Technique, Results, and Complications Related to Robot-Assisted Stereoelectroencephalography

BACKGROUND: Robot-assisted stereoelectroencephalography (SEEG) may represent a simplified, precise, and safe alternative to the more traditional SEEG techniques.

OBJECTIVE: To report our clinical experience with robotic SEEG implantation and to define its utility in the management of patients with medically refractory epilepsy.

METHODS: The prospective observational analyses included all patients with medically refractory focal epilepsy who underwent robot-assisted stereotactic placement of depth electrodes for extraoperative brain monitoring between November 2009 and May 2013. Technical nuances of the robotic implantation technique are presented, as well as an analysis of demographics, time of planning and procedure, seizure outcome, in vivo accuracy, and procedure-related complications.

RESULTS: One hundred patients underwent 101 robot-assisted SEEG procedures. Their mean age was 33.2 years. In total, 1245 depth electrodes were implanted. On average, 12.5 electrodes were implanted per patient. The time of implantation planning was 30 minutes on average (range, 15-60 minutes). The average operative time was 130 minutes (range, 45-160 minutes). In vivo accuracy (calculated in 500 trajectories) demonstrated a median entry point error of 1.2 mm (interquartile range, 0.78-1.83 mm) and a median target point error of 1.7 mm (interquartile range, 1.20-2.30 mm). Of the group of patients who underwent resective surgery (68 patients), 45 (66.2%) gained seizure freedom status. Mean follow-up was 18 months. The total complication rate was 4%.

CONCLUSION: The robotic SEEG technique and method were demonstrated to be safe, accurate, and efficient in anatomically defining the epileptogenic zone and subsequently promoting sustained seizure freedom status in patients with difficult-to-localize seizures.

KEY WORDS: Complications, Epilepsy surgery, In vivo application accuracy, Robotic surgery, Seizure outcome, Stereo-electroencephalography

The stereoelectroencephalography (SEEG) methodology enables precise recordings from deep cortical areas, multiple noncontiguous lobes, and bilateral explorations while avoiding the need for large craniotomies. As originally described by Bancaud, Talairach, and colleagues, the SEEG approach consists of a multistep and intricate method in which the Talairach stereotactic frame and the double-grid system are applied in association with telementrography, allowing the placement of multiple recording-depth electrodes with unparalleled precision and safety. Despite its extensive success, with almost 60 years of clinical use, the technical complexity involved in the placement of SEEG depth electrodes may have restricted its use in centers outside of Europe.

Benefiting from new radiological and computational innovations, a wide range of neurosurgical robotic applications, including precise stereotactic guidance (as the implantation of depth electrodes, with or without the SEEG methodology), are now available. The use of robots in stereotactic procedures may introduce several advantages to the technique, including the potential augmentation of precision and accuracy in a simplified fashion, allowing multiple trajectory options...
without the need for numerous and time-consuming frame coordinate adjustments, which could translate into fewer complications and shorter surgical times. In this prospective observational study, we describe our clinical experience with the robot-assisted SEEG method and define its utility in the management of patients with medically refractory epilepsy.

METHODS

Patient Selection
We analyzed prospectively all patients with medically refractory focal epilepsy who underwent robotic stereotactic placement of depth electrodes for extraoperative brain monitoring by using the SEEG methodology between November 2009 and May 2013. All procedures were performed with the ROSA robotic assistant device (Medtech, Montpellier, France). The present cohort and applied technique are fundamentally different from previously published series from our center, which described the conventional SEEG technique without the use of a robotic assistant device. The study was approved by the Cleveland Clinic Institutional Review Board. All surgical interventions were part of standard patient care, and no procedures were performed solely for research purposes.

All patients underwent preoperative evaluation, including scalp video-electroencephalography (V-EEG), magnetic resonance imaging (MRI), positron emission tomography, ictal single-photon emission computed tomography, and neuropsychological studies. As a result of incongruent noninvasive data or the absence of a visible lesion on MRI, recommendations for long-term implantations with SEEG methodology were made during multidisciplinary patient management conferences. SEEG electrodes were implanted according to preimplantation hypotheses of the presumed epileptogenic zones (EZs), taking into consideration the hypothetical anatomic locations of the ictal onset zones and regions of early spread of the epileptic activity.

SEEG was used if the following inclusion criteria were met: (1) the possibility of a deep-seated location of the EZ in areas such as the mesial structures of the temporal lobe, cingulate gyrus and other interhemispheric regions, posterior orbito-frontal areas, insula, and depths of sulci; (2) failure of previous subdural invasive studies to clearly outline the exact location of the seizure onset zone; and (3) the need for bihemispheric explorations for possible multifocal seizure onsets. Many of these patients were not considered optimal candidates for other methods of invasive explorations for possible multifocal seizure onsets. Many of these patients were not considered optimal candidates for other methods of invasive monitoring owing to the complexity of their epileptic syndromes. Patients with abnormal MRIs with well-demarcated lesions located in noneloquent areas and with concordant noninvasive data were not considered optimal candidates for extraoperative invasive monitoring and were excluded from this study. Similarly, patients with abnormal MRIs with lesions located in or near the eloquent brain regions were not considered optimal candidates for SEEG evaluation, undergoing subdural grid implantations (Figure 1). To avoid potential selection bias, recruitment was performed consecutively and prospectively on the basis of the above inclusion and exclusion criteria.

Robotic Implantation Technique
One day before surgery, volumetric and high-resolution preoperative MRIs (volumetric magnetization-prepared rapid-acquisition gradient-echo images, T1-weighted images; slice thickness, 1 mm; voxel size, 0.41 mm × 0.41 × 1 mm, contrasted with Multilance 0.1 mmol/kg) were obtained. DICOM (digital imaging and communications in medicine)-format images were then transferred to the robot’s native planning software. Subsequently, the anterior commissure/posterior commissure lines for each scan were manually defined, and the volumetric data sets were reformatted accordingly. Trajectories were selected to maximize sampling from superficial and deep cortical and subcortical areas within the preselcted zones of interest and were oriented orthogonally (in relation to the midsagittal plane defined by the anterior commissure/posterior commissure referential system) in the majority of cases to facilitate the anatomo-electrophysiological correlation during the extraoperative recording phase and to avoid possible trajectory shifts resulting from heavily angled entry points.

On the day of surgery, patients were placed under general anesthesia. For each patient, the head was placed supine and in a neutral position with a 3-point fixation head holder. The Leksell frame (Elekta, Stockholm, Sweden) was used as the fixation system to allow better registration and to avoid possible collisions with the robotic arm. Semiautomatic laser-based facial recognition was used in all patients to register the preoperative volumetric MRI. Only registrations with acceptable errors (<0.75 mm) were accepted and used for the implants.

Subsequently, after prepping and draping, 2-mm-diameter handheld drills (Stryker Medical, Kalamazoo, Michigan) were introduced through the robotic arm platform and used to create twist drill holes. The dura was then opened with insulated dura perforators, with monopolar cautery applied at low settings. Guiding bolts (Ad-Tech, Racine, Wisconsin; PMT Corp, Chanhassen, Minnesota) were screwed firmly into each twist hole. Finally, styles (0.8 mm in diameter) were passed gently into the parenchyma, guided by the implanted bolts, followed by the insertion of the premeasured electrodes (1.2 mm in diameter, 5 mm intercenter to center contact space; PMT Corp; Figure 2). All electrodes were implanted at the end of the procedures to optimize surgical flow and implantation efficiency. After SEEG implantation, patients were subjected to clinical

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**FIGURE 1.** Flow diagram showing patients’ selection criteria for the present study. The selection process was performed in 3 stages for the following reasons: to determine candidacy for resective epilepsy surgery (first column); to determine, from the cohort of patients who were considered candidates for epilepsy surgery, the need for extraoperative invasive evaluation (second column); and third, to determine, from the cohort of patients who required invasive monitoring, the invasive monitoring modality (third column). Patients were included and followed up prospectively if they were considered candidates for robotic stereoelectroencephalography (SEEG).
monitoring and electrographic recording of all seizure events at the epilepsy monitoring unit. A second patient management conference was then held for each patient, approximately 1 week after implantation, to discuss the results and implications of the SEEG study and to collectively decide on a plan for surgical resection. After this meeting and approximately 6 weeks after removal of the SEEG electrodes, patients underwent standard craniotomies for tailored resections of the hypothetical EZs. After recovery and discharge from hospital, all patients were followed up with regular visits (6 weeks, 6 months, and every year after resection) to document their seizure outcomes and possible late complications.

Data Analysis

The analyzed data included demographic and seizure semiology, number and location of implanted SEEG electrodes, time of planning, time of procedure, location of the EZ, type of surgical resection, application accuracy, and procedure-related complications. Complications related to the SEEG robotic procedures (up to 30 days after the surgical interventions) were classified as major or minor. A complication was considered major when it significantly changed the expected course of treatment, causing a permanent neurological deficit. Postoperative seizure outcome was measured with the use of a simplified Engel score classification: class I, seizure free (including auras); class II, significant improvement in seizures; class III, some improvement in seizures; and class IV, no improvement in seizures.

Application Accuracy Test

In vivo application accuracy was obtained by comparing the preoperatively planned trajectories, defined here by the correspondent planned entry points and the planned target points, with the final electrode trajectories extracted from postoperative computed tomography scans (0.5-mm thickness without gaps). Localization errors, which included the entry point errors (EPEs) and the target point errors (TPEs), were calculated as euclidean distances between the planned coordinates and those of the actual position of the implanted electrodes. We manually measured the errors separately on the \(x\), \(y\), and \(z\) coordinates using the ruler available in the planning software on the T1-weighted magnetization-prepared rapid-acquisition gradient-echo MRIs. Subsequently, the euclidean distances were calculated with the following formula:

\[
g = \sqrt{(x_2-x_1)^2 + (y_2-y_1)^2 + (z_2-z_1)^2}
\]
The values of EPE and TPE were calculated prospectively and consecutively from the analysis of 1000 measurements obtained from 500 consecutive trajectories extracted from 46 patients implanted in the most recent half of the series, from the time the implantation accuracy started to be calculated and collected in a prospective fashion (Figure 3).

Statistical Analyses
The raw data for each analyzed prognostic factor possibly associated with seizure freedom outcome were tested for significance ($P<.05$) with the chi-squared test with the Yates continuity correction in GraphPad Prism version 4.00 for Macintosh (GraphPad Software, San Diego, California). Paired $t$ test was applied to compare EPEs and TPEs from all trajectories.

RESULTS
One hundred patients with refractory focal epilepsy underwent 101 robot-assisted SEEG procedures. One patient was implanted twice. The mean age was 33.2 years (range, 3-64 years); 41 patients were male and 59 were female. The group included 14 pediatric patients (age range, 3-12 years). All patients had a diagnosis of refractory focal epilepsy, failing an average of 5 antiepileptic medications. In total, 1245 depth electrodes were implanted. On average, 12.5 electrodes were implanted per patient (ranging from 5-19 electrodes per patient). Right hemispheric implantations were performed in 28 procedures, left hemispheric placements in 38 procedures, and bilateral implantations in 35 procedures. Implantations involved at least 2 lobes, which included a combination of frontal, temporal, parietal, occipital, and insular lobes explorations. The MRI was considered nonlesional (after being reviewed by a board-certified neuroradiologist) in 39 patients (39%). MRI abnormalities were found in 61 patients. Twenty subtle forms of focal cortical dysplasia (type I), which included frontotemporal resection in 5 patients, frontalinsular resection in 3 patients, temporoparietal resection in 1 patient, and frontoparietal resection in 1 patient. Thirty-three patients (48.5%) underwent extratemporal resections. In the extratemporal resection group, 12 patients (17.6%) underwent parietal resections, and 2 patients (2.9%) underwent occipital resection. Multilobar resections were performed in 10 patients (14.8%), which included frontotemporal resection in 5 patients, frontoinsular resection in 3 patients, temporoparietal resection in 1 patient, and frontoparietal resection in 1 patient. Thirty-three patients (48.5%) underwent operations on the right side, and 35 patients (51.5%) underwent left hemispheric resections.

Regarding postresection histological analyses, pathological changes were found in 58 patients, and normal surgical pathology results were found in 10 patients. Pathological findings included subtle forms of focal cortical dysplasia (type I) in 41 patients, nonspecific gliosis in 11 patients, subtle forms of cortical dysplasia associated with mesial temporal sclerosis in 5 patients, and hippocampal sclerosis in 1 patient. Interestingly, no focal cortical dysplasia type II was observed in this series.

Application Accuracy
In vivo application accuracy demonstrated a median EPE of 1.2 mm (interquartile range, 0.78-1.83 mm) and a median TPE of 1.7 mm (interquartile range, 1.20-2.30 mm). The maximum EPE was 5.1 mm, and the minimum error was 0.3 mm. The maximum TPE was 7.1 mm, and the minimum error was 0.4 mm. Most of the calculated errors were in the <2-mm range group (91% for the entry point and 83% for the target point). Approximately 8% of the EPEs and 15% of the TPEs were included in the error group

\[ d[A\text{(planned position)}, B\text{(actual position)}] = \sqrt{(Ax - Bx)^2 + (Ay - By)^2 + (Az - Bz)^2} \]
of 2 to 5 mm. Only 1% of the EPEs and 2% of the TPEs were included in the group of >5-mm error. None of the intended targets or entry areas were missed because of errors in electrode trajectories. The statistical analysis demonstrated a significant difference between TPE and EPE ($P = 2.823 \times 10^{-14}$; Table 1).

Complications

In total, 4 patients (4%) developed complications, all corresponding to intracranial hematomas (2 subdural hematomas and 2 intraparenchymal hematomas). All intracranial hematomas were topographically related to the entry point of frontal- and parietal-located electrodes. Of the 4 patients with intracranial hematomas,
3 patients were asymptomatic with small-volume bleedings (<2 cm³) located in noneloquent cortical areas. No surgical interventions or changes in the standard treatment course or hospital stay were necessary. These were considered minor complications. The last patient developed an expansive intracerebral hemorrhage after electrode implantation that required surgical intervention and hematoma evacuation, resulting in poor neurological outcome without significant recovery. Consequently, the total major complication rate of the reported series is 1%. Given the total number of implanted electrodes (n = 1245), the risk of major hemorrhagic complications per electrodes was 0.08%. There were no late complications in this series.

Seizure Outcome and Statistical Analyses

From the group of patients who underwent resective surgery (68 patients), 45 (66.2%) were seizure-free (class I) and 11 (16.2%) had rare disabling seizures after surgery (class II). Seven patients (10.3%) had worthwhile improvement in seizures (class III), and 5 patients (7.3%) had no worthwhile improvement in seizures (class IV). The mean follow-up after robotic SEEG-guided resection was 18 months (range, 6-30 months).

The statistical analyses of possible predictors for seizure outcome in patients who underwent robotic SEEG-guided surgical resections are presented in Table 2. In this series, none of the studied variables (sex, side of implantation, type of resection, preoperative MRI findings and surgical pathology results) were associated with postoperative seizure control (P > .05).

Lastly, when the robot-assisted SEEG implantations were compared with our former frame-based SEEG series, the main statistical difference was related to the time of implantation; the robot-assisted implantations were 222 minutes shorter than the frame-based implantations (Table 3). Conversely, other variables were statistically similar, including the mean errors at the entry and target areas (median EPE, 1.2 mm [robotic, frameless based] vs 1.1 mm [nonrobotic, frame based]) and the complication rates (4% for the robotic, frameless-based series vs 3% for the nonrobotic, frame-based series).

**DISCUSSION**

**Key Results**

The present series represents one of the largest series of robot-assisted cranial procedures ever published. The results using the described robotic method parallels those previously published results on the utility and safety of the more conventional, nonrobotic SEEG method. Robot-assisted surgery has been performed for >30 years in different areas such as cardiac and general surgery, but its application in neurosurgery has been limited. More recently, advances in microsurgical techniques and surgical instruments dedicated to minimally invasive surgery, surgical navigation technologies, digitized imaging modalities, increased computational

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**TABLE 1. In Vivo Application Accuracy Tested in 500 Consecutive Trajectories From 46 Consecutive Stereoelectroencephalography Robotic Procedures**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Patients, n</th>
<th>Entry Point Error, n (%)</th>
<th>Target Point Error, n (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry Point Error, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 mm</td>
<td>Male</td>
<td>33</td>
<td>456 (91)</td>
<td>415 (83)</td>
<td>871</td>
</tr>
<tr>
<td>2-5 mm</td>
<td>Female</td>
<td>35</td>
<td>39 (8)</td>
<td>75 (15)</td>
<td>114</td>
</tr>
<tr>
<td>&gt;5 mm</td>
<td></td>
<td>5 (1)</td>
<td>5 (1)</td>
<td>10 (2)</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>500</td>
<td>500</td>
<td>1000</td>
<td></td>
</tr>
</tbody>
</table>

*Entry and target point errors were calculated with the Euclidean distance method.*

**TABLE 2. Statistical Association Between Predictor Variables and Seizure-Free Outcome in 68 Patients Who Underwent Robot Stereoelectroencephalography–Guided Resections**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Patients, n</th>
<th>Class I Outcome, n</th>
<th>Class I Outcome, %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>33</td>
<td>26</td>
<td>78.79</td>
<td>.5</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>35</td>
<td>24</td>
<td>68.57</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Children</td>
<td>14</td>
<td>9</td>
<td>64.29</td>
<td>.8</td>
</tr>
<tr>
<td></td>
<td>Adults</td>
<td>54</td>
<td>39</td>
<td>72.22</td>
<td></td>
</tr>
<tr>
<td>Side of implantation</td>
<td>Unilateral</td>
<td>45</td>
<td>31</td>
<td>68.89</td>
<td>.36</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>23</td>
<td>19</td>
<td>82.61</td>
<td></td>
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<tr>
<td>Pathology</td>
<td>Normal</td>
<td>11</td>
<td>6</td>
<td>54.55</td>
<td>.43</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>57</td>
<td>41</td>
<td>71.93</td>
<td></td>
</tr>
<tr>
<td>Magnetic resonance imaging</td>
<td>Normal</td>
<td>31</td>
<td>24</td>
<td>77.42</td>
<td>.53</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>37</td>
<td>25</td>
<td>67.57</td>
<td></td>
</tr>
<tr>
<td>Resection site</td>
<td>Temporal</td>
<td>29</td>
<td>22</td>
<td>75.86</td>
<td>.32</td>
</tr>
<tr>
<td></td>
<td>Extemporal</td>
<td>39</td>
<td>24</td>
<td>61.54</td>
<td></td>
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<tr>
<td>Side of resection</td>
<td>Left</td>
<td>33</td>
<td>24</td>
<td>72.73</td>
<td>.88</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>35</td>
<td>25</td>
<td>71.43</td>
<td></td>
</tr>
<tr>
<td>Previous surgery</td>
<td>Yes</td>
<td>17</td>
<td>11</td>
<td>64.71</td>
<td>.88</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>51</td>
<td>36</td>
<td>70.59</td>
<td></td>
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TABLE 3. Comparison of Frame-Based and Robot-Assisted Stereoelectroencephalography Procedures

<table>
<thead>
<tr>
<th></th>
<th>Frame-Based SEEG</th>
<th>Robot-Assisted SEEG</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures, n</td>
<td>103</td>
<td>101</td>
<td>.5</td>
</tr>
<tr>
<td>Age (average), y</td>
<td>30.9</td>
<td>33.2</td>
<td>.4</td>
</tr>
<tr>
<td>Electrodes (total), n</td>
<td>1367</td>
<td>1245</td>
<td>.1</td>
</tr>
<tr>
<td>Electrodes (average), n</td>
<td>13.3</td>
<td>12.5</td>
<td>.4</td>
</tr>
<tr>
<td>Accuracy (at entry), mm</td>
<td>1.1</td>
<td>1.2</td>
<td>.1</td>
</tr>
<tr>
<td>Morbidity, %</td>
<td>3</td>
<td>4</td>
<td>.1</td>
</tr>
<tr>
<td>Time of implantation (average), min</td>
<td>352</td>
<td>130</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

SEEG, stereoelectroencephalography.

processing power, and improvements in mechanical and electrical engineering have resulted in the incorporation of robotics into the field of neurosurgery.18,20,57-60 (Table 4). The debut of robotic neurosurgery was reported by Kwoh and colleagues19 in 1988. The authors used an industrial robot for holding and modifying the trajectory of biopsy cannulas. Six years later, Drake and coworkers18 reported the use of a similar robotic design as a retractor device for the surgical management of thalamic astrocytomas. Beginning in 1987, Benabid and colleagues18,20,57-60 initiated the development of the NeuroMate surgical robot (Renishaw, Gloucestershire, United Kingdom). NeuroMate uses preoperative image data to assist with surgical planning and a passive robotic arm to perform specific stereotactic procedures. Similarly, the ROSA system relies on preoperative images to perform image-guided surgery with great accuracy. The complex technical needs associated with the placement of SEEG electrodes make this procedure an ideal one to be executed with the robotic platform because multiple, time-consuming frame coordinate adjustments can be avoided, in addition to providing a rigid and stable platform for skull drilling. The technical utility of the robotic platform is exemplified by our study results.

The SEEG method and its original technique were developed by a team of physicians and investigators led by Jean Talairach and Jean Bancaud during the 1950s and have been established mostly by European centers in France and Italy as the method of choice for extraoperative invasive mapping in refractory focal epilepsy.3,5,14,43,50-54,61-80 The implantation strategy is individualized, with multiple stereotactic placements of intracerebral depth electrodes based on preimplantation hypotheses. The implantations take into consideration the anatomic location of the primary organization of the epileptiform activities and the hypothetical functional epileptic networks involved in the propagation of recurrent seizures.63 The hallmark of the methodology is the precise 3-dimensional recordings of brain electric signals from superficial, deep, and subcortical structures by analyzing the temporal-spatial evolution of seizures, allowing multiple noncontiguous lobe recordings and bilateral explorations while circumventing the need for large craniotomies.34,81,82

Despite its successful track record for safety and efficacy, the technique evolved minimally (with very few exceptions1) beyond its original principles and concepts. SEEG was described as a multiphase/complex method using the Talairach stereotactic frame and the double-grid system in association with teleangiography,17,68,83 which required intraoperative orthogonal x-rays and multiple days of surgical planning and imaging processing. Despite the development of novel radiological techniques and highly sophisticated image-guiding systems, the SEEG technique used in many centers today is still similar to the original technique. The technical complexity regarding the placement of SEEG depth electrodes may have contributed to its limited application in centers outside Europe. The use of surgical robots, as described here, has the potential to streamline the SEEG technique without compromising accuracy, safety, and efficacy.

Our study involving 100 patients operated on with the described technique demonstrates that the robotic SEEG procedure is precise, time-efficient, and comparable to other robotic systems. The average operative time of implantation and average accuracy that we observed are similar to what others have reported.1,2,19,30,32,44,68,83-87 This finding lends weight to the argument that robot-assisted stereotactic procedures are as accurate as other frame-based methods of neuronavigation but have the added benefit of a shorter time of implantation, especially given the multiple trajectories involved. In the comparison of the current robot-assisted SEEG implantations with our former frame-based SEEG series,5 it becomes evident that the main difference between the 2 series is related to the time of implantation: The robot-assisted implantations were approximately 3.5 hours shorter than the frame-based implantations (Table 3). Other variables were statistically similar, including the mean errors at the entry and target areas. These conclusions are preliminary, and further analyses are necessary to validate the impression that robotic-based application accuracy and frame-based application accuracy are similar. Other authors have suggested its possible superiority to frameless nonrobotic systems.1,18-21,88,89 Eljamal20,30,32 used a robotic device to insert depth electrodes for intraoperative epileptic focus, achieving an average registration accuracy of 1.4 mm compared with 2.6 mm with a frameless image-guided surgery system. Interestingly, in our measurements, in vivo application accuracy demonstrated maximum EPE and TPE of 5.1 and 7.1 mm, respectively, in a small percentage (2%) of the inserted electrodes. The outlier errors can be explained by differences in skull surfaces (mostly in curved surfaces such as the anterior temporal fossa and posterior occipital areas), multiple penetrated pial planes, previous craniotomies, and surgical resection cavities that can deviate the electrode from its original intended trajectory, but no statistical correlations were found. Nevertheless, from a clinical perspective, these errors did not compromise SEEG recordings because intended target areas were still reached in all patients. In addition, we did not observe an association between morbidity

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TABLE 4. The debut of robotic neurosurgery was reported by Kwoh and colleagues19 in 1988. The authors used an industrial robot for holding and modifying the trajectory of biopsy cannulas. Six years later, Drake and coworkers18 reported the use of a similar robotic design as a retractor device for the surgical management of thalamic astrocytomas. Beginning in 1987, Benabid and colleagues18,20,57-60 initiated the development of the NeuroMate surgical robot (Renishaw, Gloucestershire, United Kingdom). NeuroMate uses preoperative image data to assist with surgical planning and a passive robotic arm to perform specific stereotactic procedures. Similarly, the ROSA system relies on preoperative images to perform image-guided surgery with great accuracy. The complex technical needs associated with the placement of SEEG electrodes make this procedure an ideal one to be executed with the robotic platform because multiple, time-consuming frame coordinate adjustments can be avoided, in addition to providing a rigid and stable platform for skull drilling. The technical utility of the robotic platform is exemplified by our study results.

The SEEG method and its original technique were developed by a team of physicians and investigators led by Jean Talairach and Jean Bancaud during the 1950s and have been established mostly by European centers in France and Italy as the method of choice for extraoperative invasive mapping in refractory focal epilepsy.3,5,14,43,50-54,61-80 The implantation strategy is individualized, with multiple stereotactic placements of intracerebral depth electrodes based on preimplantation hypotheses. The implantations take into consideration the anatomic location of the primary organization of the epileptiform activities and the hypothetical functional epileptic networks involved in the propagation of recurrent seizures.63 The hallmark of the methodology is the precise 3-dimensional recordings of brain electric signals from superficial, deep, and subcortical structures by analyzing the temporal-spatial evolution of seizures, allowing multiple noncontiguous lobe recordings and bilateral explorations while circumventing the need for large craniotomies.34,81,82

Despite its successful track record for safety and efficacy, the technique evolved minimally (with very few exceptions1) beyond its original principles and concepts. SEEG was described as a multiphase/complex method using the Talairach stereotactic frame and the double-grid system in association with teleangiography,17,68,83 which required intraoperative orthogonal x-rays and multiple days of surgical planning and imaging processing. Despite the development of novel radiological techniques and highly sophisticated image-guiding systems, the SEEG technique used in many centers today is still similar to the original technique. The technical complexity regarding the placement of SEEG depth electrodes may have contributed to its limited application in centers outside Europe. The use of surgical robots, as described here, has the potential to streamline the SEEG technique without compromising accuracy, safety, and efficacy.

Our study involving 100 patients operated on with the described technique demonstrates that the robotic SEEG procedure is precise, time-efficient, and comparable to other robotic systems. The average operative time of implantation and average accuracy that we observed are similar to what others have reported.1,2,19,30,32,44,68,83-87 This finding lends weight to the argument that robot-assisted stereotactic procedures are as accurate as other frame-based methods of neuronavigation but have the added benefit of a shorter time of implantation, especially given the multiple trajectories involved. In the comparison of the current robot-assisted SEEG implantations with our former frame-based SEEG series,5 it becomes evident that the main difference between the 2 series is related to the time of implantation: The robot-assisted implantations were approximately 3.5 hours shorter than the frame-based implantations (Table 3). Other variables were statistically similar, including the mean errors at the entry and target areas. These conclusions are preliminary, and further analyses are necessary to validate the impression that robotic-based application accuracy and frame-based application accuracy are similar. Other authors have suggested its possible superiority to frameless nonrobotic systems.1,18-21,88,89 Eljamal20,30,32 used a robotic device to insert depth electrodes for intraoperative epileptic focus, achieving an average registration accuracy of 1.4 mm compared with 2.6 mm with a frameless image-guided surgery system. Interestingly, in our measurements, in vivo application accuracy demonstrated maximum EPE and TPE of 5.1 and 7.1 mm, respectively, in a small percentage (2%) of the inserted electrodes. The outlier errors can be explained by differences in skull surfaces (mostly in curved surfaces such as the anterior temporal fossa and posterior occipital areas), multiple penetrated pial planes, previous craniotomies, and surgical resection cavities that can deviate the electrode from its original intended trajectory, but no statistical correlations were found. Nevertheless, from a clinical perspective, these errors did not compromise SEEG recordings because intended target areas were still reached in all patients. In addition, we did not observe an association between morbidity
Interestingly, in previous literature shows that most published series related to the placement of stereotactic electrodes reported a morbidity rate ranging from 0% to 5.6%, 1,2,31,33,89,90. Spire and colleagues 31 described their experience with robotic implantation of depth electrodes in 4 patients concurrently undergoing craniotomy and placement of subdural monitoring electrodes for the evaluation of intractable epilepsy with 1 complication after subdural grid placement but no complications related to the depth electrode. We concluded that the morbidity results of the present series are compatible with other SEEG series that applied either conventional or robotic methods of stereotactic placement of depth electrodes for extraoperative mapping in patients with refractory epilepsy.

Regarding the efficacy of the method in promoting seizure-free outcome after guided resections, initial data show promising results that are compatible with our own previously published series using the more standard method of implantation; nevertheless, longer periods of follow-up are mandatory to definitively validate this conclusion. However, the initial seizure-free outcome is also comparable to outcomes in other SEEG-guided resection series published so far, ranging from 50% to 60% with similar follow-up periods. 31,5,6,89,90 Interestingly, in previous reports using different methods of invasive monitoring, variables such as normal preoperative MRI and extratemporal EZ localization are frequently associated with unfavorable seizure outcome. Conversely, McGonigal and colleagues 43 reported no such difference in a study based on SEEG recordings regarding postoperative seizure outcome between lesional and nonlesional MRI in patients who underwent SEEG-guided resections. Our own results are in agreement in that seizure outcome data between the 2 groups were statistically similar. Although the reason behind this is unclear, it is possibly due to the SEEG intrinsic feature of 3-dimensionally mapping the conceivable epileptic networks involved in the epileptic activity. In this regard, we can speculate that the SEEG method, now implemented by an accurate and reproducible robotic technique of implantation, can enhance the electrophysiological and anatomic definition of the brain areas responsible for the early generation and propagation of the pathological electric discharges, promoting more adequate outcome results in patients with difficult-to-localize seizures. This hypothesis can be definitively supported by the fact that the SEEG method may exclude potential misleading ictal and interictal recordings, possibly representing exit patterns that originate from deep or distantly located
epileptic foci. A controlled analysis comparing SEEG-guided resection with other methods of invasive monitoring is necessary to confirm this preliminary conclusion.

Limitations

Although the magnitude of the study group is likely adequate for the accuracy analysis, a larger cohort of operated patients with longer follow-up periods is mandatory to validate our seizure outcome and complication rate results. In addition, the study was not specifically designed to compare different methods of implantations. Consequently, discussions related to comparison among different methods of implantations, complications, outcomes, and accuracy are speculative in nature. A prospective case-control study is underway to more formally address these concerns.

Generalizability

The external reproduction of results, including accuracy, safety, and seizure outcome, is likely high, provided that the SEEG method, technique, and surgical indications are performed under similar conditions. The fundamental elements to achieve similar results are the multimodal and high-resolution imaging data, careful planning, adequate use of the robotic assistant device, and detailed and well-interpreted noninvasive data such as seizure semiology, scalp electroencephalography, and imaging data.

CONCLUSION

Technological developments in neuronavigation, better digitized imaging methods, and widespread use of robotized devices in different medical fields have contributed to the more systematic practice of robotic assistance in neurosurgery. The intrinsic features of the SEEG methodology and technique, with its need for optimal stereotactic accuracy, applied in multiple trajectories, make it the ideal procedure for the routine application of this novel concept in the field of neurosurgery. The described robotic technique was demonstrated to be safe, accurate, and efficient in anatomically defining the EZ, supporting its feasibility, minimal invasiveness, and reliability. Although we acknowledge that further studies are needed, the initial results are encouraging, possibly predicting to some extent the future of this technology in the field of epilepsy surgery.

Disclosure

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

REFERENCES

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COMMENT

Stereoelectroencephalography (SEEG) is gaining popularity, spreading out of France and Italy. Since Bancard1 first reported the electric activity of an ictal cortical onset by means of intracerebral electrodes in 1959, thousands of patients have benefited from this invasive monitoring methodology. In March 2009, 50 years later, colleagues at the Cleveland Clinic started the first comprehensive SEEG program in the United States.2 To date, they have performed >200 procedures, introducing robotic assistance in their workflow in November 2009. Kwoh et al performed in 1985 the first robot-assisted stereotactic procedure, a brain biopsy, with the PUMA 200 system. Despite initial successes, the project was ended because of safety concerns related to the operation of an industry-derived system in an operating theatre. In the mid-1980s, Benabid and coworkers3 in Grenoble developed the first device dedicated to neurosurgical applications, performing a robot-assisted cerebral biopsy in March 1989. In the following years, Benabid and colleagues3,4,5 foresaw several potential applications for such systems, and the history of the last 2 decades testifies that they were right. Passive robotic arms have been used successfully for several other stereotactic clinical applications such as SEEG, deep brain stimulation, and neuroendoscopy. Throughout the years, the pioneering work of the Gre- noble group demonstrated the value of such image-guided systems in assisting the neurosurgeon with accurate planning and positioning of the end effector, also allowing easy simulation and training. Other groups have subsequently reported such applications with similar systems. However, only the use of robots specifically developed for neurosurgical purposes has been consolidated in the last years. Industry-derived systems have been abandoned.

The number of intracerebral electrodes implanted in an SEEG procedure is generally high, often >10. Therefore, robotic assistants are ideal for such a purpose. Robots are precise and accurate devices, ideal for repetitive and constant-quality tasks, are able to move and keep steady for a long time, and are free of tremor and fatigue. Our group reported usefulness, safety, and high accuracy of robotic assistance in a large number of SEEG implantations performed at Niguarda Hospital, Milan, Italy.8,9,11 Colleagues at Cleveland Clinic reported in the present study comparable results on accuracy and safety, with the number of complications definitely smaller than with subdural grids. Their comparison with a historical control group provided evidence that surgical time was greatly reduced thanks to the use of the robotic assistant, maintaining the same accuracy of a traditional stereotactic system. Considering the number of trajectory per procedure, we can also speculate that the probability of human error is decreased because it is not necessary to manually adjust the frame coordinates for each trajectory. Summing the Cleveland and Milan experience, about 300 hundreds fully robotic SEEG procedures have been performed successfully and safely.

The results for seizures were also excellent, comparable to most SEEG published series. However, it must be noted that in this case series the number of patients who did not undergo resective surgery is higher than usual. Considering also the rate of subjects who underwent a unilobar temporal resection, it is advisable that the indications for SEEG be refined in the future.
Summarizing, the authors should be congratulated because their findings highlighted once more the helpfulness of a robotic system and the invaluable usefulness of SEEG in the definition of the epileptogenic zone in the most challenging cases of drug-resistant epilepsy.

Francesco Cardinale
Milan, Italy