<u>JNS</u>

Oblique trajectory angles in robotic stereoelectroencephalography

Patrick S. Rollo, BA,^{1,2} Matthew J. Rollo, BS,¹ Ping Zhu, PhD,^{1,2} Oscar Woolnough, PhD,^{1,2} and Nitin Tandon, MD^{1–3}

¹Vivian L. Smith Department of Neurosurgery, McGovern Medical School at UTHealth Houston; ²Texas Institute for Restorative Neurotechnologies, University of Texas Health Science Center at Houston; and ³Memorial Hermann Hospital, Texas Medical Center, Houston, Texas

OBJECTIVE Traditional stereo-electroencephalography (sEEG) entails the use of orthogonal trajectories guided by seizure semiology and arteriography. Advances in robotic stereotaxy and computerized neuronavigation have made oblique trajectories more feasible and easier to implement without formal arteriography. Such trajectories provide access to components of seizure networks not readily sampled using orthogonal trajectories. However, the dogma regarding the relative safety and predictability of orthogonal and azimuth-based trajectories persists, given the absence of data regarding the safety and efficacy of oblique sEEG trajectories. In this study, the authors evaluated the relative accuracy and efficacy of both orthogonal and oblique trajectories during robotic implantation of sEEG electrodes to sample seizure networks.

METHODS The authors performed a retrospective analysis of 150 consecutive procedures in 134 patients, accounting for 2040 electrode implantations. Of these, 837 (41%) were implanted via oblique trajectories (defined as an entry angle > 30°). Accuracy was calculated by comparing the deviation of each electrode at the entry and the target point from the planned trajectory using postimplantation imaging.

RESULTS The mean entry and target deviations were 1.57 mm and 1.89 mm for oblique trajectories compared with 1.38 mm and 1.69 mm for orthogonal trajectories, respectively. Entry point deviation was significantly associated with entry angle, but the impact of this relationship was negligible (-0.015-mm deviation per degree). Deviation at the target point was not significantly affected by the entry angle. No hemorrhagic or infectious complications were observed in the entire cohort, further suggesting that these differences were not meaningful in a clinical context. Of the patients who then underwent definitive procedures after sEEG, 69 patients had a minimum of 12 months of follow-up, of whom 58 (84%) achieved an Engel class I or II outcome during a median follow-up of 27 months.

CONCLUSIONS The magnitude of stereotactic errors in this study falls squarely within the range reported in the sEEG literature, which primarily features orthogonal trajectories. The patient outcomes reported in this study suggest that seizure foci are well localized using oblique trajectories. Thus, the selective use of oblique trajectories in the authors' cohort was associated with excellent safety and efficacy, with no patient incidents, and the findings support the use of oblique trajectories as an effective and safe means of investigating seizure networks.

https://thejns.org/doi/abs/10.3171/2020.5.JNS20975

KEYWORDS medically refractory epilepsy; seizures; MRI-negative epilepsy; stereo-electroencephalography

THERE are now several studies and recent meta-analyses showing that stereo-electroencephalography (sEEG) procedures are significantly safer than subdural electrode implantations for the intracranial evaluation of epilepsy.¹⁻⁸ Furthermore, sEEG implantation can effectively localize epileptic foci by comprehensively sampling the epileptogenic network, by accessing deeper cortical areas and multiple noncontiguous lobes, and by facilitating bilateral exploration.^{2,4,9–11}

Traditional sEEG, as devised by Jean Talairach,¹² entails the use of orthogonal trajectories guided by semiology and arteriography.^{13–17} This technique was developed when 3D imaging was nonexistent and roentgenograms obtained using parallel x-ray beams provided the only method of

ABBREVIATIONS EPD = entry point deviation; MRgLITT = MR-guided laser interstitial thermal therapy; RMS = root mean square; sEEG = stereo-electroencephalography; TPD = target point deviation.

SUBMITTED March 30, 2020. ACCEPTED May 6, 2020.

INCLUDE WHEN CITING Published online August 14, 2020; DOI: 10.3171/2020.5.JNS20975.

stereotactic localization and vasculature avoidance. The availability of volumetric MRI and CT imaging, combined with computerized 3D frameless navigation systems and stereotactic robotic arms, allows for sEEG electrode placement that does not require conventional arteriography and is unconstrained with regard to trajectory.¹⁰ Placement can range from azimuth-based to oblique trajectories, optimally oriented to sample relevant brain areas. However, the prevailing dogma has biased most centers toward orthogonal implantations. This is partly out of fidelity to tradition and partly owing to the relative ease of interpretation of sEEG data acquired in this way. However, this rigid approach introduces a systematic bias toward undersampling some regions and oversampling others.^{4,9} The localization of seizure foci by sEEG can be optimized in selected instances by using oblique angles of entry through the skull.^{18,19} Specifically, the insula and ventral temporal cortex cannot be sampled well with orthogonal trajectories, and the temporal and parietal opercula are more comprehensively sampled using oblique trajectories.^{18,20}

The rapid adoption of sEEG in North America and across the globe necessitates a careful analysis of its feasibility, safety, and efficacy. Being unconstrained with regard to trajectory allows for the exploration of many regions potentially involved by the epilepsy that would not otherwise be sampled and allows for a broader range of trajectories to avoid collisions with blood vessels.

Methods

This retrospective review of our sEEG series was performed after approval by the Committee for the Protection of Human Subjects at the McGovern Medical School at UTHealth. A total of 134 patients underwent robotic sEEG during a 6-year interval between June 2013 and 2019. A total of 2040 depth electrodes were implanted in 150 consecutive procedures performed by the senior author (N.T.). Eleven patients underwent the placement of additional electrodes in the same hospitalization, and 5 patients had a second sEEG implantation during a subsequent hospitalization. A mean of 13 ± 3 electrodes (\pm SD) were placed per case. Ages at seizure onset and at implantation were 13.7 ± 11.6 and 30.3 ± 11.9 years, respectively.

Planning of entry and target points was performed using robotic stereotactic software (ROSA, Zimmer Biomet) using T1-weighted contrasted MRI scans with 1×1 × 1-mm resolution, obtained at 3T or 1.5T. Volumetric contrast-enhanced CT scans were obtained after fiducial implantation and were coregistered with the MRI scan. Five skull fiducials were used in 135 procedures, 6 fiducials were used in 14 procedures, and 4 fiducials were used in 1 procedure. The ROSA robot was registered to the patient's head in each case using the skull fiducials. Submillimeter registration (root mean square [RMS] error provided by the ROSA navigation platform) was obtained and recorded in each case for further analysis. We implanted 0.8-mm-outer-diameter sEEG electrodes (PMT Corp.) using the ROSA arm.^{21,22} In each case, after making a stab incision in the skin at the site of electrode entry, the arm was brought as close as possible to the skull, and the outer table of the skull was gently percussed using a 2.1-

mm Salcman drill bit (Elekta) without the power driver attached to indent it to prevent skiving of the drill during the drilling process. The drill bit was then attached to a battery-powered driver, and a drill stop placed at the approximate thickness of the skull was used to protect the dura mater while the drill perforated the skull. Next, a Cosman coagulator (Boston Scientific) was then used to coagulate and open the dura. Following this, an anchor bolt was screwed into the twist drill hole in the skull using an anchor bolt driver. A guidance stylet (0.8 mm) was appropriately measured and inserted to the target, creating a path for the electrode. The electrode of appropriate length was selected and then implanted, and the anchor bolt cap was tightened around it to hold it in place. Systematically opening the dura in this fashion, combined with the use of a guidance stylet, minimizes the potential for the electrode to deviate into the epidural space or be deflected by sulci (Video 1).

VIDEO 1. sEEG implantation process. The implantation of a single sEEG electrode. All major steps in the implantation process are highlighted. Copyright Nitin Tandon. Published with permission. Click here to view.

A volumetric CT scan was obtained postimplantation and registered to the planning MRI scan to measure deviations from planned trajectories. The entry point deviation (EPD) and target point deviation (TPD) of each electrode from the planned trajectory were measured in all 3 cardinal planes using ROSA software (Fig. 1) and along an oblique plane selected along the length of each probe, with the maximal measured distance selected as the deviation.

The angle of entry for each electrode was quantified by creating a triangular face from the 3 closest vertices to the point of incidence on the patient's reconstructed skull surface and computing each electrode's angular deviation relative to the perpendicular of this face using MATLAB (MathWorks) (Fig. S1). Electrodes with measured entry angles greater than 75° were excluded as outliers on clinical practice (n = 9). An additional 53 electrodes were excluded due to poor skull surface reconstruction with resultant errors in the automated MATLAB processing pipeline described above. A total of 1978 trajectories were available for analysis. These were also classified into 4 bins based on the angle of entry $(0^{\circ}-30^{\circ}, 30^{\circ}-45^{\circ}, 45^{\circ}-60^{\circ}, \text{and } 60^{\circ}-75^{\circ})$ (Fig. 2). Electrode contact positions were projected onto a cortical surface model generated in FreeSurfer²³ and displayed on the cortical surface model for visualization.²⁴

Last, the time taken for electrode placement and the accuracy of robotic registration using fiducials were obtained from operative records.

Correlations across all variables were assessed using Spearman's rank correlation analysis. Multiple linear regression models were applied to evaluate the impact of entry angle, chronological order of the procedure, electrode length, and registration error on electrode placement accuracy at the entrance and target points—the EPD and TPD. Given the possibility that the residuals were not normally distributed, we also performed a robust regression analysis to validate the multiple linear regression. Multicollinearity was assessed using the variable inflation factor for each variable in the linear regression model (a variable inflation factor > 10 indicates the existence of multicollinear-

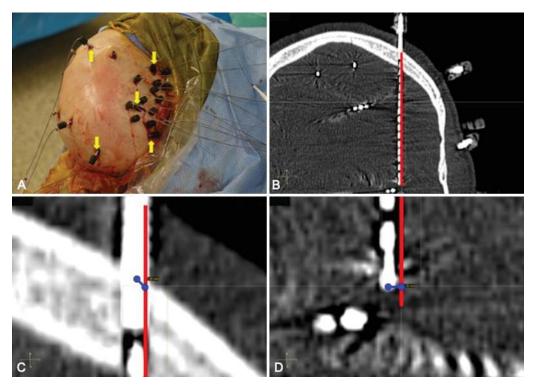


FIG. 1. Implantation and measurement. A: Postimplantation photograph of a patient with suspected right insular and temporal epilepsy. Obliquely implanted electrodes are indicated by the *yellow arrows*. B: Alignment of the planned trajectory (*red line*) with the postimplantation CT scan. C and D: Demonstration of the deviation measurements (*blue lines*) of EPD (C) and TPD (D).

ity).²⁵ Two-way interaction terms were evaluated for significance. The likelihood ratio was calculated to measure the improvement in interaction model fit over the model without an interaction term. If the model fit was improved significantly in the likelihood ratio test, we retained the interaction terms in the regression models with the other covariates. All analyses were performed using R 3.5.1, and significance tests were two-sided and considered statistically significant at p < 0.05. Mean values are presented as the mean \pm SD.

Postimplantation scans were evaluated for bleeding, and all patients were monitored for any complications related to the electrode placement (hemorrhage, swelling, neurological deficit, or infection), until their followup appointments after the removal of electrodes, at which point the decision was made for either surgical intervention, additional electrode placement, or no further surgery. The electrodes involved in seizure onsets were separately localized on the cortical surface model and, using surfacebased coregistration techniques, were depicted across the group as well.²⁶

All patients who underwent resections were followed up for as long as possible, and their neurological and seizure outcomes were also compiled.²⁷

Results

The median EPD was 1.33 mm (range 0–16.55 mm), and the median TPD was 1.47 mm (range 0–28.29 mm). The mean length of the trajectory was 48.65 ± 15.26 mm, and the mean RMS registration error was 0.51 ± 0.15 mm.

The median surgical time (incision time to completion divided by the number of probes implanted) per electrode was 5.33 minutes (range 2.33–23.00 minutes).

Summary statistics for the entire cohort are provided in Table 1. Correlations between these variables were studied in a univariate and multivariate fashion. The 4 strongest univariate correlations were between EPD and TPD (r = 0.393, p < 0.001), entry angle and case number (r = 0.393, p < 0.001)0.272, p < 0.001), EPD and case number (r = 0.193, p < (0.001), and registration error and case number (r = 0.148, p < 0.001) (Fig. 3). The remaining correlation coefficients were all $|\mathbf{r}| < 0.1$. A multiple linear regression analysis (Table 2) revealed that EPD was significantly influenced by entry angle ($\beta = 0.015$, p < 0.001), case number ($\beta =$ 0.006, p < 0.001), and electrode length ($\beta = -0.007$, p < 0.001). Similarly, TPD was significantly associated with the entry angle ($\beta = 0.025$, p = 0.001). While these values showed statistical significance, the magnitudes of their effects were not clinically relevant. A 30° increase in the entry angle would result in a 0.45-mm increase in EPD. Registration error was found to impact neither the EPD (β = -0.220, p = 0.161) nor the TPD ($\beta = -1.708$, p = 0.062). These findings remained consistent using a robust regression for validation of the analysis.

There was a significant decrease in the implantation duration, with an increasing number of cases completed as the surgical team gained more experience ($\beta = -0.043$, p < 0.001) (Fig. S2). There were no clinically significant trends in EPD, TPD, electrode length, or registration error across the 4 bins (Fig. 4). Summary statistics for each

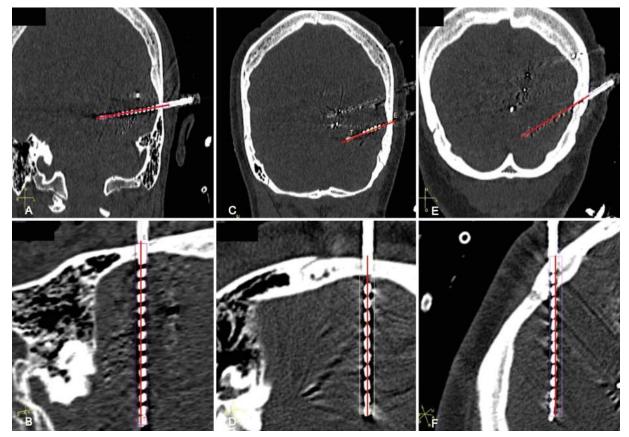


FIG. 2. Orthogonal and oblique entry angle comparison. Coronal (A, C, and E) and axial (B, D, and F) views of the postimplantation CT scans of representative electrodes demonstrating an orthogonal electrode (11°; A and B), moderately oblique electrode (31°; C and D), and highly oblique electrode (52°; E and F). The planned trajectory is highlighted in *red*.

group are provided in Table S1. Multiple linear regression and robust regression analyses demonstrated the significant differences across the entry angle bins in addition to case number and electrode length on the electrode EPD. When conducting these same analyses for TPD, only the highest entry angle group (60° -75°) was significantly associated with TPD ($\beta = -2.366$, p = 0.033) based on the multiple linear regression (Table S2).

Large EPDs relate to misregistration or an inadvertent movement of the skull after fixation and registration. All 3 of the largest EPDs were in the same patient—attributable to an undetected head shift or a misregistration. Large TPDs relate to misregistration, technical errors, or unexpected deviation from the planned trajectory. The 12 largest TPDs (> 10 mm) were examined further; they were accounted for by skiving at entry (n = 4), curved trajectory due to deviation by a sulcus (n = 4), angular deviation of the bolt from the planned trajectory (n = 2), and deviation due to a significant portion of the trajectory lying inside a large cavity (n = 2).

Seizure onset zones were identifiable and unifocal in 104 of the 134 patients. All recording and all onset electrodes were co-represented in common space, categorized also by whether or not they were involved in seizure onset (Fig. 5). Orthogonal trajectories were effective in localizing hippocampal and amygdala seizure onsets (Fig. 5A). Of 776 mesial temporal onset contacts, 664 (86%) were identified by orthogonally angled electrodes (entry angle

TABLE 1. Summary statistics of 2040 implanted electrodes

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Factor	Minimum	Maximum	Median	Mean	SD	No.
Entry angle (°)	1.0656	88.943	27.288	27.8887	13.5304	1987
RMS (mm)	0.28	1.17	0.52	0.5351	0.1509	2012
EPD (mm)	0	16.55	1.32	1.4503	1.022	2011
TPD (mm)	0	50.562	1.47	1.7962	2.0586	2011
Implant time per electrode (sec)	2.33	23	5.37	6.2415	2.9725	1876
Electrode length (mm)	9	106	46	48.6489	15.2566	2016

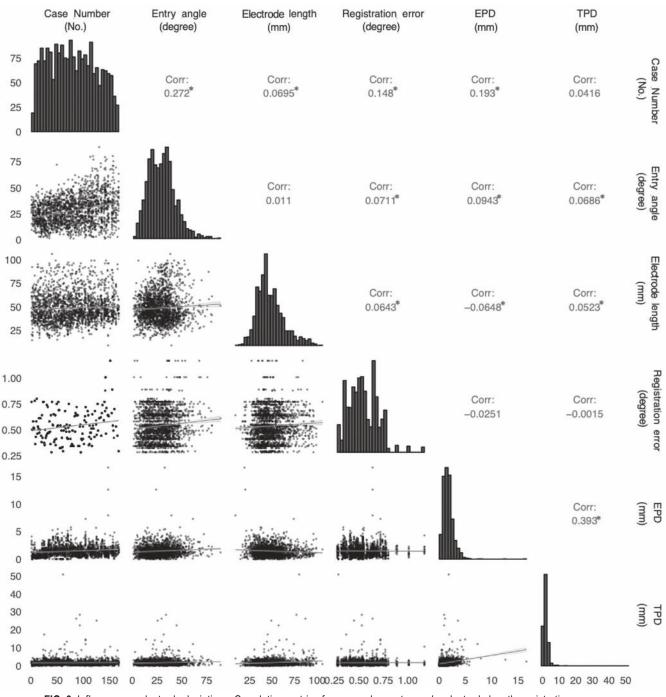


FIG. 3. Influences on electrode deviations. Correlation matrix of case number, entry angle, electrode length, registration error, TPD, and EPD using Spearman rank correlation. *Corrected p < 0.05. Corr = correlation coefficient. Figure is available in color online only.

< 30°). However, oblique trajectories were more effective at localizing extrahippocampal onsets (Fig. 5B). Of 1192 extrahippocampal onset contacts, 698 (59%) were located on obliquely angled electrodes (entry angle > 30°).

There were no clinically relevant complications in any of these 150 operations (i.e., no hemorrhages, swelling, neurological deficits, or infections) associated with electrode placement. Two patients had small asymptomatic subdural hematomas (< 3 mm thick), which were incidentally identified on postimplantation CT scans, were stable on follow-up imaging, and had no clinical correlates.

Of the 134 patients, 101 (75.4%) underwent resection or ablation, 8 (6%) had subdural electrode placement after sEEG, each followed by resection, and 25 (18.6%) underwent no subsequent resection. Within this group, seizure foci were multifocal and managed with a responsive neural stimulator in 11 patients (8.2%), epilepsy was not localizable in 13 patients (9.7%), and the remaining patient

Characteristic	EPD				TPD					
	Coefficient	SE	t	95% CI	p Value	Coefficient	SE	t	95% CI	p Value
Main effects										
Entry angle	0.015	0.004	3.630	0.007 to 0.023	<0.001	0.025	0.007	3.432	0.011 to 0.039	0.001
Case no.	0.006	0.001	5.023	0.004 to 0.008	<0.001	0.004	0.002	1.954	0.000 to 0.008	0.051
Electrode length	-0.007	0.002	-4.489	-0.010 to -0.004	<0.001	-0.008	0.010	-0.758	-0.028 to 0.012	0.449
Registration error	-0.220	0.157	-1.402	-0.527 to 0.088	0.161	-1.708	0.913	-1.870	-3.499 to 0.084	0.062
Interaction terms										
Case no. × entry angle	0.000	0.000	-2.682	0.000 to 0.000	0.007	0.000	0.000	-2.467	0.000 to 0.000	0.014
Electrode length × registra- tion error	_	_	_	_	_	0.038	0.018	2.080	0.002 to 0.073	0.038

TABLE 2. Multiple linear regression in relation to EPD and TPD adjusting the entry angle (continuous form)

- = not applicable.

(0.7%) is awaiting surgery. Of the 101 surgically treated patients, 21 underwent MR-guided laser interstitial thermal therapy (MRgLITT) ablation using the Visualase system (Medtronic) and 12 others underwent thermal MRgLITT ablation in combination with a staged open resection. Of the patients who underwent resection or ablation, 85 had follow-up durations of at least 6 months; 67 (78.8%) of these had an Engel class I or II outcome, while 55 patients (64.7%) had an Engel class I outcome. Fourteen patients (16.5%) reported an Engel class III outcome. The median follow-up period was 25 months, with a minimum of 6 months. Patients with a minimum of 12 months of followup had similar outcomes: 58 of 69 patients (84%) had an Engel class I or II outcome, with 48 patients (69.5%) having an Engel class I outcome (Fig. 6).

Discussion

To our knowledge, this is the largest reported cohort of patients in whom robotic sEEG placement accuracies were measured. Such large data sets enable us to perform multivariate analyses of the various factors that might influence the accuracy of sEEG. Our data support the efficacy and safety of oblique trajectories if these are necessary for

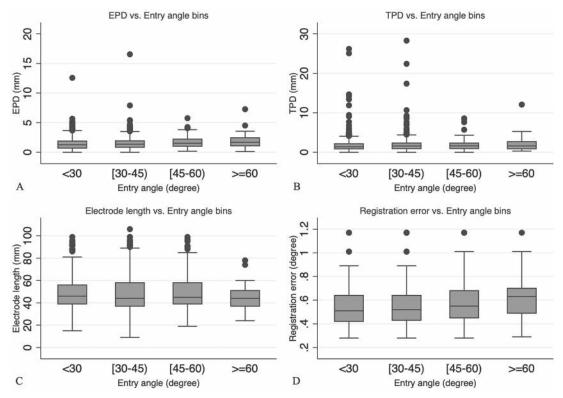


FIG. 4. Influence of entry angle on electrode implantation shown in box plots of EPD (A), TPD (B), electrode length (C), and registration error (D) by entry angle bin. *Boxes* show the median and interquartile range. *Error bars* show 95% confidence intervals with outliers highlighted.

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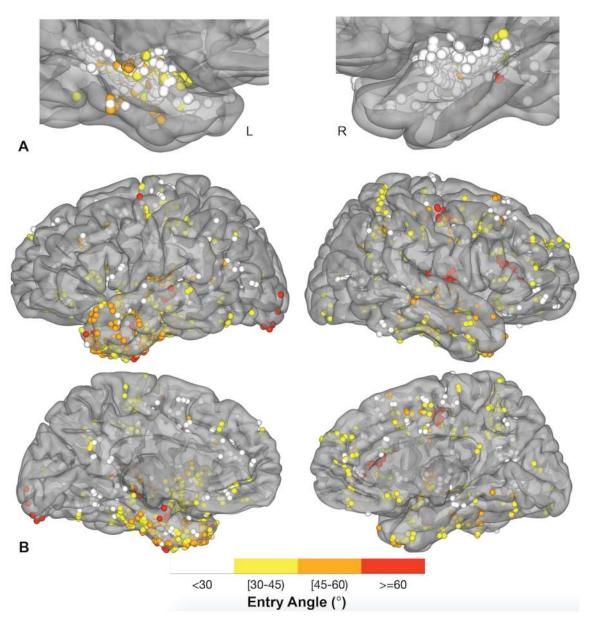


FIG. 5. Localization of seizure onsets with orthogonal and oblique trajectories. Electrode contacts within the seizure onset zone of patients with hippocampal and amygdala onsets (A) or extramesial seizure onsets (B), highlighting the entry angle of the electrode each contact was on.

clinical purposes. The hesitancy in implanting these electrodes is based, in large part, on the assumption that they will be inaccurate and possibly result in patient injury.^{4,18} The mean EPDs and TPDs reported here are comparable to those of previous studies,^{3,5,9,28} with error magnitudes well within the range of those previously reported: 92.5% of the electrodes were within 3 mm of the planned entry, and 87.3% of the electrodes were within 3 mm of the planned target points.¹⁸ Based on the multiple linear regression analysis, the entry angle did have significant effects on the entry errors; however, the clinical effect of this relationship was negligible (0.015-mm deviation per degree). Additionally, the adjusted r² values derived from both the multiple linear regression and the robust regression.

sion were less than 0.07 and 0.02 for EPD and TPD, respectively. This indicated that the variances of EPD and TPD explained by the included variables were lower than 7% and 2%, respectively. Importantly, the differences between TPD of the orthogonal electrodes were not significantly different (p < 0.05) when compared with oblique trajectories. There was a clear, though very small, impact of entry angle on the EPD, but this was not the case for the TPD. The deviation at the entry point became relatively unimportant if it was small, assuming the target point was reached and the deviation of the actual trajectory from the planned trajectory did not lead to patient harm or undersampling of intermediary brain regions.

There were no adverse events observed in associa-

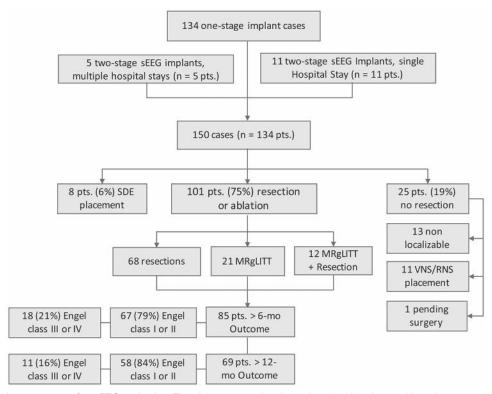


FIG. 6. Patient outcomes after sEEG evaluation. Flowchart representing the patients in this cohort and how they progressed through the epilepsy treatment process. RNS = responsive neural stimulator; SDE = subdural electrode; VNS = vagus nerve stimulator. Figure is available in color online only.

tion with the 150 procedures in this study. Based on the reported complication rate of 1.3%-5.6% (with outliers above 15%)^{5,29} per procedure as part of the implantation procedures, 3,4,7-9,11,20,28,30,31 2–8 adverse events would have been expected in this cohort, but none were seen. We attribute these outcomes to precise registration that can be accomplished using skull fiducials and a volumetric CT scan. While this is more tedious and time consuming, registration performed in this fashion is more accurate than using facial landmarks or a registration using the O-arm. Some sEEG series have reported a higher complication rate than other sEEG series.^{3–5,9,11,20,31–36} Some publications are an admixture of cases with frame-based sEEG and robotic sEEG.^{9,34} It is possible that the complication rates for frame-based procedures are higher due to human errors in the adjustment of the frame for multiple trajectories. Furthermore, there are important technical distinctions between their practice and ours that may account for these differences: during their robotic sEEG, for instance, they did not dock the robot with the head holder, and they used skin-based laser registration and implanted larger-diameter electrodes (1.2 mm). While it is impossible to definitively determine if these reasons lower accuracy and influence the higher complication rates seen in those series, given that sEEG is fundamentally a diagnostic procedure, it is obligatory for each group to devise locally relevant technical strategies to minimize risk associated with it. Given the advent of robotics in our field, we should be able to extend industrial safety cultures to the care of our patients and minimize surgical complications from sEEG electrode implantation: "Why not zero?" (https://www.dayzim.com/ about/vision-values/safety).

This study includes the largest number of reported oblique electrodes by a wide margin, in addition to being one of the larger robotic sEEG cohorts. Almost 64% (n = 54) of patients who had follow-up information of 6 months or more were seizure free, and 95% (n = 81) experienced worthwhile improvement as a result of their surgical intervention.²⁷ Fifty-five patients had Engel class I outcomes, falling within the range of seizure freedom achieved in other publications.^{3–5,7,9,11,20,28–30}

Perhaps most importantly, the ability to sample from areas that are otherwise challenging to access or to comprehensively sample using strictly orthogonal approaches—the temporal pole, the anterior medial frontal lobe, and the frontal and parietal opercula—resulted in a high percentage (75.4%) of patients undergoing definitive procedures. Of patients for whom follow-up was available for at least 1 year, 69.5% were seizure free. These numbers speak to the efficacy of oblique approaches in the localization of seizure foci.

The advantages of using oblique trajectories include minimizing the number of electrodes per procedure^{4,18} and the optimization of traditional orthogonal coverage schemes to reach previously undersampled cortex. The juxtaposition of images in Fig. 5 demonstrates the utility of oblique trajectories. Orthogonal electrodes are effective within the hippocampal region. Outside this region, the data presented here support oblique trajectories as being more effective in localizing seizures. However, the effi-

cacy of *purely* orthogonal trajectory implantation schemes is difficult to assess, as most patients had both orthogonal and oblique implants, obfuscating a direct comparison of the two approaches. Regardless of which type of trajectory is more effective, when comparing the trajectories shown in Fig. 5, it is clear that orthogonal trajectories alone would be insufficient to localize seizures in these cases.

Conclusions

Our study challenges the rationale for avoiding oblique trajectories by demonstrating a clinically insignificant impact of oblique trajectories on target deviation and on patient safety. The results clearly indicate that the judicious use of oblique trajectories does not appear to have adverse effects on patients and can be used in an effort to achieve the best potential for localizing seizure foci.

Acknowledgments

We would like to thank the clinical staff at the Texas Comprehensive Epilepsy Program—Drs. Stephen Thompson, Giridhar Kalamanagalam, Jeremy Slater, Melissa Thomas, Omotola Hope, and Sam Lhatoo—for contributing to the success of the procedures included in this study.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Tandon, MJ Rollo. Acquisition of data: Tandon, PS Rollo, MJ Rollo. Analysis and interpretation of data: Tandon, PS Rollo, Zhu, Woolnough. Drafting the article: Tandon, PS Rollo, Zhu, Woolnough. Critically revising the article: Tandon, PS Rollo, Woolnough. Approved the final version of the manuscript on behalf of all authors: Tandon. Statistical analysis: Tandon, Zhu, Woolnough. Administrative/technical/material support: PS Rollo, MJ Rollo. Study supervision: Tandon.

Supplemental Information

Videos

Video 1. https://vimeo.com/418044751.

Online-Only Content

Supplemental material is available with the online version of the article.

Supplemental Data. https://thejns.org/doi/suppl/10.3171/2020. 5.JNS20975.

Previous Presentations

Portions of this work were presented in poster form at the American Epilepsy Society Annual Meeting, Baltimore, MD, December 2019.

Correspondence

Nitin Tandon: University of Texas Health Science Center at Houston, TX. nitin.tandon@uth.tmc.edu.