

Intracranial depth electrodes implantation in the era of image-guided surgery

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ABSTRACT

The advent of modern image-guided surgery has revolutionized depth electrode implantation techniques. Stereoelectroencephalography (SEEG), introduced by Talairach in the 1950s, is an invasive method for three-dimensional analysis on the epileptogenic zone based on the technique of intracranial implantation of depth electrodes. The aim of this article is to discuss the principles of SEEG and their evolution from the Talairach era to the image-guided surgery of today, along with future prospects. Although the general principles of SEEG have remained intact over the years, the implantation of depth electrodes, i.e. the surgical technique that enables this method, has undergone tremendous evolution over the last three decades, due the advent of modern imaging techniques, computer systems and new stereotactic techniques. The use of robotic systems, the constant evolution of imaging and computing techniques and the use of depth electrodes together with microdialysis probes will open up enormous prospects for applying depth electrodes and SEEG both for investigative use and for therapeutic use. Brain stimulation of deep targets and the construction of "smart" electrodes may, in the near future, increase the need to use this method.

Key words: epilepsy, stereoelectroencephalography, depth electrode, image-guided surgery.

A implantação de eletrodos de profundidade na era da cirurgia guiada por imagem

RESUMO

O advento das modernas técnicas de cirurgia guiadas por imagem revolucionaram a técnica de implantação dos eletrodos de profundidade (EP). A estereoeletroencefalografia (E-EEG), conforme introduzida na década de 50 por Talairach, é um método invasivo de análise tridimensional da zona epileptogênica, baseado na técnica de implantação intracraniana de EP. O objetivo deste artigo é discutir os princípios da E-EEG e sua evolução, desde a era Talairach até a era atual, da cirurgia guiada por imagem, e suas perspectivas futuras. Embora os princípios gerais da E-EEG tenham permanecido intactos ao longo dos anos, a implantação de EP, que é a técnica cirúrgica que viabiliza este método, sofreu grande evolução ao longo das últimas três décadas devido ao advento das modernas técnicas de imagem, de sistemas de computação e das novas técnicas estereotáxicas. O uso de sistemas robotizados, a evolução constante das técnicas de imagem e computação e a utilização de EP com sondas para micro diálise associados a si, abre no futuro uma enorme perspectiva para a aplicação dos EP e da E-EEG, tanto para uso investigativo como terapêutico. A estimulação cerebral de alvos profundos e a fabricação de eletrodos "inteligentes", poderão incrementar, num futuro próximo, a necessidade do uso deste método.

Palavras-chave: epilepsia, estereoeletroencefalografia, eletrodo profundo, cirurgia guiada por imagem.

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Indications for epilepsy surgery depend on convergence between the results from examinations that have been performed, and this is of great importance for surgical prognoses. Convergence between the results from noninvasive preoperative investigations, particularly imaging and video-EEG examinations, does not always occur. Semi-invasive or invasive techniques for recording seizures often have to be used, in an attempt to resolve uncertainties. From an electrographic point of view, the ideal would be to make the recording as close as possible to the likely epileptogenic zone. This approach can be accomplished through semi-invasive techniques such as the use of foramen-ovale electrodes, which are indicated only when there are doubts regarding laterality in cases of mesial temporal lobe epilepsy; or through invasive techniques such as the use of subdural electrode arrays or depth electrodes. The latter are the instruments used for performing stereoelectroencephalography (SEEG), which is an invasive technique for recording seizures with the aim of achieving three-dimensional analysis of the epileptogenic zone.

In the 1950s, Talairach and Bancaud¹ were the first to indicate that the cortical regions involved in epileptic processes could be defined particularly by recording spontaneous seizures. They drew up the complete method named SEEG so that, using anatomical-electroclinical correlations, they would be able to identify the extent of the cortical areas that were involved primarily in ictal discharges, which they defined as the "epileptogenic zone". Their aim was thus to plan cortical resection procedures that would be appropriate for each particular case. The implantation strategy was very much individualized and depended on each patient's clinical, neurophysiological and anatomical characteristics, in a way that therefore distinguished it from other, similar procedures with standardized targets and paths.

In this technique, in a three-dimensional analysis model for the epileptogenic zone, the depth electrodes are inserted going towards deep targets, with intermediate contacts in the cortical and subcortical regions. Therefore, the name "depth electrode" is not adequate as used in defining SEEG, because this technique allows anatomical structures at deep, intermediate and superficial levels to be addressed².

This type of approach is currently used in presurgical assessments in different epilepsy surgical centers in Europe³⁻⁵, North America⁶⁻⁸ and Asia⁹.

The first successful attempts to record intracerebral electrical activity date from the first half of last century. Over those decades, during which the technique for intraoperative recording of signals from the cerebral cortex of epileptic patients was developed by Penfield and Jasper¹⁰, intracranial electrodes started to be implanted

with the aim of recording subcortical structures, mainly with the aim of elucidating the role of basal nuclei in seizures of "*petit mal*"^{11,12} and in presumed cases of "centrencephalic" seizures^{13,14}. In several studies, the electrodes were implanted freehand, using a technique that resulted in great imprecision in attempting to reach the intracranial targets^{15,16}. Moreover, despite the tendency towards using chronic records, the monitoring had the primary aim of inserting intracranial electrodes to record interictal discharges, following the same concepts as established for intraoperative electrocorticography.

The introduction of stereotactic methods for segmentation of intracranial structures and the introduction of the epileptogenic zone concept were fundamental for the methodological development of presurgical assessments on patients with epilepsy.

Stereotactic devices for human use were designed by Spiegel and Wycis in 1947¹⁷, and their use for recording deep cerebral structures started to be mentioned in 1950¹⁸. Stereotactic implantation of intracranial electrodes gained popularity and was mentioned as part of the evaluation of temporal lobe epilepsy at the beginning of the 1960s¹⁹. Meanwhile, in the Neurosurgical Unit of Hospital Saint-Anne, in Paris, stereotactic investigations using intracranial electrodes in epileptic patients were inspired by a recently elaborated new concept: epileptic seizures were considered to be a dynamic process with temporal-spatial organization that was sometimes multidirectional and could be better defined as a three-dimensional arrangement²⁰⁻²³. The location of origin and primary organization of this dynamic process in focal epilepsy, which, if removed, would result in controlling the crisis, was defined as the epileptogenic zone.

Following these premises, the Saint-Anne group developed the SEEG methodology^{24,25}, such that it would become possible to achieve the complex requirements of defining the organization of the ictal discharges in three-dimensional space and time. These procedures had the aim of investigating a coherent and previously formulated hypothesis regarding the epileptogenic zone that would be based on anatomical and electroclinical findings that were particular to each case. For these purposes, several prerequisites would have to be attained: the electroclinical definition of the epilepsies should be based on recordings of spontaneous seizures, and not be limited to interictal static electrical abnormalities; the structures that were previously assumed to be involved in the ictal beginnings and in the primary and secondary organization of the ictal discharges would need to be previously established and included in the exploration area, and would need to be reached with the precision of stereotactic techniques; differing from previous studies on intracranial electrodes, the primary aim in this pro-

cedure was to explore the cortical structures, given that it was presumed that the dynamic organization of the ictal discharges would follow cortical pathways. For this last proposition, because of the variability of the cortical anatomy between individuals, the stereotactic localization of different cortical areas demanded an approach based on a statistically constructed proportional reference system that would use the intercommissural line, as identified using contrasted ventriculography, as the reference basis. This method made it possible to incorporate each patient's anatomy in an anamorphous and flexible reference system²⁶.

Furthermore, stereotactic and stereoscopic teleangiography provide an excellent definition of the anatomy of the cerebral gyri and sulci^{27,28}, thereby making it possible to plan avascular paths for placement of electrodes by means of a double grid mounted on a Talairach stereotactic halo, which was manufactured commercially²⁹.

Since the pioneering experience of the Paris group, modern neuroradiology and image merging techniques have progressively developed and increased the safety of the method and the target-reaching precision, by means of stereotactic direction-finding in intracranial structures^{30,31}. However, the basic concept of a single "stereotactic environment", in which electrophysiological, morphological and functional information can be imported and entered in a dynamic correlation process for defining the three-dimensional organization of an epileptic discharge, is still of prime importance within the current era of stereoelectroencephalography, and has been of relevance for the development of modern epilepsy surgery and stereotactic neurosurgery^{32,33}.

There are many scenarios within which depth electrodes have been proven to be useful, but the extent and frequency of their use vary from one institution to another (Table).

There are several techniques for implanting depth electrodes, and these include the use of a stereotactic halo, neuronavigation without a stereotactic halo, freehand and with endoscopic assistance. Implantation of electrodes using a stereotactic halo is already well established and used in a large number of centers. Several systems are available on the market, such as the Brown-

Roberts-Wells (BRW), Cosman-Roberts-Wells (CRW) and Leksell systems, among others.

Freehand implantation of depth electrodes has been reported to have acceptable accuracy³⁴. However, this is not a viable technique for longitudinal implantation of electrodes in the hippocampus and, theoretically, there is a greater risk of hemorrhage given that the vessels along the path cannot be viewed. On the other hand, this method reduces the duration of the operation and the need for additional images.

The system without a stereotactic halo (known as a frameless system) can be used with the same precision and safety as provided by the conventional system with a halo, thereby making the procedure faster and more practical^{35,36}.

Thus, the image acquisition can be done at any time during the preoperative period, without the need to acquire the images on the day of the surgery, with the halo, as in the conventional system. In this way, the surgical planning can be done before the patient is brought to the surgical center, thereby making it possible to start work on the case quickly on the day of the operation.

By using a pair of mechanical stabilizer arms, electrodes can be implanted simultaneously on both sides of the head, by two different neurosurgeons, thereby halving the time taken for implantation. This system also provides greater flexibility in the work area during the operation, both for craniotomy construction and for the trepanation points, for implanting the electrodes in the cranium, given that there is no interposition of a stereotactic halo. Moreover, application of a stereotactic halo may be very stressful for the patient, which obviously is avoided in this type of implantation.

Finally, Song et al.³⁷ described a method for longitudinal implantation of electrodes in which the system without a stereotactic halo was combined with neuro-navigation guidance using neuroendoscopy. Through the stereotactic system, a path that places the endoscope in the lateral ventricular atrium is established. Next, with endoscopic viewing, the electrode is placed on the temporal horn, along the axis of the hippocampus, without penetrating the cerebral tissue. In this method, because the electrode does not penetrate the tissue of the hippocampus, it provides the advantage of not causing le-

Table . Common scenarios in which depth electrodes have proven to be useful.

Type of study	Structures explored
Studies on frontal lobes	Anterior cingulum, orbitofrontal region and supplementary motor area
Studies on temporal lobes	Hippocampus and amygdale
Reoperation studies	Areas in which adherences make recordings with subdural striae impossible
Deep lesions	Hypothalamic hamartomas and periventricular heterotopias

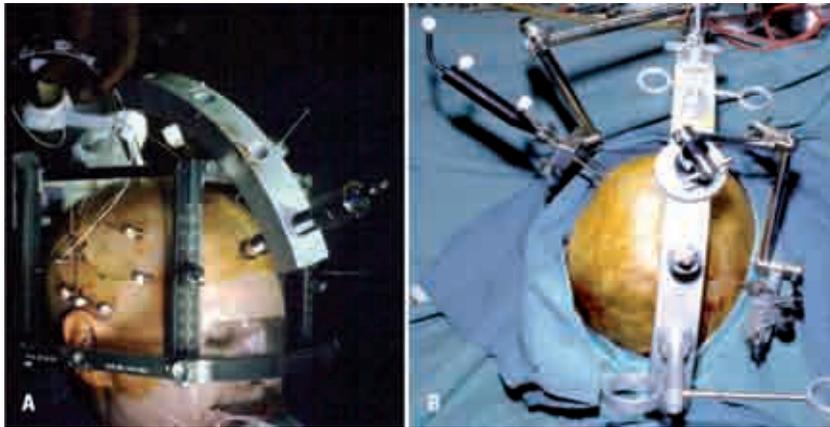


Figure. Evolution of the stereotactic system for implantation of the depth electrodes. [A] Use of stereotactic halo. [B] Use of “frameless” system with bilateral mechanical arms.

sions in the hippocampus, which will not be resected. Although the clinical significance of this remains unknown, it seems evident that this theoretically confers an advantage on this method, over the others.

While maintaining the basic principles as developed by Talairach and Bancaud¹, SEEG underwent adaptations as stereotactic, computational and imaging techniques evolved over the years, with successive incorporation of digital subtraction angiography, magnetic resonance imaging and positron emission tomography into the stereotactic methods for cerebral mapping. Although it was initially performed by implanting electrodes with the aid of a stereotactic halo, it has evolved to the present-day use of stereotactic techniques guided by neuronavigation, which does away with the need to use a stereotactic halo (i.e. becoming a frameless system).

Thus, at the start of the 1980s, tomography and digital angiography were used to locate targets, in order to implant the electrodes. From the second half of the 1980s, magnetic resonance imaging replaced tomography and, in the middle of the 1990s, digital angiography (a semi-invasive method that involves puncturing the femoral artery) was replaced by digital angiographic imaging by means of magnetic resonance, through administration of a double dose of gadolinium. This last noninvasive method, which is performed by means of puncturing a peripheral vein, enables three-dimensional analysis on the cerebral blood vessels. To simplify the method and improve its accuracy, neuronavigation systems were also introduced at that time. Over the course of these advances, during the 1990s, the implantation of electrodes (which until then had been done using a stereotactic halo) started to be performed by means of stereotactic system with an articulated arm that enabled support for the electrodes (known as a free guide and computer-assisted frameless device), which was assisted by neuronavigation without the use of a stereotactic halo (Figure).

The efficacy of invasive monitoring using SEEG has

remained constant over the years, but the evaluation of this efficacy has been based on different criteria. Guenot et al.³ and Almeida et al.³⁸ used the capacity of SEEG to provide critical information that would support or contraindicate surgery, as the criterion for evaluating the efficacy of the procedure, without taking into consideration the surgical results from patients operated after performing SEEG. Through this method, they considered that SEEG was effective in 84% and 96% of the cases, respectively.

On the other hand, other authors have considered that, in order to justify the use of invasive monitoring, there would have to be a substantial number of patients with epileptogenic foci that could be located, and who would present excellent crisis control after the resection. Using these criteria, the surgical results from different centers (with different depth electrode implantation techniques) were compiled in a study³⁹ that showed that 44% of the results were completely seizure-free. This proportion was not in line with the much more favorable results obtained among patients who underwent operations after noninvasive assessments. These findings therefore probably reflect the particular complexity of patients who require intracranial monitoring.

The efficiency and the morbidity-mortality from implantation of depth electrodes using the frameless system guided by neuronavigation and the conventional system using a stereotactic halo are similar.

The morbidity rate reported by centers that use depth electrodes ranges from 1% to 5%^{3,35,36,40-44}, and such cases almost always fall into two categories: hemorrhage or infection. Certain measures are important for preventing these two principal complications. Suspension of the use of non-steroidal anti-inflammatory drugs and asking for tests to check the duration of bleeding among patients who are taking valproic acid, prior to the operation, may reduce the risk of bleeding. In addition, the use of specific surgical techniques may reduce this risk, such as

the use of a trepanation orifice instead of small orifices of the diameter of the electrodes, made using a drill, and viewing of the path of the electrode from the entry point on the cortical surface down to the target, free of large vessels, accessed by means of neuronavigation imaging. Finally, limitation of the number of electrodes to those that are really necessary reduces the number of times that electrodes are passed through the brain and thus reduces the risk of hemorrhage.

Some institutions use intravenous or oral antibiotics for their patients during the electrode implantation period. However, there are no convincing data to support this practice⁴⁵, given that a large number of centers only use antibiotics during the operation and withdraw this medication 24 hours after the operation. Others do not even use antibiotics⁴⁶. Another technique that reduces the infection rate is care regarding the exit point for the electrode on the skin. An electrode exit point through a counter-opening in the skin, several centimeters from the electrode entry point in the cranium, with purse stitches around the exit, reduces the risk of a cerebrospinal fluid fistula. The great majority of infections are successfully treated by removing the electrode, together with the use of intravenous antibiotics. Cerebritis and abscesses are extremely rare⁴⁷. Two cases of Creutzfeldt-Jakob disease have been reported⁴⁸, and it is therefore important to avoid reuse of electrodes.

Although extremely rare, there are reports from some series regarding patients who died because of implantation of depth electrodes⁴³.

More recently, some cases of the use of depth electrodes for therapeutic purposes, causing lesions through thermocoagulation, have been described in the literature. These can be used in patients with a limited epileptogenic zone that is well confined to the region of one electrode contact, or when resection surgery is contraindicated^{49,50}. Depth electrodes have also been used for less conventional indications, such as deep cerebral stimulation, for example in relation to subthalamic nuclei or mamillothalamic tract, thus finding a new scenario of action^{51,52}.

Today, for research purposes, depth electrodes can be coupled to each other, as probes for microdialysis, thereby making it possible to examine the concentrations of substances of interest in the cerebrospinal fluid or cerebral tissue⁵³.

For the future, research is being conducted towards constructing "smart" electrodes that already have their own built-in preamplifiers, analog-to-digital converters, wireless transmission and energy generators. Phase III studies are in progress, towards producing implantable devices that continually record cerebral electrical activity and provide electrical stimulation to interrupt crisis ac-

tivity, through depth electrodes and subdural electrodes (Neuropace, La Jolla, CA, USA).

Therefore, there is an enormous future potential for increasing the applications of depth electrodes and SEEG, both for diagnostic use and for therapeutic use. Robotic systems for implanting depth electrodes, the constant evolution of imaging and computational techniques and the use of combined depth electrodes as probes for microdialysis open up the future possibility of even greater precision within the technique of depth electrode implantation and of widening the understanding of epileptogenic zones, with electrophysiological and biochemical data on this region. The brain stimulation of different deep targets and the construction of "smart" electrodes may soon increase the need for depth electrode implantation.

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