

# Safety and Efficacy of Stereoelectroencephalography in Pediatric Epilepsy Surgery

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## Abstract

Stereoelectroencephalography (SEEG) is the preoperative assessment of choice when the epileptogenic zone (EZ) is unclear in patients requiring surgery for severe, drug-refractory epilepsy. There are relatively little data on the safety and efficacy of SEEG in the pediatric epilepsy population. We, therefore, investigated the insertional complications, rate of successful identification of the EZ, and long-term seizure outcomes following surgery after SEEG in children. This was a retrospective study of drug-resistant pediatric epilepsy patients treated with surgery between 2005 and 2020 and who underwent presurgical SEEG. Rationale for and coverage of SEEG, identification of the EZ, and ultimate seizure outcome following SEEG-tailored resections were collected and analyzed. Thirty patients (15 male, mean age:  $12.4 \pm 5$  years) who underwent SEEG were studied. SEEG-related complications occurred in one case (3%). A total of 190 multicontact electrodes (mean:  $7.0 \pm 2.5$  per patient) were implanted across 30 insertions capturing 440 electrographic seizures (mean:  $17.5 \pm 27.6$  per patient). The most common rationale for SEEG was normal magnetic resonance imaging with surface EEG that failed to identify the EZ (17/30; 57%). SEEG identified a putative EZ in all cases, resulting in SEEG-tailored resections in 25/30 (83%). Freedom from disabling seizures was achieved following resections in 20/25 cases (80%) with  $5.9 \pm 4.0$  years of postoperative follow-up. SEEG is a safe and effective way to identify the EZ in the presurgical evaluation of children with refractory epilepsy and permits effective and long-lasting SEEG-tailored resections.

## Keywords

- ▶ pediatric epilepsy surgery
- ▶ depth electrode
- ▶ safety

## Introduction

Surgery is the main treatment for pediatric drug-resistant epilepsy, and the epileptogenic zone (EZ) can often be adequately characterized based on standard noninvasive preoperative evaluation.<sup>1–4</sup> Stereoelectroencephalography (SEEG) is

the invasive assessment method of choice when the EZ remains unclear, such as when magnetic resonance imaging (MRI) does not reveal a lesion, the MRI abnormality does not correspond to a broad EEG field, there is a diffuse MRI abnormality, when disabling seizures continue after previous surgery, or the suspected EZ is in or near eloquent cortex.<sup>3,5</sup>

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While numerous reports exist on the safety and efficacy of SEEG in adult and mixed adult and pediatric populations,<sup>5–8</sup> few studies have focused specifically on safety and efficacy of SEEG in pediatric populations. A recent meta-analysis of nine reports representing 277 children (mean age: 7.4 years; average of 11.6 SEEG electrodes) compared the safety and efficacy of SEEG to subdural grids, and SEEG led to surgery in 213 (77%) patients.<sup>9</sup> The overall complication rate of SEEG in studies reporting directly-attributable complications was 4/222 (1.8%) and included two intracerebral hemorrhages, one fatal case of cerebral edema, and a fractured depth electrode.<sup>9</sup> A recent multicenter UK study of pediatric stereotactic depth electrode placement showed that only 3% of 135 children had any bleeding-related complication.<sup>10</sup> In contrast, the published complication rate of subdural grid or strip implantation is between 5 and 15%, with higher rates of intracerebral hemorrhage, infection, and cerebrospinal fluid leak reported for these procedures.<sup>9,11–15</sup>

Given the relative paucity of data on the safety and efficacy of SEEG in children, the goal of this study was to examine our institutional experience with pediatric SEEG for the evaluation of drug-resistant epilepsy to characterize insertional complications, successful identification of the EZ, and surgical outcomes following subsequent SEEG-guided resections.

## Materials and Methods

### Patients

This was a retrospective review of pediatric drug-resistant epilepsy patients evaluated by the Comprehensive Epilepsy Program at the University of Alberta between 2005 and 2020 who underwent SEEG as part of the presurgical evaluation. This retrospective study was approved by University of Alberta Health Research Ethics Board. The characteristics of the 30 identified patients are detailed in ▶Table 1.

### Preoperative Evaluation

All patients underwent standardized preoperative assessment including clinical evaluation, seizure log, continuous noninvasive scalp electroencephalography (baseline EEG and long-term video EEG with 32 leads [16 channels]), and epilepsy protocol MRI. All patients underwent standard neuropsychological testing, and some underwent ancillary neuroimaging. Each patient was presented to our epilepsy multidisciplinary team prior to and following SEEG-implantation.

### Stereoencephalography

The rationale for invasive monitoring in patients with disabling, drug-resistant epilepsy who were deemed candidates for SEEG was retrospectively classified according to the categories proposed by Cossu et al.<sup>16</sup> We used a neuronavigational system from MEDTRONICS (Minneapolis, Minnesota, United States). DIXI electrodes (DIXI Medical Marchaux-Chaudefontaine, France) were used. The intracranial length was 20 cm × 0.8 mm, and there was a 7 mm distance between each electrode. The number of electrodes varied from 4 to 16, depending on the patient. We used a frameless stereotactic

**Table 1** The characteristics of 30 pediatric patients with drug-resistant epilepsy who underwent SEEG to identify the EZ

Characteristic	n (%) or [mean ± SD]
Sex	
Male	15 (50%)
Age of onset (y; mean ± SD)	4.8 ± 3.0
Semiology	
Focal seizures with preserved awareness	5 (17%)
Focal seizures with impaired awareness	23 (77%)
Generalized seizure	2 (7%)
MRI findings	
Normal	17 (57%)
Hippocampal sclerosis	2 (7%)
Focal cortical dysplasia	9 (31%)
Low grade glioma	2 (7%)
Rationale for SEEG [5]	
Normal MRI, EEG failed to identify EZ	17 (57%)
Abnormal MRI, broad EEG field	6 (21%)
Large, multifocal, or bilateral MRI with focal ictal EEG	0
MRI abnormality near eloquent area	6 (21%)
Previous epilepsy resection failure	1 (3%)

Abbreviations: EZ, epileptogenic zone; MRI, magnetic resonance imaging; SD, standard deviation; SEEG, stereoelectroencephalography.

robotic arm (“Olivier arm,” Hybex Industries). A 2 mm twist drill was made for electrode insertion and the electrode was passed to the target. The electrodes are fixed in place by a guide screw and cap (DIXI Medical) and a head dressing was then applied. The trajectory was individualized using blood vessel mapping software and a robotic arm was used to insert the electrode into the target. Data on SEEG coverage, electrographic seizures, duration, complications, and successful identification of an EZ were collected retrospectively by epilepsy conference note review. SEEG insertion complications were defined as adverse clinical or radiographic events occurring within 30 days that could conceivably be directly related to depth electrode insertion or removal. All patients except one underwent post-SEEG MRI to verify depth electrode location and to rule out any adverse events. The single case without post-SEEG MRI was a 3-year-old with frontal focal cortical dysplasia who underwent a SEEG-tailored resection during the same admission following electrode explantation and who did not have a clinical need for post-implantation imaging.

### Surgery

SEEG-tailored resections were undertaken at a separate admission (except for the case described above) following synthesis of SEEG data and presentation at the epilepsy conference. The surgical details are presented in ▶Table 2. Resection of the EZ and intracranial mapping (Brain Laboratory, Munich, Germany)

**Table 2** Surgical characteristics of the 30 pediatric patients investigated with SEEG

Characteristic	n (%) or [mean ± SD]
Total electrodes	190
Electrodes per patient (mean ± SD)	7 ± 3
Age at SEEG implantation (y; mean ± SD)	12.4 ± 5.0
Electroencephalographic seizures per patient (mean ± SD)	18 ± 28
Duration of SEEG (d; mean ± SD)	8.5 ± 3
Complications of SEEG	1 (3%)
Neurogenic pulmonary edema	1 (3%)
Intracerebral hemorrhage	0
SEEG-tailored resections	25 (83%)
Lesionectomy	1 (4%)
Frontal cortical resection	8 (33%)
Supplementary motor area	4 (17%)
Orbitofrontal	4 (17%)
Occipital	4 (17%)
Anterior temporal lobectomy	10 (40%)
Selective amygdalohippocampectomy	2 (8%)

Abbreviations: SD, standard deviation; SEEG, stereoelectroencephalography.

resulted in individualized resection around the electrode area. The area around the target electrode was 1 to 2 cm in all directions. Intraoperative mapping and intraoperative electrocorticography were not used. In our experience, this did not help provide additional information beyond the SEEG. If the EZ was near the eloquent cortex, it was resected up to the eloquent cortex with incomplete resection. If EZ was near eloquent cortex, EZ was resected up to the eloquent cortex with incomplete resection.

### Postoperative Evaluation

Seizure outcome was assessed using the Engel classification system.<sup>17</sup> Briefly, Class I describes patients who are free of disabling seizures even if they have or have had some auras or intervening episodes strictly related to a change in their medication. Class II describes patients who have rare disabling seizures or whose seizures only occur while they are sleeping. Class III and Class IV describe patients with less favorable outcomes. This information was collected based on the most recent chart notes from the treating pediatric neurologist. Histopathological analysis was performed by an experienced neuropathologist. Standardized postoperative neuropsychological testing was performed at 1-year follow-up.

## Results

### Patient Characteristics

Thirty pediatric patients (15 male; mean age: 12.4 ± 4.6 years; range: 3–17 years) who underwent SEEG were included.

Preoperative patient characteristics including age at onset, semiology, MRI findings, and rationale for SEEG are shown in ►Table 1. The mean postoperative surveillance for seizure control in the subgroup that underwent SEEG-tailored resection was 5.9 ± 4.0 years.

### SEEG Safety and Efficacy

A total of 190 multicontact electrodes (mean: 7.0 ± 2.5 per patient) were implanted across 30 insertions and captured 440 electrographic seizures (mean: 17.5 ± 27.6 per patient). The most common rationale for SEEG was normal MRI with surface EEG that failed to identify the EZ (17/30; 57%), and the second most common rationale for SEEG was an abnormal MRI but a wide field demonstrated on surface EEG (6/30; 20%). SEEG-related complications occurred in 1/30 patients (3%), a case of neurogenic pulmonary edema.<sup>18</sup> The patient developed neurogenic pulmonary edema in the operating room as the depth electrode was being implanted in the temporal lobe, specifically the amygdala, and there was no brain stem involvement. The patient was immediately treated by the anesthesiologist and the implantation was aborted. Immediate postoperative MRI was performed in all but one case (as outlined above), with no intracerebral hemorrhages documented.

The EZ was successfully characterized and resulted in subsequent SEEG-tailored resections in 25/30 (83%) patients, as summarized in ►Table 2. Four of the five patients who did not undergo epilepsy resections following SEEG had evidence of multifocality, and the other patient became seizure-free following SEEG. Durable freedom from disabling seizures was achieved following SEEG-guided resection in 20/25 cases (80%) after 5.9 ± 4.0 years of postoperative follow-up. Surgical pathology of the resection specimens was consistent with focal cortical dysplasia (11/25; 44%), hippocampal sclerosis (5/25; 20%), gliosis (3/25; 12%), normal (3/25; 12%), Rasmussen's encephalitis (2/25; 8%), or tuberous sclerosis (1/25; 4%).

## Discussion

Here, we report a low (~3%) rate of SEEG-related complications occurring as part of the evaluation of pediatric drug-resistant epilepsy. Furthermore, SEEG resulted in resections in most patients (83%). In this study, the most common reason for invasive recording was disabling epilepsy with a normal MRI and surface EEG that failed to identify the EZ. SEEG-tailored resections resulted in freedom from disabling seizures in 80% of study patients with an average of 5 years of postoperative seizure surveillance.

Our data represented a unique contribution to the existing literature examining the safety and efficacy of pediatric SEEG, which consists of fewer than 200 reported cases with over 2 years of postoperative seizure surveillance. Overall, SEEG-related complications appear to be rare in the literature, with bleeding, infection, and hardware malfunctions most commonly reported.<sup>7,19,20</sup> Other rarely reported complications include infarction, cerebral edema, photopsia, and transient amnesia in mixed populations.<sup>19</sup>

Robot-assisted and MRI-based SEEG studies of pediatric patients also showed a similar excellent safety profile,<sup>21,22</sup> and a recent meta-analysis of only pediatric patients reported total complication rate of 2.9% for SEEG.<sup>9</sup> Overall, our reported SEEG complication rate of 3%, attributable to a single case of neurogenic pulmonary edema previously described in detail,<sup>18</sup> falls well within the range reported in the literature of 0 to 7%.<sup>5,8,9,13,16,20,23</sup> In contrast, subdural investigations carry a 5 to 15% risk of complications.<sup>9,11–15</sup>

SEEG can be helpful to correctly identify the EZ without undergoing unnecessary craniotomy, especially when MRI is normal or there are multiple lesions. Engle Class I outcomes occurred in all the patients for whom the EZ was not identified, who underwent subdural grid placement, followed by SEEG and surgery.<sup>24</sup> In our study, patients underwent SEEG-guided resections of the identified EZ in 83% of cases, similar to reported in the literature,<sup>5,25,26</sup> thereby avoiding unnecessary craniotomy, an extended hospital stay, and increased health resource utilization.

The direct efficacy of SEEG implantation may be difficult to assess as it depends on multiple factors including, patient selection, preimplantation hypothesis, and adequacy of coverage of the area of interest as well as the experience of the treating epilepsy team. Taussig et al<sup>20</sup> and Cardinale et al<sup>27</sup> reported seizure-free outcomes in 60 to 67% of patients, but in a very recent multicenter retrospective study of 135 patients undergoing SEEG-guided surgery, only 34.8% of patients were seizure free after a median follow-up of 1.3 years.<sup>10</sup> In contrast, 80% of our cohort were free of seizures, comparable to some other reported studies,<sup>26</sup> and these favorable outcomes may represent out rigorous selection process of optimal patients, correct preoperative hypothesis, ancillary testing, and an experienced team.

This report is limited by its single-center, retrospective analysis of a limited number of patients and the absence of a meaningful control arm, as subdural grids were largely abandoned at our institution during the study period in all but exceptional circumstances. Nevertheless, in all our patients, we searched and reported all major and minor complications. Our data clearly demonstrate that pediatric patients with drug-resistant epilepsy investigated by SEEG are frequently candidates for epilepsy resections associated with a high chance of long-term seizure freedom and a low risk of complications.

## Conclusions

In summary, intracranial monitoring plays a crucial role in the management of pediatric patients with refractory epilepsy. Our study, although relatively small and retrospective, shows that SEEG is a safe and effective way to identify the EZ in the presurgical evaluation of children with drug-resistant epilepsy and permits effective SEEG-tailored resection. SEEG avoids unnecessary craniotomy and may even be beneficial in areas challenging to cover with subdural grids. Larger studies are needed to establish a standardized protocol for SEEG and surgical assessment to further improve safe seizure control.

## Conflict of Interest

None declared.

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