Stereoelectroencephalography Implantation Using Frameless Neuronavigation and Varioguide: Prospective Analysis of Accuracy and Safety in a Case Series of 11 Patients

Vincent Joris[1], José Geraldo Ribeiro-Vaz[1], Patrice Finet[1], Riëm El Tahry[2], Lior M. Elkaim[3], Christian Raftopoulos[1], Susana Ferrao-Santos[2]

■ BACKGROUND: **Stereoencephalography (SEEG) is becoming a widespread diagnostic procedure for drug-resistant epilepsy investigation. Techniques include frame-based and robot-assisted implantation, and more recently, frameless neuronavigated systems (FNSs). Despite its recent use, the accuracy and safety of FNS are still under investigation.**

■ OBJECTIVE: **To assess in a prospective study the accuracy and safety of a specific FNS use for SEEG implantation.**

■ METHODS: **Twelve patients who underwent SEEG implantation using FNS (Varioguide [Brainlab]) were included in this study. Data were collected prospectively and included demographic data, postoperative complications, functional results, and implantation characteristics (i.e., duration and number of electrodes). Further analysis included accuracy at entry point and target using measurements of the euclidean distance between planned and actual trajectories.**

■ RESULTS: **Eleven patients underwent SEEG-FNS implantation from May 2019 to March 2020. One patient did not undergo surgery because of a bleeding disorder. The mean target deviation was 4.06 mm, and mean entry point deviation was 4.2 mm, with insular electrodes significantly more deviated. Results excluding insular electrodes showed a mean target deviation of 3.66 mm and a mean entry point deviation of 3.77 mm. No severe complications occurred; a few mild to moderate adverse events were reported (1 superficial infection, 1 seizure cluster, and 3 transient neurologic impairments). The mean implantation duration by electrodes was 18.5 minutes.**

■ CONCLUSIONS: **Implantation of depth electrodes for SEEG using FNS seems to be safe, but larger prospective studies are needed to validate these results. Accuracy is sufficient for noninsular trajectories but warrant caution for insular trajectories with statistically significantly less accuracy.**

INTRODUCTION

The use of intracranial electroencephalography (EEG) in the workup of patients with pharmacoresistant epilepsy has become a gold standard in many centers treating epilepsy.[1] When noninvasive evaluation with magnetic resonance imaging (MRI) and surface EEG are insufficient to identify the epileptogenic focus, implantation of intracranial electrodes is sometimes necessary using subdural grids or depth electrodes.[1-3] Over the past decade, the use of depth electrodes implanted percutaneously, so-called stereoencephalography (SEEG),[4] has gained popularity, notably with the appearance of surgical robot.

There have been several major advances in SEEG since Talairach et al.[5] first described the technique, perhaps most notably with the

Key words
- Case series
- Pharmacoresistant epilepsy
- Safety
- Stereoencephalography

Abbreviations and Acronyms
CT: Computed tomography
EEG: Electroencephalography
FNS: Frameless neuronavigated system
MRI: Magnetic resonance imaging
SEEG: Stereoencephalography
SOZ: Seizure onset zone

From the Departments of [1]Neurosurgery and [2]Neurology, Cliniques Universitaires St-Luc, Woluwe-St-Lambert, Belgium; and [3]Division of Neurology and Neurosurgery, McGill University, McGill University Health Center, Montreal, Quebec, Canada

To whom correspondence should be addressed: Vincent Joris, M.D. [E-mail: vincent.j.joris@saintluc.uclouvain.be]

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use of robot or neuronavigational systems. The accuracy and safety of frame-based or robot-assisted SEEG have been well described, including in several meta-analyses.[6-13] The accuracy at target is an estimated 1.9 mm with a frame-based technique[11] and an estimated 1.7 mm with a robot-assisted technique.[7] Complication rates vary but have been estimated at 1.3% with frame-based and robot-assisted SEEG, with the most concerning complication being hemorrhage.[6] The safety and efficacy of implantation of SEEG with a frameless neuronavigated system (FNS), remains under investigation.[14-17] Accuracy at target ranges between 2.47 mm[18] and 11.8 mm[19]; hematoma is (to our knowledge) unfrequently reported.[14-26]

Our center has recently shifted from an open to a percutaneous FNS implantation assisted with the Varioguide (Brainlab, Munich, Germany). This study aims to assess the accuracy and safety of this technique in 11 consecutive patients implanted with 94 electrodes.

METHODS

Patient Population

This observational study was approved by our institution's hospital ethics committee, and written informed consent was obtained from all patients and/or parents. Data were collected prospectively on 11 consecutive patients with drug-resistant epilepsy from May 2019 to March 2020. All patients underwent comprehensive neurologic assessment, including neurologic examination, 3T magnetic resonance imaging (MRI), fluorodeoxyglucose positron emission tomography, video EEG monitoring, and neuropsychological testing. One patient was excluded because of a diagnosis of bleeding disorder made during preoperative workup. Patients were allocated a study number.

Preoperative Planning

The location of electrodes was planned during a multidisciplinary meeting and relied on preoperative data to identify the most likely site of the epileptogenic focus. Planning of implantation was defined on an anatomic MRI (T1-weighted image or fluid-attenuated inversion recovery–weighted image in case of existing lesion). Insular electrodes were planned with a vertical trajectory (and not transopercular) to avoid sylvian fissure vessels. Preoperatively, T1 MRI with contrast (angio-MRI) was obtained to identify venous anatomy, and a computed tomography (CT) scan with contrast (angio-CT) was obtained to identify arterial anatomy. Between 6 and 7 skin fiducials (3 on the forefront and 3 or 4 on the side of implantation, more for bilateral implantation) were placed for the neuronavigation before imaging. The implantation was then planned on the neuronavigation system (Iplannet [Brainlab]) with a fusion of angio-MR, angio-CT, and anatomic magnetic resonance. The trajectory was reassessed as needed by changing the entry point but keeping the target to avoid vascular structures (no systematic margins were applied). Imaging and neuronavigation planning were performed the day before surgery except in children who needed general anesthesia (to avoid motion), in which case both were performed on the day of the surgery.

Surgical Implantation

Implantation was performed by a senior neurosurgeon and senior resident (postgraduate year 6). All implantations were performed under general anesthesia. During the implantation, the head was turned at 90° and fixed in a Mayfield clamp. Coregistration of neuronavigation was then performed using skin fiducials. If the measurement accuracy was unsatisfactory (i.e., obvious deviation when controlling for skin landmarks), coregistration was corrected or repeated. Hair was shaved in a small area around the implantation site (<1 cm²). The implantation procedure used DIXI implantation material (DIXI, Besançon, France) and the Varioguide with an adapted technique from the one suggested by Budke et al.[14] The accepted inaccuracy was <0.3° in each freedom angle and <0.3 mm in translation. If a new entry site was needed because of conflict with other electrodes, the entry site could be replanned during surgery. Data could not be registered for further analysis in such cases because the newly planned trajectory was not recorded in the software.

After the Varioguide was in position, the channel was used to hold the different instruments needed for the implantation. The details of implantation are described elsewhere.[14] A skin puncture was made before burr hole and dural coagulation. Subsequently, the bolt was implanted, with the length dependent on the thickness of the patient's skin. The accuracy of bolt implantation was assessed in real time, and the Varioguide was adjusted as needed. After the bolt was implanted, the Varioguide was removed and the electrode length was calculated with a neuronavigated pointer. A probe was then inserted at the defined length, followed by electrode insertion through the bolt. After the implantation of all electrodes on 1 side, the head was turned, and the process was repeated (including coregistration) if bilateral implantation was necessary. MRI was performed postoperatively to assess electrode position and assess for acute complications. **Figure 1** shows some of the key steps of implantation.

The distance between the planned electrode and the real electrode was then measured on the neuronavigation system. The euclidean distance was measured using X, Y, Z coordinates for each electrode at target and the skull-entry point (**Figure 2**) using the formula $\sqrt{(Xa - Xb)^2 + (Ya - Yb)^2 + (Za - Zb)^2}$, a being the planned trajectory and b being the real trajectory. The angles of penetration of the skull (coronal and anteroposterior) were also analyzed. We defined the arc angle as the angle formed between the entry point and the vertex as measured from the skull base (**Figure 3**).

Electrodes caused a magnetic artifact, which needed an approximation of target location for correction (**Figure 4**). The fixation of 1 electrode in 1 patient was not possible and resulted in a loose bolt. However, because the inaccuracy of the trajectory of this electrode is independent of the neuronavigation method, this electrode was not considered in the accuracy measurement. Electrodes that missed the intended target (i.e., no contact of the electrodes with the targeted white matter) were considered as inaccurately positioned.

Postoperative Data

Acute complications were defined as occurring during the first 24 hours after implantation or electrode removal. Adverse events were defined as occurring after the first 24 hours and until the most recent follow-up, at post-SEEG visit or after at least 1 month after electrode removal. Adverse events were subdivided into mild

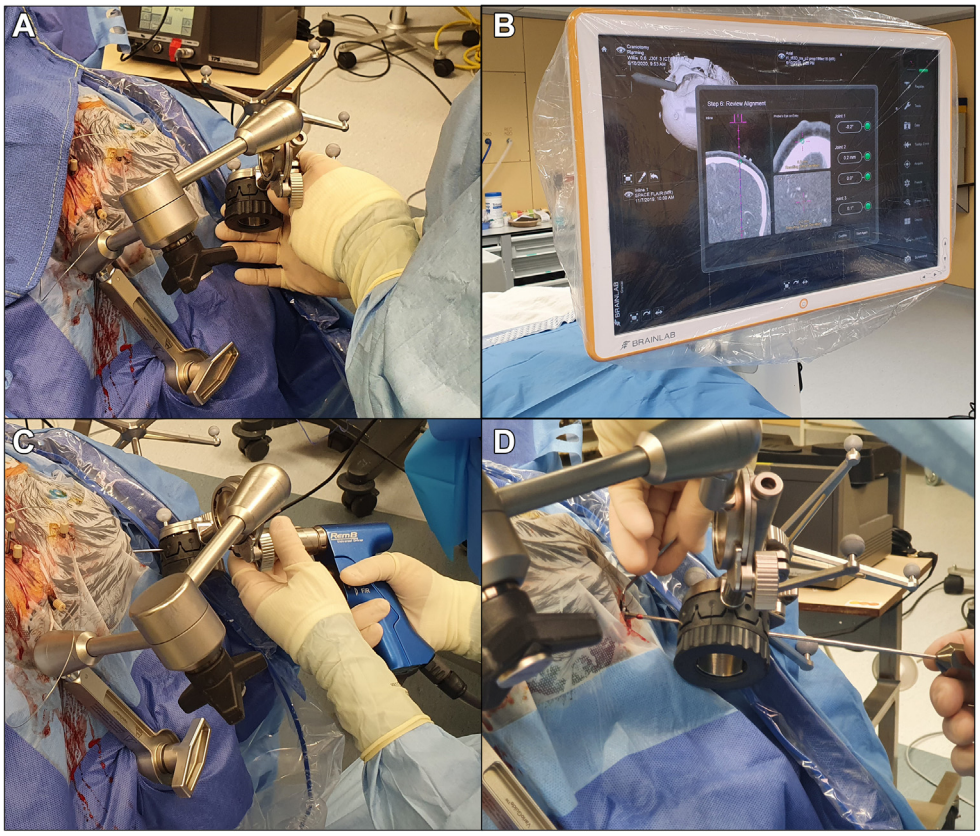

Figure 1. Key steps of the implantation. The Varioguide is positioned in the correct trajectory (**A**) using the 3 joints with feedback of inaccuracy given by the Brainlab Station (**B**). After skin puncture, the skull is drilled through the Varioguide (**C**) and the bolt is implanted in the same way (**D**). Afterward, the desired length of electrode is measured using the pointer and the electrode is implanted (not shown).

(no clinical repercussion), moderate (transient clinical symptoms without permanent sequelae), or serious (needing reoperation or associated with permanent sequelae).

The clinical yield of SEEG was also qualitatively appraised, by defining cases in which results allowed a full localization of the seizure onset zone (SOZ), versus a partial localization or cases in which results were nonlocalizing.

Literature Review

We queried the PubMed database with the term "SEEG" [AND] "accuracy." All abstracts were screened and only series using the FNS technique were further analyzed to extract accuracy and safety data on those techniques.

Statistical Analysis

All statistical analyses were conducted in R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) and X Quartz version 2.7.11 (The X Window System, X.org foundation, Portland, Oregon, USA). Shapiro-Wilk normality tests were used. Simple linear and multiple regressions (1-way and 2-way analysis of variance) were performed to estimate the association between quantitative variables. The quality of the statistical models was evaluated using the R^2 value. A P value ≤ 0.05 was considered statistically significant.

Reporting

This case series has been reported in line with the PROCESS (Preferred Reporting of Case Series in Surgery) guideline.[27]

RESULTS

Eleven patients underwent SEEG implantation, with a mean age at implantation of 25.5 years (range, 4–46 years). The cohort included 5 male and 6 female patients, with a mean epilepsy duration of 15.5 years (range, 2–26 years). Two implantations were bilateral and 9 were unilateral (2 right and 7 left). The cause of epilepsy was structural in 6 (dysplasia in 4, bilateral mesiotemporal sclerosis in 1, and hippocampal atrophy in 1) and unknown in 5. A total of 94 electrodes were implanted using this technique with mean implantation of 9 electrodes (range, 5–12). Demographic data are summarized in Table 1.

The implantation was uneventful in 8 patients. For 1 patient, coregistration had to be repeated during surgery. For another

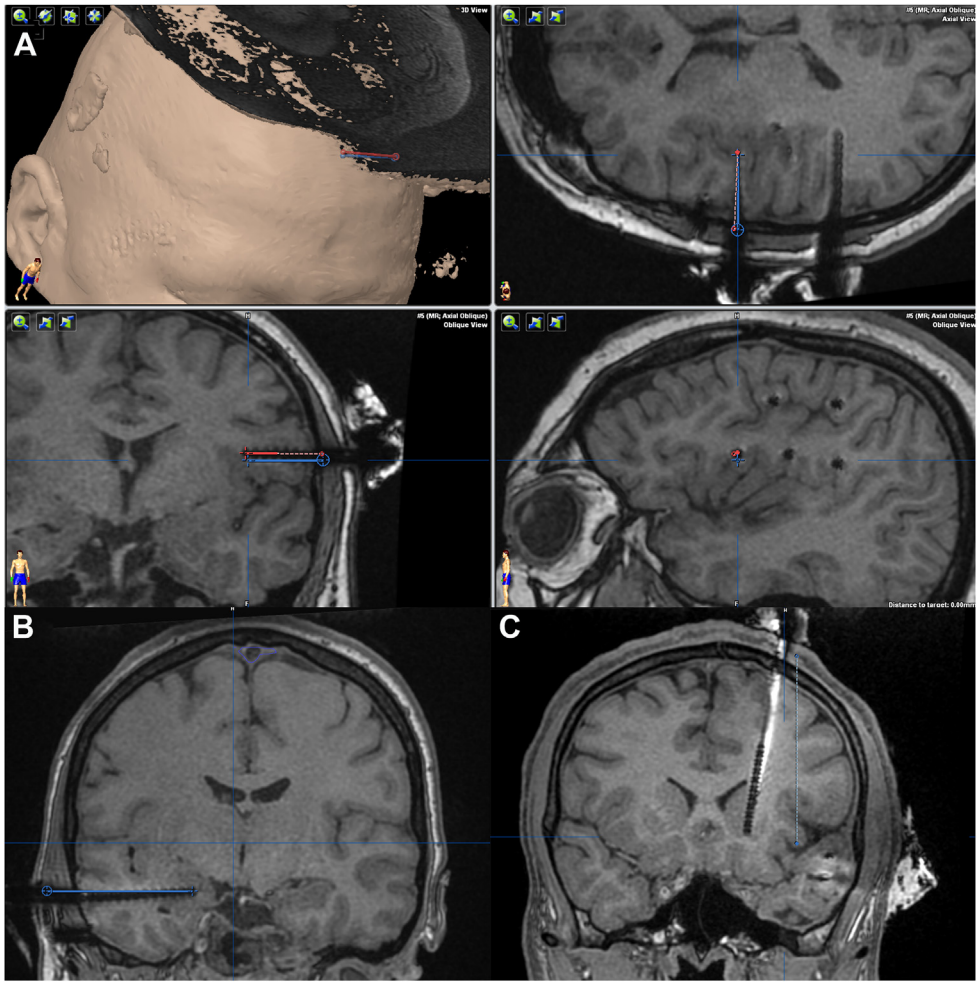

Figure 2. Postoperative magnetic resonance imaging (MRI) of different patients. (**A**) Image from Iplannet (Brainlab), showing the postoperative MRI in the 3 axes, and reconstructed three-dimensional model of the head of the patient. The planned electrode is in *blue* and the real electrode in *red*. The distance is measured using X, Y, Z coordinates. (**B**) Postoperative MRI showing an accurate and concordant real trajectory (patient 1, electrode 2). (**C**) Postoperative MRI of an electrode with an important deviation (patient 6, anterior insular electrode, worst electrode of our series).

patient, coregistration with skin fiducials was not sufficiently accurate (significant deviation between skin landmarks and neuronavigation), and a surface matching technique was performed. Technical difficulty resulted in prolonged drilling and 1 loose bolt in 1 patient.

The mean target deviation was 4.06 mm in all patients (standard deviation, 2.5 mm; range, 0.38–20.63 mm; Table 2). Entry point deviation could not be measured in 6 electrodes because of intraoperative modification. The mean entry point deviation was 4.2 mm (standard deviation, 2.47 mm; range, 0.61–12.25 mm; Table 3). The mean deviation and accuracy varied between patients, as shown in Figure 5, with 1 notable outlier (patient 6) who had a large deviation (>20 mm) for an insular electrode. The mean length of electrodes was 46.5 mm (range, 17.3–89.5 mm). The mean implantation duration by electrodes was 18.5 minutes (range, 16–23.8 minutes), with an overall mean implantation time of 158 minutes and a resulting mean total operative time of 246 minutes.

Insular electrodes were less accurate on average, with a mean deviation of 7.44 mm at target (vs. 3.66 mm in noninsular electrodes) and 7.53 mm at entry point (vs. 3.77 mm in noninsular electrodes; $P < 0.001$). Further, entry points closer to the vertex with an arc angle $<30^{\circ}$ were statistically less accurate than the others ($P = 0.006$), with an accuracy of 5.9 mm for target (vs. 3.6 mm) and 6.1 mm for entry (vs. 3.8 mm).

The univariate analysis showed a strong association between accuracy at target and the following factors: location ($R^2 = 0.23$; $P < 0.001$), accuracy at entry point ($R^2 = 0.4$; $P < 0.001$), arc angle at entry point ($R^2 = 0.04$; $P = 0.0062$) and electrode length ($R^2 = 0.13$; $P < 0.001$). Further multivariate analysis showed that

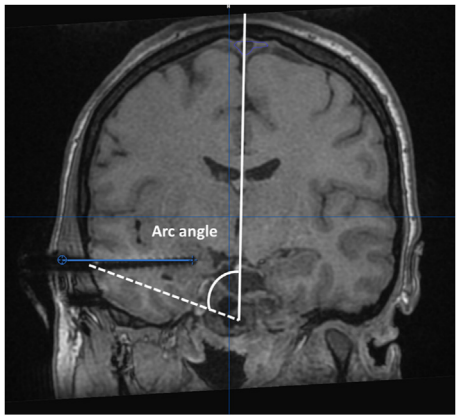

Figure 3. Definition of arc angle on a postoperative T1-weighted magnetic resonance imaging in the Brainlab software. The arc angle was defined as the angle between the vertex and the entry point. It was measured by calculating the angle between the midline and a line joining the entry point and the midline at skull base (*white lines*).

Table 1. Demographics

Demographic	Value
BMI (kg/m^2)	28.2 (17.1–39.5)
Age at implantation (years)	25.5 (4–46)
Duration of epilepsy (years)	15.5 (2–26)
Cause	
Unknown	5
Structural	6
Dysplasia	*4*
Mesiotemporal sclerosis	*1*
Vascular	*1*
Implanted electrodes	94
Electrodes/patient	8.5 (5–12)
Side of implantation	
Left	7
Right	2
Bilateral	2

insular electrodes were correlated with longer electrodes ($R^2 = 0.52$; $P < 0.001$) and smaller arc angles ($R^2 = 0.74$; $P < 0.001$). Length of electrodes was statistically significantly longer for insular exploration, with a mean length of 73.7 mm (range, 65.9–89.5 mm) versus 42.9 mm (range, 17.3–66.46 mm) for noninsular electrodes ($P < 0.001$). Mean arc angle was statistically different ($P < 0.001$), with a mean angle of 19.2° for insular electrodes (range, 11.3°–27.2°) versus 55.3° for noninsular electrodes (range, 9.1°–87.5°).

From a qualitative standpoint, 7 electrodes (7.4%) were deemed misplaced. Six (85%) were insular (3 anterior and 3 posterior) and 1 was parietal; overall, 60% of insular electrodes missed their targets. After analysis of SEEG results, neurologists estimated to have fully localized the SOZ for 7 patients. For 2 patients, SEEG was nonlocalizing and for 2 other patients, SEEG only partially showed the SOZ.

Deep infection or hematomas were not observed in any patient. One patient presented with skin necrosis at the entry point of 1 electrode at follow-up (prolonged drilling during surgery) categorized as a superficial skin infection. Three patients reported transient neurologic impairment without radiologic abnormalities (2 had contralateral hypoesthesia and 1 had dysphasia). One patient also presented with a postictal altered mental status with behavioral impairment, during which he pulled out most

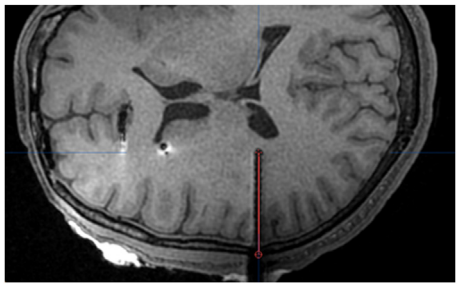

Figure 4. Artifact generated by a parietal electrode on a postoperative magnetic resonance imaging. The generated artifact measures 3.5 mm and the electrode measures 0.8 mm. The real target and entry point were thus estimated by calculating a new trajectory (*red line*) compared subsequently with the planned trajectory (not shown on this image for clarity).

Table 2. Accuracy at Target

	n	Mean Deviation (mm)	Range (mm)	Relative Deviation (%)*
All regions	93	4.06	0.38–20.63	9 (1–29)
Noninsular	83	3.66	0.37–7.34	9 (1–25)
Frontal	20	3.79	1.78–7.05	8 (3–14)
Parietal	21	3.24	0.81–6.84	9 (1–25)
Occipital	1	3.99	—	9
Temporal	34	3.76	0.38–7.34	10 (1–24)
Cingular	7	3.94	1.94–6.36	8 (4–12)
Insular	10	7.44	4.18–20.63	10 (6–29)

*Relative deviation represents the mean deviation divided by the length of the electrode.

Table 3. Accuracy at Entry Point

	n	Mean Deviation (mm)	Range (mm)
All regions	87	4.2	0.61—12.25
Noninsular	77	3.77	0.61—8.13
Frontal	19	3.92	0.61—8.13
Parietal	21	3.01	0.67—7.14
Occipital	1	3.36	—
Temporal	29	4.26	1.62—7.69
Cingular	7	3.73	1.37—6.22
Insular	10	7.53	1.41—12.25

electrodes at day 9 (surgical removal was performed rapidly afterward). One patient developed a seizure cluster on withdrawal of antiseizure medication. Safety data are summarized in Table 4.

SEEG allowed for preoperative planning in 7 patients: 2 for lesional resections and 5 for temporal lobe surgery (4 anterior temporal lobe disconnections with amygdalohippocampectomy and 1 without). Three patients were offered palliative surgery with vagus nerve stimulation. For 1 patient, the exploration was deemed insufficient because of insufficient sampling and a new SEEG was proposed. Overall surgical outcomes are summarized and presented in Table 5.

In our literature review (Table 6), we identified 13 studies over an 8-year period including 236 patients with a total of 1874 electrodes. In a pooled analysis, mean accuracy was 3.84 mm at target (range, 2.47—11.8 mm), with 8 reported cases of hematomas, leading to a risk for 3% per procedure, or 0.4% by electrode. Four cases of infection were reported, leading to a risk of 1.5% per procedure. No death was reported.

DISCUSSION

This prospective case series included 11 patients with 94 electrodes implanted through a percutaneous FNS technique. The mean accuracy at target was 4.06 mm, and when excluding insular

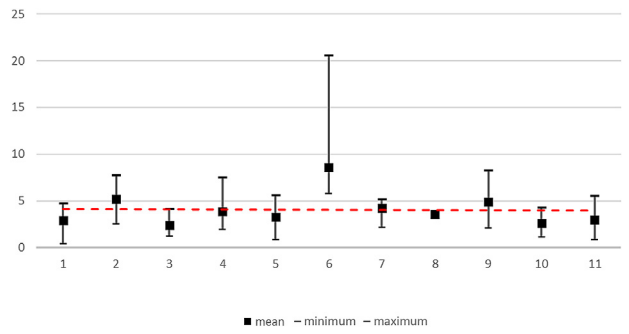

Figure 5. Distribution of the electrode deviation among patients, showing an important inaccuracy in patient 6. The dotted line represents the total mean target deviation (4.06 mm).

Table 4. Safety

Acute Complication (in the 24 hours After Surgery)	n (%)
Hematoma	0
Loose fixation bolt	1 electrode (1)
Transient neurologic deficit without radiologic abnormalities	2 (18)
Adverse events*	
Seizure cluster	1 (10)
Auto explantation	2 (18)
Sepsis	0
Deep infection	0
Superficial skin infection	1 (10)
Transient neurologic deficit without radiologic abnormalities	2 (18)
Procedural incidents	
Material failure	1 electrode (1)
Transient neuronavigation incident	3 procedure
Freezing	1
Perprocedural shift	1
Uneffective fiducial coregistration	1
Duration (minutes/electrodes)	
Total operative time	28.87 (24.66—37)
Implantation time	18.6 (15.44 —23.75)

*2 patients presented with 3 and 4 of the reported complications.

Table 5. Outcomes

Outcome	n
Malpositioned electrodes*	7 (7.4%)
Localization of seizure onset zone	
Full localization	7
Partial localization	2
No localization	2
Post-SEEG decision	
Resection or disconnection	7
Lesionectomy	2
Anterior temporal lobectomy	5†
Neurostimulation (vagus nerve stimulation)	3
New SEEG	1

SEEG, stereoencephalography.
*Electrodes that missed the target, †4 with amygdalohippocampectomy, 1 with multiple subpial transection.

Table 6. Review of Accuracy and Safety of FNS Technique Reported in the Literature

Study	Year	Implantation Technique	N	Electrodes (n)	Mean Electrodes/ Patient (n)	Target Deviation ± SD (mm)	Entry Deviation ± SD (mm)	Reported Deviation	Hematoma	Death	Infection	Implantation Time by Electrodes (min)	Total Implantation Time (min)	Total Operative Time (min)
Current series	2022	Bolt Varioguide	11	94	8.5	4.06 ± 2.5	4.2 ± 2.47	ED	0	0	1 (9%)	18.6	158	246
Nowell & al.[15]	2014	Bolt Suretrack	22	187	8.5	3.66 ± 2.21	/	LD	1 (0.5%)	0	0	16.11§	137	/
Verburg & al.[26]	2016	Bolt Varioguide	7	89	12.7	3.5‡	/	ED	/	/	/	/	/	/
Roessler & al.[16]	2016	Bolt Leyla-arm	6	58	9.6	3.2 ± 2.2	1.4 ± 1.2	ED	0	0	0	11.8	115	/
Budke & al.[14]	2017	Bolt Varioguide	15	111	7.4	2.96 ± 1.49	3.64 ± 1.78	ED	1 (6.6%)	0	0	15.7	90	/
Sharma & al.[24]	2019	Bolt Vertek	6	/	10	4.6‡	5.5‡	ED	0	0	0	/	/	/
Gross & al.[17]	2020	No bolt Vertek	68	413	6.1	6.19 ± 4.13	/	ED	2 (3.2%)	0	3 (4.8%)	/	/	/
Rodionov & al.[23],*	2020	Bolt Vertek	23	202	8.8	3.2 ± 1.8	1.4 ± 0.8	ED	/	/	/	/	/	/
Girgis & al.[19]	2020	No bolt Vertek	13	45	3.5	11.8 ± 4.1	/	ED	/	/	/	/	/	/
Kim & al.[20],†	2020	No bolt Vertek	25	177	7.1	/	/	/	3 (12%)	0	1 (4%)	25.2	173.4	301
Ladisich & al.[22]	2021	Bolt Varioguide	17	220	12.9	2.7 ± 2	3.2 ± 2.4	ED	0	0	1	15.3§	197.3	/
Tay & al.[25]	2021	Bolt Autoguide	9	102	11.3	4.67 ± 0.27	/	ED	1	0	0	/	/	/
Song & al.[18]	2021	Bolt Varioguide	19	141	7.4	2.47 ± 0.79	1.96 ± 0.47	ED	0	0	0	14.16	/	/
Kojima & al.[21]	2022	No bolt Vertek	4	18	4.5	5.12 ± 1.4	4.29 ± 1.92	ED	0	0	0	70.35	/	/
		No bolt Autoguide	2	17	8.5	3.59 ± 2.22	1.99 ± 0.9	ED	0	0	0	35.45	/	/

SD, standard deviation; ED: Euclidian distance; LD, lateral deviation.
*Only last group analyzed.
†Only FNS-arm analyzed.
‡No SD available.
§Timing derived from available data.

Table 7. Comparison of Operative Time and Implantation Time in Different techniques

Technique	Mean Implantation Time/Electrode (minutes)	Mean Total Operative Time (minutes)
Frameless neuronavigated system*	19.6	284
Frame[30,31]	20.4	Not available
Robot[10,20,30]	11.6	276.5

*Data derived from articles cited in Table 6.

electrodes that were significantly less accurate, the mean deviation improved to 3.66 mm. Accuracy was influenced by location (insular electrodes being less accurate), accuracy at the entry point, and length of electrodes (longer electrodes being less accurate), as well as proximity to the vertex (i.e., arc angle <30°). In 7 patients, the SEEG allowed full localization of the SOZ, in 2 patients only partially, and in 2 patients, the SOZ could not be localized. No postoperative hemorrhage was recorded, and only 1 patient developed a skin infection. Three patients presented with transient neurologic symptoms, which resolved within a few days. A summary of the results from this study and comparisons with other series on FNS techniques are presented in Table 6.

No meta-analysis has been performed of FNS techniques, but our literature review (Table 6) showed a global accuracy at target of 3.84 mm when pooling data, with an important range of error (2.47–11.8 mm). However, those results must still be taken with caution, because the techniques were heterogenous. Our series show slightly lower accuracy (4.06 mm). The case series using FNS that showed worse accuracy[17,19,21] have in common the lack of use of an anchoring bolt. The absence of a bolt could lead to less control over the direction of the electrode and facilitate bending when piercing the parenchyma.

The accuracy reported for FNS is less than robot and frame implantation, as shown in a recent meta-analysis[7] with an accuracy of 2.89 mm (95% confidence interval, 2.34–3.44 mm) for frame-based implantation and 1.17 mm (95% confidence interval, 1.66–1.75 mm) for robot-assisted implantation. This difference can be explained by different factors. The stability of the implantation system in FNS (usually a neuronavigated arm) is probably worse than the stability of a frame or a robot, which benefits from multiple anchoring points. This question cannot be addressed in our study. Another potential cause of increased error is the coregistration technique, which is more rigid in frame[12] or robot[13] implantation than in neuronavigation. Rodionov et al.[23] showed how adding bone fiducials instead of skin fiducials, as well as using a "trajectory guidance" technique instead of a "target guidance" technique, could increase their accuracy.

Electrodes targeted at the insula were significantly less accurate and accounted for 6/7 misplaced electrodes (85%); overall, 60% of insular electrodes missed their target. If we exclude them from the analysis, our accuracy reaches 3.66 mm (comparable to other FNS techniques). A vertical oblique trajectory protocol was chosen in our study when implanting insular electrodes to avoid damaging the vessels of the sylvian fissure. The trajectory choice led to an insertion point closer to the vertex, increased angle with the skull, and longer electrodes, which all were significantly associated with increased target deviation. Those results are contradictory to the

Table 8. Tips for Error Avoidance and Lessons Learned

Problem	Case	Resulting Outcome	Suspected Reason	Suggested Solution
Inadequate registration	11	—	Excessive mobility of skin fiducials because of thick and elastic skin	Repeat coregistration until satisfactory Use alternative methods if available Never settle if insufficient accuracy
Loss of accuracy during surgery	2	Large deviation of electrode with inadequate mapping	Displacement of reference between acquisition and implantation	Verify tightness of joints in the reference arm Mark entry point at first registration and verify accuracy again at each implantation Pay attention for unwanted blow to the reference arm during draping Allow for sterile registration reacquisition during surgery if needed (e.g.. leave enough exploitable skin fiducials in the surgical field) Reacquire registration as soon as inaccuracy is noted If enough accuracy cannot be reached in sterile condition, remove drapes, and acquire registration again
Prolonged drilling	7	Loose bolt because of excessive burr hole width	Insufficient skin opening	Verify skin perforation before drilling
	7	Postoperative skin necrosis because of heat injury	Prolonged drilling	Apply saline on the skin during drilling to prevent heat injury
Slow drifting of the drill	6, 7	Large deviation of electrodes and inadequate mapping (insular)	Unfavorable angle of drilling	Favor orthogonal trajectory (>30° to the skull) Verify tightness of every joint Apply rugine on the skin to constrain the drill Avoid applying excessive force on the drill

series of Ladisich et al.,[22] who showed that shorter trajectories were related to worse accuracy. Further, Rollo et al.[28] showed that oblique trajectories using a robot were as accurate as orthogonal trajectories in 2040 electrodes. This finding was confirmed by Machetanz et al.,[29] who compared frame-based implantation with frameless robot implantation in the insula via an oblique trajectory and showed equivalent accuracy between insular and noninsular electrodes with both techniques. Those data could suggest that oblique trajectories are safe with robot or frame implantation but should be avoided in FNS implantation. However, our study as well as the analysis of the literature cannot address this specific point.

Even although FNS seem less accurate, the main factor to consider is safety and usefulness of electrodes. No hematoma or deep infection was observed in our case series. When looking at data from our literature review, complication rates for infection range from 0% to 4.8%, 0% to 12% for hemorrhage,[20,26] and 0% to 2.3% for other complications including transient neurologic impairments. When pooled together, we obtain a hemorrhage risk of 0.4% for each electrode and 3% for each implantation. Those numbers are comparable to numbers reported for robot and frame implantation. In 2 large meta-analyses, including 2624 patients and 22,085 electrodes for one[6] and 2959 patients and 18,200 electrodes for the other,[8] complication rates were evaluated at 1%–2% for hemorrhage, 0.8%–1% for infection, 0.6%–1% for transient neurologic impairment, 0.6%–1% for permanent neurologic impairment, and 0.3% for death. We still advise caution on oblique insular implantation, which led to useless electrodes in 60% of cases in our experience and which need a safety margin of 7.5 mm based on our result.

Another factor to consider is duration of implantation. which is linked to cost-effectiveness. Implantation time ranged between 11.8 minutes[16] and 70.5 minutes[21] between FNS series, putting our implantation time of 18.5 minutes in the reported range. Robot-assisted implantation time is estimated at between 10.4 minutes[30] and 13.5 minutes.[20] Yet, when pooling data, FNS is longer for implantation but similar to robot for global operative time (see Table 7). This finding indicates that FNS may lead to a longer implantation time but a quicker setup than robot, which makes it also more interesting for less extensive implantation protocol. Comparatively, FNS may cut time by up to 50% compared with classic frame-based techniques.[16] Our analysis supports this aspect because implantation time is already similar, but the additional timing needed for frame fixation and scanner acquisition is expected to largely exceed the timing needed for FNS installation. Further, some consider FNS as a more cost-effective alternative compared with other techniques. Specifically, studies have shown a reduced price for FNS compared with robot-assisted[20] (10%) and frame-based[16] (28%). One of the main advantages of FNS might thus be cost-effectiveness with a sufficient safety profile.

Even although this series is small, this prospective trial has allowed us to identify points of attention for improving our implantations. Most of the problems were identified after patient 6, precluding any statistical analysis of accuracy or safety improvement, but we compiled some tips and tricks in Table 8.

This study has several limitations. The number of patients included in this study is relatively small. We still managed to assess the safety and accuracy of FNS in our institution. Even although this was a prospective study, some data were missing on the entry point because of peroperative modification of trajectory.

CONCLUSIONS

This case series details the implantation of 94 intracranial EEG electrodes using frameless neuronavigation in 11 patients. The mean implantation time was 18.5 minutes per electrode, with a mean accuracy of 3.66 mm at target for noninsular electrodes and 7.44 mm for insular electrodes, in line with the reported literature. Insular implantation was statistically less accurate than noninsular implantation, potentially because of the length of electrodes and proximity of implantation site to the vertex. The lack of accuracy led to missed targets and could limit the effectiveness of the technique for insular exploration. Implantation was globally safe in our case series; however, larger studies are necessary before meaningful conclusions regarding safety can be made, especially regarding oblique insular exploration.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Vincent Joris: Conceptualization, Methodology, Writing – original draft, Investigation, Formal analysis, Commented on previous versions of the manuscript, Read and approved the final manuscript. **José Geraldo Ribeiro-Vaz:** Conceptualization, Methodology, Writing – original draft, Investigation, Commented on previous versions of the manuscript, Read and approved the final manuscript. **Patrice Finet:** Conceptualization, Methodology, Commented on previous versions of the manuscript, Read and approved the final manuscript. **Riëm El Tahry:** Conceptualization, Methodology, Commented on previous versions of the manuscript, Read and approved the final manuscript. **Lior M. Elkaim:** Conceptualization, Methodology, Commented on previous versions of the manuscript, Read and approved the final manuscript. **Christian Raftopoulos:** Conceptualization, Methodology, Commented on previous versions of the manuscript, Read and approved the final manuscript. **Susana Ferrao-Santos:** Conceptualization, Methodology, Writing – original draft, Investigation, Formal analysis, Writing – review & editing, Commented on previous versions of the manuscript, Read and approved the final manuscript.

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