The Value of Diagnostic Bilateral Intracranial Electroencephalography in Treatment-Resistant Focal Epilepsy

Travis C. Hill[1], Benjamin A. Rubin[1], Vineet Tyagi[2], Jason Theobald[2], Alyson Silverberg[1], Mary Miceli[1], Patricia Dugan[1], Chad Carlson[3], Werner K. Doyle[1]

■ OBJECTIVES: **We assessed the efficacy and risks of diagnostic bilateral intracranial electroencephalography (bICEEG) in patients with treatment-resistant epilepsy (TRE) with poorly lateralized epileptogenic zone on noninvasive studies as reflected by progress to resection, Engel outcome, and complication rate.**

■ METHODS: **This is a retrospective chart review of 199 patients with TRE who had diagnostic bICEEG at New York University Medical Center between 1994 and 2013. Study end points were progress to resection, surgical outcome, and perioperative complications. Univariate analysis was performed with analysis of variance, *t* test, or Fisher exact test; multivariable analysis was performed using discriminant function analysis.**

■ RESULTS: **bICEEG lateralized the epileptogenic zone and the patient had resection in 60.3% of cases. The number of depth electrodes used was positively correlated with resection, and surgical complications during bICEEG negatively correlated. Vagal nerve stimulators were implanted in 58.2% of patients who did not undergo resection and 20.7% of those who did. Among the 87 patients who progressed to resection and had more than 1-year follow-up, 47.1% were seizure free compared with 12.7% of the 55 who did not. Male sex correlated with good postoperative seizure control. The most common complication was infection requiring debridement, occurring in 3.1% of admissions (9 of 290).**

■ CONCLUSIONS: **At our center, 60% of patients undergoing bICEEG progress to resection and 57% of these had more than 90% reduction in seizures. We conclude that bICEEG allows the benefits of epilepsy surgery to be extended to patients with poorly lateralized and localized TRE.**

INTRODUCTION

An estimated 10%–30% of patients with epilepsy fail to respond to antiepileptic drugs.[1-3] These patients are at increased risk for adverse seizure-related events, cumulative risk of neurologic damage from ongoing seizures, and account for most epilepsy-related health care costs.[4] If the epileptogenic zone (EZ) can be localized, the patient may be a candidate for potentially curative epilepsy surgery. Although seizure control after surgery is affected by the location of the EZ, association with a structural lesion, and the underlying pathology, seizure freedom is attained in 34%–74% of patients.[5] Complete control is rarely seen in medically managed treatment-resistant epilepsy (TRE), yet it remains a realistic goal of surgery if surgery can be offered.[6,7] Because of the potential for rendering patients seizure free, low operative risk, and increasing disability associated with TRE, many opine that epilepsy surgery remains an underused therapy.[8,9]

Presurgical evaluation consists of a thorough medical and neurologic examination, review of seizure semiology, neuropsychological evaluation, interictal and ictal video electroencephalography (vEEG),

Key words
- Epilepsy surgery
- Intracranial EEG
- Treatment-resistant epilepsy
- Vagus nerve stimulation

Abbreviations and Acronyms
bICEEG: Bilateral intracranial electroencephalography
EZ: Epileptogenic zone
MDC: Multidisciplinary conference
MRI: Magnetic resonance imaging
TRE: Treatment-resistant epilepsy
vEEG: Video electroencephalography
VNS: Vagal nerve stimulator

From the [1]Department of Neurosurgery, New York University School of Medicine, New York, New York; [2]New York University School of Medicine, New York, New York; [3]Department of Neurology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

To whom correspondence should be addressed: Werner K. Doyle, M.D. [E-mail: wkd1@nyu.edu]

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and structural magnetic resonance imaging (MRI). If these studies adequately localize the EZ, the patient can undergo resection. When noninvasive studies yield discordant or ambiguous data, more extensive workup may be required. These additional studies may include positron emission tomography, ictal single-photon emission computed tomography, ^{1}H magnetic resonance spectroscopy, magnetoencephalography, functional MRI, intracarotid amobarbital, or Wada test.

At our center, we have extensive experience with the use of diagnostic bilateral intracranial electroencephalography (bICEEG) to lateralize the EZ in patients when data from noninvasive studies failed to identify a surgical target. The decision to pursue bICEEG depends on careful consideration of the risks of an invasive diagnostic procedure against the potential benefit of EZ resection. We report the experience with bICEEG at a single institution by a single neurosurgeon from 1994 to 2012, with particular focus on progression to resection, seizure outcomes, and surgical complications.

METHODS

Study Design and Patient Selection

After obtaining institutional review board approval, we reviewed the charts of all patients with focal TRE who underwent bICEEG under the care of a single surgeon (W.K.D.) between 1994 and 2012. We did not exclude patients for any reason (e.g., previous epilepsy surgery, lesional/nonlesional, specific semiology), but all patients were prescreened at a multidisciplinary conference (MDC). Investigators not involved with patient care reviewed operative reports and clinical records. Data collection was managed with REDCap electronic data capture tools.[10] A total of 199 patients were identified and included in analysis, 142 of whom had more than 1 year of follow-up.

Multidisciplinary Conference and Indications for bICEEG

All patients with TRE who were considered for epilepsy surgery were referred from the New York University Comprehensive Epilepsy Center after team consensus evaluation at the MDC. The MDC comprised representatives from the neurology (epileptology), neuropsychology, neuroradiology, and neurosurgery teams. The group evaluated all relevant clinical data for evidence of localization and lateralization, and a consensus recommendation was made. For patients with poorly lateralized data, the group may recommend to proceed with bICEEG, undergo further noninvasive evaluation, pursue palliative procedures (vagal nerve stimulator [VNS] or corpus callosotomy), or continue with medical management. Our study population consisted of patients recommended for bICEEG by the MDC because of nonuniformly lateralized data but who were believed to be likely candidates for curative resection if the EZ could be localized.

Table 1. Subject Demographics Before Bilateral Intracranial Electroencephalography

	>1 Year Follow-Up	Follow-Up <1 Year	Overall
Number of patients	142	57	199
Age at last surgery (years)	30.0 (4.7—55.3)	28.2 (10.2—47.1)	29.5 (4.7—55.3)
Age of onset (years)	11.6 (0.0—46.0)	9.0 (0.0—31.0)	11.6 (0.0—46.0)
Duration of disease (years)	18.8 (0.8—50.1)	19.2 (—2.4 to 40.4)	18.8 (0.8—50.1)
Follow-up interval (years)	7.1 (1.0—19.2)	0.3 (0.0—6.0)	5.1 (0.0—19.2)
Sex			
Male	74 (52.11)	25 (43.86)	99 (49.75)
Female	68 (47.89)	32 (56.14)	100 (50.25)
Handedness			
Right-handed	117 (82.39)	45 (78.95)	162 (81.41)
Left-handed	19 (13.38)	10 (17.54)	29 (14.57)
Other	6 (4.23)	2 (3.51)	8 (4.02)
Baseline seizure frequency			
Unable to assess	4 (2.82)	2 (3.51)	6 (3.02)
1—6 per year	2 (1.41)	0 (0.00)	2 (1.01)
7—11 per year	0 (0.00)	1 (1.75)	1 (0.50)
1—3 per month	21 (14.79)	11 (19.30)	32 (16.08)
1—6 per week	79 (55.63)	29 (50.88)	108 (54.27)
1—2 per day	13 (9.15)	7 (12.28)	20 (10.05)
>2 per day	23 (16.20)	7 (12.28)	30 (15.08)
Vagal nerve stimulator implant before surgery			
Yes	22 (15.49)	10 (17.54)	32 (16.08)
No	120 (84.51)	47 (82.46)	167 (83.92)
Outcome category			
No further surgery or resection	50 (35.2)	23 (40.35)	73 (36.7)
Surgery but no resection	5 (3.5)	1 (1.75)	6 (3.0)
Surgery with resection	87 (61.3)	33 (57.89)	120 (60.3)

Values are number or mean (% or range).

Preoperative Diagnostic Workup

All patients evaluated for bICEEG underwent a detailed medical interview and physical examination, vEEG, structural neuroimaging (MRI), and neuropsychological testing before MDC presentation. Additional studies, ordered for some patients based on the recommendations of either the MDC or the primary epileptologist, included positron emission tomography, single-photon emission computed tomography, Wada test, and magnetoencephalography.

Surgical Procedure

All bICEEG implantation/explantation procedures were performed under general anesthesia with frameless stereotactic guidance. Surgical details varied with the specific plan for each patient and are