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The Usefulness of Intraoperative Cerebral C-Arm CT Angiogram for Implantation of Intracranial Depth Electrodes in Stereotactic Electroencephalography Procedure

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Key Words
Cerebral angiogram · Electroencephalography · Epilepsy · Stereotactic surgery

Abstract
Background: Stereotactic electroencephalography (SEEG) is an invasive diagnostic tool for localizing the epileptic zone in patients with medically refractory focal epilepsy. Despite technical and imaging advances in guiding the electrode placement, vascular injury is still one of its most serious complications. ***Object:*** To investigate the usefulness of intraoperative cerebral C-arm CT angiogram (CCTA) in avoiding intracranial hemorrhagic complications during SEEG electrode implantation. ***Methods:*** Trajectory data from 12 patients who underwent SEEG electrode implantation were studied in detail. This included an analysis of the implantation of 146 SEEG electrodes, which were guided by intraoperative CCTA, as well as the standard planning based on preoperative contrast-enhanced MRI. In addition, a prospective analysis of SEEG hemorrhagic complications using the studied methodology was performed in a total of 87 patients receiving 1,310 electrodes. ***Results:*** There was no complication related to the CCTA itself. Intraoperative CCTA entailed modification of the original trajectory based on the preoperative MRI in 27 of 146 electrode implantations (18.5%). In 10 of them, a severe vascular complication was adverted by intraoperative CCTA. The safety of this new approach was also confirmed by the analysis of postinterventional CT, which revealed a symptomatic hematoma caused by 1 single electrode out of the 1,310 implanted. ***Conclusions:*** This study showed that intraoperative CCTA in addition to preoperative MRI is useful in guiding a safer SEEG electrode implantation. The combination of both imaging modalities essentially minimizes the risk of serious hemorrhagic complications.

Introduction

Following the introduction of scalp electroencephalography (EEG) recording by Berger [1] in 1929, intracranial recording started in the middle of the last century [2–6]. First, intracranial electrodes for seizure localiza-

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tion were implanted freehandedly [2, 7–9]. Later, this procedure was guided by the stereotactic technique [10–12]. In the 1960s Talairach and Bancaud [13] developed the methodology and technique of stereotactic EEG (SEEG) for the evaluation of patients with medically refractory partial epilepsy. Since then, SEEG has been a well-utilized procedure in a large number of patients with medically refractory partial epilepsy [14, 15].

In terms of safety and morbidity, intracranial hemorrhagic events due to vascular injury during electrode implantation are considered the most feared complication [16–19]. In recent years, advances in structural and functional neuroimaging techniques, such as CT and MRI, improved the safety, accuracy and efficacy of the SEEG implantation technique [20–23]. Beyond the general well-known cortical anatomical landmarks, the patient's individual vasculature is one of the most important anatomical nuances to be recognized and understood in order to avoid possible vascular injuries. While SEEG electrode implantation has been guided by ventriculography and conventional cerebral angiography in the past, advanced imaging modalities, such as the angio-CT and angio-MRI, are now used to guide SEEG electrode implantation more precisely [12, 22–24].

Our group has been performing SEEG procedures since 2009, applying the C-arm CT angiogram (CCTA) during SEEG implantation. The role of cerebral angiography and CCTA in preventing vascular injury during SEEG procedures has been unclear. The aim of this study was to investigate the utility of intraoperative cerebral CCTA during SEEG implantation in the diagnosis and treatment of refractory focal epilepsy.

Methods

Part I: Accuracy

Twelve consecutive patients with the diagnosis of refractory focal epilepsy who were implanted with SEEG electrodes were prospectively studied. In total, 146 electrodes were analyzed regarding the accuracy of implantation and complication rate. The study was approved by the Cleveland Clinic Institutional Review Board.

Patient Selection for SEEG

The indications for SEEG as well as the planning of implantation were individualized and previously discussed at our weekly patient management conference. On average, 15 electrodes were implanted per patient. The selection criteria for SEEG procedures were as follows:

1 The possibility of the epileptogenic zone being located in deep areas in the cortex, specifically in limbic and paralimbic structures such as the mesial structures of the temporal lobe, cingulate gyrus, posterior orbitofrontal areas and insula
2 The clinical impression that the epileptogenic zone had a more widespread location in the cortex, corresponding to a more diffuse epileptogenic zone, indicated the need for a better mapping of the epileptogenic network
3 Previous subdural invasive study and/or previous multiple operations
4 The need for bilateral implantation

Planning and Procedure

The SEEG methodology implies a rigorous preimplantation inquiry of all available findings obtained during the noninvasive phase of investigation in order to define a coherent hypothesis of the anatomical localization of the epileptogenic zone. In this decision-making process, the respective significance of presurgical evaluation testing may vary greatly, depending on each patient. After a localizing hypothesis is formulated, a tailored implantation strategy is planned, with the goal of confirming or rejecting the preimplantation hypothesis. In this phase, the exploration is focused to sample the anatomic lesion (if present) and to determine the more likely structure(s) of ictal onset and the possible pathway(s) of propagation of the seizures. The desired targets are reached using commercially available depth electrodes (AdTech, Racine, Wis., USA; Integra, Plainsboro, N.J., USA) implanted using a conventional stereotactic technique through 2.5-mm drill holes. Depth electrodes are implanted using orthogonal or oblique orientation, allowing intracranial recording from lateral, intermediate or deep cortical and subcortical structures in a three-dimensional (3D) arrangement, thus accounting for the dynamic, multidirectional spatiotemporal organization of the epileptic seizures.

As part of our routine practice, the patient is admitted to hospital on the day of surgery. The day before surgery, a stereotactic contrast-enhanced volumetric T1 sequence MRI is performed. Images are then transferred to our stereotactic neuronavigation software (iPlan Cranial 2.6; Brainlab AG, Feldkirchen, Germany) where trajectories are calculated the following day. On the day of surgery, while the patient is under general anesthesia, the Leksell stereotactic frame (Elekta, Sweden) is applied using the standard technique. Once the patient's head is attached to the angiography table a noncontrast C-arm CT and a contrast-enhanced, subtracted C-arm CT are performed. The injection protocol for the subtracted C-arm CT used a prolonged X-ray delay of about 9 s to allow the visualization of both the arterial and the venous system in the resulting 3D images. The noncontrast C-arm CT images including the N-fiducial box are sent to the neuronavigation software for localization of the N-fiducial markers and for 3D registration with the MRI data set. The preoperative MR images and the contrast-enhanced C-arm CT images are then digitally processed using dedicated fusion software (syngo XWP; Siemens Healthcare, Forchheim, Germany). These fused images are overlaid on live fluoroscopic images and used during the time of implantation to confirm the accuracy of the final entry point of each electrode and to ensure the absence of vascular structures along the electrode pathway (which were not previously noted with the contrasted MRI). After planning with the stereotactic software, trajectory coordinates are recorded and transported to the operating room. Trajectories are in general planned in orthogonal orientation in relation to the skull's sagittal plane in order to facilitate implantation and later interpretation of the electrodes positions. In a few trajectories, electrodes are implanted in nonorthogonal trajectories, with the entry point closer to the vertex. Targets for nonorthogonal trajec-

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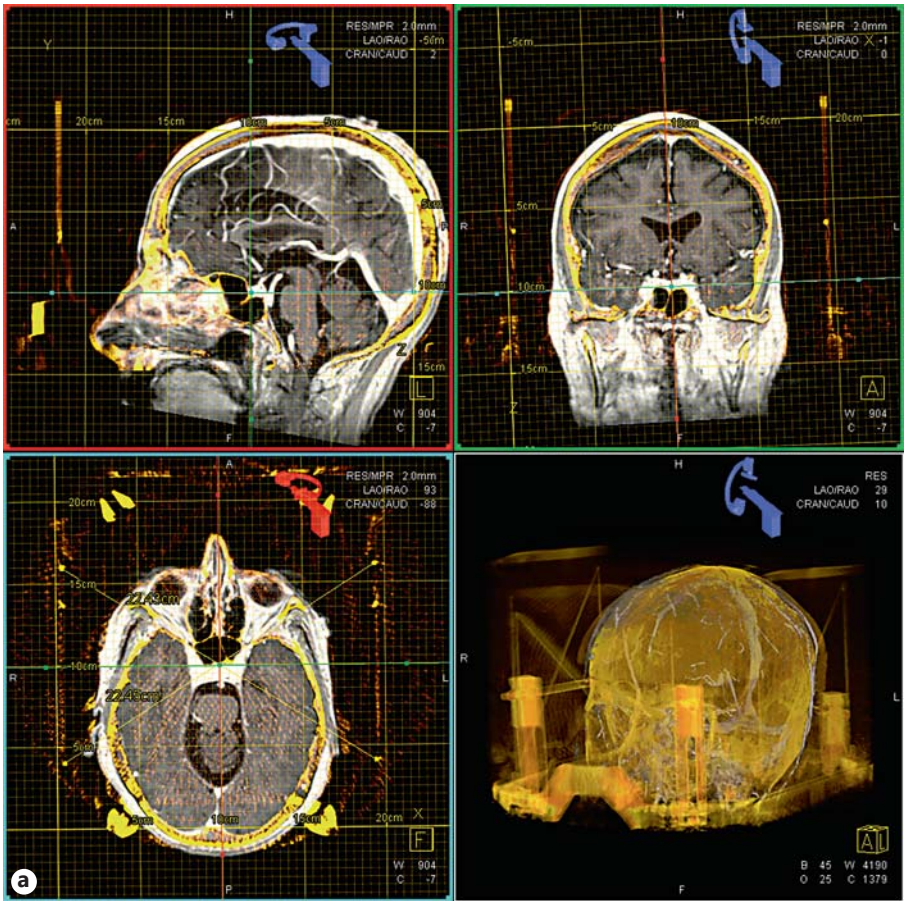


Fig. 1. a, **b** Fusion of data sets 1, 3 and 5 with data set 2 making the aligned measurement grid of data set 2 available in these data sets.

(For figure 1b see next page.)

tories include the posterior orbitofrontal cortex, superior frontal gyrus and superior parietal lobule. The coordinates for each trajectory are then adjusted in the stereotactic frame and a fluoroscopic image, in lateral view, is performed in each new position. Care is taken to ensure that the central beam of the fluoroscopic system is centered at the middle of the implantation probe to guarantee that the 3D image of the vasculature overlaid onto the live fluoroscopic image is not distorted due to parallax effects. If a vessel is recognized along the pathway during fluoroscopy, the implantation probe is manually moved a few millimeters until the next avascular space is recognized. If the implantation probe is aligned correctly, corresponding to the planned trajectory and passing along an avascular space, the implantation is then performed, with skull perforation, dura opening, placement of the guiding bolt and placement of the electrode under fluoroscopic guidance. The implantation progress is observed under fluoroscopic control in a frontal view to confirm the straight trajectory of each electrode. For additional guidance a coronal MRI slice corresponding to the level of each electrode implantation is overlaid onto the fluoroscopic image.

A C-arm CT control scan is performed after each SEEG electrode implantation. The reconstructed images are then fused with the MRI data set using the previously described fusion software. The resulting merged data sets are displayed and reviewed in axial, sagittal and coronal planes, allowing the verification of the correct placement of the electrodes.

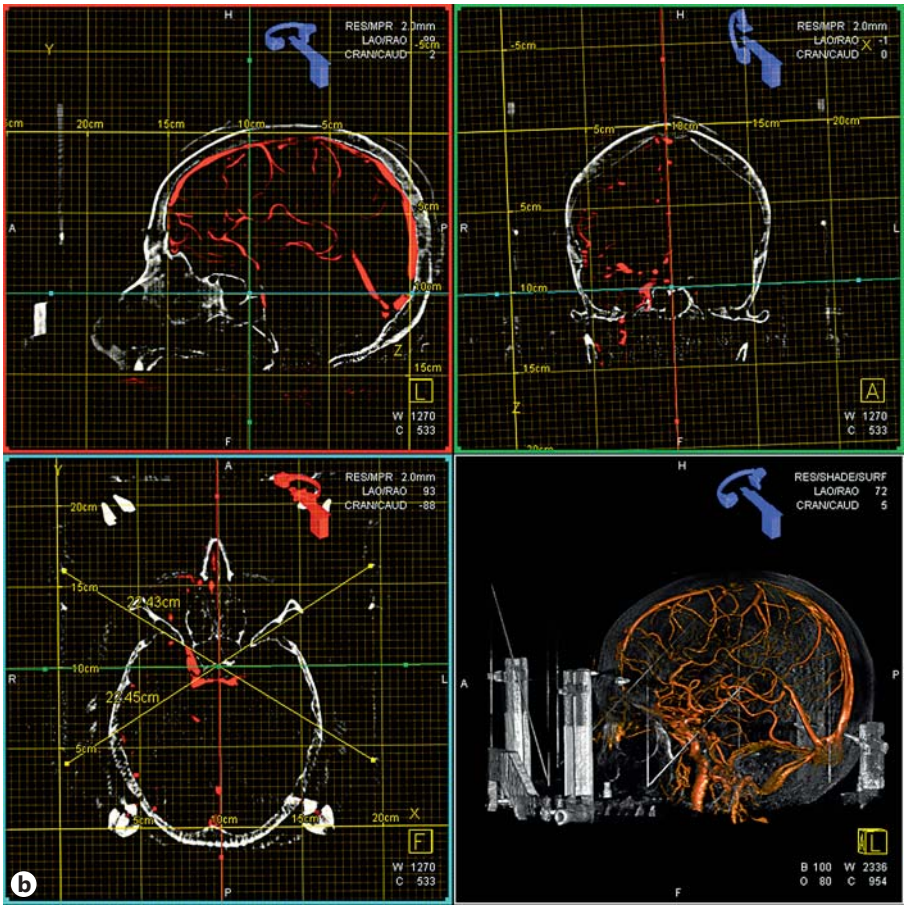
The SEEG electrodes remain for several days (on average 7 days) for presurgical evaluation. After the presurgical evaluation and removal of the electrodes, a regular noncontrast CT is performed in every patient. The integrity of the removed electrodes is confirmed.

Implantation Accuracy Analysis

Postoperative analysis was performed by two 'blind' investigators (M.J.M. and M.v.R.) who had no information about the intraoperative changes in the trajectory due to the presence of vascular structures. The data analysis was performed using 3D software (syngo InSpace) on a dedicated 3D workstation (syngo XWP; Siemens Healthcare).

The following data sets were used for the postoperative analysis:

- MRI images (data set 1)
- Noncontrast C-arm CT images with the fiducial box (data set 2)
- 3D DSA C-arm CT images (data set 3) with corresponding mask images (data set 4)
- Noncontrast C-arm CT images with the implanted electrodes (data set 5)
- Control postimplantation CT images for hemorrhage detection acquired after the removal of electrodes (data set 6)
- List with coordinates of planned electrode trajectories from the stereotactic planning software (Brainlab system; data set 7)



As a first step, a measurement grid was aligned within data set 2 (noncontrast C-arm CT images with the fiducial box) to represent the coordinate system of the stereotactic frame defined by the N-fiducials of the fiducial box. Data sets 1, 3 and 5 (MRI images, 3D DSA C-arm CT images, noncontrast C-arm CT images with the implanted electrodes) were fused with data set 2 to make the aligned measurement grid of data set 2 available in these data sets (fig. 1a, b). Based on the measurement grid applied to data set 5 the coordinates of the entry points of the implanted electrodes were documented (fig. 2) and compared to the original implantation plan (fig. 3). The average difference in distance of the planned entry point versus the actual entry point (in x, y and z orientations) was recorded and analyzed.

In terms of accuracy, the stereotactic y and z coordinates of the actual entry point for each electrode were identified. These coordinates were recorded in the Excel file containing the preoperative intended x, y and z coordinates. The distance D between the planned and actual entry points was now calculated according to the formula:

$$D = \sqrt{\left(y_{act} - y_{plan}\right)^2 + \left(x_{act} - x_{plan}\right)^2}.$$

Electrodes with Modified Trajectories

Trajectories with a distance greater than 3 mm between the planned entry point and the actual entry point were considered to be modified trajectories due to the presence of vascular structures along the planned trajectory during the implantation (information provided by the live overlay of the intraoperative CCTA). Modified trajectories were later confirmed by the senior author (J.G.-M.). For these electrode trajectories, further analyses were performed to characterize the presence or not of vascular structures along the trajectory:

- The planned and actual coordinates of dura entry and target point as well as the corresponding trajectories were marked both in data set 1 (MRI) and data set 3 (subtracted C-arm CT)
- The marked trajectories were then visually checked for interferences with any vessel

Part II: Complication Rate

Hemorrhagic complications were prospectively collected and analyzed. Eighty-seven consecutive patients were studied, including the 12 patients studied for the accuracy measurement. In total, 1,310 electrodes were implanted and complications were analyzed by recording the hemorrhagic events observed in the immediate postoperative CT scans.

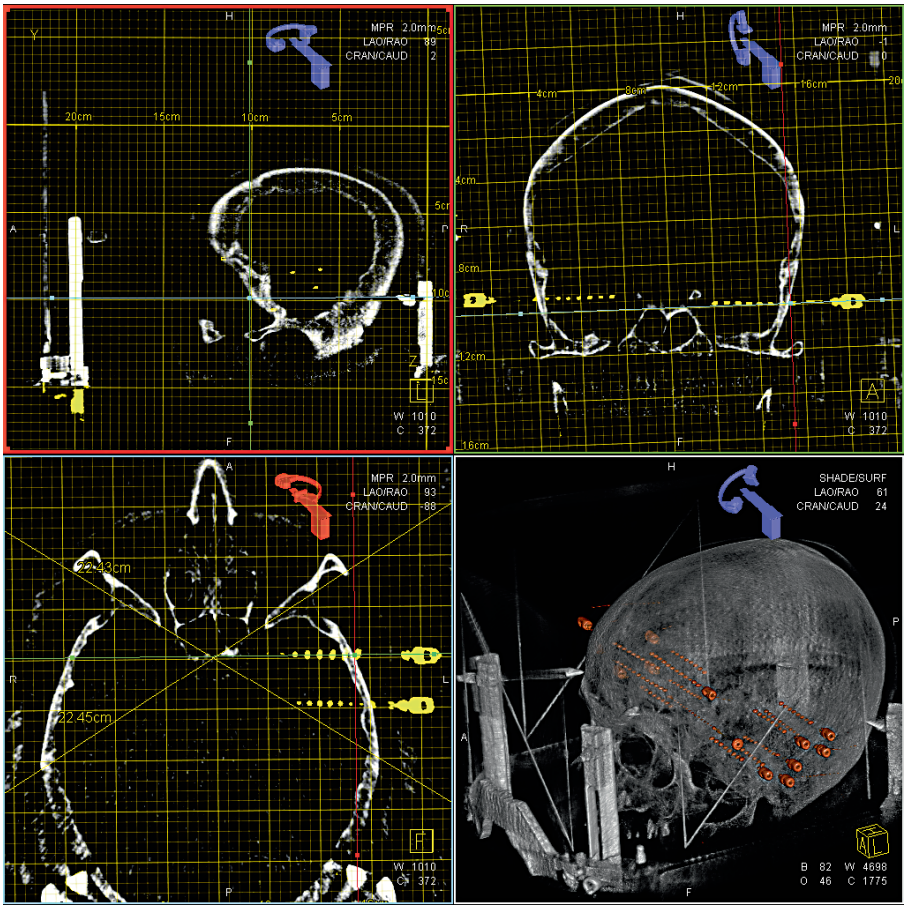


Fig. 2. Analysis of the actual entry points based on the measurement grid applied to data set 5.

Results

Part I: Accuracy

As mentioned in Methods, 12 consecutive patients were studied with a total of 146 electrode trajectories analyzed. The 12 patients included 7 females and 5 males, ranging in age from 24 to 43 years. All patients had refractory focal epilepsy with an indication for extraoperative invasive monitoring in order to further anatomically define the location of the epileptogenic zone. Fifty electrodes were located on the left and 96 on the right. Electrode locations were as follows: frontal (n = 47), mesial temporal (hippocampal, n = 10), insular (n = 6), parietal (n = 43), lateral temporal (n = 30) and occipital (n = 10). No severe adverse event, such as hemorrhagic or infective complications, was seen in this study group. No complications were associated with the CCTA procedures.

The mean accuracy was 0.88 ± 0.92 mm (range 0–2.9) for the electrodes which were implanted as preoperatively intended. Readjustment of the entry point of the electrodes was performed for 27 electrode trajectories (18%) according to the additional information gained by direct intraoperative CCTA and confirmed by the operating neurosurgeon (J.G.-M.). In the modified trajectory group (27 in total), 15 trajectories were located in the frontal lobe, 10 in the temporal lobe and 2 in the parietal lobe. In 6 trajectories, both the intended and the modified trajectory had some minor interference with the vasculature, but no clear vessel/electrode collision. No interference with the vasculature was evident for 2 of the electrodes. In 10 electrodes, the intended trajectory (based on contrast-enhanced MRI images only), but not the actual trajectory (corrected after the analysis with the digitally fused 3D DSA C-arm CT images), would have had serious interference with the vasculature.

Part II: Complication Rate and Seizure Outcome

The review of postinterventional CT of the 87 consecutive patients (42 males and 45 females, mean age of 35 years) implanted with 1,310 SEEG electrodes showed

1 intracerebral hemorrhagic contusion (fig. 4). No complications due to the angiographic procedure were observed. The cerebral hemorrhagic contusion was located in the mesial frontal lobe cortex (leg area in the Rolandic cortex), causing transitory leg weakness which recovered after 15 days with no residual deficits. Repeated CT at this time revealed a complete resolution of the contusional area. None of the 146 electrode trajectories analyzed in part I resulted in hemorrhagic complications. For the entire studied group (87 patients – 1,310 implanted electrodes), the rate of hemorrhagic complications/implanted electrodes was 0.07%. In the retrospective analysis of the 87 patients, 65 patients underwent resections (75%). From this group, 62% remained seizure free after 1 year.

Discussion

The use of angiograms for SEEG implantation is controversial. Respecting the cerebral vasculature of each individual patient is of paramount importance to ensure the safety of SEEG implantation. Therefore, advanced imaging modalities like cerebral angiography, CT and contrast-enhanced MRI have been used [12, 19–23, 25, 26]. Although the use of CCTA is not new in SEEG, its utility in avoiding vascular injury has never been demonstrated. Our results support previous concepts that the use of CCTA in association with other imaging modalities may drastically diminish the incidence of vascular injuries in SEEG procedures.

According to the results of this recent investigation and previous publications, no single vascular imaging modality provides 100% safety for the implantation of SEEG [12, 19–23, 25, 26]. While others have advocated MRI to be sufficient for preoperative planning [24, 27], we observed an additional benefit of intraoperative CCTA, refining the final electrode position in order to avoid collision with vascular structures, preventing potential devastating complications. In our series, 18% of the trajectories, which had previously been planned using contrast-enhanced MRI only, were modified after using the intraoperative CCTA as an overlay on the live fluoroscopic image. Conversely, in 6 trajectories with potential vascular collisions on the intended and actual trajectories, no hemorrhagic events were observed. In this clinical scenario, we can speculate that it is quite possible that even with eminent vascular collisions, vessels may shift away from the electrodes, preventing vascular injury.

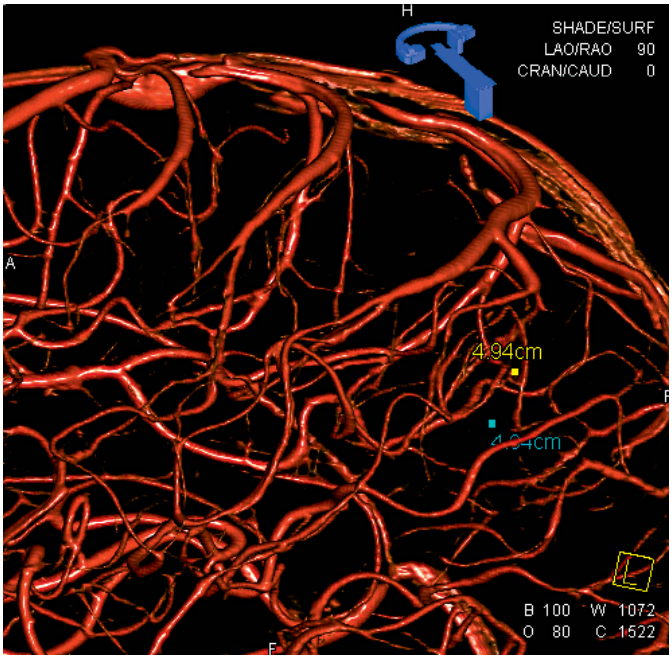


Fig. 3. 3D angiographic reconstruction (lateral view) showing the intended SEEG electrode trajectory (yellow), with clear vascular collision and the moved (blue) trajectory, now through an avascular space.

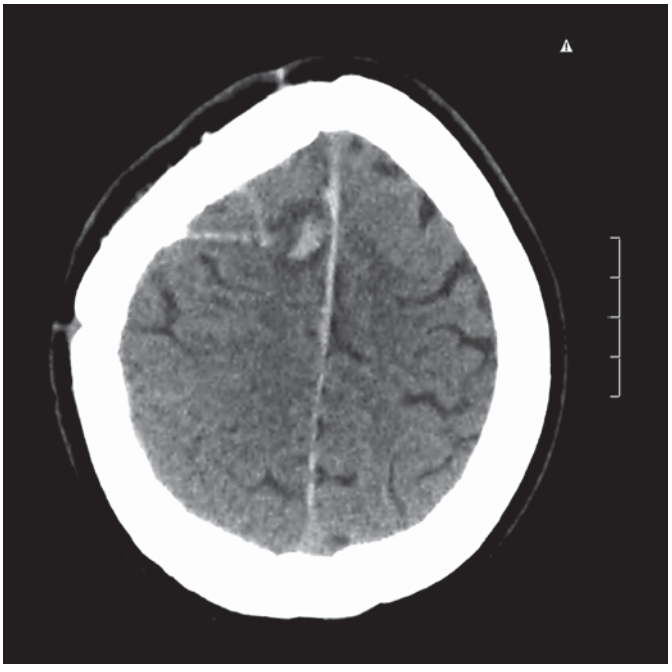


Fig. 4. CT scan of the only hemorrhagic complication among the 1,130 implanted SEEG.

It is important to emphasize that these 6 trajectories were all located in the perisylvian/insular areas where arteries are generally located within large cisternal spaces and, despite the maximal effort to avoid such collisions, the clinical necessity to explore these cortical areas overcame the risks of possible hemorrhagic events. Based on this discussion, we can argue that an electrode-vessel collision on the matched images (preimplantation DSA and postoperative CT) is not reliable to prove a real collision. This assumption is further supported by our results, as we had no intra-axial bleeding on postoperative CT despite the predictable electrode-vessel collision on the fused images. The most reasonable explanation might be the mobility of the vessels, as they become mechanically displaced rather than penetrated by the inserting electrode. This is mostly true in arterial vessels rather than veins due to the fact that arteries are located in cisternal spaces, allowing a certain degree of mobility, unlike veins, which are attached to the brain, with very limited movement. Despite the possibility of vascular dislodgement in particular areas, the use of the CCTA allowed us to perform more aggressive and extensive exploration, especially in areas surrounded by an intense vascular network, such as the insula, perisylvian cortex and posterior orbitofrontal area.

The safety and usefulness of our approach was also confirmed by the fact that only 1 electrode caused a symptomatic contusion among the 1,310 inserted electrodes and no clear hematomas were observed in the entire series. Although the relatively large experience with SEEG implantation at the Cleveland Clinic Epilepsy Center confirms a very low risk for vascular injury using the current method of implantation, a residual risk may remain unavoidable. While the presented risk of vascular injury seems to be negligible in most experienced hands performing this procedure almost daily, these results may not reflect the general outcome at every center, and caution has to be practiced.

Several authors have reported acceptable complication rates without the angiogram but with the use of other vascular imaging modalities, such as double-dose gadolinium-contrasted MRIs, where vessels can be clearly visualized and electrode trajectories can be planned accordingly [28, 29]. Nevertheless, when reviewing the literature, the rate of complications using MRI only (without angiogram) tends to be higher than with the angiogram. De Almeida at al. [22], using the MRI technique only, reported a rate of hemorrhagic complication to be almost 3 times higher (0.7% per electrode) compared to other groups using the angiographic technique. It is likely that for the higher complication rates reported, especially in extratemporal implantations in surgical series utilizing the MRI technique only, the implantations tended to be less aggressive, with few electrodes implanted in the insula or frontal/Rolandic areas and more electrodes implanted in the temporal areas. In addition, the double-dose gadolinium technique, a possible alternative to the angiographic technique, is problematic, being associated with renal complications due to surpassing the maximal dose considered to be safe. Although our opinion favors the use of the cerebral angiogram, further studies are necessary to clarify the utility of this technique in preventing vascular complications in SEEG procedures.

Since its conceptualization, the SEEG technique has been closely associated with the use of the cerebral angiogram. However, Talairach and Bancaud [13] had to operate on 0.5% of their patients because of severe intracerebral hematoma following SEEG implantation. However, this series was from the pre-CT era and we can possibly speculate that the real incidence of hemorrhagic complications could have been even higher. Later, a study published by Espinosa et al. [25] described a risk of subdural hematoma in 0.6% of their patients and Engel et al. [29] even described a mortality rate of 1.4% with the placement of depth electrodes. Also, Guenot et al. [19] reported 1 death due to intracranial hematoma. Conversely, in a large SEEG series, Cossu et al. [20] had serious hemorrhagic complication in 9 (4.2%) of their patients with a need for emergency surgical evacuation in 3 patients, despite the use of cerebral angiogram. Although the methodology used by Cossu et al. [20] is quite similar to the described method, the cerebral angiogram was used in the preimplantation planning and not during the intraoperative procedure, perhaps contributing to fewer intracranial bleedings. Nevertheless, a fair comparison in terms of morbidity cannot be completely performed since size and demographical characteristics are quite different in both series.

Conclusion

In addition to contrast-enhanced MRI, SEEG-implanted patients benefit from intraoperative cerebral CCTA during the insertion of intracranial depth electrodes. The proposed combined approach drastically minimizes the risk of hemorrhagic complications, allowing more aggressive implantation in more vascularized cortical areas.

Acknowledgments

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Disclosure Statement

M.v.R. is employed by Siemens Medical Solutions USA, Inc. All other authors have no financial interest in the materials and devices used in this study.

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