Chapter 6
Robotics in Epilepsy Surgery

Hussam Abou-Al-Shaar, Arka N. Mallela, Danielle Corson, James Sweat, and Jorge Alvaro González Martínez

Introduction

The practice of epilepsy surgery has significantly changed in the last decade although fundamentals and core concepts have remained largely unchanged. With recent radiological and computational innovations, modern techniques, including the use of robotic devices, are increasingly utilized in many surgical fields. In this sense, epilepsy surgery is not an exception [1–17]. At present, assistant robotic devices have been mainly applied for stereotactic localization and placement of recording electrodes or different types of probes that require precise placement, as in stereoelectroencephalography (SEEG), deep brain stimulation (DBS), responsive nerve stimulators (RNS), and laser interstitial thermal therapy (LITT) procedures. The application of robotic devices has reshaped the practice of epilepsy surgery, bringing relevant advantages in relation to the more standard stereotactic frame-based methods. Namely, robots have the potential to increase the accuracy and the capability of performing numerous insertion trajectories without the need for time-consuming coordinate adjustments. These technical aspects can potentially translate to relevant clinical advantages, creating reproducible surgical results and a more acceptable margin of error in the implantations, reducing peri-operative complications and overall operative time [2, 5, 9, 17].

H. Abou-Al-Shaar · A. N. Mallela · D. Corson · J. Sweat · J. A. González Martínez (✉)
Department of Neurological Surgery and Epilepsy Center, University of Pittsburgh Medical Center, Pittsburgh, PA, USA
e-mail: aboualshaarh@upmc.edu; mallelaan@upmc.edu; wagnerdm@upmc.edu; sweatj@upmc.edu; gonzalezjo@upmc.edu

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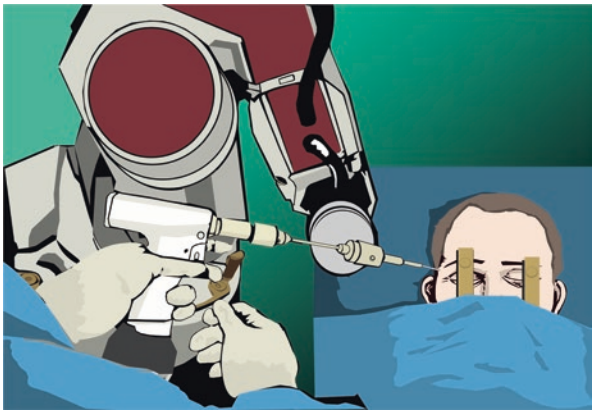

Fig. 6.1 Artist representation of Robotic SEEG demonstrating the robotic device incorporated into the epilepsy surgery armamentarium

One of the most widespread applications of robotics in epilepsy surgery is the stereotactic placement of depth electrodes through the SEEG method (Fig. 6.1) [18]. Briefly, the SEEG is a presurgical invasive monitoring method that allows precise intracortical recordings in multiple non-contiguous lobes, within the three-dimension stereotaxic space, following a highly formulated hypotheses of implantation that seeks to understand the spatiotemporal organization of the epileptiform activity. In many centers, mostly outside Europe, the method represents a shift in the diagnostic and treatment paradigms as compared to the practice of invasive monitoring through the subdural implantation technique. Among other advantages, the avoidance of large craniotomies and their related complications are clear benefits of SEEG procedures [5, 11, 17, 19–31].

The SEEG stereotaxic method and related stereotactic technique were originally developed and described by Jean Talairach and Jean Bancaud. In the initial implantations by Tailarach and Bancaud, and still utilized in some surgical centers, stereotactic frames and the double grid system, in association with teleangiography, were used as the main instruments for precisely implanting the depth electrodes [32–37]. Despite its long-reported clinical successful application, we could speculate that the technical complexity regarding the placement of SEEG depth electrodes using conventional stereotactic frames might have contributed to the limited and late widespread clinical application in centers outside France and Italy. The multiple steps procedures, the need for multiple coordinate adjustments and verifications, and the complexity of imaging fusion are examples of how technical challenges associated with the placement of depth electrodes might have delayed the more general application of this method. The availability of modern robotic devices, with multiples advantages related to versatility, practicality, and precision, was an important driving force in the utilization of the SEEG method in centers outside Europe. Over the past decade, there has been an exponential increase in robotic SEEG procedures in the United States and this may be related, among other factors, to the availability of robotic devices [18].

Robotic SEEG

SEEG Planning

It is important to note that the basic stereotaxic principles related to conventional (non-robotic) and robotic implantations are similar. The development of the SEEG robotic implantation plan demands a clear formulation of the specific anatomo-electro-functional hypotheses to be tested [38–42]. Similar to conventional SEEG, the hypotheses are typically generated during multidisciplinary patient management conferences (PMCs) based on the results of various non-invasive evaluations that include semiology, scalp EEG, imaging, neuropsychology, and other types of non-invasive information. In general sense, SEEG depth electrode placements are designed to sample the anatomic lesion (if identified), potential structure(s) related to the ictal onset, and possible pathway(s) of early and late propagation of epileptiform activity. The entry, intermediate points of interest, and targets are reached using commercially available depth electrodes in various lengths and variable number of contacts, depending on the specific brain region of interest to be explored. Depth electrodes are inserted using orthogonal/semiorthogonal or oblique/semi-oblique orientations, allowing intracranial recording from lateral, intermediate, and/or deep cortical and subcortical structures in a three-dimensional (3D) arrangement, thus accounting for the dynamic, spatiotemporal organization of the epileptic discharges (Fig. 6.2). It is fundamentally important to separate the SEEG method (a stereotaxic method of seizure localization) from techniques related to the implantation of depth electrodes (a stereotactic technique: frame-based, frameless-based, robotic or conventional).

The protocol and procedures related to SEEG robotic implantation will vary from center to center, but the fundamental principles of explorations and interpretation of SEEG recordings should remain similar, regardless of the applied technique. Specifically, at our center, the discussions related to the hypotheses of implantation and the potential location of electrodes are carried out during multidisciplinary patient management conferences, which take place days or weeks before the implantation. The conclusions of the discussions are documented in the patient's medical record, including the hypotheses of implantation and the possible location of electrodes. The electrodes are then represented in the Talairach stereotactic space as a common stereotactic coordinate system, allowing the precise translation of the original implantation map to the robot stereotactic software (Fig. 6.2). Volumetric preoperative magnetic resonance images (T1, contrasted with Gadolinium contrast, e.g., Multihance®—0.1 mmol/kg) are obtained the day before surgery, DICOM format images are digitally transferred to robot's native planning software, and 3D volumetric reconstructions are generated (axial, coronal, and sagittal) and reformatted based on the topographic location of the anterior commissure (AC)-posterior commissure (PC) line. Trajectories are created to maximize sampling from

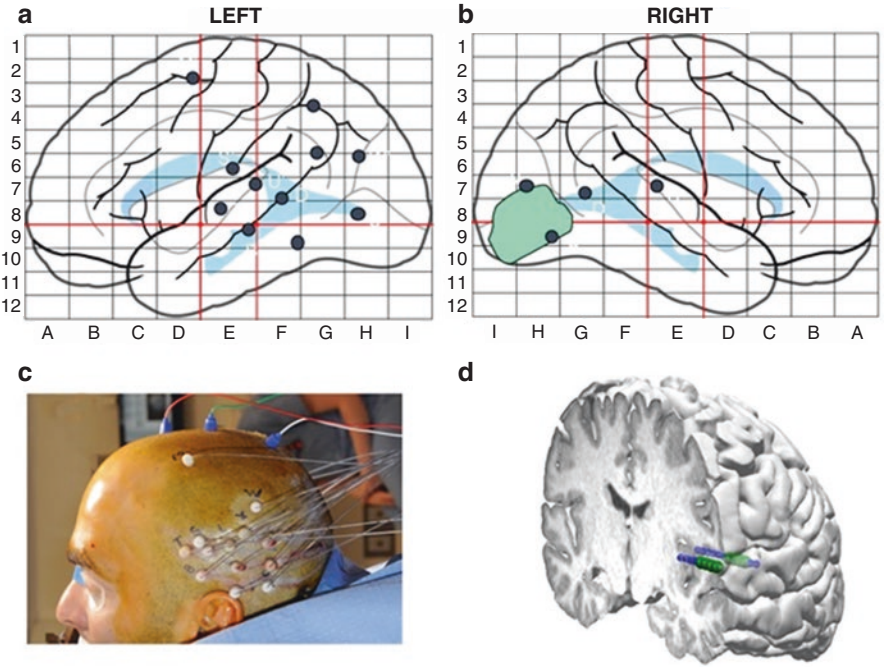

Fig. 6.2 SEEG planning and anatomical representation in Robotic SEEG. (**a**) and (**b**) illustrate the SEEG planning before the implantation. In this patient, we demonstrate the plan for bilateral SEEG implantation in temporal-occipital regions. The green area in the (**b**) panel represents a possible lesion observed on preoperative MRI. (**c**) illustrates the intraoperative aspect of robotic SEEG implantation. (**d**) depicts the three-dimensional representation of electrodes (blue) in the superior temporal gyrus on the left hemisphere. The green circles represent the areas where ictal recordings demonstrated the onset on the epileptiform activity

superficial and deep cortical and subcortical areas within the pre-selected zones of interest. The trajectories are oriented orthogonally (or semi-orthogonally) in the majority of cases to facilitate the anatomo-electrophysiological correlation during the extra-operative recording phase and to avoid possible trajectory shifts due to excessive angled entry points. All trajectories are evaluated for safety and target accuracy in their individual reconstructed planes (axial, sagittal, and coronal), and any trajectory that appears to compromise vascular structures is adjusted appropriately without affecting sampling from the areas of interest (Fig. 6.3). A set working distance of 200 mm from the drilling platform to the target is initially utilized for each trajectory as starting point, later adjusted in order to maximally reduce the working distance and consequently increase the implantation accuracy. The overall implantation schemas are analyzed using the 3D cranial reconstruction capabilities, and external trajectory positions are examined for any entry sites that would be prohibitively close (less than 1.5 cm distance) at the skin level.

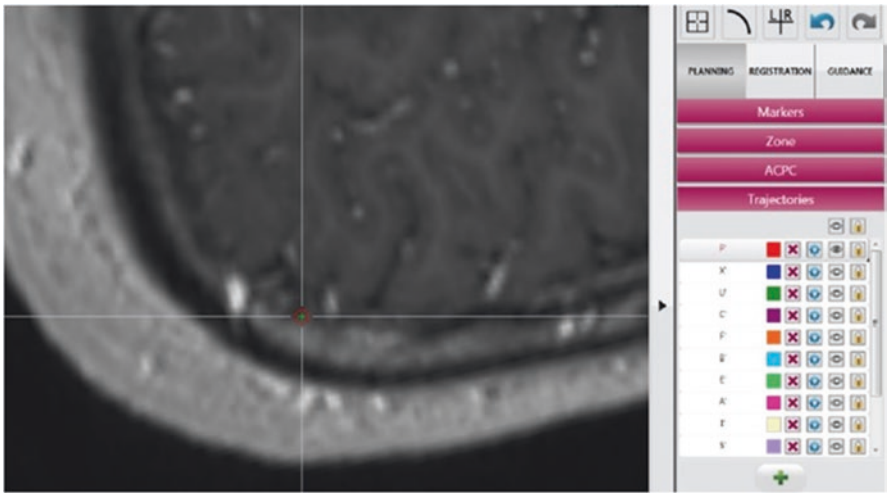

Fig. 6.3 Aspect of robotic SEEG planning using the robotic device native software. The picture illustrates that the entry point is in the preoperative contrasted MRI. Note the absence of vascular structures at the entry point location

The Surgical Implantation

The following description is related to the implantation technique applied to ROSA robotic system (Zimmer Biomet). Initially, patients undergo general anesthesia. For each patient, the head is placed into a three-point fixation head holder. The robot is then positioned such that the working distance (distance between the base of the robotic arm and the midpoint of the cranium) is fixed and approximately 70 cm. The robot is locked into position, and the head holder device is secured to the robot. No additional position adjustments are made to the operating table or to the robot during the implantation procedure. The operating table bed control is disconnected to prevent inadvertent movements of the patient. After positioning and securing the patient to the robot, image registration takes place. For SEEG procedures, we apply semi-automatic laser based facial recognition or fiducial-based registration (Fig. 6.4). Accuracy of the registration process is then confirmed by correlating additional independently chosen surface landmarks with the registered MRI. If calculated error is higher than 2 mm, the registration process is repeated, until an optimal registration accuracy is reached.

After prepping, draping, and trajectory confirmation, the arm movement is initiated using a foot pedal. A 2 mm diameter handheld drill is introduced through the platform and used to create a small opening in the skin and then skull, enough to support the guiding bolt. The dura is opened with an insulated dura perforator and monopolar cautery at low settings. Guiding bolts are screwed into the skull firmly,

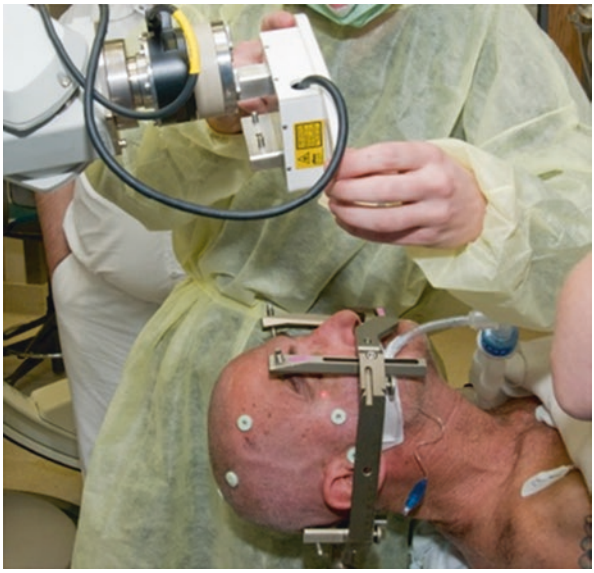

Fig. 6.4 Robotic laser registration in SEEG procedure

and the distance from drilling platform to the retaining bolt is measured. This process is repeated for each trajectory. A small stylet (2 mm in diameter) is then set to the previously recorded electrode distance. The stylet is passed gently into the parenchyma, guided by the implantation bolt, followed immediately by the insertion of the pre-measured electrode.

After implantation of all electrodes, the patient is removed from the fixation device. Fluoroscopy is then utilized in the AP plane to confirm the general accuracy of implanted electrode trajectories. A postimplantation volumetric computed tomography (CT) scan of the brain without contrast, with 1 mm cuts, is obtained for each patient. Following SEEG implantation, patients are subjected to clinical monitoring and electrographic recording of all seizure events at the epilepsy monitoring unit [43].

Results of SEEG Robotic Implantations

In a recent report, the authors analyzed a large series of patients with medically refractory focal epilepsy who underwent robotic stereotactic placement of depth electrodes for extraoperative brain monitoring using the SEEG technique [43]. The analyzed data included demographic and seizure semiology, number and location of implanted SEEG electrodes, time of planning, time of procedure, location of the epileptogenic zone, type of surgical resection, application accuracy, and procedure-related complications. Postoperative seizure outcome was measured using the Engel classification [44]. In total, one hundred patients with refractory focal epilepsy

underwent 101 robotic-assisted SEEG procedures. All procedures were completed without cancellations due to hardware or software malfunctioning. The time for planning was 30 min in average (ranging from 15 to 60 min). The average operative time was 130 min (range from 45 to 160 min). Analyses of the robot-assisted SEEG recordings resulted in hypothetical localization of the epileptogenic zone in 97 patients (97%). Sixty-eight patients underwent surgical resection guided by robot-assisted SEEG evaluations, corresponding to 70.1% of the patients with localizable seizures.

In vivo application accuracy, tested in 500 consecutive trajectories, demonstrated the mean entry point error of 1.38 mm (±0.8 mm) and the mean target point error of 2.31 mm (±0.9 mm). Despite the tendency of higher target point errors when compared to entry point errors, statistical analyses failed to demonstrate a statistically significant difference. Regarding the occurrence of adverse events, the authors reported a total of 4 patients (4%) with surgical complications related to intracranial bleeding (2 subdural hematomas and 2 intraparenchymal hematomas). All events of intracranial bleeding were 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 bleeds (<2 cm^3) located in non-eloquent cortical areas. These were considered minor complications, and no surgical intervention or changes in the standard treatment course or hospital stay were necessary. The major complication rate of the reported series was 1%. Given the total number of implanted electrodes (n = 1245), the risk of major hemorrhagic complication per electrodes was 0.08%. Regarding seizure outcome reported in the series, the mean follow-up after robotic SEEG-guided resection was 18 months (ranging from 6 to 30 months). From the group of patients who underwent resective surgery (68 patients), 45 (66.2%) had class I seizure-free outcome postoperatively at last follow-up 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 authors concluded that the results using the reported robotic method parallel previous reports regarding the utility and safety of the traditional SEEG method in the treatment of patients with medically refractory and difficult to localize seizures. This demonstrates that the robotic SEEG method is a reliable, safe, simplified, and time-efficient alternative to the more conventional methods of SEEG implantation. Various studies have also reported similar results and conclusions demonstrating that robotic-assisted stereotactic procedures are safe, accurate, efficient, and comparable to frame-based devices [11, 14, 25, 32, 43, 45].

Reports describing and analyzing comparisons between robotic versus conventional depth electrodes implantations are sparse and a controversial topic. Authors advocating robotic implantation have described its possible superiority to frameless non-robotic systems, but a “head-to-head” comparison is still missing. Eljamel and colleagues [46] have used a robotic device to insert depth electrodes for intraoperative epileptic focus, achieving an average registration accuracy of 1.4 mm compared to 2.6 mm with an image-guided surgery system. Among several factors, the rigid

and stable platform for skull drilling provided by robotic devices may have contributed to the difference in accuracy between these two techniques.

Beyond the SEEG method and technique, there are multiple reports of robotics applications in other areas of epilepsy and functional neurosurgery. In particular, there has been novel and innovative use of these technologies in ablative procedures such as MR-guided laser interstitial thermal therapy (MRgLITT or LITT) or radiofrequency ablations, in neuromodulation procedures such as responsive neurostimulation (RNS), and in deep brain stimulation (DBS). We detail the further robotic application in the field of epilepsy surgery in the subsequent sections.

Robotic Ablative Procedures

Stereotactic ablative procedures require the accurate placement of an ablative probe (for laser or radiofrequency procedures) into a specific target previously defined in stereotactic space, often determined by prior SEEG exploration or by MRI visible lesions that are thought to be the epileptogenic zone. As such, robots have two immediate roles: first, for the accurate stereotactic placement of the ablative device, and second, the steerable control of the inserted ablative probe. Previous authors have successfully demonstrated the ablation of epileptogenic periventricular nodular heterotopias in patients with medically resistant epilepsy [47]. After appropriate preoperative imaging, the authors utilized the ROSA® system to accurately guide the placement of the laser catheter (Visualase, Medtronic, Dublin, Ireland) in conjunction with intraoperative MRI. In this report, there were no complications following the ablation. In a similar method, other authors utilized the ROSA® system to guide the placement of a radiofrequency ablation catheter in 5 patients (ages 6 months to 13 years) with hypothalamic hamartomas and consequent gelastic seizures [48]. Four of five patients had grade I seizure outcome, and there were no permanent complications.

Robotic Placement of Responsive Neurostimulation Electrodes

Responsive neurostimulation (RNS) (NeuroPace Inc., Mountain View, CA) is an alternative to ablative therapies for medically refractory focal epilepsy. RNS can detect epileptiform patterns and delivers electrical stimulation along two stereotactically implanted electrodes to terminate seizures. As with other epilepsy implantation procedures, accurate placement of the electrodes is paramount. As such, robotic stereotaxy is a powerful surgical adjunct for RNS implantation (Fig. 6.5). McGovern and colleagues [9] demonstrated robotic implantation of RNS electrodes in 12

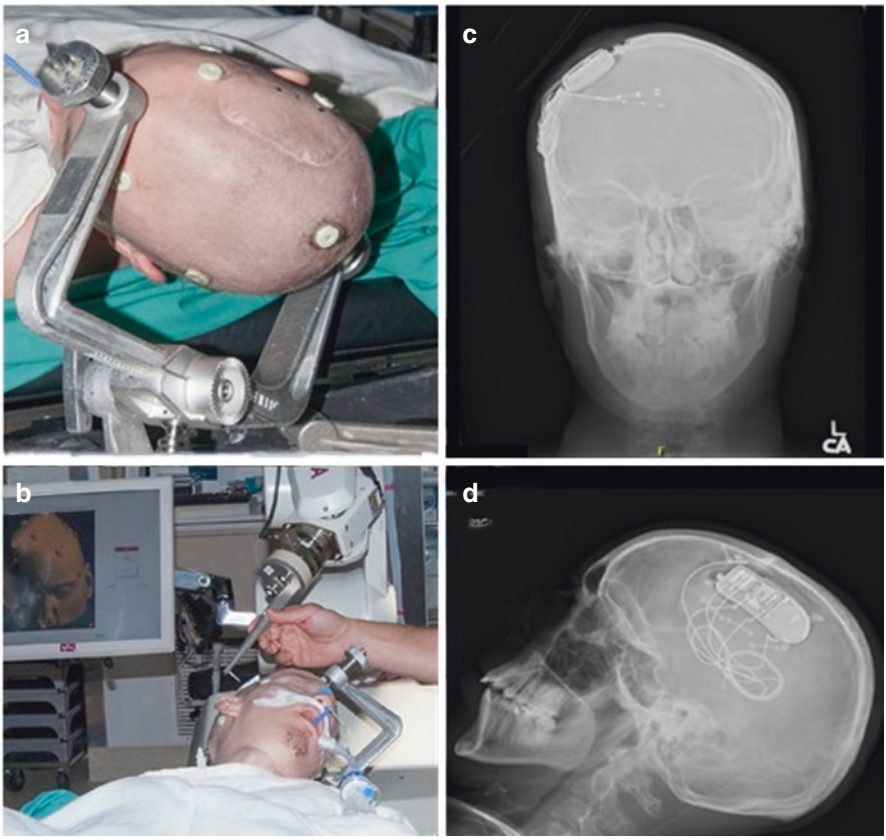

Fig. 6.5 Robotic implantation of response neuro stimulation device. (**a**) Head position using Mayfield head holder. (**b**) Robotic registration using scalp fiducials. Panels (**c**) and (**d**) showing AP and lateral postimplantation RNS device X-rays using the robotic technique

patients, with an overall seizure reduction rate of approximately 40% at 2 years. Notably, 10 of the 12 patients had implantation in temporal lobe structures, with the other two in orbitofrontal cortex and premotor cortex. Similarly, Chan et al. demonstrated successful robotic implantation of RNS in eight patients with mesial temporal lobe epilepsy. Four patients had one-year follow-up, of which one had a grade I outcome and 2 had grade II outcomes. Finally, Tran and colleagues have recently reported ROSA-based RNS implantation in 16 patients. At 1-year follow-up of 8 patients, there was an average of 90% seizure reduction [49]. There is demonstrably increasing usage of robotic stereotaxy in RNS, but further studies will be required to understand the benefits in terms of electrode accuracy, operative efficiency, and seizure freedom.

Conclusions

Stereotactic robots can precisely guide the placement of electrodes and laser probes in 3D space and accurately perform multiple stereotactic trajectories using a frameless setup with adequate precision and in a short period of time. These capabilities avoid the need for multiple, time-consuming frame coordinate adjustments, making the procedures less susceptible for human errors and consequently complications. These advantages suggest that surgical robots are an ideal platform for the placement of SEEG electrodes. Other reports related to DBS, RNS, and LITT procedures using robotic capabilities have been described, highlighting the feasibility and similar advantages in comparison with the SEEG robotic [9, 50, 51].

Concerning safety, the SEEG robotic technique has been demonstrated to be a safe technique, with major morbidity rate of 1% compatible with other SEEG series that applied more conventional stereotactic guidance techniques. Most of the published series reported a morbidity rate ranging from 0 to 5.6% [1, 17, 23, 43]. Spire and colleagues [52] described their experience with robotic implantation of depth electrodes in four patients concurrently undergoing craniotomy and placement of subdural monitoring electrodes for the evaluation of intractable epilepsy with one complication after subdural grid placement but no complication related to depth electrode implantation. By obtaining compatible results with our larger series, the authors also believed that the SEEG system allows the safe and accurate placement of depth electrodes in an efficient manner while obviating the need of reposition the patient or removing the stereotactic frame. The main disadvantage of robotic surgery is its initial cost.

Technological developments in imaging guidance, digital imaging methods, and the more widely use of robotized devices in different medical fields have contributed to the recent and progressive systematic application of robotic surgery in neurosurgery. This statement is specifically relevant in epilepsy surgery and particularly relevant for the SEEG method. The intrinsic features of the SEEG method and technique, with its absolute necessity for high accuracy in multiple trajectories, provide the ideal clinical scenario for the routine application of robotics. The robotic technique is demonstrated to be safe, accurate, and efficient in anatomically defining the epileptogenic zone, proving its feasibility, minimal invasiveness, and reliability, without compromising efficiency. Although further studies are needed, the initial promising results are encouraging and possibly predictive of the further widespread application of this technology in the field of epilepsy surgery as well as in other neurosurgery subspecialties in the near future.

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