

# Analysis of Morbidity and Outcomes Associated With Use of Subdural Grids vs Stereoelectroencephalography in Patients With Intractable Epilepsy

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**IMPORTANCE** A major change has occurred in the evaluation of epilepsy with the availability of robotic stereoelectroencephalography (SEEG) for seizure localization. However, the comparative morbidity and outcomes of this minimally invasive procedure relative to traditional subdural electrode (SDE) implantation are unknown.

**OBJECTIVE** To perform a comparative analysis of the relative efficacy, procedural morbidity, and epilepsy outcomes consequent to SEEG and SDE in similar patient populations and performed by a single surgeon at 1 center.

**DESIGN, SETTING, AND PARTICIPANTS** Overall, 239 patients with medically intractable epilepsy underwent 260 consecutive intracranial electroencephalographic procedures to localize their epilepsy. Procedures were performed from November 1, 2004, through June 30, 2017, and data were analyzed in June 2017 and August 2018.

**INTERVENTIONS** Implantation of SDE using standard techniques vs SEEG using a stereotactic robot, followed by resection or laser ablation of the seizure focus.

**MAIN OUTCOMES AND MEASURES** Length of surgical procedure, surgical complications, opiate use, and seizure outcomes using the Engel Epilepsy Surgery Outcome Scale.

**RESULTS** Of the 260 cases included in the study (54.6% female; mean [SD] age at evaluation, 30.3 [13.1] years), the SEEG (n = 121) and SDE (n = 139) groups were similar in age (mean [SD], 30.1 [12.2] vs 30.6 [13.8] years), sex (47.1% vs 43.9% male), numbers of failed anticonvulsants (mean [SD], 5.7 [2.5] vs 5.6 [2.5]), and duration of epilepsy (mean [SD], 16.4 [12.0] vs 17.2 [12.1] years). A much greater proportion of SDE vs SEEG cases were lesional (99 [71.2%] vs 53 [43.8%];  $P < .001$ ). Seven symptomatic hemorrhagic sequelae (1 with permanent neurological deficit) and 3 infections occurred in the SDE cohort with no clinically relevant complications in the SEEG cohort, a marked difference in complication rates ( $P = .003$ ). A greater proportion of SDE cases resulted in resection or ablation compared with SEEG cases (127 [91.4%] vs 90 [74.4%];  $P < .001$ ). Favorable epilepsy outcomes (Engel class I [free of disabling seizures] or II [rare disabling seizures]) were observed in 57 of 75 SEEG cases (76.0%) and 59 of 108 SDE cases (54.6%;  $P = .003$ ) amongst patients undergoing resection or ablation, at 1 year. An analysis of only nonlesional cases revealed good outcomes in 27 of 39 cases (69.2%) vs 9 of 26 cases (34.6%) at 12 months in SEEG and SDE cohorts, respectively ( $P = .006$ ). When considering all patients undergoing evaluation, not just those undergoing definitive procedures, favorable outcomes (Engel class I or II) for SEEG compared with SDE were similar (57 of 121 [47.1%] vs 59 of 139 [42.4%] at 1 year;  $P = .45$ ).

**CONCLUSIONS AND RELEVANCE** This direct comparison of large matched cohorts undergoing SEEG and SDE implantation reveals distinctly better procedural morbidity favoring SEEG. These modalities intrinsically evaluate somewhat different populations, with SEEG being more versatile and applicable to a range of scenarios, including nonlesional and bilateral cases, than SDE. The significantly favorable adverse effect profile of SEEG should factor into decision making when patients with pharmacoresistant epilepsy are considered for intracranial evaluations.

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 Author Audio Interview

 Supplemental content

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Patients with pharmacoresistant epilepsy constitute approximately one-third of the population with epilepsy. This population has a high incidence of accidental injuries, status epilepticus, and sudden unexpected death.<sup>1</sup> Three randomized prospective trials<sup>2-4</sup> have shown that epilepsy surgery is of great benefit in pharmacoresistant epilepsy, but epilepsy surgery continues to be underused. Although the reasons are multifactorial, an important factor is the perceived risk of surgical procedures, particularly in nonlesional cases or those that need intracranial evaluations to clarify the role of a lesion in a patient's epilepsy. Overall, intracranial electroencephalographic (EEG) recordings are necessary to localize the epileptogenic zone<sup>5-7</sup> in 30% to 50% of candidates for epilepsy surgery.<sup>8,9</sup>

Subdural electrode (SDE) implantation via a craniotomy has been the principal approach for intracranial EEG recordings in North America, the United Kingdom, and Germany.<sup>10-17</sup> In contrast, the French,<sup>16,18-20</sup> Italian,<sup>16,21-24</sup> and Brazilian<sup>25</sup> approaches to the evaluation of epilepsy follow the Talairach stereoelectroencephalographic (SEEG) approach,<sup>26,27</sup> in which depth electrodes are inserted into the brain to desired targets without requiring a craniotomy.<sup>28-30</sup> SEEG is optimized to record electrical activity from deep brain structures and sulci and in cases where bilateral evaluations are necessary.<sup>31,32</sup> Both approaches have existed in parallel, relatively isolated from each other, for the better part of a half-century, until the recent advent of SEEG in North America,<sup>30,33-35</sup> a development driven principally by the availability of stereotactic robots with 3-dimensional (3D) navigational platforms.<sup>36,37</sup> Although SDE and SEEG techniques have specific relative advantages, in most patients needing intracranial EEG, either approach could be used, although bilateral SDE implantations are challenging.

Mounting evidence during the last few years<sup>28,33,38-43</sup> suggests that SEEG procedures are safer than SDE implantations. The reported rates of complications after SDE implantations range from 5% to 17% per procedure.<sup>44-57</sup> In comparison, the complication rate per SEEG procedure is less than 1%, as revealed in a large recent meta-analysis.<sup>33</sup> Given that intracranial monitoring is a diagnostic technique for determining candidacy for and the targets of resection, the morbidity of these procedures detracts from the larger goal of improving the quality of life of patients with medically intractable epilepsy<sup>48,49,58-61</sup> and contributes to the underuse of epilepsy surgery.<sup>62</sup>

The relatively abrupt transition from SDE to SEEG in select centers in North America allows for a comparative analysis of outcomes using these 2 distinct techniques. The surgical outcomes and procedural morbidity are ideally evaluated in the context of a relatively homogenous population and by the same team involved in the decision-making process regarding the candidacy and strategies for epilepsy surgery. At our center, we switched from performing chiefly SDE evaluations to SEEG in 2013. No appreciable change in the types of patients referred to us for evaluation and treatment of epilepsy has occurred. Therefore, although this study is retrospective, the populations being compared are similar and roughly equal in number, allowing for evaluations of the efficacy of SDE vs SEEG in localizing the epileptogenic focus vis-à-vis their adverse effect profiles.

## Key Points

**Question** Does stereoelectroencephalography change the landscape around the management of medically intractable epilepsy?

**Findings** This comparative analysis of 239 patients undergoing 260 consecutive intracranial evaluations of intractable epilepsy found that stereoelectroencephalography implantation took less time and was less painful and less morbid for patients compared with subdural electrode implantations. Despite being less likely to have lesions on magnetic resonance imaging, patients who had definitive procedures had better outcomes at 1 year if they underwent evaluation using stereoelectroencephalography (57 of 75 [76.0%]) compared with subdural grid electrode evaluation (59 of 108 [54.6%]).

**Meaning** Stereoelectroencephalography has distinctly better procedural morbidities and, in selected cases, may have better outcomes than subdural grid electrodes, features that should influence decision making and lower the barrier to candidacy for resection or ablation among patients with intractable epilepsy.

## Methods

All patients undergoing implantation of intracranial electrodes by a single neurosurgeon from November 1, 2004, through June 30, 2017, were included (ensuring at least 12 months of follow-up in each case). The patient history, video-EEG, imaging, and neuropsychological evaluation as reviewed at a multidisciplinary patient management conference drove surgical decision making in each case. Written informed consent for prospective data collection was obtained from all patients undergoing electrode implantation. All research data collection was performed after approval by the local committee on the protection of human subjects at the University of Texas Health Science Center at Houston.

We used the electronic medical record to compile demographics, age at epilepsy onset, number of anticonvulsant drugs failed, duration of epilepsy, type of implantation (SDE vs SEEG), duration of the surgical procedure, number of contacts implanted, blood products transfused during implantation, opiate requirements after surgery (a surrogate for pain and discomfort), duration of intracranial monitoring, definitive procedure performed (resection, neuromodulation, or ablation), complications, and postoperative seizure outcome. All patients underwent magnetic resonance imaging (MRI) at 3 T (213 [81.9%]) or 1.5 T (47 [18.1%]) with sequences specifically designed to optimize detection of epileptogenic foci. All preoperative MRI findings were evaluated by a board-certified neuroradiologist (E.R.F.) blinded to the procedure and outcomes. In all cases where focal abnormalities were identified in the surgical specimen by the neuropathologist, a secondary unblinded review was performed by the neuroradiologist to evaluate any subtle cortical abnormalities that might have been missed initially. A handful of cases were recharacterized as lesional based on this second look, but given the importance of imaging for outcome after epilepsy surgery, we believed it was important to categorize all cases in which imaging abnormalities

were detected at any point in time and therefore these were considered lesional.

Choices of implant type and locations for electrode placement were motivated in each case by the putative epileptogenic zone as implicated by noninvasive data. The SDE implantations were performed using standard techniques,<sup>63</sup> via a craniotomy to implant platinum iridium electrodes (PMT Corp) embedded in polymeric silicone sheets placed in the subdural space, coupled with dural expansion. SEEG implantations were performed in most cases (>95%) using a ROSA robot (Medtech) registered to each patient's head using stereotactic skull screws and guided by a computed tomographic angiogram coregistered to a high-resolution 3D-contrasted T1-weighted MRI scan.<sup>30,38,64,65</sup> We implanted 0.8-mm diameter electrodes (PMT Corp). The earliest patients in this series underwent SEEG implantation using a stereotactic arm (Vertek; Medtronic Neuronavigation) or a coordinate frame (Leksell; Elekta).

A major contributor to use of medical resources, in addition to length of hospital stay, is the duration of surgical time. Use of the operating room (OR) was computed as the total OR time ("wheels-in to wheels-out") and the time of the actual procedure (incision to closure time). All patients underwent a postoperative computed tomographic scan after electrode implantation to localize electrodes<sup>66</sup> and to detect hemorrhagic complications. Patients were monitored via 24-hour video-EEG in the epilepsy monitoring unit after implantation. The duration of monitoring depended on the time taken to obtain adequate ictal recordings to localize the epileptogenic zone or to conclude that localization was unlikely to be accomplished.

Doses of narcotics administered postoperatively were converted to oral morphine milligram equivalents (MME) using standardized conversion tables from the Centers for Disease Control and Prevention for oral opioids<sup>67</sup> and GlobalRxPh (<https://www.globalrph.com>) for intravenous opioids.<sup>68</sup> Postoperative seizure outcomes were assessed using the Engel Epilepsy Surgery Outcome Scale.<sup>43</sup> Unpaired *t* tests for numerical data and Pearson  $\chi^2$  tests for categorical data were used to evaluate distinctions between the 2 groups. An a priori level of .05 was used such that any result with 2-sided *P* < .05 was deemed statistically significant (eMethods in the Supplement). Unless otherwise indicated, data are expressed as mean (SD).

### Statistical Analysis

Statistical tests used included the Pearson  $\chi^2$  test, paired and unpaired *t* tests, Wilcoxon rank sum test, and log-rank test. An a priori level of significance of .05 was used throughout and hypothesis tests were 2-sided. MATLAB with the Statistics and Machine Learning Toolbox (version (version R2018b; MathWorks) was used to run these tests.

## Results

### Population

A total of 239 patients underwent 260 intracranial evaluations during a 150-month interval (260 cases; 118 male [45.4%]

and 142 female [54.6%]; mean age at evaluation, 30.3 [13.1] years). The SDE group included 139 SDE implantations in 136 patients (3 patients had 2 distinct SDE implantations in 2 hospital stays). Six of these 136 patients underwent additional SDE electrode placements during the same hospital stay, which was therefore attributed as a single evaluation. The mean age at surgery in the SDE cohort was 30.6 (13.8) years; 78 cases (56.1%) were female and 61 (43.9%) were male. Mean age at onset of epilepsy was 13.4 (11.9) years; mean epilepsy duration was 17.2 (12.1) years; and these patients had experienced preoperative failure of anticonvulsant therapy with a mean of 5.6 (2.5) anticonvulsants. Ninety-nine cases (71.2%) were lesional by MRI and 44 had hippocampal sclerosis of varying severity (International League Against Epilepsy types 1-3).<sup>69</sup>

The SEEG group included 121 cases in 116 patients (5 patients had 2 distinct SEEG implantations in 2 hospital stays). Six of the 116 patients underwent additional SEEG electrode placements performed during the same hospital stay and attributed to as a single hospital procedure. Mean age at surgery was 30.1 (12.2) years; 64 (52.9%) were female and 57 (47.1%) were male; mean age at epilepsy onset was 13.7 (11.6) years. The mean duration of epilepsy was 16.4 (12.0) years, and they had experienced preoperative failure of a mean of 5.7 (2.5) anticonvulsant drugs. Fifty-three cases (43.8%) were lesional, and 22 had hippocampal sclerosis of varying degrees of severity. Thus, the 2 cohorts were not significantly different in demographics or epilepsy severity (Table 1); however, a larger proportion of the SDE cases (71.2% vs 43.8%) were lesional (*P* < .001). This difference reflects the tendency to evaluate nonlesional cases more readily with SEEG than with SDE implantation and affects the likelihood of these patients undergoing resection.

### Distinctions in Utilization and Morbidity

By all measures, SEEG procedures took significantly less time (mean total OR time, 322.0 [75.7] minutes; mean actual surgery time, 121.3 [48.2] minutes) than SDE procedures (mean total OR time, 429.4 [68.1] minutes; mean actual surgery time, 308.2 [62.5] minutes; *P* < .001). The OR times for SDE and SEEG procedures trended to decrease over time (Figure 1), indicating greater surgical efficiency with experience. To account for this secular (long-term temporal) trend, we compared mean total OR times and implantation times for the last 50 SDE procedures (426.3 [67.4] and 302.1 [59.3] minutes, respectively) vs the last 50 SEEG procedures (297.7 [39.2] and 96.9 [20.3] minutes, respectively), and both were significantly shorter (*P* < .001). Even with these shorter surgical times, a greater number of electrode contacts were implanted in SEEG vs SDE cases (mean, 186.9 [38.6] vs 114.3 [30.9]; *P* < .001). The median number of SEEG probes implanted per patient was 15 (range, 9-20), and the median time for implantation of each SEEG electrode was 5.3 minutes (range, 2.1-23 minutes).

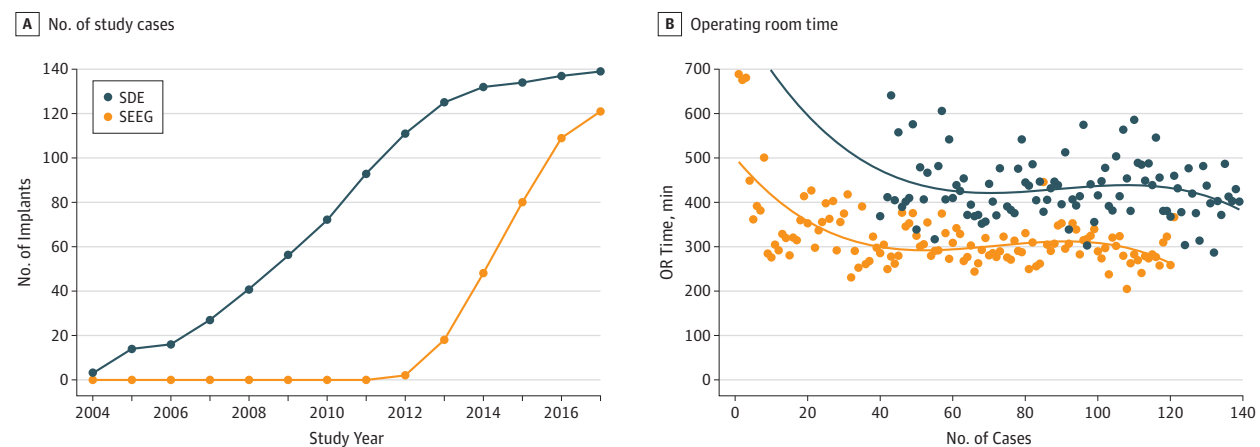
Blood transfusions were administered to correct acute anemia due to blood loss, coagulopathy, or both, intraoperatively or in the acute postoperative period. One SEEG procedure needed platelet transfusion (0.8%, due to a preexisting thrombocytopenia) in contrast to the 19 SDE procedures (13.7%) requiring intraoperative transfusions (*P* < .001) (Table 1). Of

Table 1. Comparison of the 2 Groups

Characteristic	Study Group		Statistical Comparison	P Value <sup>a</sup>
	SDE (n = 139)	SEEG (n = 121)		
Male, No. (%)	61 (43.9)	57 (47.1)	$\chi^2$ Test	.60
Age at surgery, mean (SD), y	30.6 (13.8)	30.1 (12.2)	Unpaired t test	.75
No. of failed anticonvulsants, mean (SD)	5.6 (2.5)	5.7 (2.5)	Rank sum test	.99
Age at onset, mean (SD), y	13.4 (11.9)	13.7 (11.6)	Unpaired t test	.86
Duration of epilepsy, mean (SD), y	17.2 (12.1)	16.4 (12.0)	Unpaired t test	.60
Implant OR time, mean (SD), min	429.4 (68.1)	322.0 (75.7)	Unpaired t test	<.001
Implant surgery time, mean (SD), min	308.2 (62.5)	121.3 (48.2)	Unpaired t test	<.001
No. of electrodes per patient, mean (SD)	114.3 (30.9)	186.9 (38.6)	Unpaired t test	<.001
Patients receiving transfusions, No. (%)	19 (13.7)	1 (0.8)	$\chi^2$ Test	<.001
Duration of monitoring, mean (SD), d	8.1 (2.8)	7.7 (3.9)	Unpaired t test	.29
Narcotic use, mean (SD), MME	356 (233)	201 (176)	Unpaired t test	<.001
Major complications, No. (%)	10 (7.2)	0	$\chi^2$ Test	.003
Lesional, No. (%)	99 (71.2)	53 (43.8)	$\chi^2$ Test	<.001
Hippocampal sclerosis, No. (%)	44 (31.7)	22 (18.2)	$\chi^2$ Test	.013
Definitive procedures, No. (%)				
Resection or ablative surgery	127 (91.4)	90 (74.4)	$\chi^2$ Test	<.001
Mesial temporal vs neocortical locus, No. of cases	58 vs 69	42 vs 46	$\chi^2$ Test	.77
No cranial intervention	12 (8.6)	17 (14.0)	$\chi^2$ Test	.17
Pending intervention	0	5 (4.1)	$\chi^2$ Test	.02

Abbreviations: MME, milligram morphine equivalents; OR, operating room; SDE, subdural grid electrode; SEEG, stereoelectroencephalography. <sup>a</sup>  $P < .05$  indicates significance. Hippocampal sclerosis was defined as any subtle (type 3) to prominent (type 1) imaging change that met ILAE defined criteria.<sup>69</sup>

Figure 1. Overall Comparison of Numbers of Study Cases and Operating Room (OR) Times



Data were acquired in consecutive cases from November 1, 2004, through June 30, 2017. SDE indicates subdural electrode; SEEG, stereoelectroencephalography.

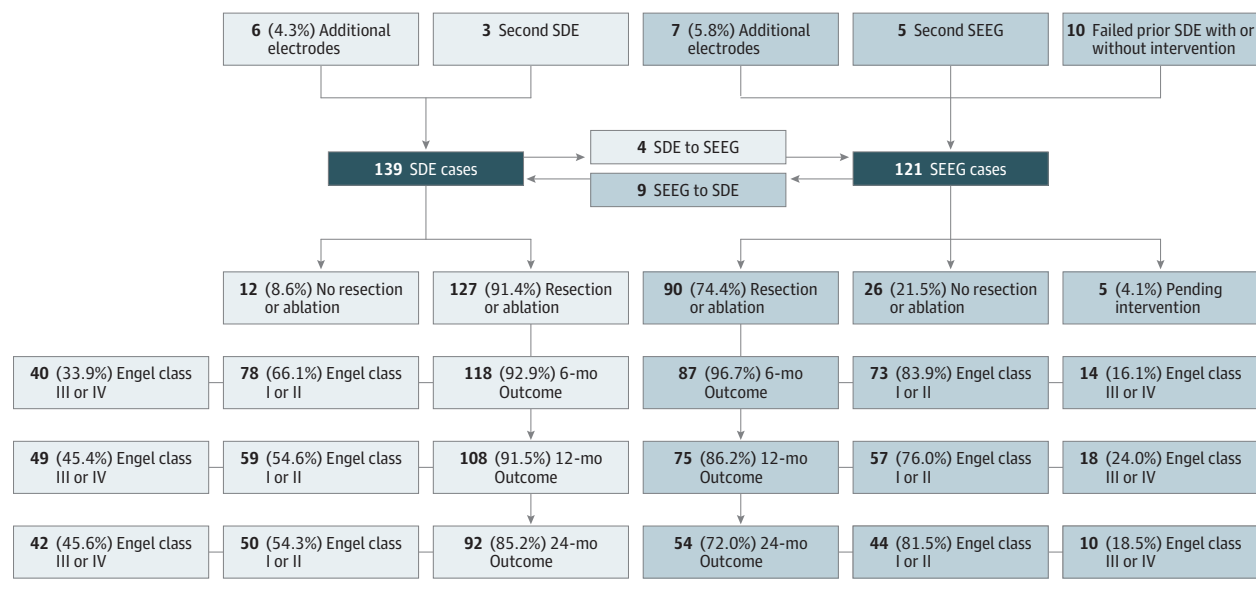
these 19 procedures, 5 involved a second SDE implantation or the management of an intracranial hematoma in the same hospital stay. Transfusions occurred in 7 of the last 50 SDE cases and 1 of the last 50 SEEG cases ( $P = .03$ ).

Seven symptomatic hemorrhagic sequelae and 3 infections related to SDE implantation occurred, and 1 of these cases experienced long-term neurologic sequelae. Two hematomas and 1 infection occurred in the last 50 SDE cases. No symptomatic complications of any kind occurred in the SEEG cohort, a very significant difference in compli-

cation rates ( $P = .003$ ) (Table 1). Two patients in the SEEG cohort had small asymptomatic subdural hematomas (<3 mm thick), incidentally identified on postimplantation computed tomographic scans with no clinical correlate. Patients in the SDE cohort received significantly greater dosages of narcotics (mean, 356 [233] MME/patient) compared with those in the SEEG cohort (mean, 201 [176] MME/patient;  $P < .001$ ). The mean MME used in the last 50 SDE cases was 394 (249) per patient; in the last 50 SEEG cases, 199 (196) per patient ( $P < .001$ ) (Table 1).



Figure 2. Overview of Characteristics and Management of Subdural Electrode (SDE) and Stereoelectroencephalography (SEEG) Groups



Outcomes were measured with the Engel Epilepsy Surgery Outcome Scale, where class I indicates free of disabling seizures; II, rare disabling seizures; III, worthwhile improvement; and IV, no worthwhile improvement.

### Comparative Epilepsy Outcomes

A significantly greater proportion of SDE cases underwent resection or ablative (laser interstitial thermal therapy [LITT]) surgery compared with SEEG cases (127 [91.4%] vs 90 [74.4%];  $P < .001$ ). Of the last 50 cases of each type, 48 SDE cases (96.0%) vs 36 SEEG cases (72.0%) underwent resection or LITT ( $P = .001$ ). Twelve SDE cases (8.6%) and 17 SEEG cases (14.0%) were thought to not be candidates for focal resection or ablation after evaluation. Of the last 50 cases, 8 (4.0%) SDE cases and 16 (8.0%) SEEG cases were not thought to be candidates for further intracranial intervention. In addition, 5 SEEG cases (4.1%) were not willing (due to concerns of cognitive decline) or not able (due to lapse in medical insurance coverage) to undergo a definitive procedure or are still awaiting intervention. Thus, the SEEG and SDE cohorts were significantly different in the proportions of cases that were lesional, suggesting that these modalities were used to evaluate somewhat different populations, although the same group of physicians at the same center managed and referred these cases. However, this shift in the patient pool would be expected to bias outcomes against SEEG, because these patients generally have less favorable outcomes. Definitive procedures performed in each group are summarized in Table 1 and Figure 2. We analyzed these 2 groups in the following 3 ways: all those who underwent resection, the subgroup of nonlesional cases (the most challenging class of patients in epilepsy surgery), and all cases undergoing evaluation by either modality.

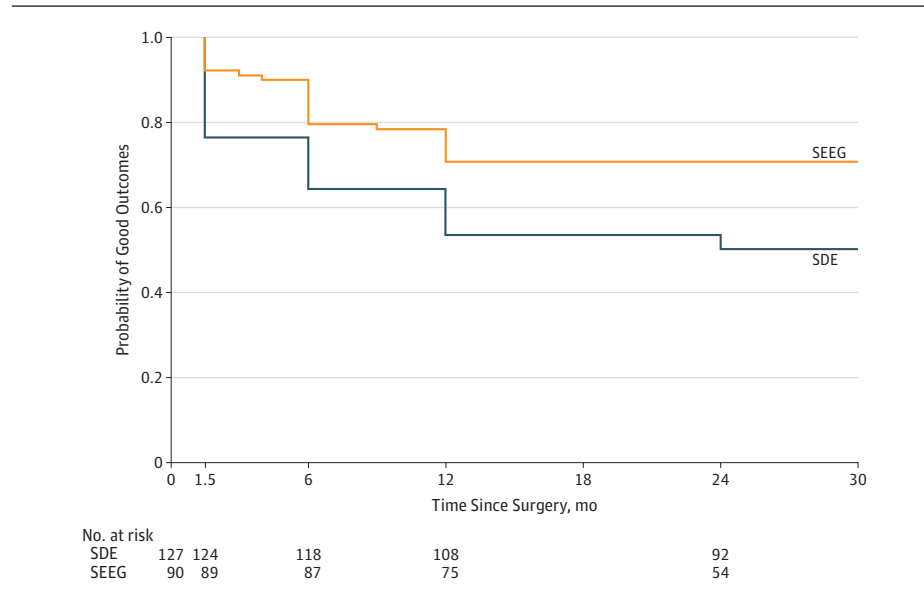
A significantly greater proportion of the SEEG cohort had a good outcome (Engel class I [free of disabling seizures] or II [rare disabling seizures]) compared with the SDE cohort at 6 months (73 of 87 [83.9%] vs 78 of 118 [66.1%];  $P = .004$ ) and 12 months (57 of 75 [76.0%] vs 59 of 108 [54.6%];  $P = .003$ ) after resection. When comparing just the last 50 cases in each

group at 1 year, 23 of 30 SEEG cases (83.3%) had a good outcome (Engel class I or II) compared with 26 of 41 of the last SDE cases (63.4%) of the last 50 SDE cases ( $P = .07$ ). Survivor function analysis of good outcomes (Engel class I or II) at 1 year was 70.6% for SEEG vs 53.4% for SDE; at 2 years, 70.6% and 50.2% respectively (log-rank  $P = .16$ ; 95% CI, 0.9046-2.1997). Survivor functions for seizure freedom (Engel class I) at 1 year were 58.4% for SEEG and 45.7% for SDE cases. At 2 years, survivor functions were 56.6% for SEEG cases and 43.6% for SDE cases (significantly different log-rank  $P = .03$ ; 95% CI, 1.0844-2.4719). The relatively recent introduction of SEEG implies a shorter follow-up duration, and so the Kaplan-Meier curves are plotted to end at 30 months (Figure 3).

Given the differences in the proportion of cases in the 2 cohorts that were lesional, we also performed subgroup analyses based on the presence of imaging abnormalities. Compared with the lesional SDE cohort, a significantly greater proportion of the lesional SEEG cohort had good outcomes (Engel classes I and II) at 6 months (36 of 40 [90.0%] vs 64 of 87 [73.6%];  $P = .04$ ) and at 1 year (30 of 36 [83.3%] vs 50 of 79 [63.3%];  $P = .03$ ). The distinction was more significant for nonlesional cases; good outcomes were seen at 6 months (37 of 47 [78.7%] vs 13 of 28 [46.4%];  $P = .004$ ) and 12 months (27 of 39 [69.2%] vs 9 of 26 [34.6%];  $P = .006$ ) in the cohorts.

As mentioned above, 91.4% of the SDE group and 74.4% of the SEEG group underwent resections or LITT. A substantial component of these were patients with bitemporal epilepsies, preferentially undergoing evaluation with SEEG, who were unlikely to undergo resections. Even so, to demonstrate non-inferiority of SEEG relative to SDE, we evaluated outcomes in all patients (not just those in whom definitive procedures were performed) undergoing intracranial evaluations. In this analysis, favorable outcomes (Engel class I or II) for SEEG com-

Figure 3. Kaplan-Meier Survivor Analysis



Analysis evaluates the probability of good outcomes (Engel Epilepsy Surgery Outcome Scale class I [free of disabling seizures] and II [rare disabling seizures]) in subdural electrode (SDE) and stereoelectroencephalography (SEEG) groups. No follow-up was recorded at 18 months.

Table 2. Engel Class at 12 Months for the Entire Cohort Undergoing Electrode Placement and for Those Patients Deemed Appropriate Candidates for Resection or Ablation

Engel Class <sup>a</sup>	Study Group		P Value <sup>b</sup>
	SDE	SEEG	
<b>Cases Undergoing Resection or Ablation</b>			
No. of cases	108	75	
Class I or II	59 (54.6)	57 (76.0)	.003
Class III	41 (38.0)	16 (21.3)	.02
Class IV	8 (7.4)	2 (2.7)	.17
<b>Cases Evaluated Using SDE or SEEG<sup>c</sup></b>			
No. of cases	139	121	
Class I or II	59 (42.4)	57 (47.1)	.45
Class III	41 (29.5)	16 (13.2)	.002
Class IV	8 (5.8)	2 (1.7)	.09

Abbreviations: SDE, subdural grid electrode; SEEG, stereoelectroencephalography.

<sup>a</sup> Measured on the Engel Epilepsy Surgery Outcome Scale, where class I indicates free of disabling seizures; II, rare disabling seizures; III, worthwhile improvement; and IV, no worthwhile improvement.

<sup>b</sup> Calculated using  $\chi^2$  test.  $P < .05$  indicates significance.

<sup>c</sup> Performed at 12 months.

pared with SDE were noninferior at 6 months (73 of 121 [60.3%] vs 78 of 139 [56.1%];  $P = .49$ ) and at 1 year (57 of 121 [47.1%] vs 59 of 139 [42.4%];  $P = .45$ ) (Table 2 and eResults in the Supplement).

## Discussion

Implantation of SDEs has been the criterion standard<sup>11-13</sup> for delineating epileptogenic zones, especially in North America, but SEEG techniques are being increasingly adopted.<sup>70</sup> Implantation of SDEs allow for precise functional mapping of brain surfaces relative to epileptogenic zones.<sup>34</sup> On the other hand, the improved coverage and precise targeting of deeper structures gives SEEG an advantage in sampling deep lesions and bilateral explorations.<sup>18,28,29,34</sup> In addition, the ability of the SEEG method to map distributed epileptic networks involved in epileptic activity has been hypothesized to be responsible for improved outcomes in patients with epilepsy that is difficult to localize.<sup>18,28,42</sup> During the course of our institu-

tion's rapid adoption of SEEG, we noticed a marked distinction in patient tolerance for this procedure compared with SDE placement and also that outcomes in patients who underwent resection or LITT after SEEG tended to be better. This analysis of a large series of patients undergoing intracranial EEG quantifies both of these impressions.

The availability of surgical robots, such as the ROSA and NeuroMate,<sup>71</sup> allows for a combination of accuracy and efficiency<sup>39</sup> in the placement of depth electrodes for SEEG. With recent and ongoing advancements in robotic surgical assistance,<sup>72</sup> the time taken for the placement of intracranial electrodes has diminished significantly. Mean surgical time was 121.3 (48.2) minutes for SEEG cases vs 308.2 (62.5) minutes for SDE ( $P < .001$ ). When comparing the most recent 50 cases, these differences are further amplified at 96.9 (20.3) minutes for SEEG vs 302.1 (59.3) minutes for SDE placement ( $P < .001$ ).

Implantation of SDEs can be associated with an increased risk of hemorrhage,<sup>73</sup> specifically subdural hematomas.<sup>33,39,40,74</sup> Our SDE cohort had 7 hemorrhage-related complications and 3 infections, significantly higher than the complication rate in the

SEEG cohort ( $P = .003$ ). We found a secular trend in complications after SDE implantation; 7 occurred in the first 70 cases and 3 in the last 69 cases, suggesting that increasing surgical expertise results in diminishing complications with SDE implantations. However, the morbidity between the 2 groups was notable even in the last 50 cases of each type (3 [6.0%] vs 0;  $P = .08$ ). The absence of intracerebral bleeding associated with depth electrode placement<sup>73</sup> is attributable to meticulous stereotactic techniques.<sup>33</sup>

Implantation of SDEs is also associated with an increased need for blood products compared with SEEG.<sup>65</sup> In our series, 1 SEEG procedure and 19 SDE procedures involved the use of blood products during implantation. The SEEG cases also required significantly lower amounts of narcotics ( $P < .001$ ), which reduces downstream sequelae such as vomiting, constipation, somnolence, and respiratory depression.<sup>75</sup>

Significantly distinct proportions of SEEG and SDE cohorts were lesional, suggesting that despite not being consciously aware of this, our group evolved to expand the pool of patients being referred for surgical consideration. Given that nonlesional cases generally have worse outcomes, this evolution would be expected to bias the seizure outcomes against SEEG, but this was not borne out in the results. Also, in keeping with other SEEG series, a smaller percentage of SEEG cases underwent resection than SDE cases. The purpose of intracranial recordings is to determine candidacy for resection procedures. Indeed, if this investigative technique allows for better selection of the best candidates for such approaches, it should result in a lower rate of patients undergoing resection and a higher rate of good outcomes, thereby limiting the numbers of “double losers,” that is, those who lose cognitive function but continue to have seizures.<sup>76</sup> Indeed, the type of patient evaluated and the proclivity to perform a resection are intrinsic to each of these modalities and cannot be further disambiguated. Thus, all these caveats should factor into deriving interpretations from the comparisons between epilepsy outcomes in these 2 groups.

Our evaluation of seizure outcomes included the entire data set and the last 50 cases in each cohort, followed up at 6 and 12 months, in addition to a survivor analysis. These analyses significantly favored SEEG, trended toward SEEG, or, when looking at all patients undergoing intracranial evaluations, showed that SEEG is noninferior. Fifty-seven of 75 SEEG case (76.0%) had good outcomes at 1 year after resection, compared with 59 of 108 SDE cases (54.6%) ( $P = .003$ ) and 48 of 75 case (64.0%) vs 48 of 108 cases (44.4%) were seizure free. These outcomes (or lack of inferiority when considering all patients undergoing implantation) in SEEG vs SDE cohorts are especially striking when considering that only 43.8% of the SEEG cases were lesional by MRI, compared with 71.2% of the SDE cohort. This better outcome despite lack of lesions, a major contributor to good outcomes in prospectively validated nomograms,<sup>77</sup> argues for superiority of SEEG relative to SDE.

One factor that could contribute to the differences in surgical outcomes is the propensity in most centers to be biased toward resection in cases with equivocal data after SDE monitoring. These patients have already had a craniotomy, and a second operative procedure is necessary to remove the SDEs. This bias

may be responsible for some of the poor outcomes in the SDE cohort but is an intrinsic and likely immutable aspect of this surgical approach.

In our series, a relatively high percentage of the SEEG cohort underwent resection or LITT after SEEG (74.4%; compared with 67% in Serletis et al<sup>78</sup>; 45% in Mullin et al<sup>79</sup>; 68% in González-Martínez et al<sup>64</sup>; and 74% in Cardinale et al<sup>39</sup>) with outcomes as favorable or better than those reported in recent SEEG case series.<sup>32,64,79,80</sup> This discrepancy could be accounted for by some diversity between patient populations at different institutions, the greater number of electrodes implanted per case at our center, or perhaps by a more judicious sampling of the putative epileptogenic sites.

To conclude, SEEG methods are better tolerated and are likely less resource intensive. Although superior outcomes are seen in those patients with SEEG who undergo resection or LITT compared with outcomes after SDE, especially marked in nonlesional cases, distinctions in patient characteristics in these 2 cohorts should temper conclusions that can be drawn from these observations. These features have clear import when there is equipoise in considering the use of a modality for invasive intracranial monitoring and should predispose us to consider SEEG preferentially over SDE placement to localize epileptogenic networks in those cases. Last, the minimally invasive nature of SEEG allows for its integration with laser ablation of mesial temporal structures or heterotopia,<sup>81,82</sup> that makes the entire surgical approach—localization plus therapy—minimally invasive.

A question that emerges from this work is, which patients should undergo SDE and SEEG? Our transition from SDE to SEEG, which mirrored in the experience at other North American centers, was incremental, with SEEG initially used mostly in bilateral cases, deep lesions, or patients with prior surgery. However, after this initial learning period, and driven by the availability of robotic technology, SEEG became the predominant modality for intracranial recordings to localize epilepsy. This process was driven by experience, observations of the distinct difference in the patient experience, and a major cognitive transition on the part of the neurosurgeon and the team of epilepsy neurologists in learning to evaluate these data. In centers such as ours that have reached maturation in their use of SEEG, SDEs are now used chiefly to evaluate neocortical epilepsy located around eloquent cortex and in young children, whose skull is too thin to hold the anchor bolts for SEEG.

### Limitations

Certain limitations are inherent to a retrospective analysis such as this. Although a prospective randomized trial comparing these 2 approaches would be ideal, whether such a study is practically feasible, given poor accrual rates in prior prospective trials in epilepsy surgery, is unclear. Further, given the vastly different complication rates, whether equipoise or the possibility of randomizing patients to evaluate these differences prospectively is also unclear. Data sets such as these are therefore crucial because they provide the best evidence possible for us to compare intracranial recording techniques used to evaluate intractable epilepsy.

## Conclusions

The SEEG method is associated with less narcotic use for pain management and lower rates of complications and is generally far better tolerated than SDEs. Comparing populations studied

by these 2 techniques, confounded though by the propensity for a resection regardless of the quality of localization in the SDE cohort, reveals greater efficacy in seizure localization and therapy of SEEG compared with that of SDE, the current criterion standard.<sup>11-13</sup> These features of the SEEG method should lower the barrier for surgical candidacy in intractable epilepsy.

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*Concept and design:* Tandon, Tong.

*Acquisition, analysis, or interpretation of data:* All authors.

*Drafting of the manuscript:* Tandon, Tong, Friedman.

*Critical revision of the manuscript for important intellectual content:* Tandon, Tong, Johnson, Von Allmen, Thomas, Hope, Kalamangalam, Slater, Thompson.

*Statistical analysis:* Tong.

*Administrative, technical, or material support:* Tandon, Johnson, Von Allmen.

*Supervision:* Tandon, Kalamangalam.

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