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Localization yield and seizure outcome in patients undergoing bilateral SEEG exploration

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Summary

Objective: We aimed to determine the rates and predictors of resection and seizure freedom after bilateral stereo-electroencephalography (SEEG) implantation.

Methods: We reviewed 184 patients who underwent bilateral SEEG implantation (2009-2015). Noninvasive and invasive evaluation findings were collected. Outcomes of interest included subsequent resection and seizure freedom. Statistical analyses employed multivariable logistic regression and proportional hazard modeling. Preoperative and postoperative seizure frequency, severity, and quality of life scales were also compared.

Results: Following bilateral SEEG implantation, 106 of 184 patients (58%) underwent resection. Single seizure type ($P = 0.007$), a family history of epilepsy ($P = 0.003$), 10 or more seizures per month ($P = 0.004$), lower number of electrodes ($P = 0.02$), or sentinel electrode placement ($P = 0.04$) was predictive of undergoing a resection, as were lack of nonlocalized ($P < 0.0001$) or bilateral ($P < 0.0001$) ictal-onset zones on SEEG. Twenty-six of 81 patients (32% with follow-up greater than 1 year) remained seizure-free. Predictors of seizure freedom were single seizure type ($P = 0.01$), short epilepsy duration ($P = 0.008$), use of 2 or fewer antiepileptic drugs (AEDs) at the time of surgery ($P = 0.0006$), primary localization hypothesis involving the frontal lobe ($P = 0.002$), sentinel electrode placement only ($P = 0.02$), and lack of overlap between ictal-onset zone and eloquent cortex ($P = 0.04$), along with epilepsy substrate histopathology ($P = 0.007$). Complete resection of a suspected focal cortical dysplasia showed a trend to increased likelihood of seizure freedom ($P = 0.09$). The 44 of 55 patients (80%) who underwent resection and experienced seizure recurrence had >50% seizure reduction, as opposed to 26 of 45 patients (58%) who continued medical therapy alone ($P = 0.003$). Seventy-two percent of patients had a clinically

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DISCLOSURE

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

meaningful quality of life improvement (>10% decrease in the Quality of Life in Epilepsy [QOLIE-10] score) at 1 year.

Significance: A strong preimplantation hypothesis of a suspected unifocal epilepsy increases the odds of resection and seizure freedom. We discuss a tailored approach, taking into account localization hypothesis and suspected epilepsy etiology in guiding implantation and subsequent surgical strategy.

Keywords

epilepsy; intracranial EEG; outcome; stereo-electroencephalography; surgery

1 | INTRODUCTION

A recent North American shift from subdural electrodes (SDEs) to stereo-electroencephalography (SEEG),¹ an intracranial method long favored by European epileptologists,^{2,3} reflects an appreciation of the need to explore epileptic networks in a three-dimensional (3D) manner in an effort to accurately define the epileptogenic zone, and ultimately to optimize seizure outcomes after epilepsy surgery. Yet, a parallel increase in the rates of intracranial recordings without subsequent resection⁴ highlights the urgent need for better patient selection. In this context, patients undergoing bilateral SEEG (B-SEEG) implantations represent a particular challenge. Despite complex and costly noninvasive presurgical testing, these patients ended up with one or more epilepsy localization hypotheses that require bilateral exploration, with recent data suggesting worse seizure outcomes following surgery in this cohort as opposed to SEEG patients with preimplantation hypotheses restricted to one hemisphere.¹ On one hand, “sick” patients with frequent seizures, poor quality of life, and high risk of sudden death have much to gain by seizure freedom. On the other hand, the societal and personal burden of diagnostic and therapeutic interventions is high and a clear understanding of the extent of expected benefits is necessary. Although multiple retrospective reports describe general outcomes following SEEG implantations,^{1,3,5} no data currently exist on the epilepsy localization yield, rates, and determinants of seizure control in the particularly challenging population of B-SEEG.

In this study, we examine the odds of undergoing a resection and achieving seizure freedom after B-SEEG implantations. We explore preinvasive and invasive characteristics associated with the likelihood of resection and seizure freedom. Finally, to explore the role of resective surgery in reducing seizure burden when curative resective surgery may not be possible, we describe the extent of postoperative improvement in seizure frequency and severity.

2 | METHODS

2.1 | Patient selection

We included all 184 patients who underwent B-SEEG implantations (defined as electrodes implanted in both hemispheres in a single implantation) at the Cleveland Clinic Epilepsy Center between March 2009 and December 2015.

2.2 | Preimplantation evaluation protocol

All patients were first assessed in the outpatient clinic, where in addition to undergoing history taking and physical examination, they were asked to complete electronically delivered questionnaires on various aspects of their seizure severity and psychosocial functioning as part of our institution's "Knowledge Program" (KP) for systematic comprehensive outcome assessment.⁶ Measures evaluated included the Liverpool Seizure Severity Scale (LSSS)⁷ and Quality of Life in Epilepsy (QOLIE-10) scale.⁸ The LSSS is a 12-item questionnaire pertaining to seizure severity and seizure impact on daily function (if no seizures occur in the last 4 weeks, the score is 0; scores range from 0 to 100, with higher scores indicating worse seizure severity). The QOLIE-10 is a 10-item questionnaire covering general and epilepsy-specific domains (epilepsy effects, mental health, and role functioning), with higher scores denoting worse quality of life.

When a diagnosis of medically intractable focal epilepsy was suspected or made, patients were admitted to the epilepsy monitoring unit (EMU) for video-scalp EEG monitoring. Additional noninvasive testing included 3T magnetic resonance imaging (MRI) in all patients, as well as fluorodeoxyglucose positron emission tomography (FDG-PET), ictal single-photon emission computed tomography (SPECT), magnetoencephalography (MEG), and neuropsychological testing, as deemed appropriate. Then, the patient's case was presented at a multidisciplinary patient management conference (PMC), attended by epileptologists, epilepsy neurosurgeons, neuroradiologists, nuclear imaging radiologists, neuropsychologists, psychiatrists, epilepsy nurses, and a bioethicist. If SEEG was deemed necessary, a second preimplantation PMC took place, where a dedicated group of expert epileptologists and neurosurgeons refined localization hypotheses and generated a preimplantation map to test hypotheses regarding the localization of the ictal-onset zone (IOZ) and its propagation network.

2.3 | Indications for B-SEEG

Indications for bilateral implantation included one or more of the following factors:

1. Localization hypothesis that involves bilateral highly connected networks with rapid interhemispheric spread (n = 139; Figure 1).
2. Discordant lateralizing data (semiology, ictal EEG, PET, ictal SPECT, MEG; n = 21). In cases with suspected lateralization but some data raising concerns about contralateral or bilateral epilepsy, sentinel electrodes were utilized on the contralateral hemisphere. Such was the case most frequently in temporo-perisylvian hypotheses.
3. Bilateral MRI lesions (most commonly in the setting of periventricular nodular heterotopia [PNH]; n = 37).

SEEG implantation was then completed according to previously published methodology,¹ with some technical evolution during the study period, such as the incorporation of robotic implantation in 2013.

2.4 | Postimplantation evaluation protocol

Patients were transferred from the operating room to the postanesthesia care unit, and then to the EMU, where after 24 hours, antiepileptic drugs (AEDs) were progressively withdrawn as needed. After the recording of an adequate number of seizures and the completion of electrical brain stimulation, the invasive EEG data were discussed at a PMC led by the dedicated invasive team (epileptologist, epilepsy neurosurgeon), the patient's primary epileptologist, and the remainder of the available members of the epilepsy center. A decision was made about whether resective surgery should be offered.

2.5 | Variables definition

Epilepsy characteristics: Malformations of cortical development included suspected focal cortical dysplasia, PNH, and polymicrogyria (Table 1). Additional baseline characteristics (KP data), semiology, previous interventions, and scalp ictal EEG patterns are available in Table S1. Bilateral version denotes head version to both sides in separate seizures. A patient was considered to have discordant lateralizing signs when contradictory lateralizing signs (such as version or unilateral clonic activity) were recorded in a single seizure or separate seizures. Preimplantation hypothesis was determined on the basis of the PMC reports, in which the network thought to be most consistent with the noninvasive data was stated.

SEEG and surgery characteristics: Asymmetric implantations denoted 2 or more electrode differences between 2 hemispheres (Table 1). Sentinel electrodes consisted of 1-2 electrode sampling regions in one hemisphere in an asymmetric implantation. Implantation schemes, although never identical, followed particular network explorations, with modifications on the basis of secondary hypotheses, and were categorized between the temporo-parietooccipital junction (TPOJ), perisylvian regions, temporo-perisylvian, temporo-frontal, frontoparietal, and frontal hypotheses (as exemplified in Figure 1). Eloquent cortex was defined as cortex holding visual, sensory, motor, or language function, as confirmed by electrical cortical stimulation and/or expected functional neuroanatomy. If MRI was lesional, completeness of lesion resection was documented on the basis of postoperative MRI. Further details on the extent and location of resection are available in Table S1, along with histopathologic findings.

2.6 | Outcome

Three different levels of SEEG implantation outcomes were analyzed:

Occurrence of resection: Resection was defined as open resection or laser ablation. Implantation of a neurostimulation device (responsive neurostimulation) was defined as no resection.

Curative outcomes: Seizure outcomes were assessed at 2 different levels. (a) Completely seizure-free from any seizure recurrence (even if provoked), and (b) Engel classification at the last follow-up visit; a favorable outcome was defined as Engel class I (seizure-free or no more than a few early, nondisabling seizures, or seizures upon drug withdrawal only). Acute postoperative seizures (occurring within the first postoperative week) and auras were not

counted as seizure recurrence. If the exact date of first seizure recurrence was not available in the medical records, the date of recurrence was taken as the midpoint between the follow-up visit or phone call indicating a recurrence and the previous follow-up date. For patients who underwent a repeat resection or invasive recording, the last follow-up date was taken as the last date before the repeat intervention. Only patients with follow-up greater than 1 year were included in this analysis.

Palliative outcomes: Seizure frequency at the last visit was compared to that reported preoperatively. Monthly seizure frequency at last follow-up was averaged from reported frequency over the previous 6 months. More than 50% reduction in seizure frequency and worsening of seizure frequency were determined. Only patients with follow-up greater than 1 year were included in this analysis. In addition, Liverpool Seizure Severity Scale (LSSS) and Quality of Life in Epilepsy Questionnaire-10 (QOLIE-10) were administered at 1 and 2 years, and scores were compared to the preoperative score. The 10% decrease in QOLIE-10 score was chosen to reflect “clinically meaningful thresholds” of improvement, based on previously published reports.^{9,10}

2.7 | Statistical methods

First, descriptive statistics were performed for each variable including means, medians, and standard deviations for continuous variables and frequencies for categorical variables. Univariate analysis was first performed using Wilcoxon rank-sum, chi-square, and Fisher’s exact tests to compare patients undergoing resections to those with continued medical management and to compare seizure-free patients to those with seizure recurrence in those with at least 6 months of follow-up. Variables identified on each analysis with $P < 0.1$ were then subjected to a multivariate linear regression model to study the probability of resection, and a Cox proportional hazards regression model to study postoperative seizure freedom. Preimplantation and postimplantation variables were run separately because they are typically considered at different clinical decision-making points. Results with $P < 0.05$ after multivariate analysis were considered statistically significant.

Kaplan-Meier survival curves were then constructed to illustrate the probability of seizure freedom, first in the overall group and then with each of the significant prognostic variables.

2.8 | Research ethics boards and consent

This study was approved by the Cleveland Clinic Institutional Review Board. Due to the retrospective nature of the study, written consent was waived.

3 | RESULTS

3.1 | Patient characteristics

Characteristics of the 184 patients who underwent B-SEEG implantations are summarized in Table 1. Patients were taking a mean of 2.4 AEDs and experienced a mean of 32.2 seizures per month (median 9.5, range 0.5-600). Many signs of a challenging epilepsy localization were found, including discordant lateralizing signs (11%), multiple clinical seizure types (mean 1.67), and challenging ictal scalp EEG patterns that were nonlocalized (17%),

multiple (53%), and at times bilateral independent (25%). Family history of epilepsy showed a trend to association with a frontal hypothesis (9/41 [22%] vs 7/65 [11%]; $P = 0.12$).

SEEG evaluation results are summarized in Table 1. Multiple ictal-onset zones were seen in 48% of patients. A TPOJ primary hypothesis was predictive of bilateral independent ictal-onset zones (22/41 [54%] of TPOJ-hypothesized epilepsies vs 51/140 [36%] of other epilepsies, $P = 0.05$). Of note, 15 of 69 (22%) patients implanted with sentinel electrodes (1-2 sampling one hemisphere) had seizures recorded from the sentinel electrodes. SEEG recordings failed to localize an ictal onset in 8% of patients.

3.2 | Likelihood of resection

Following the SEEG implantations, 106 patients (58%) underwent resections. Resection was not offered for several reasons, highlighted in Table 1, the most common being multifocality of the epileptogenic zone (48%). Pathology results are shown in Table S1, the most common being focal cortical dysplasia type 1 (50/97 [51%]).

3.3 | Overall seizure outcome

Seizure outcome was analyzed in patients who underwent resection and had follow-up greater than 1 year ($n = 81$). Mean follow-up was 3.1 years (range 1-75.4). Twenty-six patients (32%) achieved and maintained seizure freedom after resection (Figure 2), corresponding to 26 of 159 (16%) of the overall analyzed SEEG implanted cohort. The mean time to seizure recurrence was 0.61 years. As illustrated in Figure 2, a steep slope of recurrence was observed in the early postoperative period. Fifty-five percent of patients were seizure-free at 6 months, dropping to 33% of seizure freedom by 2 years after surgery and stabilizing at 22% by 4 years. A slightly higher number of patients achieved Engel class I outcome at last follow-up (29 patients, 36%). The remainder had the following Engel outcomes: 14 patients (17%) Engel class II, 22 (27%) Engel class III, and 16 (20%) Engel class IV. In comparison, 62% of patients undergoing unilateral SEEG implantation ($n = 204$ implanted; 159 resected) were seizure-free at 6 months, dropping to 52% at 2 years and 43% at 5 years; therefore faring better than the bilateral SEEG cohort.

In addition, 10 patients underwent responsive neurostimulation (RNS) placement after SEEG recordings, due to overlap with eloquent cortex ($n = 4$) or multifocality ($n = 6$), most frequently involving bilateral mesial temporal regions ($n = 5$). One patient achieved seizure freedom in the last 6 months of follow-up. Patients experienced a median seizure frequency reduction of 12.8% (interquartile range [IQR] -61.8% to 75%). Seizure frequency worsened in 3 of 10 patients. All 6 patients who experienced generalized tonic-clonic seizures prior to RNS placement started having focal seizures only.

3.4 | Tailoring of SEEG implantations

Further tailoring of the SEEG implantation was performed either in the setting of the initial SEEG, with additional electrode implantation (8/184 [4%] of cohort), or with a repeat invasive evaluation at a later date (5/184 [3%] of cohort). In the latter group, subdural grids for language mapping were later performed in 2 patients, and a repeat SEEG evaluation was performed in 3 patients (bilateral in 2, unilateral in one). Subsequently, 3 patients were

considered surgical candidates. One resection and 2 laser ablations were performed. The surgical outcomes of all 3 cases were classified as Engel class III.

3.5 | Predictors of resection

Univariate analysis of predictors of resection is outlined in Table 2.

Across preimplantation data variables, multivariate linear regression model revealed a single seizure type ($P = 0.007$, odds ratio [OR] 2.52, 95% confidence interval [CI] 1.29-4.93), higher seizure frequency (greater than 10 seizures/month; $P = 0.004$, OR 2.67, 95% CI 1.36-5.22), family history of epilepsy ($P = 0.0025$, OR 3.13, 95% CI 1.49-6.56), and lower number of electrodes ($P = 0.02$), along with placement of sentinel electrodes only ($P = 0.04$, OR 2.05, 95% CI 1.02-4.08) as predictive of resection. After similar multivariate analysis of invasive evaluation data variables, absence of bilateral independent IOZs ($P < 0.0001$, OR 7.38, 95% CI 3.57-15.24) and absence of nonlocalized IOZs ($P < 0.0001$) remained predictive of resection. Of note, no noninvasive data variables could predict a localized vs nonlocalized SEEG ictal onset.

3.6 | Predictors of seizure freedom

Univariate analysis of predictors of seizure freedom is highlighted in Table 3.

After proportional hazard modeling, the following variables remained predictive of seizure freedom among preimplantation variables: epilepsy duration less than 10 years ($P = 0.008$, OR 4.24, 95% CI 1.45-13.54); 2 or fewer AEDs at the time of surgery ($P = 0.0006$, OR 18.5, 95% CI 3.78-89.51); single seizure type ($P = 0.01$, OR 5.76, 95% CI 1.49-26.59); frontal hypothesis ($P = 0.002$, OR 6.7, 95% CI 2-22.62); and placement of sentinel electrode only ($P = 0.02$, OR 3.3, 95% CI 1.2-10). Among postimplantation variables, overlap with eloquent cortex ($P = 0.04$, OR 2.16, 95% CI 1.04-4.19) and gliosis or normal pathology ($P = 0.007$, OR 2.69, 95% CI 1.33-5.16) were predictive of seizure recurrence. Notable factors that did *not* modify likelihood of seizure freedom were the presence of an MRI lesion ($P = 0.3$) and the completeness of an MRI lesion resection ($P = 0.8$). However, on subgroup analysis per type of lesion, complete resection of suspected focal cortical dysplasia (FCD) lesions ($n = 7$) showed a trend to better seizure outcome ($P = 0.09$).

We also explored whether our data support a “learning curve” in our application of the SEEG method by comparing outcomes of patients operated between 2009 and 2012 vs 2012 and 2015. As seen in Figure 3, there is no clear evidence of improved outcomes after 2012 ($P = 0.94$). However, after 2012, there was a higher proportion of implantations that led to a resection (63% vs 46%; $P = 0.03$), suggesting an improved ability to define the epileptogenic zone (EZ). In patients who had subsequent resections, there was a further suggestion of “learning” over the study period, with less resections in patients who had multiple seizure types (31% of resections after 2012 vs 46% before 2012; $P = 0.16$) and in the dominant hemisphere (33% vs 62% before 2012; $P = 0.009$), reflecting better identification of patients who could realistically benefit from a resection. This occurred in parallel with an improved recognition of the extent of the EZ with a growing proportion of multilobar resections (25% of resections after 2012 vs 8%; $P = 0.11$). Figure 3 highlights seizure outcome Kaplan-Meier curves per significant outcome predictor in addition to procedure year variables.

3.7 | Seizure burden and severity after resection compared to medical management

Beyond the 26 patients who achieved seizure freedom, an additional 44 patients achieved a 50% or greater reduction in seizure frequency (44/55 [80%]) compared to a 50% or more reduction in seizures in 26 of 45 (58%) of patients who did not undergo a resection ($P=0.003$).

LSSS and QOLIE-10 scales were recorded from postoperative visits of some patients who did not achieve seizure freedom after resection ($n=56$; Table S2). Seventy-two percent of patients had a clinically meaningful quality of life improvement ($>10\%$ decrease in QOLIE-10 score) at 1 year, and 56% maintained that improvement at 2 years.

4 | DISCUSSION

We report the first longitudinal outcome series of patients undergoing B-SEEG implantations and demonstrate rates and predictors of resection and seizure freedom while evaluating a palliative role for resective surgery.

4.1 | Implantations without resection—Taking into account noninvasive heralds of multifocality

The first striking finding in this series is the lower rate of resection (58%) compared to that reported in nonselected SEEG implantation cohorts (75%-87%) at our center¹ and elsewhere.^{3,5} This rate of resection is similar to other invasive recording techniques (subdural grids/strips, with or without depths) when implanted bilaterally (60%-65%).^{11,12} The lack of confidence in lateralization and need for bilateral implantation may in part reflect noninvasive data suggesting bilateral, multifocal, or diffuse epileptogenicity, and herald SEEG results precluding patients from curative resective surgery. The presence of 2 or more clinical seizure types was indeed predictive of not undergoing a resection after SEEG implantation and of seizure recurrence. The predictive value of multiple seizure types was suggested previously in the setting of subdural grid implantations without subsequent resections.¹³ Our finding that the predominant reasons for not undergoing a resection in this cohort were multifocality (48%) and nonlocalized ictal onset (8%) supports this hypothesis (Table 1). Although the use of invasive recordings has been associated with a promising increase in resective surgical options in multifocal lesional etiologies previously thought to be “nonsurgical,” such as tuberous sclerosis¹⁴ and polymicrogyria,¹⁵ there has also been an increase in invasive recordings without subsequent resections.⁴ Our findings highlight the importance of taking into account noninvasive heralds of multifocality, which currently are likely to preclude patients from a curative resective surgical option.

The role of noninvasive data in determining seizure outcomes after SEEG-guided resection has also been demonstrated by the finding that complete resection of a tight MEG cluster is associated with better seizure outcomes,¹⁵ including in patients with prior failed resection.¹⁶ Concordance of interictal (eg, MEG) and ictal (eg, SPECT) noninvasive data may further support a well-delineated EZ amenable to successful resection.¹⁷ We examined the impact of SEEG interictal patterns on the likelihood of resection and seizure freedom and found that on univariate analysis, a lower number of interictal populations and a dominant interictal

population were correlated with higher likelihood of resection and seizure freedom. However, the significance of interictal SEEG data was not independently associated with seizure outcome when SEEG factors related to the IOZ were considered in a multivariate analysis. A confined irritative zone, as determined by noninvasive (MEG) or invasive (SEEG) recordings, may be associated with better seizure outcomes due to a less distributed epileptic pathology, which may be more amenable to resection, but its impact on seizure outcomes independent of other seizure outcome predictors remains to be determined.

4.2 | The impact of the preimplantation hypotheses

We demonstrated the role of suspecting a single epilepsy localization from noninvasive data as the first step in crafting an implantation likely to lead to a resection. The second step is formulating strong and testable anatomo-functional hypotheses, in which a bilateral implantation is a carefully adapted tool to answer specific questions. Indeed, certain hypotheses require bilateral implantations due to the network-specific interhemispheric connectivity, recognized with perisylvian, TPOJ, frontoparietal, and frontal epilepsies. The use of sentinel electrodes to rule out contralateral propagation was associated with a higher likelihood of resection and seizure freedom, providing support for such an approach. Better seizure outcomes noted with frontal hypothesis (after multivariate analysis) and perisylvian resection (on univariate analysis) also support that in the setting of a strong preimplantation hypothesis with highly localizing but poor lateralizing value, a bilateral implantation can be used to craft a successful surgical strategy. Meanwhile, the independent predictive value of the number of implanted electrodes in the likelihood of performing a resection reflects the crucial step of the preimplantation meeting, in which an electrode map is produced after formulation of hypotheses based on the noninvasive data. A trend to the predictive value of a higher number of electrodes for seizure recurrence or no resection had similarly been shown with subdural grids.^{13,18} Conversely, a bilateral subdural grid and depth electrode series showed that a higher number of depth electrodes was predictive of better seizure outcomes,¹² perhaps suggesting that the decision to implant depth electrodes in the context of an otherwise convexity coverage specifically reflects the formulation of a strong hypothesis implicating deeper regions (not covered by subdural grids).

Despite the formulation of strong preimplantation hypotheses, certain epilepsy localizations may be associated with truly bilateral EZs, as suggested by worse seizure outcomes in TPOJ epilepsies, with which bilateral independent seizures were frequently recorded (54%). Furthermore, 22% of implantations utilizing sentinel electrodes revealed seizures arising from the less-sampled hemisphere. In these situations, the ability to localize the epileptogenic zone to a single area amenable to a resective surgical strategy may be mitigated by wide epileptogenicity reflecting bilaterally connected networks.

This generation of implantation hypotheses requires lengthy training and is honed by experience. Although there was no significant improvement in outcomes in 2012-2015 compared to 2009-2012, we found some suggestion of an evolution in our ability to define and select appropriate SEEG candidates. This learning is an ongoing process, however, as we have a similar proportion of patients with bilateral ictal onset in the 2-time cohorts, and

similar seizure-free outcomes, reflecting the challenging nature of this patient population and the limitations of this invasive EEG method or our ability to apply it.

4.3 | Independent role of etiology in determining surgical strategy

Previous studies have shown conflicting results either highlighting a role for nonlesional MRI as a predictor of seizure recurrence^{3,19,20} or failing to show such a role^{5,21,22} with or without subdural grids or SEEG guidance. One meta-analysis suggested improved seizure outcomes in lesional cases.²³ The importance of interpreting all other noninvasive testing and in the setting of discordant data delineating an EZ with the use of invasive recordings such as SEEG, is therefore of the utmost importance. But beyond the importance of a confident localization hypothesis, our data support the recent call for an integrated localization and etiology-centric approach to epilepsy surgery.²⁴ Thus far the impact of etiology on seizure outcome has been shown in the setting of better seizure outcomes in patients with tumors^{25,26} and malformations of cortical development,^{27,28} specifically FCD IIb,²⁹ without strong data to support tailoring of surgical strategy in relation to suspected etiology. In this cohort, we showed that surgical strategy (completeness of lesion resection) affected outcome differentially in suspected FCD lesions as opposed to other malformations of cortical development (PNH, polymicrogyria), hippocampal sclerosis, and encephalomalacia. When pooling multiple lesion types, completeness of lesionectomy has been correlated with seizure freedom in one large cohort of SEEG-guided resections.³ Indeed, completeness of lesionectomy has classically been associated with seizure freedom in the setting of epilepsy-associated tumors,³⁰ FCD,^{31,32} cavernoma,³³ and posttraumatic encephalomalacia involving the frontal lobe.³⁴ However, completeness of lesionectomy has not been shown to correlate with seizure freedom in other lesion types such as polymicrogyria^{3,15} and PNH.^{35,36} In addition, invasive recordings have documented a complex relationship between the lesion and the EZ, which may extend beyond the lesion (eg, in the setting of encephalomalacia due to early insults)³⁷ or occupy only part of the lesion or lie in cortical areas remote from the lesion (eg, in polymicrogyria¹⁵ and PNH).³⁶ The conflicting literature on the impact of lesional MRI and completeness of lesionectomy on outcome may therefore reflect heterogeneous patient groups, with completeness of lesion resection playing a role in some but not all lesion types and reflecting a primary role for the underlying epilepsy pathology in dictating the overlap of the EZ with the lesion. In this cohort, subgroup analysis per lesion type indeed revealed a trend toward improved seizure outcome with complete resection of suspected FCD, but not with other types of lesions. We propose that completeness of lesionectomy is crucial in suspected FCD type IIb, whereas SEEG is necessary to delineate the EZ in certain types of malformations of cortical development (polymicrogyria, PNH) and encephalomalacia, where multilobar lesions may not necessarily be associated with multilobar EZs.

Furthermore, family history of epilepsy showed a trend toward predicting a frontal hypothesis and was associated with a higher chance of undergoing a resection, highlighting that the epilepsy substrate may not only play a role in the surgical approach, but also in successful localization of the epilepsy. Refining further the biologic understanding of genetic epilepsies and its impact on epilepsy surgery will be essential to use these data for prediction

of seizure outcomes, as epilepsy surgery outcomes have been shown to vary widely according to genetic mutation.³⁸

4.4 | A silver lining: Palliative role of resective surgery

Given the characteristics of the patient population undergoing B-SEEG implantation, it is not surprising that lower rates of seizure freedom (32%) were observed compared to that in unselected SEEG,^{1,3,5} unilateral SEEG implantations (43% at 5 years, unpublished data), and subdural grid cohorts (33%-70%).^{25,39,40} When considering the entire cohort prior to SEEG implantation, the proportion of patients who underwent a resection and were subsequently seizure-free was lower (16%). If the noninvasive characteristics of the cohort undergoing B-SEEG implantations are taken into account, expecting similar rates of seizure freedom from a surgical intervention may be unrealistic. High seizure frequency (>10 seizures/month) was a predictor of resection in this cohort, highlighting a population in which there may be motivation for noncurative procedures. Preoperative QOLIE-10 scores (mean 29.8) were also higher (ie, worse) than those reported previously in the outpatient epilepsy population in our institution (mean 22.1 in Jehi et al¹⁰). Average seizure frequency far exceeded that of an unselected SEEG cohort published previously by our center (32.2 seizures/month compared to 20/month in Gonzalez-Martinez et al¹).

Palliation, defined by the World Health Organization⁴¹ as a treatment that provides relief from distressing symptoms (such as high seizure burden), then becomes a desirable goal in the absence of a curative care option. Indeed, with the advent of less-invasive resective surgery approaches such as thermocoagulation, there has been a change to using responder rate (>50% seizure reduction) as a primary outcome of epilepsy surgery in patients for whom resection is expected to be palliative.²⁵ Meanwhile, there has been an increase in palliative surgical approaches such as vagus nerve stimulation (VNS) and responsive neurostimulation (or RNS).⁴² In a patient population with medically intractable focal epilepsy without a curative resective strategy, management options without pursuing further SEEG evaluation would include the following: (a) continued medical management with further AED trials (4%-7% chance of seizure freedom, 51% chance of >50% seizure reduction in this cohort), (b) VNS (0-1% chance of seizure freedom, 16%-21% chance of >50% seizure reduction), and (c) RNS (14%-15% chance of seizure freedom for at least 1 year, 29% chance of >50% seizure reduction).⁴³ The responder rate in our cohort (80%) was comparatively higher than any of these, suggesting that pursuing a B-SEEG implantation to craft a resective surgery may have greater potential to reduce seizures than continued medical management and traditional “palliative” procedures, even in suspected multifocal epilepsy.

4.5 | Limitations

Our study was limited by its retrospective nature and heterogeneous patient population, which may have hindered the significance of some variables, for example, in the setting of completeness of resection, which showed a trend to significance in FCD-type lesions only. Furthermore, seizure severity and quality of life scales were only completed in some patients postoperatively, thereby limiting the interpretation of the results. Additional noninvasive data

may be informative to seizure outcome, but in the setting of a retrospective study, we were limited to analysis of video-EEG and MRI results.

5 | CONCLUSIONS

We demonstrated rates of resection and seizure freedom after B-SEEG implantation to be comparatively lower than that reported in unselected cohorts, largely related to multifocality, heralded by noninvasive features (eg, multiple seizure types). Odds of curative resective surgery may be better after B-SEEG implantation in select groups of patients, with suspected unifocal epilepsy and a strong preimplantation hypothesis requiring exploration of bilaterally connected networks. However, in patients with suspected multifocal epilepsy, there may still be a role for B-SEEG implantation to craft a palliative resection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Gonzalez-Martinez J, Bulacio J, Alexopoulos A, et al. Stereoelectroencephalography in the “difficult to localize” refractory focal epilepsy: early experience from a North American epilepsy center. *Epilepsia*. 2013;54:323–30. [PubMed: 23016576]
2. Bancaud J, Angelergues R, Bernouilli C, et al. Functional stereotaxic exploration (SEEG) of epilepsy. *Electroencephalogr Clin Neurophysiol*. 1970;28:85–6.
3. Cossu M, Cardinale F, Csatan L, et al. Stereoelectroencephalography in the presurgical evaluation of focal epilepsy: a retrospective analysis of 215 procedures. *Neurosurgery*. 2015;57:706–18.
4. Jehi L, Friedman D, Carlson C, et al. The evolution of epilepsy surgery between 1991 and 2011 in nine major epilepsy centers across the United States, Germany, and Australia. *Epilepsia*. 2015;56:1526–33. [PubMed: 26250432]
5. McGonigal A, Bartolomei F, Regis J, et al. Stereoelectroencephalography in presurgical assessment of MRI-negative epilepsy. *Brain*. 2007;130:3169–83. [PubMed: 17855377]
6. Katzan I, Speck M, Dopler C, et al. The Knowledge Program: an innovative, comprehensive electronic data captured system and warehouse. *AMIA Annu Symp Proc*. 2011;2011:683–92. [PubMed: 22195124]
7. Scott-Lennox J, Bryant-Comstock L, Lennox R, et al. Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale. *Epilepsy Res*. 2001;44:53–63. [PubMed: 11255073]
8. Cramer JA, Perrine K, Devinsky O, et al. A brief questionnaire to screen for quality of life in epilepsy: the QOLIE-10. *Epilepsia*. 1996;37:577–82. [PubMed: 8641236]
9. Wiebe S, Elisziw M, Matijevic S. Changes in quality of life in epilepsy: how large must they be to be real? *Epilepsia*. 2001;42:113–8. [PubMed: 11207794]
10. Jehi L, Tesar G, Obuchowski N, et al. Quality of life in 1931 adult patients with epilepsy: seizures do not tell the whole story. *Epilepsy Behav*. 2011;22:723–7. [PubMed: 22019018]

11. Placantonakis DG, Shariff S, Lafaille F, et al. Bilateral intracranial electrodes for lateralizing intractable epilepsy: efficacy, risk and outcome. *Neurosurgery*. 2010;66:274–83. [PubMed: 20087126]
12. Hill TC, Rubin BA, Tyagi V, et al. The value of diagnostic bilateral intracranial electroencephalography in treatment-resistant focal epilepsy. *World Neurosurg*. 2017;103:1–10. [PubMed: 28185968]
13. Pestana Knight EM, Loddenkemper T, Lachhwani D, et al. Outcome of no resection after long-term subdural electroencephalography evaluation in children with epilepsy. *J Neurosurg Pediatr*. 2011;8:269–78. [PubMed: 21882919]
14. Carlson C, Teutonico F, Elliott RE, et al. Bilateral invasive electroencephalography in patients with tuberous sclerosis complex: a path to surgery? *J Neurosurg Pediatr*. 2011;7:421–30. [PubMed: 21456917]
15. Maillard LG, Tassi L, Bartolomei F, et al. Stereoelectroencephalography and surgical outcome in polymicrogyria-related epilepsy: a multicentric study. *Ann Neurol*. 2017;82:781–94. [PubMed: 29059488]
16. Murakami H, Wang ZI, Marshly A, et al. Correlating magnetoencephalography to stereo-electroencephalography in patients undergoing epilepsy surgery. *Brain*. 2016;139:2935–47. [PubMed: 27567464]
17. El Tahry R, Wang ZI, Thandar A, et al. Magnetoencephalography and ictal SPECT in patients with failed epilepsy surgery. *Clin Neurophysiol*. 2018;129:1651–7. [PubMed: 29920428]
18. MacDougall KW, Burneo JG, McLachlan RS, et al. Outcome of epilepsy surgery in patients investigated with subdural electrodes. *Epilepsy Res*. 2009;85:235–42. [PubMed: 19380212]
19. Berkovic SF, McIntosh AM, Kalnins RM, et al. Preoperative MRI predicts outcome of temporal lobectomy: an actuarial analysis. *Neurology*. 1995;45:1358–63. [PubMed: 7617198]
20. Jeha LE, Najm I, Bingaman W, et al. Surgical outcome and prognostic factors of frontal lobe epilepsy surgery. *Brain*. 2007;130:574–84. [PubMed: 17209228]
21. Jeha LE, Najm IM, Bingaman WE, et al. Predictors of outcome after temporal lobectomy for the treatment of intractable epilepsy. *Neurology*. 2006;66:1938–40. [PubMed: 16801667]
22. Simasathien R, Vadera S, Najm I, et al. Improved outcomes with earlier surgery for intractable frontal lobe epilepsy. *Ann Neurol*. 2013;73:646–54. [PubMed: 23494550]
23. Tellez-Zenteno JF, Hernandez Ronquillo L, et al. Surgical outcomes in lesional and non-lesional epilepsy: a systematic review and meta-analysis. *Epilepsy Res*. 2010;89:310–8. [PubMed: 20227852]
24. Blumcke I, Lo Russo G, Najm I, et al. Pathology-based approach to epilepsy surgery. *Acta Neuropathol*. 2014;128:1–3. [PubMed: 24879580]
25. Bulacio JC, Jehi L, Wong C, et al. Long-term seizure outcome after resective surgery in patients evaluated with intracranial electrodes. *Epilepsia*. 2012;53:1722–30. [PubMed: 22905787]
26. Hanakova P, Brazdil M, Novak Z, et al. Long-term outcome and predictors of resective surgery prognosis in patients with refractory extratemporal epilepsy. *Seizure*. 2014;23:266–73. [PubMed: 24378203]
27. Catenoix H, Mauguire F, Guenot M, et al. SEEG-guided thermocoagulation. A palliative treatment of nonoperable partial epilepsies. *Neurology*. 2008;71:1719–26. [PubMed: 19015488]
28. Lamberink HJ, Boshuisen K, van Rijen PC, et al. Changing profiles of pediatric epilepsy surgery candidates over time: a nationwide single-center experience from 1990 to 2011. *Epilepsia*. 2015;56:717–25. [PubMed: 25847357]
29. Bonini F, McGonigal A, Scavarda D, et al. Predictive factors of surgical outcome in frontal lobe epilepsy explored with stereoelectroencephalography. *Neurosurgery*. 2018;83:217–25. [PubMed: 28673029]
30. Pelliccia V, Deleo F, Gozzo F, et al. Early and late epilepsy surgery in focal epilepsies associated with long-term epilepsy-associated tumors. *J Neurosurg*. 2017;127:1147–52. [PubMed: 28084910]
31. Krsek P, Maton B, Jayakar P, et al. Incomplete resection of focal cortical dysplasia is the main predictor of poor postsurgical outcome. *Neurology*. 2009;72:217–23. [PubMed: 19005171]

32. Oluigbo CO, Wang J, Whitehead MT, et al. The influence of lesion volume, perilesion resection volume, and completeness of resection on seizure outcome after resective epilepsy surgery for cortical dysplasia in children. *J Neurosurg Pediatr.* 2015;15:644–50. [PubMed: 26030332]
33. Jehi LE, Palmini A, Aryal U, et al. Cerebral cavernous malformations in the setting of focal epilepsies: pathological findings, clinical characteristics, and surgical treatment principles. *Acta Neuropathol.* 2014;128:55–65. [PubMed: 24831066]
34. Kazemi NJ, Son EL, Mosewich RK, et al. Resection of frontal encephalomalacias for intractable epilepsy: outcome and prognostic factors. *Epilepsia.* 1997;38:670–7. [PubMed: 9186249]
35. Li LM, Dubeau F, Andermann F, et al. Periventricular nodular heterotopia and intractable temporal lobe epilepsy: poor outcome after temporal lobe resection. *Ann Neurol.* 1997;41:662–8. [PubMed: 9153529]
36. Mirandola L, Mai RF, Francione S, et al. Stereo-EEG: diagnostic and therapeutic tool for periventricular nodular heterotopia epilepsies. *Epilepsia.* 2017;58:1962–71. [PubMed: 28880999]
37. Ghatan S, McGoldrick P, Palmese C, et al. Surgical management of medically refractory epilepsy due to early childhood stroke. *J Neurosurg Pediatr.* 2014;13:58–67.
38. Stevelink R, Sanders MW, Tuinman MP, et al. Epilepsy surgery for patients with genetic refractory epilepsy: a systematic review. *Epileptic Disord.* 2018;20:99–115. [PubMed: 29620010]
39. Asano E, Juhasz C, Shah A, et al. Role of subdural electrocorticography in prediction of long term seizure outcome in epilepsy surgery. *Brain.* 2009;132:1038–47. [PubMed: 19286694]
40. Mullin JP, Sexton D, Al-Omar S, et al. Outcomes of subdural grid electrode monitoring in the stereoelectroencephalography era. *World Neurosurg.* 2016;89:255–8. [PubMed: 26893042]
41. World Health Organization. Palliative care – fact sheet. Available at: <http://www.who.int/mediacentre/factsheets/fs402/en/> Accessed February 15th 2018.
42. Kaiboriboon K, Malkhachroum AM, Zrik A, et al. Epilepsy surgery in the United States: analysis of data from the National Association of Epilepsy Centers. *Epilepsy Res.* 2015;116:105–9. [PubMed: 26310969]
43. Jehi L, Jette N. Not all that glitters is gold: a guide to surgical trials in epilepsy. *Epilepsia Open.* 2016;1:22–36. [PubMed: 29588926]

Key Points

- Targeted coverage of a strong hypothesis increases the odds of resection and subsequent seizure freedom after bilateral SEEG
- Electroclinical features of unifocal epilepsy increase the odds of seizure freedom, even in the setting of multifocal lesions
- Completeness of lesionectomy is correlated with good seizure outcome in some (eg, focal cortical dysplasia [FCD] type IIb) but not all pathologies
- Even in the absence of seizure freedom, resection is associated with improved seizure reduction compared to medications alone

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FIGURE 1.

SEEG implantation schemes of selected patients of the cohort studied, represented on Talairach grids. A, Temporoparietooccipital junction hypothesis, with sentinel electrodes placed on the left hemisphere to rule out propagation from the contralateral hemisphere. B, Temporofrontal hypothesis (temporal pole, orbitofrontal, and anterior cingulate were the top 3 hypotheses), with suspected left lateralization but placement of right-sided electrodes in key regions. C, Primary hypothesis involved the supplementary sensorimotor area, with exploration of the frontoparietal network propagation. D, Temporo-perisylvian hypothesis (with secondary hypothesis involving the anterior cingulate), with contralateral electrodes sampling the amygdala and perisylvian regions. E, Perisylvian hypothesis, with sentinel electrodes on the left to exclude propagation from the contralateral hemisphere. F, Frontal hypothesis, with symmetric exploration given lack of strong lateralizing data

Time since surgery	6 mo	1 yr	2 yrs	3 yrs	>4 yrs
N at risk	54	40	22	7	4
% seizure-free	55%±5%	46%±5%	33%±5%	26%±5%	22%±6%

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FIGURE 2.

Kaplan-Meier plot of postoperative seizure freedom following resection guided by bilateral SEEG implantation

FIGURE 3.

Differences in postoperative seizure freedom according to variables identified as significant in the multivariate analysis: epilepsy duration less than 10 years, single seizure type, use of 2 or fewer AEDs at the time of surgery, use of sentinel electrodes only, lack of overlap with eloquent cortex, and pathology suggestive of epileptic substrate (focal cortical dysplasia, hippocampal sclerosis) were predictive of a higher chance of seizure freedom. An additional Kaplan-Meier curve representing seizure outcomes in the early (2009-2012) and later (2012-2015) period of our SEEG program showed no significant differences

TABLE 1

Baseline characteristics of the overall cohort

	Overall group (n = 184)
Female (%)	98 (53%)
Adult (%)	160 (87%)
Mean age at SEEG, years (SD, range)	30.9 ($\pm$ 13.4, 5-69)
Epilepsy characteristics	
Mean age at seizure onset, years (SD, range)	14.4 ($\pm$ 12.3, 0-65)
Mean epilepsy duration at the time of surgery (SD, range)	17.1 ($\pm$ 12.3, 1-55)
Mean number of seizure types (SD, range)	1.67 ($\pm$ 0.93, 1-5)
Mean monthly seizure preoperative seizure frequency/month (median, range)	32.2 (9.5, 0.5-600)
Epilepsy etiology	
Unknown (%)	97 (53%)
Suspected MCD (%)	41 (22%)
Encephalitis (%)	17 (9%)
Suspected HS (%)	16 (9%)
Encephalomalacia (ischemic or posttraumatic; %)	12 (6.5%)
Tumor ^a (%)	1 (0.5%)
Family history (%)	57 (31%)
Imaging	
Nonlesional (%)	109 (59%)
Lesional (%)	75 (41%)
Type of MRI lesion	
MCD (%)	38 (21%)
HS (%) ^b	24 (13%)
Unilateral HS (%)	10 (42%)
Bilateral HS (%)	14 (58%)
Encephalomalacia (%)	12 (7%)
Other (%)	1 (1%)
Extent of MRI lesion (lesional, n = 75)	
Unilobar (%)	32 (43%)
Multilobar (%)	43 (57%)
Bilateral (%)	37 (49%)
Primary hypothesis	
Temporo-parietooccipital (%)	42 (23%)
Perisylvian (%)	30 (16%)
Temporal (%)	26 (14%)
Temporo-perisylvian (%)	13 (7%)
Bilateral temporal (%)	12 (7%)
Frontal (%)	20 (11%)
Parietal (%)	12 (7%)

	Overall group (n = 184)
Frontoparietal (%)	11 (6%)
Temporofrontal (%)	11 (6%)
Cingulate (%)	5 (3%)
Occipital (%)	2 (1%)
SEEG evaluation	
Mean number of electrodes implanted (SD, range)	13.7 (± 2.3 , 4-21)
Mean number of electrodes implanted on the left (SD, range)	6.9 (± 3.7 , 1-16)
Mean number of electrodes implanted on the right (SD, range)	6.6 (± 3.8 , 1-14)
Mean ratio of number of electrodes on side with most electrodes to side with least electrodes (SD, range)	4.2 (± 3.5 , 1-16)
Sentinel (1-2) electrodes on one side (%)	71 (39%)
Symmetric (2 electrode or less difference between sides; %)	36 (20%)
Implantation scheme	
Temporo-parietooccipital junction (%)	54 (29%)
Temporo-perisylvian (%)	41 (22%)
Perisylvian (%)	18 (10%)
Bilateral temporal (%)	6 (3%)
Frontoparietal (%)	24 (13%)
Frontal (%)	6 (3%)
Temporofrontal (%)	17 (9%)
Broad (frontal, parietal, temporal, $\pm$ occipital; %)	18 (10%)
Additional electrode implantation (%)	8 (4%)
Mean number of interictal populations (SD, range)	4.1 (± 2.3 , 0-13)
Presence of a dominant (>50%) interictal population (%)	126 (68%)
Ictal-onset zones ^C (n = 181)	
One (%)	81 (45%)
Multiple (%)	86 (48%)
Nonlocalized (%)	14 (8%)
Bilateral independent (%)	73 (40%)
Overlap with eloquent cortex (%)	43 (24%)
Seizures from sentinel electrode (n = 69) ^d (%)	15 (22%)
Resection	
Resective surgery performed (open resection and laser ablation; %)	106 (58%)
Open resection (%)	97 (92%)
Laser ablation (%)	9 (5%)
Responsive neurostimulation (%)	10 (5%)
Reason for no resection (n = 78)	
Multifocal (%)	43 (55%)
Nonlocalized (%)	14 (18%)
Risk of deficit (%)	12 (15%)
Seizure-free on AED (%)	3 (4%)
Patient declined (%)	3 (4%)

	Overall group (n = 184)
No seizures recorded (%)	3 (4%)
Relationship of lesion and resection (n = 38)	
Complete	11 (29%)
Incomplete	19 (50%)
Resection did not include lesion	8 (21%)

n = 184.

AED, antiepileptic drug; FCD, focal cortical dysplasia; MCD, malformation of cortical development; HS, hippocampal sclerosis; MRI, magnetic resonance imaging (MRI); SD, standard deviation.

^aThis patient's MRI showed an intraventricular mass arising from the margin of the caudate head with invasion of the mesial frontal and orbitofrontal regions. SEEG was recommended to map the epileptogenic zone and determine the cortical borders of the resection.

^bFour patients had concurrent HS with MCD (1) or encephalomalacia (3) (these patients were considered to have the latter as the “predominant” imaging characteristic”).

^cA total of 181 of 184 patients had seizures recorded—the remaining 3 did not have spontaneous or stimulation induced seizures.

^dn = 71 with sentinel electrode implanted, of which 2 did not have recorded seizures.

TABLE 2

Univariate analysis of predictors of resection (significant predictors only)

	Overall group (n = 184) ^a	Resection (n = 106)	No resection (n = 78)	P value
Preimplantation data				
Pediatric (%)	24	18 (75%)	6 (25%)	0.06
Adult (%)	160	88 (55%)	72 (45%)	
Family history of epilepsy (%)	57	41 (72%)	16 (28%)	0.008
No family history of epilepsy (%)	127	65 (51%)	62 (49%)	
1 Seizure type (%)	107	71 (66%)	36 (34%)	0.005
>1 Seizure type (%)	77	35 (45%)	42 (55%)	
No bilateral version (%)	176	104 (59%)	72 (41%)	0.06
Bilateral version (%)	8	2 (25%)	6 (75%)	
10 Seizures per month (%)	92	60 (65%)	32 (35%)	0.04
<10 Seizures per month (%)	92	46 (50%)	46 (50%)	
Absence of bilateral independent scalp ictal EEG patterns (%)	138	85 (62%)	53 (38%)	0.06
Presence of bilateral independent scalp ictal EEG patterns (%)	46	21 (46%)	25 (54%)	
Primary hypothesis other than TPOJ (see Table 1; %)	142	88 (62%)	54 (38%)	0.03
Primary hypothesis TPOJ (%)	42	18 (43%)	24 (57%)	
Confined hypothesis-driven scheme (%)	166	99 (59%)	67 (40%)	0.09
Broad implantation scheme (%)	18	7 (39%)	11 (61%)	
Sentinel electrode(s), %	71	48 (68%)	23 (32%)	0.03
>1-2 Sentinel electrodes (%)	113	58 (51%)	55 (49%)	
Number of electrodes (SD, range)		13.3 (±0.2, 4-20)	14.2 (±0.3, 10-21)	0.006
Postimplantation data				
4 Interictal populations (%)	120	77 (64%)	43 (36%)	0.01
5 Interictal populations (%)	64	29 (45%)	35 (55%)	
Presence of dominant interictal population (>50% of the interictal discharges; %)	126	80 (63%)	46 (37%)	0.02
Lack of dominant interictal population (%)	58	26 (45%)	32 (55%)	
Absence of bilateral independent ictal-onset zones (%)	108	84 (78%)	24 (22%)	<0.0001
Bilateral independent ictal-onset zones (%)	73	22 (30%)	51 (70%)	
Absence of overlap between ictal-onset zones and eloquent cortex (%)	138	86 (62%)	52 (38%)	0.07

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	Overall group (n = 184) ^a	Resection (n = 106)	No resection (n = 78)	P value
Overlap between ictal-onset zone and eloquent cortex (%)	43	20 (47%)	23 (53%)	
Localized ictal-onset zone (%)	167	106 (63%)	61 (37%)	<0.0001
Nonlocalized ictal-onset zone (%)	14	0 (0%)	14 (100%)	
One ictal-onset zone (%)	81	66 (82%)	15 (18%)	<0.0001
Multiple ictal-onset zones (%)	86	40 (47%)	46 (53%)	

^a Ictal-onset zone data available in 181 patients due to absence of recorded seizures in 3 patients.

TABLE 3

Univariate analysis of predictors of seizure freedom (significant predictors only)

	Overall group (n = 81)	Seizure-free (n = 26)	Seizure recurrence (n = 55)	P value
Preimplantation data				
Epilepsy duration 10 y (%)	26	12 (46%)	14 (54%)	0.07
Epilepsy duration >10 y (%)	55	14 (25%)	41 (75%)	
2 AEDs (%)	50	21 (42%)	29 (58%)	0.005
3 AEDs (%)	30	4 (13%)	26 (87%)	
1 Seizure type (%)	56	23 (41%)	33 (59%)	0.006
2 Seizure types (%)	25	3 (12%)	22 (88%)	
No history of encephalitis (%)	74	26 (35%)	48 (65%)	0.02
History of encephalitis (%)	7	0 (0%)	7 (100%)	
No history of failed resective surgery (%)	66	24 (36%)	42 (64%)	0.07
Previous failed resective surgery (%)	15	2 (13%)	13 (87%)	
1-2 Sentinel electrodes (%)	35	15 (43%)	20 (57%)	0.07
More than 1-2 sentinel electrodes (%)	46	11 (24%)	35 (76%)	
Frontal hypothesis (%)	12	7 (58%)	5 (42%)	0.04
Other than frontal hypothesis (%)	69	19 (28%)	50 (72%)	
Other than TPOJ hypothesis (%)	66	24 (36%)	42 (63%)	0.07
TPOJ hypothesis (%)	15	2 (13%)	13 (87%)	
Postimplantation data				
4 Interictal populations (%)	62	23 (37%)	39 (71%)	0.07
5 Interictal populations (%)	19	3 (16%)	16 (84%)	
One ictal-onset zone (%)	48	19 (40%)	29 (60%)	0.08
Multiple ictal-onset zones (%)	33	7 (21%)	26 (79%)	
Absence of bilateral independent ictal-onset zones (%)	61	23 (38%)	38 (62%)	0.05
Bilateral independent ictal-onset zones (%)	20	3 (15%)	17 (85%)	
Absence of overlap between ictal-onset zones and eloquent cortex (%)	67	24 (36%)	43 (64%)	0.09
Overlap between ictal-onset zone and eloquent cortex (%)	14	2 (14%)	12 (86%)	
Perisylvian resection (%)	6	4 (67%)	2 (33%)	0.07

	Overall group (n = 81)	Seizure-free (n = 26)	Seizure recurrence (n = 55)	P value
Resection outside perisylvian region (%)	75	22 (29%)	53 (71%)	
Pathology result other than gliosis/normal (FCD type 1, 2A, 2B, HS, Other; %) ^a	61	23 (38%)	38 (62%)	0.01
Gliosis or normal (%)	14	1 (7%)	13 (93%)	

Only patients with follow-up > 1 year were included.

^aN = 74 given laser ablation.