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## Factors Associated With Failed Focal Neocortical Epilepsy Surgery

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### Abstract

**BACKGROUND**—Seizure outcomes after focal neocortical epilepsy (FNE) surgery are less favorable than after temporal lobectomy, and the reasons for surgical failure are incompletely understood. Few groups have performed an in-depth examination of seizure recurrences to identify possible reasons for failure.

**OBJECTIVE**—To elucidate factors contributing to FNE surgery failures.

**METHODS**—We reviewed resections for drug-resistant FNE performed at our institution between 1998 and 2011. We performed a quantitative analysis of seizure outcome predictors and a detailed qualitative review of failed surgical cases.

**RESULTS**—Of 138 resections in 125 FNE patients, 91 (66%) resulted in freedom from disabling seizures (Engel I outcome). Mean  $\pm$  SEM patient age was  $20.0 \pm 1.2$  years; mean follow-up was 3.8 years (range, 1-17 years); and 57% of patients were male. Less favorable (Engel II-IV) seizure outcome was predicted by higher preoperative seizure frequency (odds ratio = 0.85; 95% confidence interval, 0.78-0.93), a history of generalized tonic-clonic seizures (odds ratio = 0.42; 95% confidence interval, 0.18-0.97), and normal magnetic resonance imaging (odds ratio = 0.30; 95% confidence interval, 0.09-1.02). Among 36 surgical failures examined, 26 (72%) were related to extent of resection, with residual epileptic focus at the resection margins, whereas 10 (28%) involved location of resection, with an additional epileptogenic zone distant from the resection. Of 16 patients who received reoperation after seizure recurrence, 10 (63%) achieved seizure freedom.

**CONCLUSION**—Insufficient extent of resection is the most common reason for recurrent seizures after FNE surgery, although some patients harbor a remote epileptic focus. Many patients with incomplete seizure control are candidates for reoperation.

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#### Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

## Keywords

Epilepsy surgery; Extratemporal; Failure; Neocortical; Outcome

Focal epilepsy is a common and devastating disorder, particularly when seizures are refractory to antiepileptic drugs. Many cases of drug-resistant epilepsy are surgically remediable after localization and resection of the epileptogenic zone. Anterior temporal lobectomy for mesial temporal lobe epilepsy (MTLE) has been shown by Class I evidence to be effective and safe, resulting in seizure freedom in approximately two-thirds of patients.<sup>1,2</sup> However, treatment of drug-resistant focal neocortical epilepsy (FNE), including extra-temporal lobe epilepsy, is more challenging. Approximately one-half of children and adults who undergo targeted resection for FNE continue to have seizures postoperatively.<sup>3,4</sup> Thus, significant room for improved surgical strategies exists in FNE treatment.

Although epilepsy surgery failures have been studied by many groups, the underlying reasons for persistent or recurrent seizures after resection for FNE remain poorly understood.<sup>5,6</sup> FNE is a more heterogeneous disorder than MTLE, with much variability in localization, pathology, and response to antiepileptic drugs.<sup>3,4</sup> Accurate localization of the epileptogenic zone typically requires long-term electroencephalography (EEG) recordings with video monitoring, correlated with anatomic and functional neuroimaging studies.<sup>7,8</sup> Invasive intracranial electrocorticography (ECoG) recordings are also often necessary, particularly in the absence of a distinct pathological lesion on magnetic resonance imaging (MRI).<sup>7,9</sup> Planning a safe surgical resection requires an appreciation of both the seizure onset zone and eloquent cortical regions such as those involved in motor function, language, and vision. Presumably, epilepsy surgery will fail if the epileptogenic zone is incorrectly localized, the extent is incompletely delineated for resection, or another epileptogenic zone distant from the resection is undetected or untreated. The relative contribution of these reasons for failed epilepsy surgery is not well understood, but an improved appreciation of their prevalence may help improve surgical planning and outcome prediction.

In this study, we review 138 resections in 125 patients with drug-resistant FNE performed at our institution. As in previous investigations of epilepsy surgery, we report a quantitative analysis of potential seizure outcome predictors. However, unlike most epilepsy surgery series, we also perform further qualitative review of cases with less favorable seizure outcomes, examining post-operative diagnostic findings. Our goal is a better understanding of the reasons for failed FNE surgery to help guide treatment strategies going forward.

## METHODS

### Patients and Data Collection

We examined the medical records of 148 consecutive patients who underwent 135 targeted resections for FNE at the University of California, San Francisco between January 1, 1998, and December 31, 2011. After the exclusion of 10 patients without at least 1 year of postoperative follow-up, 138 resections in 125 patients were analyzed. All patients had drug-resistant epilepsy and had failed  $\geq 2$  antiepileptic drug regimens. Resections for MTLE,

hemispherectomies, disconnection procedures, and device implantations were excluded. All procedures in the study were in full compliance with University of California, San Francisco clinical research policies, with research protocol approval by university's Committee on Human Research.

Surgical decisions were made by a comprehensive team of epileptologists, neurosurgeons, neuropsychologists, neuroradiologists, and other practitioners. Standard preoperative evaluation included EEG and structural MRI and often included neuropsychological evaluation, magnetoencephalography (MEG), positron emission tomography (PET), and long-term video-EEG monitoring with or without extra-operative ECoG using surgically implanted subdural or depth electrodes. Resections were customized to incorporate epileptogenic regions or cerebral lesions and to preserve eloquent cortex when applicable. Intra-operative ECoG was often used to further guide resection. Surgical specimens were analyzed by neuropathologists.

We reviewed all outpatient and inpatient provider notes, diagnostic and laboratory reports, operative records, and pathology reports. Clinical and demographic data, including patient sex, age, handedness, epilepsy duration, surgical history, medication history, MRI results, MEG findings, EEG findings, PET results, use of implanted electrodes for long-term recording, side and lobe(s) of surgery, and use of intraoperative ECoG, were recorded. Details on patients' epilepsy history and seizure semiology, including seizure type and frequency, were obtained from preoperative and postoperative assessments by epileptologists. Epilepsy risk factors were recorded and tallied, including a history of cerebral palsy or birth injury, developmental delay or static encephalopathy, febrile seizures, head trauma, central nervous system infection, family history of epilepsy, drug or alcohol abuse, cerebral ischemia, and status epilepticus. Seizure outcome was determined at the latest patient follow-up by an epileptologist using a modified Engel classification system, with Engel class I outcome signifying freedom from disabling seizures.<sup>10</sup> To allow insight into factors associated with surgical failure, we then performed further chart review for patients with recurrent postoperative seizures (Engel II-IV outcome) who had sufficient diagnostic data with new postoperative electrographic data (long-term EEG or ECoG) and neuroimaging studies.

### Statistical Analysis

To examine factors for statistical association with postoperative seizure freedom (Engel I outcome) vs less favorable seizure outcome (Engel II-IV), we first performed univariate analysis with the  $\chi^2$  test for categorical variables (eg, sex) or an unpaired Student *t* test for continuous variables (eg, age). Before using parametric tests, we verified normality of data and used the Levene test for equality of variances. Only variables showing a value of  $P < .20$  on univariate analysis were then entered into a multivariate logistic regression model in a backward fashion. Thus, the multivariate model was built to identify variables significantly associated with seizure outcome and potential interactions between these variables. Odds ratios were calculated with a 95% confidence interval, and statistical significance was assessed at  $P < .05$ , with statistical analyses performed with SPSS version 22 (IBM, Somers, New York).

## RESULTS

We analyzed 138 focal neocortical resections for drug-resistant epilepsy in 125 patients, including 15 repeat surgeries in patients who underwent previous resection. Postoperative follow-up ranged from 1 to 17 years, with a mean of 3.8 years. Seventy-one patients (57%) were male, and the mean  $\pm$  SEM age at the time of surgery was  $20.0 \pm 1.2$  years. Epilepsy was localized to the frontal lobe in 57 patients (46%), the lateral temporal lobe in 30 individuals (24%), and the parietal or occipital lobes in 28 individuals (22%), and 21 patients (20%) underwent resection involving  $>1$  lobe. Other patient characteristics are summarized in Table 1.

At the last follow-up, 90 patients (72%) were free of all disabling seizures (Engel IA-ID), including 65 individuals (52%) who were completely seizure free (Engel IA). Given that some patients received  $>1$  resection in this series, 91 surgeries overall (66%) resulted in an Engel I outcome. Rates of Engel II to IV outcome are listed in Tables 2 and 3, and seizure outcomes by age range are shown in Table 4. The mean  $\pm$  SEM age of patients with Engel I ( $20.4 \pm 1.5$  years) vs Engel II to IV ( $18.6 \pm 2.4$  years) outcomes did not differ appreciably ( $t = 0.7$ ;  $P = .8$ ).

The most common primary pathological findings in descending order were malformation of cortical development, mainly focal cortical dysplasia, gliosis only, and brain tumor (Table 5). Among these 3 pathologies, seizure freedom was achieved most frequently in patients with tumoral epilepsy (82%) and least often in those with gliosis only (61%), although this relationship was not significant ( $\chi^2 = 3.1$ ;  $P = .21$ ). Other pathologies observed are shown in Table 5. In 10 patients, including 7 children (age  $<18$  years), 2 distinct pathological findings were noted (eg, tuber and malformation of cortical development). Outcomes were less favorable in patients with dual pathology (30% seizure free) compared with those with a single pathology (76% seizure free;  $\chi^2 = 9.5$ ;  $P < .01$ ).

Seizure outcomes were stratified across various factors of interest, including those listed in Table 1, to investigate potential predictors of postoperative seizure freedom. Variables with possible relationship to seizure outcome on univariate analysis ( $P < .20$ ) were entered into multivariate analysis (Figure 1). Patients with a higher preoperative seizure frequency were significantly less likely to achieve seizure freedom than those with less frequent seizures (odds ratio = 0.85; 95% confidence interval, 0.78-0.93;  $P < .01$ ), and Engel I outcome was less common in individuals with a history of generalized tonic-clonic seizures (odds ratio = 0.42; 95% confidence interval, 0.18-0.97;  $P = .04$ ). In addition, a normal MRI predicted worse seizure outcome with borderline significance (odds ratio = 0.30; 95% confidence interval, 0.09-1.02;  $P = .05$ ). Univariate analysis of other factors investigated did not reveal a relationship to seizure outcome, including age; sex; handedness; epilepsy duration; number of antiepileptic drug regimens failed; number of epilepsy risk factors; presence of preoperative neurological deficit; localized findings on EEG, MEG, or PET; use of extraoperative or intraoperative ECoG; or surgery lobe or side. Notably, among 46 patients who harbored a distinct radiological lesion such as tumor, tuber, or vascular malformation, Engel I outcome was significantly more common with gross total (85% seizure free) compared with subtotal (33% seizure free) resection based on postoperative MRI ( $\chi^2 = 8.2$ ,

$P = .02$ ). Gross total vs subtotal resection and single vs dual pathology were not entered into the multivariate regression analysis, given their relevance to only a smaller subset of patients.

In addition to quantitative analysis of seizure outcome predictors, we performed further qualitative chart review for patients with less favorable (Engel II-IV) seizure outcomes to better understand the reasons for surgical failure (Figure 2). Of the 47 cases with recurrent seizures after surgery, sufficient diagnostic data with new postoperative electrographic (long-term EEG or ECoG) and neuroimaging studies were available for 36 cases (77%), allowing further insight into seizure focus localization. In 26 of these 36 cases (72%), seizure recurrence was most likely related to extent of resection, with data suggesting residual seizure focus adjacent to the surgical cavity. In 10 of the 36 cases (28%), recurrent seizures most likely originated from an additional seizure focus distant from the area of resection. Additional factors associated with seizure recurrence in both of these patient subsets are listed in Figure 2. More than 1 factor was present in several cases.

Among 26 cases of seizure recurrence related to extent of resection (Figure 2), we noted 10 cases in which the borders of resection were intentionally limited to preserve eloquent cortex (eg, primary motor cortex), despite evidence suggesting potential epileptogenicity. Ten cases existed in which epileptiform activity was observed beyond the region of resection on intraoperative ECoG. The resection was not extended in these surgeries because of any 1 or combination of the following reasons: Residual interictal spikes were less prominent than those within the area of resection; residual spikes did not colocalize with the radiological lesion; or the involved cortex was eloquent. We noted 6 cases with residual lesion present on postoperative MRI (eg, brain tumor, focal cortical dysplasia) that likely contributed to persistent seizures. In 7 cases, seizures recurred after a focal resection in a patient ultimately determined to have a hemispheric epilepsy syndrome (eg, Rasmussen syndrome, hemimegalencephaly). Hemispherectomy was not performed as first-line surgical therapy in these patients either because of an uncertain diagnosis of hemispheric epilepsy or to limit neurological deficits associated with hemispherectomy. Of 26 cases in the extent of resection category, 12 went on to have further resection, after which 8 patients (67%) ultimately achieved seizure freedom. These included 5 patients with hemispheric epilepsy who subsequently received hemispherectomy, allowing 4 to become seizure free.

In all 10 cases of seizure recurrence related to location of resection, postoperative EEG suggested epileptiform activity in a separate location distant from the resection (Figure 2). Five of these cases involved patients with tuberous sclerosis complex (TSC) harboring multiple cortical tubers in whom other epileptogenic tuber(s) may have contributed to persistent epilepsy. As an example, a 1-year-old boy experienced recurrent seizures several months after resection of a large epileptogenic tuber in the right frontal lobe, and repeat EEG suggested epileptiform activity colocalizing with smaller tubers on the contralateral side. Three cases in this category involved patients harboring dual pathology with mesial temporal sclerosis after a focal neocortical resection. These included a 5-year-old boy who underwent resection of a left frontal focal cortical dysplasia, with postoperative evaluation suggesting hippocampal sclerosis contributing to persistent seizures. In the location of resection group, we also observed 1 case of multifocal glioma and a case involving an

additional focus of focal cortical dysplasia. Among these 10 cases, 4 patients went on to receive an additional resection, resulting in freedom from seizure in 2 patients: the aforementioned boy with dual pathology who received amygdalohippocampectomy and a 3-year-old boy with TSC.

Given that 50% of surgical failures in the location of resection category were in patients with tubers and that TSC represents a unique clinical entity, we also repeated our analyses excluding this population. After excluding TSC patients, we analyzed 130 surgeries in 118 patients. Overall, Engel I outcome was achieved in 87 patients (74%) at the last follow-up or after 88 surgeries (68%) overall. On multivariate analysis, seizure recurrence remained significantly associated with higher preoperative seizure frequency ( $P < .01$ ) and normal MRI ( $P = .01$ ), but a history of generalized seizures was not a significant outcome predictor ( $P = .16$ ) in this population. Among these patients, sufficient postoperative data were available for 31 cases, allowing further evaluation of surgical failures. Of these cases with persistent seizures, 26 (84%) were related to extent of resection, with seizures originating from the resection cavity margins, whereas 5 (16%) were more likely related to a separate epileptogenic focus distant from the resection. Thus, when patients with TSC are excluded from the analysis, a smaller proportion of surgical failures are related to location of resection.

Finally, among all 125 patients, there were 9 cases of perioperative morbidity and no perioperative mortality. Three patients had postoperative wound infection requiring surgical debridement and intravenous antibiotics, and there were 2 cases of surgical site hematoma requiring evacuation, all without long-term sequelae. Two patients had mild hemiparesis postoperatively, and 1 patient experienced a transient oculomotor nerve palsy related to strip electrode position, which resolved after electrode repositioning. Finally, we noted a single case of postoperative pneumonia, which resolved with antibiotics.

## DISCUSSION

The surgical treatment of FNE is typically more challenging than that of MTLE, with fewer FNE patients achieving seizure freedom postoperatively, but the reasons for surgical failure are incompletely understood. In the present study, we reviewed 138 resections in 125 patients with drug-resistant FNE performed at our institution to better understand factors associated with recurrent seizures. In addition to a quantitative analysis of seizure outcome predictors, we performed qualitative examination of circumstances surrounding failed epilepsy surgery, reviewing postoperative diagnostic studies in patients who did not achieve freedom from seizure. Whereas 66% of surgeries resulted in a favorable Engel class I seizure outcome, recurrent debilitating seizures (Engel II-IV) were present in 34% of cases. On multivariate analysis, less favorable seizure outcome was predicted by a higher preoperative seizure frequency, generalized tonic-clonic seizures, and a normal MRI. These results are not surprising because previous investigations have suggested that worse preoperative seizure profile is associated with decreased likelihood of seizure freedom after surgery for both MTLE and FNE.<sup>11-13</sup> Of 32 cases with Engel II to IV outcome examined in detail, seizure onset was localized to residual epileptic focus adjacent to the resection cavity in 72% of resections but to an additional epileptogenic zone distant from the surgical site in

28% of cases. Thus, it is likely that FNE surgery failure is more often related to extent of resection than location of resection.

Determining the optimal extent of resection is an essential and intricate aspect of epilepsy surgery planning. In the setting of a focal radiological lesion, gross total resection has consistently been associated with better seizure outcomes than subtotal excision such as in surgery for brain tumors, cavernous malformations, and focal cortical dysplasia.<sup>14-16</sup> The presence of residual lesion identified on postoperative MRI was also associated with worse seizure outcome in our series. Thus, whenever safe and possible, gross total resection of identified epileptogenic lesions is an important goal. We also observed 3 cases in which dual pathology with mesial temporal sclerosis was not fully appreciated during initial MRI evaluation and likely contributed to seizure recurrence after focal neocortical resection. Our center routinely performs 3-T MRI with epilepsy-specific sequences as part of our preoperative evaluation. However, the ability to detect subtle epileptogenic lesions, including changes in hippocampal architecture, will likely be further enhanced as 7-T MRI becomes more widely used.<sup>17</sup>

The ideal extent of resection may be more ambiguous in the setting of MRI without a clearly circumscribed unifocal epileptogenic lesion or when neuroimaging is not fully concordant with electrophysiological findings. A main concern is that although a larger resection may increase the likelihood of complete epileptic focus obliteration, it may also increase the risk of new neurological or neuropsychological deficit.<sup>18,19</sup> It is important to consider, however, that persistent seizures themselves can lead to progressive neurocognitive issues and neurological deficits<sup>20,21</sup> and that freedom from seizure is the single biggest predictor of quality of life in epilepsy.<sup>22,23</sup> In 1 large patient series at a major epilepsy center, a trend toward more aggressive surgical resections did not lead to an increased rate of neurological morbidity.<sup>24</sup> These findings are prone to subjective interpretation, however, and only children were included in this series.

In 10 cases of failed epilepsy surgery we studied, epileptiform activity on ECoG was noted outside the region of resection, but additional resection was not pursued. Reasons for this included concern for eloquent cortex, relatively low spike frequency, and the lack of a radiological lesion. Given the challenge of localization in FNE, our group uses either extraoperative ECoG with implanted electrodes or intraoperative ECoG in the majority of cases. The predictive value of ictal ECoG for incomplete resection of epileptiform tissue has been reported by others.<sup>25</sup> Asano et al<sup>26</sup> examined 61 children who underwent extraoperative ECoG, finding that subtotal excision of the area of electrographic abnormality was the only independent predictor of seizure recurrence after surgery. Although interictal ECoG is also widely used to modify resections in epilepsy surgery, including in our practice, there is conflicting evidence about its predictive value.<sup>9,27</sup> For instance, in 1 series of 52 resections for pediatric epilepsy, Wray and colleagues<sup>28</sup> reported that residual epileptiform activity was seen on intraoperative ECoG in the majority of cases (71%), yet 73% of these patients were seizure free postoperatively. On the other hand, Palmieri and colleagues<sup>29</sup> found that three-quarters of patients with cortical dysplasia and complete excision of continuous epileptiform discharges became seizure free whereas all those with incomplete resection continued to have seizures. Therefore, caution must be used



when planning resection margins on the basis of interictal ECoG findings, and consideration should be given to the type of residual epileptiform activity, potential for cortical eloquence, congruence of radio-logical findings, and gross tissue appearance. Additional study is needed to guide proper interpretation of interictal and ictal ECoG and to explore its potential role in more novel localization techniques such as high-frequency oscillation mapping and resting-state functional connectivity analysis.

In 10 cases we examined, an additional epileptic focus distant from the surgical site likely contributed to postoperative seizures. Five of these cases involved patients with TSC harboring >1 cortical tuber. Seizures become refractory to medications in the majority of children with TSC by 2 years of age, leading to developmental retardation and marked cognitive impairment.<sup>30,31</sup> Therefore, early operative intervention is often considered for those with severe drug-resistant epilepsy. However, bilateral or multiple epileptogenic lesions are more common in TSC than in other lesional epileptic disorders, likely because of the frequent multiplicity of cortical tubers.<sup>32,33</sup> A recent meta-analysis of 20 studies found that 56% of TSC patients undergoing epilepsy surgery for epileptogenic tubers achieve Engel class I seizure outcome.<sup>34</sup> The authors reported that favorable seizure outcome was predicted by a lack of generalized seizures, focal EEG results, congruence of electrographic and imaging findings, and the absence of significant developmental delay. Similar results were reported in another systematic review of 25 articles in which TSC patients achieved an approximately 90% decrease in seizure frequency after resection.<sup>35</sup> Some groups have advocated for the use of MEG for localization of the epileptic focus in TSC, citing more favorable accuracy than with EEG.<sup>31,36</sup> Finally, there is also disagreement about whether fewer tubers are associated with more favorable surgical outcomes.<sup>35,37,38</sup> Although epilepsy surgery remains a worthwhile option for TSC patients, perioperative family counseling must include a detailed discussion about the risk of persistent seizures in this disorder.

For some patients with persistent postoperative seizures, resulting from either incomplete resection or multiplicity of epileptic foci, reoperation may be warranted. Of the patients we examined in detail, 16 received repeat resection at our institution, resulting in freedom from seizure in 10 individuals (63%). Two large retrospective series of >50 reoperations for intractable epilepsy each reported a seizure freedom rate of approximately 40% after the second surgery.<sup>39,40</sup> In particular, reoperation can be considered for patients with a seemingly insufficient extent of resection after the initial surgery, although hemispherectomy may be required in children ultimately determined to have a hemispheric epilepsy syndrome.<sup>41,42</sup> As with all epilepsy surgery, the presence of congruent diagnostic data strongly supporting a focal epileptogenic zone and patient debilitation by continued seizures are required before repeat resection can be considered.

## Limitations

Important limitations of this study are its single-centered, retrospective nature and the absence of control. Many of the factors associated with surgical failures in our series are subjective and examined in hindsight after seizures persist postoperatively. Given the number of variables examined here, spurious statistical relationships and failure to detect

outcome predictors are both possible considerations. FNE includes a spectrum of focal epileptic disorders, so caution must be used when patient-level observations are generalized to the overall population. In addition, both children and adults are included in our series, and although age was not a significant predictor of outcome, it is possible that some conclusions may not be generalizable to all age groups, given the differences between these populations. Nevertheless, the qualitative nature of our analysis also allows insight into the complex scenarios associated with epilepsy surgery failures that may be overshadowed in purely quantitative analyses of seizure outcome predictors.

## CONCLUSION

Drug-resistant FNE represents a more diverse and surgically challenging disorder than MTLE, and it is critical that we understand the factors associated with surgical success and failure. In the present series of 138 surgeries in 125 FNE patients, a lower preoperative seizure frequency, the absence of generalized seizures, and an abnormal MRI predicted a favorable seizure outcome. Of the cases involving recurrent seizures after resection, 72% were more closely related to extent of resection given residual epileptogenic tissue adjacent to the surgical site, whereas the location of resection was important in 28% of cases involving an additional epileptic focus. Important considerations in FNE surgery include accurate and complete delineation and resection of the epileptogenic zone(s), as well as family counseling about the likelihood of a favorable seizure outcome. Some patients may be candidates for reoperation after an initial failed procedure.

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## ABBREVIATIONS

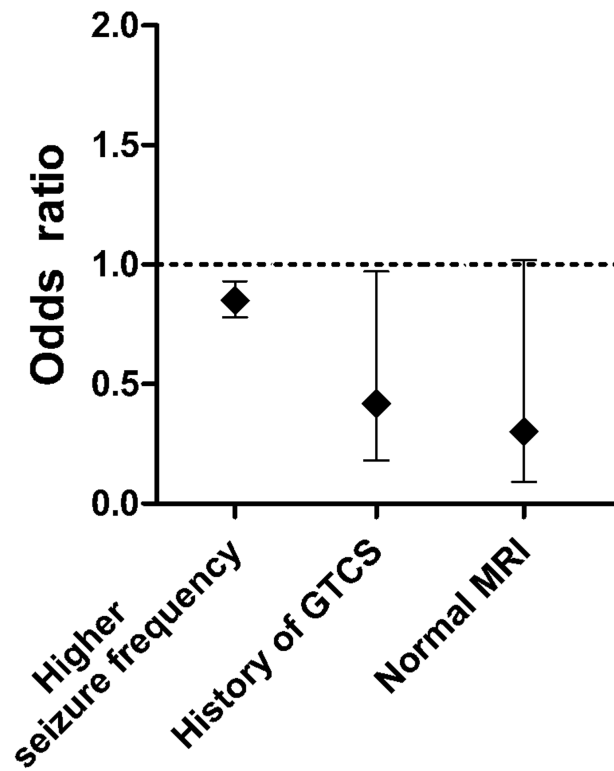
<b>ECoG</b>	electrocorticography
<b>EEG</b>	electroencephalography
<b>FNE</b>	focal neocortical epilepsy
<b>MEG</b>	magnetoencephalography
<b>MTLE</b>	mesial temporal lobe epilepsy
<b>TSC</b>	tuberous sclerosis complex

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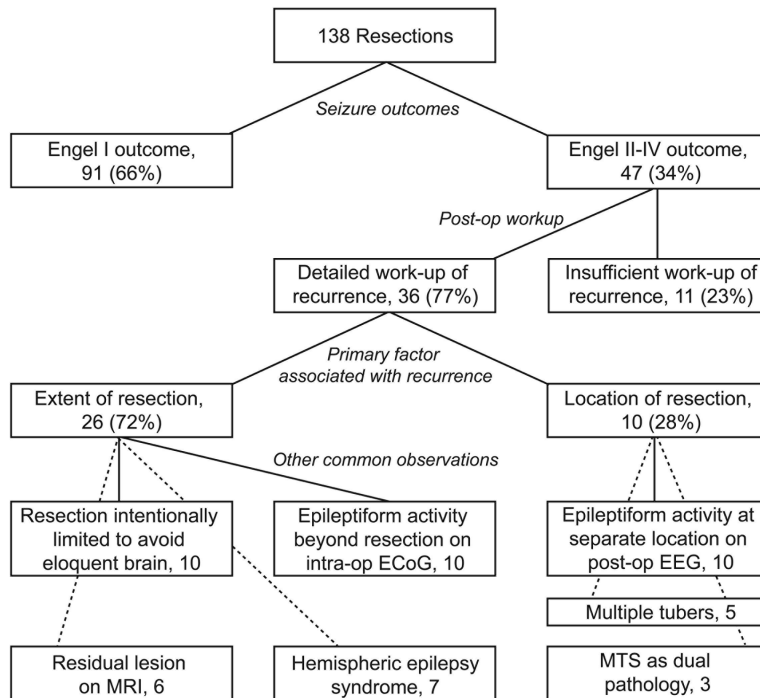
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**FIGURE 1.**

Predictors of Engel I seizure outcome from multivariate analysis. Shown are the results of multivariate logistic regression analysis of potential predictors of favorable (Engel I) seizure outcome, with data represented as odds ratio & 95% confidence interval. Among all variables examined (see Methods and Tables 1-5), only those with a value of  $P < .20$  on univariate analysis were included in the multivariate model. A higher preoperative seizure frequency, history of generalized tonic-clonic seizures (GTCS), and normal magnetic resonance imaging (MRI) were associated with a less favorable (Engel II-IV) seizure outcome. Seizure frequency was entered into the multi-variate model as a continuous variable, whereas history of GTCS and MRI findings are dichotomized categorical variables.

**FIGURE 2.**

Flow chart summarizing factors associated with seizure recurrence. Among 47 cases with less favorable (Engel II-IV) seizure outcome, 36 had sufficient postoperative diagnostic workup available for further qualitative analysis. Of these 36 resections, 26 cases of seizure recurrence (72%) were associated primarily with extent of resection, with evidence suggesting residual epileptogenic tissue adjacent to the resection cavity, and 10 cases (28%) were more closely associated with location of resection, with evidence of an additional epileptic focus distant from the resection. Within these 2 categories, other commonly observed factors potentially related to seizure recurrence are also listed, with >1 factor noted in some cases. ECoG, electrocorticography; EEG, electroencephalography; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis.

TABLE 1

Patient Characteristics<sup>a</sup>

Demographics	
Age, y	20.0 ± 1.2
Sex, n (%)	
<i>Male</i>	71 (57)
<i>Female</i>	54 (43)
Handedness, n (%)	
<i>Right</i>	67 (64)
<i>Left</i>	16 (15)
<i>Ambidextrous</i>	4 (4)
<i>Not yet lateralized/unknown</i>	18 (17)
Epilepsy characteristics	
Duration epilepsy, y	10.7 ± 0.9
Daily seizure frequency, n (%)	
<i>No</i>	3.3 ± 0.5
Antiepileptic drug regimens trialed, n (%)	
<i>No</i>	5.0 ± 0.3
History of generalized seizures, n (%)	
<i>Yes</i>	68 (54)
<i>No</i>	57 (46)
Epilepsy risk factors, n (%)	
0	54 (43)
1	45 (36)
2	26 (21)
Focal neurological deficit, n (%)	
<i>No</i>	99 (79)
<i>Yes</i>	26 (21)
Previous epilepsy resection, n (%)	
<i>Yes</i>	110 (88)
<i>No</i>	15 (12)
Preoperative diagnostics, n (%)	
MRI	
<i>Abnormal</i>	113 (90)
<i>Normal</i>	12 (10)
24-h EEG	
<i>Localized</i>	63 (50)
<i>Lateralized</i>	34 (27)
<i>Not lateralized</i>	20 (16)
<i>Not done</i>	8 (6)
MEG	
<i>Localized</i>	42 (34)

<i>Not localized</i>	17 (14)
<i>Not done</i>	66 (53)
PET	
<i>Abnormal</i>	22 (18)
<i>Normal</i>	8 (6)
<i>Not done</i>	95 (76)
Implanted extraoperative ECoG	
<i>Performed</i>	55 (44)
<i>Not performed</i>	70 (56)
Operative factors, n (%)	
Lobe of resection	
<i>Frontal</i>	57 (46)
<i>Lateral</i>	30 (24)
<i>Parietal</i>	10 (8)
<i>Occipital</i>	8 (6)
<i>Multiple</i>	20 (16)
Side of surgery	
<i>Right</i>	66 (53)
<i>Left</i>	59 (47)
Intraoperative ECoG	
<i>Performed</i>	97 (78)
<i>Not performed</i>	28 (22)

<sup>a</sup>ECoG, electrocorticography; EEG, electroencephalography; MEG, magnetoencephalography; MRI, magnetic resonance imaging; PET, positron emission tomography. Data are n (%) for categorical variables or mean  $\pm$  SEM for continuous variables for 125 patients who underwent 138 surgeries.



**TABLE 2**

Seizure Outcomes: Final Outcomes by Patient

<b>Final Outcomes by Patient (n = 125)</b>	<b>n (%)</b>
Engel I	90 (72)
Engel IA	65 (52)
Engel IB-ID	25 (20)
Engel II	8 (6)
Engel III	14 (11)
Engel IV	13 (10)

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**TABLE 3**

Seizure Outcomes: Overall Outcomes by Surgery

<b>Overall Outcomes by Surgery (n = 138)</b>	<b>n (%)</b>
Engel I	91 (66)
Engel IA	65 (47)
Engel IB-ID	26 (19)
Engel II	9 (7)
Engel III	18 (13)
Engel IV	20 (14)

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**TABLE 4**

Seizure Outcomes: Outcomes by Age

Age (n = 125 Patients), y	Engel I, n (%)	Engel II-IV, n (%)
0-9.9	18 (60)	12 (40)
10-19.9	39 (83)	8 (17)
20-29.9	11 (61)	7 (39)
30-39.9	12 (75)	4 (25)
40-49.9	8 (67)	4 (33)
50-59.9	1 (100)	0 (0)
60-69.9	1 (100)	0 (0)

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**TABLE 5**

Seizure Outcomes: Outcomes by Pathology

<b>Pathology (n = 125 Patients)</b>	<b>Engel I, n (%)</b>	<b>Engel II-IV, n (%)</b>
Malformation of cortical development	29 (71)	12 (29)
Gliosis only	19 (61)	12 (39)
Tumor	23 (82)	5 (18)
Vascular malformation	6 (100)	0 (0)
Tuber (tuberous sclerosis complex)	3 (43)	4 (57)
Ischemia/hypoxia	4 (100)	0 (0)
Infection	3 (75)	1 (25)
Normal brain	2 (100)	0 (0)
Cyst	1 (50)	1 (50)

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