Published in final edited form as:

J Clin Neurophysiol. 2014 June ; 31(3): 199–202. doi:10.1097/WNP.0000000000000047.

Diagnostic Outcome of Surgical Revision of Intracranial Electrode Placements for Seizure Localization

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Abstract

Purpose—We aimed to determine the yield of revising intracranially implanted electrodes and the factors contributing to the yield.

Methods—Patients were identified from the Mayo Clinic Epilepsy Surgery Database between 1997 and 2010. Twenty patients had revision of intracranial electrode placements because initial implantation did not localize seizure onset adequately.

Results—Seizures were captured in 18 of 20 patients who underwent intracranial electrode revision, of which 10 (55.6%) showed localized seizure onset that led to a surgical resection. Seizures were improved in 9 of 10 patients who underwent resection; of these, 5 were seizure free. The only factors found to be statistically significant in localizing ictal onset zone after revised implantation were prior focal scalp interictal discharges and an initial intracranial EEG showing ictal onset at the edge of the electrode grid. No permanent complication was associated with revised implantation, but 1 patient had transient apraxia of the right foot.

Conclusion—Revised implantation could be useful in selected patients with inadequate seizure localization on initial intracranial EEG. Resective surgery was performed in 50% of patients who underwent revision of intracranial electrodes, with the majority of these patients experiencing an improvement in seizure control.

Keywords

epilepsy surgery; intracranial EEG monitoring; seizure

Introduction

Despite optimal medical therapy, up to a third of persons with epilepsy continue to have recurrent seizures (Sander et al, 1990; Schuele and Luders, 2008). If a focal ictal onset zone

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Presented at the annual meeting of the American Epilepsy Society, San Diego, California, November 30–December 4, 2012.

Conflict of interest: None.

Funding disclosure: None.

can be accurately localized and safely removed, epilepsy surgery can be an effective therapeutic option. On the basis of noninvasive studies, intracranial EEG (iEEG) recording is indicated to improve seizure localization in patients with discordant or indeterminate seizure localization (Rosenow and Luders, 2001). However, iEEG is expensive and labor intensive. In addition, investigators have reported that iEEG is associated with risk of transient and permanent neurologic deficits, infections, hematoma, non-habitual seizures, cerebral infarction, cerebral edema, and increased intracranial pressure (Fountas et al, 2004; Hamer et al, 2002; Van Gompel et al, 2008; Wong et al, 2009). Because increased complication rates are related to longer monitoring with a greater number of electrodes (Hamer et al, 2002), the extent of iEEG should be determined judiciously and limited to reduce the risk of complications.

Although iEEG implantation is guided by thorough presurgical evaluations, situations still occur in which iEEG is not able to localize the ictal onset zone. Studies have shown that between 30% and 40% of iEEGs do not produce adequate localizing information of seizure origin (Pondal-Sordo et al, 2007; Schiller et al, 1998; Van Gompel et al, 2008; Wetjen et al, 2009). Therefore, repeat surgery is sometimes required to revise the intracranial electrode placement for better source localization. Given the increased risk of repeat brain surgery, we believe it is important to identify the diagnostic outcome of revising intracranially implanted electrodes, as well as the determining factors that contribute to diagnostic yield of the revision.

Methods

Patient Population

Patients were identified retrospectively from the Mayo Clinic Epilepsy Surgery Database between 1997 and 2010. Twenty patients had revision of intracranial electrode placements during a single inpatient evaluation because the initial implantation did not localize the seizure onset adequately. Adult and pediatric patients were included in the study population.

Presurgical Evaluations

All patients had comprehensive presurgical evaluations, including history and neurologic evaluation, outpatient awake and asleep EEG, epilepsy protocol magnetic resonance imaging (MRI), and inpatient video-EEG monitoring. Single-photon emission computed tomography (SPECT) was performed in 15 patients through subtraction ictal SPECT coregistered to MRI (SISCOM), as described previously (O'Brien et al, 1998a; O'Brien et al, 1998b; O'Brien et al, 2000). Positron emission tomography was performed in 6 patients. All patients were reviewed at our multidisciplinary epilepsy surgery conference, where the decision for intracranial electrode implantation and the number and location of electrode placements were determined by group consensus.

Intracranial EEG Data Collection and Analysis

Continuous iEEG was recorded with EEG software (XLTEK; Natus Medical Inc). Bipolar and referential electrode montages were used to review the EEG recordings. A digital 60-Hz

notch filter was used when necessary to eliminate line noise. Seizure onset was determined by visual analysis of the EEG tracings.

Statistical Analysis

Data entry and statistical analysis were performed using statistics software (IBM SPSS Statistics 19; IBM Corp). Two-sided Fisher exact test was used in the analysis of categorical data. *P* values less than .05 were considered statistically significant.

Results

Demographic Characteristic

Between 1997 and 2010, 336 patients underwent intracranial EEG monitoring in our center. Twenty patients (6%) had revision of their intracranially placed electrodes during the same hospitalization because the initial implantation did not produce adequately localizing information. At presurgical evaluation (Table 1), the median (interquartile range) number of seizures of the patients was 9 (2, 42.5) seizures per month. The median (interquartile range) number of antiepileptic medications that had been tried was 5.5 (4, 7). Two patients had a history of right anterior temporal lobectomy; 1 patient, vagus nerve stimulation (VNS); and 1 patient, both VNS implantation and a history of right anterior temporal lobectomy.

Presurgical Evaluations

Seventeen of the 20 patients had seizures with lateralizing clinical semiology (Table 1). Focal interictal discharges were present in prior scalp EEG recordings in 6 patients. The rest had either generalized (n=1), multifocal (n=5), generalized plus multifocal (n=2), or no interictal (n=6) epileptiform abnormalities. Twelve patients had prior focal scalp ictal EEG onset. The other 8 patients had nonlateralizing scalp ictal EEG onset, and the result from imaging studies were used to guide the implantation of intracranial electrodes. MRI showed focal lesions in 9 of the 20 patients, and 12 of 15 patients had localizing SISCOM findings. The majority of patients (85%) were considered to have extratemporal lobe epilepsy based on the epilepsy surgery conference consensus after reviewing all presurgical data.

iEEG Recording

The median (interquartile range) number of seizures recorded before the decision to revise the intracranial electrodes was 5.5 seizures (4.5, 11.5). During the first iEEG recording, a median (interquartile range) of 5 (4, 7) subdural grids, strips, and depth electrodes and 76 (64, 91) of electrode contacts were placed. A combination of intracranial grid and strip electrodes were used in 15 patients, whereas the remaining 5 patients had additional depth electrodes implanted for seizure localization. No complication was associated with the first implantation. For 9 patients, iEEG showed ictal onset zone at the border of coverage (Table 2); the other iEEGs showed late or diffuse ictal EEG discharges. EEG discharge was considered late when clinical seizure was already in progress before ictal EEG onset.

In 7 of 11 patients with iEEG showing late or diffuse ictal onset, reimplantation was guided through SISCOM, MRI, or semiology findings. In 4 patients, the initial implantation did not cover the SISCOM abnormality adequately (Nos. 2, 5, 6, and 19). Three patients had

bilateral seizure onset on iEEG. However, 2 of these 3 patients had lateralizing or localizing seizure semiology (Nos. 12 and 15). The final patient (No. 16) had focal lesion on MRI.

The patients were monitored for a median of 4 days (interquartile range, 3–6 days) after revision of intracranial electrodes. The revised iEEG consisted of a median (interquartile range) of 7 (3.5, 8.5) subdural grids, strips, and depth electrodes and 82 (52, 119) electrode contacts. A combination of intracranial grid and strip electrodes was used in 16 patients, whereas the remaining 4 patients had additional depth electrodes implanted for seizure localization. In 15 of 20 patients, the revision involved repositioning of intracranially placed electrodes. The remaining 5 patients had a median of 16 additional electrode contacts (interquartile range, 12–24) implanted for seizure localization. One patient had transient right foot apraxia after revision of intracranial implantation. Two patients did not have further seizure after the revision of electrode placements (Table 3). Revised implantation and recording localized the seizure onset in 10 (55.6%) of the other 18 patients. Statistically significant factors in localizing an ictal onset zone after implantation revision were prior focal scalp interictal discharges (100% in focal vs 38.5% in nonfocal; $P=.04$) and initial iEEG showing ictal onset at the edge of the electrode grid (100% in ictal onset at the edge of the electrode grid vs 20% in late indeterminate ictal EEG onset; $P=.001$). The rate of localizing the ictal onset zone after revising iEEG implantation was 100% (3/3) when both predictive factors were present vs 0% (0/8) when neither factor was present ($P=.006$). Factors that did not reach statistical significance were prior focal scalp ictal EEG onset (80% in focal vs 25% in nonfocal; $P=.054$) and lateralizing seizure semiology (66.7% in lateralizing vs 0% in nonlateralizing semiology; $P=.07$). Findings on SISCOM (localizing vs nonlocalizing) and MRI head (normal vs abnormal) did not show an association with the yield of the revised implantation. Because of the small sample size, positron emission tomographic findings were not analyzable as prognostic factors.

Outcome of Resective Epilepsy Surgery

Twelve patients underwent resective surgery. Two patients did not have localizing iEEG on revised implantation, and their resections were guided by SISCOM or MRI findings. One of these 2 patients continued to have seizures after surgery, whereas the other did not return for further follow-up (Table 3). The other 10 patients all had localizing seizure focus on the revised iEEG recording. Five of these 10 patients were free of seizure during follow-up (follow-up duration, 1 month–4 years). The other 5 patients continued to have seizures after resective surgery; however, the seizures were less frequent and less intense (Engel class III postoperative outcome) in 4 patients (Nos. 6, 9, 13, and 17). Patients Nos. 6 and 17 each had 2 seizure types identified on revised iEEG; both underwent palliative surgery to remove the predominant seizure focus. Patient No. 13 did not have complete resection of seizure focus due to the overlap with eloquent cortex. The final patient (No. 11) had no improvement of seizure control after surgery. This patient later had a VNS implanted.

Discussion

Because of the potential morbidities associated with iEEG, the extent of iEEG coverage has to be determined judiciously to reduce the risk of complications. This determination creates

a fundamental problem of potential sampling error in iEEG. Schiller et al (Schiller et al, 1998) postulated that recurrence of seizures after epilepsy surgery may be from either incorrect localization of the epileptogenic zone or erroneous determination of its boundaries. They also suggested that extending the coverage by implanting additional electrodes may improve outcome.

Data have been limited on the yield of revising intracranially placed electrodes. Siegel et al (Siegel et al, 2000) reported a case series that evaluated the role of reimplanting intracranial electrodes after a failed initial iEEG recording. Seven (77.7%) of their 9 patients had adequate seizure localization during repeat evaluation, and 5 (83.3%) of 6 patients became seizure free after resective surgery. The higher yield of their iEEG reevaluation than ours may be due to the following reasons. First, their patients had further noninvasive tests after the first intracranial recordings failed to detect the ictal onset zone. The repeat intracranial electrode implantation was performed during hospitalization that was separate from the first implantation. The repeat implantation was further guided by results of the additional noninvasive tests that were performed. In contrast, the revision of original implantation in our study was conducted during a single hospitalization, with the revision based on the results of the initial intracranial recordings and the presurgical data available. Second, prior surgeries and VNS treatments had failed in 4 of our patients.

Lee et al (Lee et al, 2004) reported their experience of revising intracranial electrodes during a single hospitalization. In their study, 11 of 18 patients (61%) were found to have a new focal ictal onset zone after revision of intracranial electrodes, which is similar to our rate of 56%. However, our study is the first to identify predictive factors for seizure localization after revising the implantation. We found that EEG seizure onset at the edge of subdural grid coverage was a positive prognostic factor. This finding is not surprising because the purpose of reimplantation in these patients was to further delineate the boundary of the seizure focus. If the initial iEEG had showed diffuse or late-onset ictal discharge, the discharge possibly had corresponded to propagated seizure activity instead of seizure-onset activity—in which case the epileptogenic zone could be deeper or distant from the discharge location. This possibility could explain the low yield of reimplantation in 20% in these patients with initially indeterminate iEEG recording. Information from seizure semiology and MRI and SISCOM scans were used to guide the reimplantation in these patients. However, none of the noninvasive measures (lateralizing semiology, 0/2; focal MRI lesion, 0/1; and localizing SISCOM abnormality, 2/4) were particularly helpful. In contrast, a noninvasive measure that is significantly associated with high yield of revised iEEG implantation is the presence of scalp interictal discharges before the first implantation. Surprisingly, presence of prior focal scalp ictal discharges did not reach statistical significance, but this result may be due to the relatively small sample of patients in our study.

We have previously reported in 2 studies that the overall rates of iEEG in localizing the ictal onset zone were 61% and 79% (Van Gompel et al, 2008; Wetjen et al, 2009). From this perspective, the modest seizure-localizing rate of 56% after revising iEEG implantation in the current study is understandable. Moreover, the use of predictive factors identified in our current study may further increase the yield. The rate of localizing the ictal onset zone after revising the iEEG implantation is 100% when both predictive factors are present (ie, prior

focal scalp interictal discharges and ictal onset at the edge of prior implantation) and 0% when neither factor is present.

Patients should be carefully selected before proceeding with a revision of implanted electrodes. Hamer and colleagues (Hamer et al, 2002) reported that the risk of complications increases with longer duration of monitoring and greater number of electrodes. In our study, 1 patient had transient right foot apraxia after revision of intracranial implantation. Our complication rate of 5% for revision of iEEG implantation is comparable to the overall rates of 3% to 27% reported in previous series of mostly first-time intracranial electrode implantations (Schiller et al, 1998; Hamer et al, 2002; Van Gompel et al, 2008; Wong et al, 2009) and also 0% in patients with repeat implantation (Lee et al, 2004).

Our study showed that 90% of our patients had either complete or incomplete but improved seizure control from resective surgery performed following revised iEEG recording, with 50% being seizure free. Of the 4 seizure patients who had incomplete postsurgical seizure control, resective surgery was palliative in nature in 2 patients who had multifocal seizures and in 1 patient whose ictal onset zone was not completely resected because of overlap with functioning cortex. Widdess-Walsh et al (Widdess-Walsh et al, 2007) demonstrated that an ictal spread pattern from the edge of the subdural grids was an independent predictor of seizure recurrence. Our study showed that reimplantation of intracranial electrodes can lead to seizure freedom in 50% of these patients. These findings further confirm that the extent of resection of the ictal onset zone is a major determinant of outcome of epilepsy surgery following iEEG recording (Kim et al, 2010).

In summary, among patients with inadequate localization of seizure focus on initial iEEG recording, revised implantation could be useful in selected patients. In addition, revision of intracranial implantation is not associated with increased complication rate. Patients who are good candidates for revision of iEEG are those whose prior scalp EEG had showed focal interictal discharges and those whose initial iEEG had shown ictal onset at the edge of the implantation.

Abbreviations

iEEG	intracranial EEG
MRI	magnetic resonance imaging
SISCOM	subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging
SPECT	single-photon emission computed tomography
VNS	vagus nerve stimulation

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Table 1

Demographic and Presurgical Evaluation Data of 20 Patients Who Had Revision of Intracranially Placed Electrodes

Characteristics	Values ^a
Age, median (interquartile range), y	23 (17.25, 31.75)
Pediatric patients ^b	5 (25)
Sex, M/F	10/10
Age at seizure onset, median (interquartile range), y	11.5 (5.5, 15)
AEDs tried, median (interquartile range), No.	5.5 (4, 7)
Monthly seizure frequency, median (interquartile range), No.	9 (2, 42.5)
Lateralizing seizure semiology	17 (85)
Discharges in scalp interictal EEG findings	
Focal	6 (30)
Multifocal	5 (25)
Generalized	1 (5)
Generalized and multifocal	2 (10)
None	6 (30)
Discharges in scalp ictal EEG findings	
Focal	12 (60)
Bilateral	3 (15)
Indeterminate	3 (15)
None	2 (10)
MRI with focal lesion	9 (45)
SISCOM with focal findings (n=15)	12 (80)
PET with focal hypometabolism (n=6)	4 (67)

Abbreviations: AED, antiepileptic drug; F, female; M, male; MRI, magnetic resonance imaging; PET, positron emission tomography; SISCOM, subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging.

^aValues are presented as number and percentages unless stated otherwise.

^bAge <18 years.

Table 2

Predictive Factors of Localizing the Ictal-Onset Zone on Revised Implantation of Intracranial Electrodes

Predictive Factor	Ictal Onset Zone (Ratio; %)		P Value
Semiology	Lateralizing (10/15; 66.7)	Nonlateralizing (0/3; 0)	.07
Head MRI	Abnormal (4/8; 50)	Normal (6/10; 60)	.52
SISCOM	Localizing (6/12; 50)	Nonlocalizing (2/3; 66.7)	.43
Scalp interictal EEG discharges	Focal (5/5; 100)	Nonfocal (5/13; 38.5)	.04 ^a
Scalp ictal EEG discharges	Focal (8/10; 80)	Nonfocal (2/8; 25)	.054
Initial iEEG ictal discharges	Edge of grid (8/8; 100)	Late indeterminate (2/10; 20)	.001 ^a

Abbreviations iEEG, intracranial EEG; MRI, magnetic resonance imaging; SISCOM, subtraction ictal single-photon emission computed tomography coregistered to magnetic resonance imaging.

^aStatistically significant.

Table 3

Individual Result of iEEG Recordings and Surgical Outcome

Patient No.	iEEG No. 1, Seizure Onset	iEEG No. 2, Localizing Seizure Onset	Resection	Outcome After Resection of Seizure Focus (Duration of Follow-up) ^a
1	Late EEG onset ^b	No	Right frontal ^c	No further follow-up
2	Late EEG onset	No ^d	No	N/A
3	Onset at edge of grid	No seizure recorded	No	N/A
4	Diffuse EEG onset	No seizure recorded	No	N/A
5	Diffuse EEG onset	No ^d	Right parietal ^e	IV (1 y)
6	Diffuse EEG onset	1st seizure-type, yes ^d ; 2nd type, no ^f	Right temporal	III (4 y)
7	Onset at edge of grid	Yes	Right temporal	I (4 y)
8	Onset at edge of grid	Yes	Right parietal	I (4 y)
9	Onset at edge of grid	Yes	Left frontal	III (2 y)
10	Onset at edge of grid	Yes	Left parietal	I (1.5 y)
11	Onset at edge of grid	Yes	Left frontal	IV (2 y)
12	Diffuse EEG onset	No ^g	No	N/A
13	Onset at edge of grid	Yes	Left frontal ^h	III (1 y)
14	Onset at edge of grid	Yes	Right frontal	I (4 y)
15	Diffuse EEG onset	No ^g	No	N/A
16	Diffuse EEG onset	No ⁱ	No	N/A
17	Onset at edge of grid	1st seizure type, yes; 2nd seizure type, no ^f	Right temporal	III (6 y)
18	Diffuse EEG onset	No	No	N/A
19	Late EEG onset	Yes ^d	Right frontal	I (6 mo)
20	Diffuse EEG onset	No	No	N/A

Abbreviations: iEEG, intracranial EEG; N/A, not applicable.

^aEngel class postoperative outcome.^bClinical seizure in progress before EEG seizure onset.^cResection guided by SISCOM finding.^diEEG No. 2 implantation guided by SISCOM findings.^eResection guided by SISCOM and MRI findings.^fiEEG No. 2 recorded 2 seizure types; No. 1, predominant right temporal ictal onset; No. 2, rare diffuse ictal onset.^giEEG No. 2 implantation guided by semiology findings.^hIncomplete seizure focus resection due to overlapping with eloquent cortex.ⁱiEEG No. 2 implantation guided by MRI findings.