is based on EEG recordings, it does not require sedation, which is particularly interesting in pediatric patients. ESI represents an important imaging tool in focal epilepsies due to cortical dysplasia, which might be difficult to detect on standard imaging.

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1. Introduction

Focal cortical dysplasia (FCD) is a cerebral malformation due to a developmental defect in cortical organization (Taylor et al., 1971). Pathogenesis of FCD includes abnormalities of lamination, neuronal differentiation and neuronal maturation ranging from

mild to severe. Mild cortical dysplasia, currently classified as FCD type I, is usually very subtle or even undetectable on magnetic resonance imaging (MRI). More severe FCD, classified as type II, presents mostly in young children, often with frequent seizures, status epilepticus and infantile spasms. This type of dysplasia is divided into IIa and IIb, with IIb showing balloon cells and being more likely visible in the MRI. In the more recent classification (Blümcke et al., 2011), FCD type III, was introduced, which associates FCDs with other brain pathologies.

FCD is a common cause of drug resistant focal epilepsy in children and adults. It is also the most frequent etiology in children undergoing epilepsy surgery (Blümcke et al., 2017; Lerner et al.,

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2009), which often represents the only option to obtain long term seizure control. Overall, postsurgical seizure freedom ranges from 42 to 70% in pediatric patients (Chen et al., 2014; Hader et al., 2004; Hudgins et al., 2005; Krsek et al., 2009a, 2009b; Park et al., 2006; Phi et al., 2010; Ramantani et al., 2013), on average 55.8 +/- 16.2% in a meta-analysis 37 studies on 2014 patients (Rowland et al., 2012).

Given that FCD are often undetectable on MRI, additional algorithms to localize the epileptogenic zone with good sensitivity and specificity were developed. Recent advances in morphometric MRI analysis increased the sensitivity of detecting dysplasia type II, in particular IIb (Wagner et al., 2011). Multimodal imaging with combined analysis of MRI, positron emission tomography (PET) and ictal single-photon emission computed tomography (iSPECT) also helps to detect subtle lesions (Juhász and John, 2020).

Electric source imaging (ESI) allows to noninvasively localize the epileptogenic zone if based on high density EEG (64 electrodes or more, HD-ESI). The technique has been particularly well studied in adults (Brodbeck et al., 2011; Mégevand et al., 2014) but clinical applications in children are limited and reports on ESI in children with dysplasia remain scarce (Russo et al., 2016a; Sperli et al., 2006).

In the present study, we investigated the yield of HD-ESI in a cohort of patients with childhood-onset epilepsy due to FCD managed by surgical resection. Our goal was to correlate ESI findings with epilepsy outcome and to compare its localization value with other non-MRI imaging techniques, such as PET and iSPECT.

2. Materials and methods

This study was approved by the local Research Ethics Committee, in agreement with the Declaration of Helsinki.

The study was conducted at the Geneva University Hospitals, a tertiary referral center for presurgical and surgical management of adults and children with drug-resistant epilepsy. Overall more than 900 patients have been evaluated since its opening in 1995. Among them, approximately 40% are children at the time of presurgical evaluation.

Inclusion criteria for our study were: diagnosis of FCD on the basis of histopathology, onset of epilepsy before 18 years and surgically treated, ESI using 64 electrodes or more, follow-up of at least two years. Patients with FCD suspected on MRI but not confirmed at histopathology were excluded.

2.1. Patients

Systematic ESI was introduced in 2000. We therefore retrospectively searched our database between 2000 and 2019, and identified 52 patients (adults and children) with a diagnosis of FCD. Twenty-five patients were excluded because HD-ESI was not performed. Seven patients were excluded because they did not have surgery yet or because the follow-up was too short. Finally, 20 patients matched our inclusion criteria.

The following data were analyzed: gender, age at seizure onset and at surgery, duration of epilepsy before surgery, seizure type, seizure frequency, FCD localization and histopathological subtype, associated cerebral lesions, developmental or cognitive level, number and types of preoperative anti-epileptic treatments, as well as family history of seizures or developmental delay. Preoperative development was formally assessed by a neuropsychologist in all patients.

We also collected all data of the presurgical evaluation procedures, which in our center typically includes prolonged video-electroencephalogram (EEG), 3 Tesla cerebral MRI, interictal PET-scan, ictal and interictal SPECT-scans, including subtraction

analysis (referred to together as “ictal SPECT” or “iSPECT”), and high-density ESI based on EEG with 64 electrodes or more. Finally, type and number of resective surgical procedures, post-operative complications and seizure frequency, as well as duration of the follow-up were also collected. Post-operative seizure outcome was assessed according to the Engel Classification (Wieser et al., 2001).

2.2. Electric source imaging

In these 20 patients, eleven EEGs were recorded with 256 electrodes, four with 128 electrodes and five with 64 electrodes. We used HydroCel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR, USA), allowing 1–2 h recording sessions during wakefulness and light sleep (sampling rate of 1 kHz, band-pass 0.1–400 Hz). The Vertex (Cz) electrode was used as recording reference and data were referenced offline to the average reference. The recording duration was 1–2 h and carried out in the patient's bed, usually after lunch to allow light sleep. Since HD-EEG required the removal of the long-term monitoring EEG electrodes, it was obtained at the end of the monitoring period when medication was partially resumed. No sound or light restriction was imposed.

Epileptogenic discharges (summarized as “spikes”) were manually selected from the EEG by a board certified EEG reader, unblinded to the patient's history. Discharges consisted of focal spikes, spike-waves and sharp waves. If a burst of discharges occurred, the first one was chosen for analysis. Channels with artifacts were removed and interpolated from the analysis. Only the most frequent spike type was subject to analysis. Spikes were averaged to increase signal-to-noise ratio.

Source estimation was done using the linear distributed inverse solution called local autoregressive average (LAURA) (de Peralta et al., 2004; Michel et al., 2004a) by one of us (LS, blinded to clinical data), coregistered with the patient's MRI as described elsewhere (Brodbeck et al., 2011).

In short, 5000 solution points are distributed evenly in the extracted grey matter and serve as the solution space (Brunet et al., 2011; Spinelli et al., 2000). The lead field matrix is then computed using the known analytical solutions for an advanced three-shell spherical head model with anatomical constraints (Ary et al., 1981), and incorporated in the linear inverse solution algorithm which allows the localization of the electric source. The potential map at 50% of the rising phase of the averaged spike was used for source analysis. This information is fused with the patient's MRI.

We also determined the localization of the ESI maximum compared to the resected area. For that, we measured the distance of the ESI maximum to the surgical resection border on a postoperative MRI coregistered to the preoperative MRI.

ESI was described as “localizing” when the ESI maximum was located in the resected area in patients with favourable outcome.

2.3. MRI, PET and iSPECT

All patients had MRI as part of the presurgical evaluation acquired with a 3 Tesla machine based on established imaging protocols.

All 20 patients also underwent conventional FDG-PET during the interictal state, monitored with EEG. The administered activity was 200–250 MBq for adults and was adapted to body weight in children. Images were obtained 30 min after tracer administration, reconstructed with an iterative ordered subset expectation maximization algorithm and corrected for attenuation, decay and scatter. Five PET tomographs were used, namely a Siemens Biograph (17 subjects), Biograph mCT (one subject), Biograph Vision (one subject) and an ECAT-Exact PET (one subject).

Ictal and interictal SPECT were performed in 16 patients using tracer injection (99mTc-Ethyl cysteinat dimer, 740 MBq for adults and weight-adapted doses for children) during seizure or in the interictal phase (with a minimum interval of 24 h since the last seizure). Images were obtained 20–60 min after the radioisotope injection. Images were acquired with fan beam collimators and reconstructed correcting for uniform attenuation using a Chang method and for scatter with a double window method. Two SPECT systems were used, namely a Toshiba three head tomograph (14 subjects) and a Siemens Symbia T6 two head tomograph (two subjects).

All images were reviewed by a trained neuroradiologist and nuclear medicine specialist during the presurgical evaluation. For this study, we reviewed only the clinical reports made by imaging experts at the time of the evaluation.

2.4. Surgery

All cases were reviewed in a multidisciplinary discussion between epileptologists, paediatric neurologists, neurosurgeons, neuroradiologists and neuropsychologists to determine the degree of agreement between the different imaging modalities. Based on this review, decision for surgery, type and extent of resection were taken by the consortium.

2.5. Statistical analysis

Data were analyzed with univariate and multivariate logistic regression models to measure their relationship with the post-operative epilepsy outcome. We analyzed the following parameters: histological diagnosis (FCD type), results of the intracranial EEG recordings, location of the lesion (temporal versus extratemporal), presence or absence of another cerebral lesion, number of surgical interventions and completeness of resection. Categorical data were analyzed using contingency tables and Chi-square test and Fisher's exact test were used to test for differences. For all analyses, p -values < 0.05 were considered as statistically significant.

We also calculated sensitivity and specificity of ESI, ictal SPECT and PET. The imaging modality was described as "true positive" in a given patient when the maximum of abnormality (source, hypometabolism or hyperperfusion) was located in the resected lobe in patients with postoperative seizure control. "False positive" refers to patients where the abnormality was included in the resection, but the patient continued to present seizures post-operatively. The result was labeled as "true negative" if the pathology was outside the resection volume and the patient continued to suffer from seizures. "False negative" refers to cases where the abnormality was not resected, but the patient became seizure-free.

We used Chi-square and Fisher exact tests to assess the statistical significance of the difference between sensitivity and specificity of PET, iSPECT and ESI.

3. Results

3.1. Demographic data

General characteristics of our patients are summarized in Table 1. Age at seizure onset varied from one week to 18 years. Patients data are summarized in Table 1.

3.2. Postoperative seizure outcome

Overall 12 of the 20 patients (60%) had Engel I post-surgery outcome. Details of patients' outcome can be found in Table 2.

Table 1
General patients characteristics (n = 20).

Gender male/female	8/12
Age at seizure onset: median/range (years)	1.1/0–18
Age at surgery: median/range (years)	11.4/1–35
Epilepsy duration: median/range (years)	8.8/0.8–34.3
Post-op follow-up time: median/range (years)	2/2–11
FCD localization	
Temporal	6 (30%)
Extra-temporal	14 (70%)
FCD type	
Type I	8 (40%)
Type II	12 (60%)
Type III	0
Side of lesion	
Left	10 (50%)
Right	10 (50%)
Both	0
Type of surgery	
Lesionectomy	13 (65%)
Lobectomy	5 (25%)
Multilobectomy	2 (10%)
Hemispherectomy	0
Imaging and EEG	
Video-EEG monitoring	20 (100%)
Intracranial EEG recording	9 (45%)
MRI	20 (100%)
MRI positive for FCD lesion	16 (80%)
PET	20 (100%)
iSPECT	16 (80%)
ESI	20 (100%)

n, number of patients.

Ten of them were seizure-free after the first intervention. Two became seizure-free after a second intervention. In both cases, an incomplete resection was identified to be the reason of persistent seizures. For those patients, ESI localization was concordant with the second resection. Types of surgery are summarized in Table 1.

According to the ILAE classification of focal cortical dysplasias,² eight patients (40%) had type I FCD, 12 (60%) had type II FCD. Among patients with type II, four were type IIa and eight were type IIb. There were no significant differences regarding seizure outcome between patients with FCD type I or II ($p = 0.09$).

Extratemporal localization was more often associated with a younger age at epilepsy onset ($p = 0.0044$). However, there were no significant differences between temporal and extratemporal foci regarding seizure outcome.

3.3. EEG and imaging

All patients underwent MRI and PET, and 16 patients had ictal SPECT. All of them also underwent high density EEG with ESI analysis.

First, correct localization with respect to the affected lobe was evaluated to allow the comparison with other imaging techniques. ESI results were localized within the affected lobe (concordant) in 70% of the cases. This was significantly superior to ictal SPECT, co-localizing in 41.7% ($p = 0.04$). Similar localization value was obtained with PET, which showed concordant unifocal hypometabolism in 59.5% (no difference to ESI, $p = 0.4$).

Comparing sensitivity and specificity of the different non-MRI imaging modalities (ESI, PET and iSPECT), ESI showed the highest sensitivity with 91.7%, followed by 75% for PET ($p = 0.3$), and iSPECT with low sensitivity (55.6%; $p = 0.06$) but higher specificity (100%) ($p = 0.2$). This amounted to an accuracy of 80% for ESI, and 75% for PET and for iSPECT. All the characteristics of ESI, PET and SPECT are summarized in Table 3.

Table 2
Postoperative outcome according to FCD localization and type.

	Engel Class I (%)	Engel Class II (%)	Engel Class III (%)	Engel Class IV (%)
All patients	12 (60)	3 (15)	4 (20)	1 (5)
Localization				
Temporal	3 (25)	1 (33.3)	2 (50)	0
Extratemporal	9 (75)	2 (66.7)	2 (50)	1 (100)
FCD type				
Type I	3 (25)	3 (100)	1 (25)	1 (100)
Type II	9 (75)	0	3 (75)	0

We found no differences ($p = 0.8$) in ESI localization precision between extratemporal (66.7 %) and temporal epilepsy (71.4 %). Table 4 summarizes the localizing power of the different imaging techniques in temporal and extratemporal lesions. ESI was localizing in ten patients (83 %) with FCD type II and only in four patients (50 %) with FCD type I ($p = 0.11$). Table 5 summarizes the features of each patient.

In nine of 20 patients (45 %), the distance of ESI maximum to the surgical resection border was equal to zero (i.e. the ESI maximum was located inside the resected area). In 11 patients, the source maximum was located outside the resection volume. The distance to the lesion was between 4.8 and 40.7 mm (mean: 22.1 mm). Six patients had a source maximum outside the resected area but that was still correct on a lobar level.

Seizure freedom was observed in nine out of ten patients (90 %) when ESI and PET showed concordant localizing results, but only in five patients (60 %) if the results of ESI and PET were discordant ($p = 0.24$). Similarly, concordant results of ESI and iSPECT were associated with seizure freedom in all of the five patients who underwent both exams. If the ESI and SPECT showed divergent results ($n = 6$), only 50 % experienced seizure control ($p = 0.18$). When ESI, PET and iSPECT all pointed to the same cortical regions, the outcome was Engel I in all four patients (100 %). Examples of co-registration of ESI, PET and iSPECT images are shown in Fig. 1 and Fig. 2.

Table 3
Characteristics of ESI, PET and iSPECT.

	ESI (n = 20)	PET (n = 20)	iSPECT (n = 16)	p-Value
Sensitivity (%)	91.7	75.0	55.6	0.3* 0.06**
Specificity (%)	62.5	75.0	100	0.6* 0.2**
PPV (%)	78.6	81.8	100	0.8* 0.5**
NPV (%)	83.3	66.7	60.0	0.5* 0.4**

PPV, positive predictive value; NPV, negative predictive value; n, number of patients.

* p-Value calculated by comparison of ESI versus PET.

** p-Value calculated by comparison of ESI versus SPECT.

Table 4
Localizing value according to temporal and extratemporal FCD.

	ESI	PET	iSPECT	p-Value
Temporal (%)	66.7	60	53.3	0.76* 0.55**
Extratemporal (%)	71.4	55.6	28.6	0.31* 0.01**

* p-Value calculated for localizing value of ESI versus PET.

** p-Value calculated for localizing value of ESI versus SPECT.

ESI were done using different numbers of electrodes. Eleven EEGs were recorded with 256 electrodes, four with 128 electrodes and five with 64 electrodes. When 256 electrodes were used, ESI was localizing in nine out of eleven patients (82 %), compared to 50 % with use of 128 electrodes and 60 % with 64 electrodes ($p = 0.5$). Seizure freedom was more frequently found in patients who had 256 electrodes recordings. Ten out of eleven patients (91 %) with 256 electrodes recordings were Engel I after surgery, compared to none with 128 electrodes and two out of five (40 %) with 64 electrodes ($p = 0.0015$).

Four patients (20 %) were MRI negative. In that case, ESI was localizing in only two patients (50 %). In MRI positive patients, ESI was able to localize the lesion in 12 out of 15 patients (80 %). The mean distance of ESI maximum to resection border for MRI negative patients was 18.7 mm (range 0 – 40.68 mm), compared to a mean distance of 10.2 mm for MRI positive patients.

The percentage of Engel II-IV was higher in temporal lesions than extratemporal. Three out of six patients (50 %) with temporal FCD were Engel II-IV compared to only five out of 14 patients (36 %) with extratemporal lesions. This result is not statistically significant ($p = 0.64$) and might be due to the small population.

4. Discussion

The findings of our study show that HD-ESI provides excellent localization precision of FCD in the presurgical evaluation of surgical candidates. This method based on non-invasive EEG is easily applicable in children. Adding ESI results to nuclear imaging analyses improve patient outcome.

Patients with FCD often have abundant interictal discharges, as in our population, which allows computing an excellent signal-to-noise ratio of the averaged spikes. We found highest accuracy (80 %) and sensitivity (91.7 %) for ESI, which was superior to ictal SPECT and PET, although non significantly. Concordance of ESI with either PET or SPECT was associated to 90–100 % chance of complete seizure control, which underlines the value of multimodal imaging.

As the postoperative prognosis of FCD is modest (Rowland et al., 2012), in particular if the MRI is negative or ambiguous, additional tools are needed to determine the localization of the FCD. The yield of PET and iSPECT might be limited by the presence of multifocal abnormalities, mainly due to propagation of ictal activity and recruitment of remote structures, and in case of PET, large hypometabolic zones which match only partially with the seizure-onset zone (Tomas et al., 2019). ESI results lack information of the extent of source, but are unambiguous regarding the neuronal activity. As such, ESI provides complementary information to PET and iSPECT if MRI is negative or multifocal.

Our results corroborate the findings of Russo et al. in 14 pediatric patients with cortical dysplasia, who also found superiority of ESI over other imaging exams (Russo et al, 2016b). Using 32 channel recordings in 40 FCD patients, a sensitivity of 66 % and a specificity of 37 % with regard to surgical outcome after one year of follow-up was described (Russo et al, 2016a). The relatively

Table 5
Main features of each patient.

	Histology	MRI	Localization	Outcome (Engel)	PET localizing	iSPECT localizing	ESI localizing
Patient 1	FCD IIb	Positive	E	I	Yes	Yes	Yes
Patient 2	FCD IIa	Positive	E	I	Yes	No	Yes
Patient 3	FCD IIb	Positive	T	III	No	No	Yes
Patient 4	FCD I	Positive	E (multifocal)	IV	No	No	No
Patient 5	FCD IIb	Positive	E	I	Yes	Yes	Yes
Patient 6	FCD I	Positive	E	II	No	No	No
Patient 7	FCD I	Positive (only on 3 T)	E	III	No	No	No
Patient 8	FCD I	Negative	T	I	Yes	Yes	Yes
Patient 9	FCD IIb	Negative	E	III	Yes	No	No
Patient 10	FCD IIa	Positive	E	I	Yes	No	Yes
Patient 11	FCD IIb	Positive	E	I	Yes	Yes	Yes
Patient 12	FCD IIb	Positive	T	III	Yes	No	Yes
Patient 13	FCD I	Positive	T	II	No	No	No
Patient 14	FCD I	Positive	E	I	Yes	Yes	Yes
Patient 15	FCD I	Positive	E	I	Yes	No	Yes
Patient 16	FCD IIa	Positive	E	I	Yes	No	Yes
Patient 17	FCD IIb	Negative	T	I	No	No	No
Patient 18	FCD IIb	Positive	E	I	No	No	Yes
Patient 19	FCD I	Positive	E	II	No	No	Yes
Patient 20	FCD IIa	Negative	T	I	No	Yes	Yes

3 T, 3 Tesla MRI; T, Temporal, E, Extratemporal.

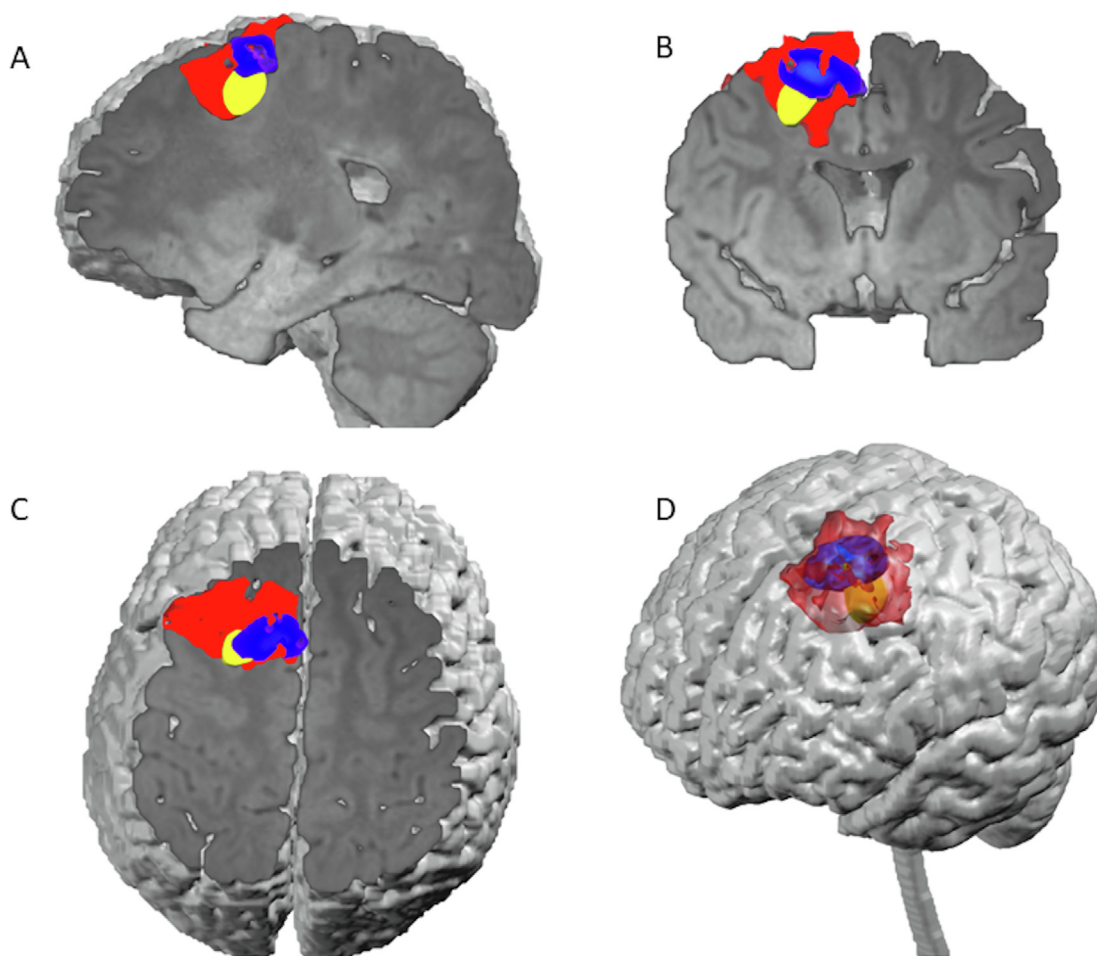


Fig. 1. Multimodal imaging from patient suffering from a left frontal epilepsy. Resection is displayed in red, ictal SPECT in yellow and ESI in blue. (A) sagittal view, (B) coronal view, (C) axial view, (D) 3D rendering of the different volumes. Images are displayed in normal convention (left is left). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

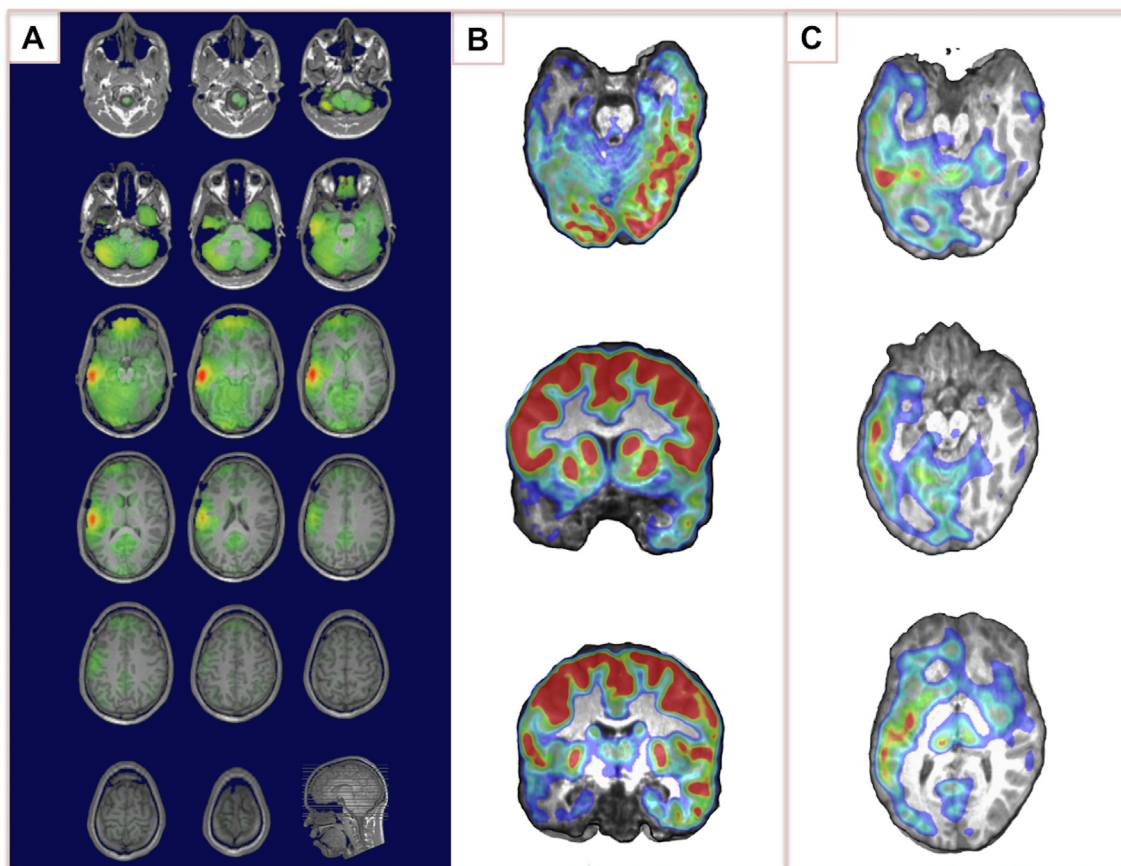


Fig. 2. Example of comparison of ESI, PET and iSPECT before surgery. (A) 256-channel ESI found the source maximum (red) in left lateral temporal lobe. (B) PET showed hypometabolism of the entire left temporal lobe, which extends to the occipital lobes. (C) Extensive hyperperfusion of left temporal and occipital lobe, but also posterior insula, was seen in iSPECT. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

low channel count may explain the lower performance of ESI compared to our study. Electrode coverage should include inferior-basal parts of the frontal, temporal and occipital lobe to allow optimal source imaging. Recent studies suggest that at least a 64-channel equipment should be used to improve significantly localization (Brodbeck et al., 2010, 2011; Lantz et al., 2003; Michel et al., 2004b; Plummer et al., 2008). Sperli et al. (2006) studied a population of 30 pediatric patients with various causes of epilepsy. Patients had ESI with either a 64 or a 128-channel equipment. They reported a localizing value of 90 % for HD-ESI, which is similar to our results with 256.

Using HD-ESI, we did not find any differences in the localizing power between temporal and extra-temporal foci, and consequently similar surgical success. ESI in extratemporal lobe FCD showed superior localizing value compared to iSPECT, but there were no differences compared to PET. Relationship between seizure onset zone and PET hypometabolism has been studied in pediatric patients with intractable epilepsy, with the help of intracranial EEG monitoring. These studies showed that PET localization of epileptic foci has a good accuracy of 70 % on the lobar level but has a low sensitivity to delineate the exact seizure onset zone within the lobes (Jeong et al., 2017; Juhász and John, 2020). PET seems to better localize epileptic foci in temporal lobes (particularly in the mesial region) than in extratemporal regions (Rathore et al., 2014; Tomas et al., 2019). In a recent retrospective study, subtraction ictal single-photon emission CT coregistered to MRI (SISCOM) in 113 patients (of which 31 % were non-lesional), an

accuracy of 52 % was obtained. Ictal SPECT requires a major investment in staff and supervision and is therefore mainly employed for complex cases, such as non-lesional extratemporal epilepsy, and carried out only in selected centers (Aungaroon et al., 2018; Sighu et al., 2018).

The present study has several limitations, which includes its retrospective nature, a relatively small and heterogeneous sample size. A prospective study of a larger group of patients would help to better assess the proper value of ESI in the presurgical work-up of patients with FCD and drug-resistant epilepsy.

We did not include MRI as another imaging exam, since we were interested to evaluate the yield of supplementary imaging modalities like ESI, PET and ictal SPECT. However, 75 % of our patients had subtle or clear abnormalities, which may result in a selection bias, i.e. operation is more often proposed to patients with a more or less clear MRI finding. FCD is often associated with only subtle changes on MRI, so ESI can guide a secondary MRI reading and lead to the detection of a dysplastic lesion (like in cases with a very small transmantle sign on MRI, for example). Moreover, despite morphometry or in-depth visual analysis of the candidate regions, no lesion can be identified in a significant proportion of patients (Wagner et al., 2011). In our experience, MRI-negative cases are on the rise, which is also underlined by a recent large retrospective single center study (Cloppenburg et al., 2016) of more than 3000 patients. Thus, more knowledge on the benefit of the localizing precision of non-MRI exams is necessary, alone or in combination.

5. Conclusions

In conclusion, this study shows that ESI allows highly accurate localization of the epileptogenic area in children with drug-resistant epilepsy caused by FCD, both in temporal and in extratemporal lobe regions. Co-registration with PET or ictal SPECT/SISCOM increases its yield in this patient group. ESI is a powerful technique, which has been demonstrated in several prospective and retrospective studies (Mouthaan et al., 2019). This non-invasive method is especially interesting for pediatric patients, who often require sedation during standard imaging procedures. In addition, given its relatively low costs, we believe that ESI should be implemented in the workflow of presurgical epilepsy evaluation centers, either by an in-house team or through out-sourced analysis.

Disclosure

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All authors have participated in the article preparation or in the research and have approved the final version of the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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