

Evaluation of intractable epilepsy

Invasive monitoring

Tarafa S. Baghdadi, MD, Marwan W. Najjar, MD.

ABSTRACT

إن التحديد الدقيق للمنطقة المولدة للصرع هو العامل الأهم لجراحة الصرع الناجحة. على الرغم من التقدم الحاصل في ميدان التصوير الإشعاعي العصبي، لا يزال تخطيط داخل القحف المسيطر هو المعيار الأهم والذي يساعد في معرفة زمرة مرضى الصرع الذين سيستفيدون من الجراحة. إن الزرع الدقيق للإلكترودات داخل القحف، والمعالجة الحكيمة لما ينتج عنهم من معلومات هما حاجة حتمية لبناء برنامج ناجح لمعالجة الصرع. كما أن عدد المراكز المعنية بهذا المجال في العالم العربي قليل. إضافة إلى ذلك، أن ثقافة المجتمع ليست كافية لإدراك إمكانيات العلاج الجراحي للاضطرابات الصرع. سوف نستعرض في هذه المراجعة أنواع مختلفة للتخطيط داخل القحف، نناقش استعمالاتهم، والتعديلات الأخيرة لكل واحد. كما سنوضح أمثلة سريرية لحالات تم علاجها في المركز الطبي للجامعة الأمريكية - بيروت - لبنان. ثم سنلقي الضوء على مستقبل تخطيط داء الصرع.

Accurate localization of the epileptogenic zone is the fundamental key factor for successful epilepsy surgery. Despite the progress achieved in the field of neuroimaging, invasive intracranial recording is still the gold standard that helps recognize the patient population who may profit from surgery. Meticulous implantation of intracranial electrodes and judicious interpretation of their data is a definite need in a successful epilepsy program. Few centers in the Arab world are involved in that domain. Moreover, the society itself is not well informed to appreciate the potentials of surgical treatment of seizure disorders. In this review article, we will go over various types of intracranial recordings, discussing their indications, and the last updates for each. Some of the cases carried out at the American University of Beirut Medical Center, Beirut, Lebanon will be illustrated as examples of our current practice. Then, the future of epilepsy monitoring will be highlighted in brief.

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From the Department of Surgery-Neurosurgery, American University of Beirut Medical Center, Beirut, Lebanon.

Address correspondence and reprint request to: Dr. Marwan W. Najjar, Assistant Professor of Clinical Surgery-Neurosurgery, American University of Beirut, PO Box 11-0236, Riad El Solh 1107 2020, Beirut, Lebanon. Tel. +961 (1) 350000 Ext. 5260 / 3043704. Fax. +961 (1) 363291. E-mail: mwnajjar@yahoo.com / mn12@aub.edu.lb

The debate still exists on the definition of the epileptogenic zone.¹⁻³ The most acceptable definition among epileptologists is, however, that area of the brain necessary and sufficient to generate seizures and that, when resected, will result in seizure freedom.¹ This renders the concept of “localization” a leader in guidance of the whole invasive and non-invasive preoperative investigations performed for remedy. The degree of concordance among different presurgical evaluations for epilepsy will dictate the need for invasive intracranial recordings. A spectrum extends between 2 extremes. On one hand, there are the straightforward cases where the semiology, scalp EEG, neuroimaging, and neuropsychological testing are sufficient to build up a strong indication for surgery. On the other hand, there are the complicated ones with divergent results of noninvasive tests that mandate invasive methods. Our review aims to highlight various invasive intracranial recording techniques, illustrating some cases from our current practice at the American University of Beirut Medical Center (AUB-MC), Beirut, Lebanon as examples.

General indications. Resective epilepsy surgery is an essential treatment in several intractable epilepsies. In most instances, surgery can be carried out based on confluence of non-invasive data, such as video-EEG findings and semiology, MRI, PET, SPECT, and others. Concordance of data pointing to the epileptic focus may not be achieved in all patients, however. Invasive monitoring may be performed to further define the epileptogenic region of interest, and its relationship to eloquent cortex, after establishing a working hypothesis. Enough non-invasive data are necessary in forming the hypothesis and ensuring optimal results. Invasive monitoring may include strip electrodes, grids, or stereotactically placed depth electrodes.

Dimensions of the epileptogenic zone. The exact location and extent of the epileptogenic zone may not be surely delineated by non-invasive means.⁴ Many reasons stand behind this limitation, but the rapid spread of ictal discharges may be the most influential one. Tailored resection cannot be carried out without

accurate estimation of the ictal onset zone extent and distribution. Non-lesional patients impose a specific preoperative challenge since their treatment theories are mainly based on semiology, surface EEG, and other noninvasive neuroimaging modalities, but not guided by a lesion seen on the MRI. In their non-lesional pediatric epilepsy series, Jayakar et al⁵ used intraoperative electrocorticography in 22 patients with convergent preoperative data and chronic subdural recordings in the rest of their cohort of patients (n=80).⁵ The dilemma of asymptomatic seizure onset cannot be resolved without an invasive means that enables us to discriminate between the real site of kindling and the symptomatogenic zone. The most common seizure type was complex partial in the occipital lobe epilepsy series by Caicoya et al.⁶ The neurophysiological observation that the occipital lobe has different routes of propagation gives it the ability to simulate other types of lobar epilepsy, and thus makes intracranial EEG of paramount importance.⁷ The need for intracranial electrode recording in cases of failure may be more desperate, since those patients may still have strong clues of localization, but failed to profit from surgery.⁸ Residual epileptogenic tissues may be the source of seizure activity continuation. However, the dilemma of epileptic spell recurrence should be handled with a high level of skepticism. Hennessy et al,⁹ documented an ipsilateral but neocortical temporal involvement in the epileptogenesis of recurrence in mesial temporal sclerosis (MTS). Moreover, exclusive contralateral temporal seizure onset was noticed in 25% of MTS relapses. The dilemma of multifocality, and the concepts of epilepsy networks and syndromes rather than localization are well discussed by Bertram in a recent paper.¹⁰ To avoid failure, Bauman et al¹¹ used multistage epilepsy surgery in children. According to their objectives, some patients' resection could not be claimed satisfactory after the first surgery, as cortical eloquence, and the equivocality of epileptogenic zone might hamper the conventional 2-stage monitoring approach.

Epileptogenic zone versus structural lesion. Better comprehension of the mechanisms of epileptogenesis has imposed new challenges to the management strategies in intractable epilepsy. In some instances, the presence of a well-defined lesion might be the trap that leads to failure if not analyzed properly in the context of the pathology itself and the ictal potentials of the surrounding cortex. The presence of a temporal epileptogenic lesion in association with an overtly atrophic ipsilateral hippocampus is a strong indication to include the mesial temporal structures in the resective surgery.¹² Mathern et al¹³ detected the highest neuron losses when the mesial temporal lesion was adjacent to the body of the hippocampus. Dual pathology urges the need to include both lesions, or to exclude one of them from the circuitry of epilepsy. More attention is being

paid to the association between MTS and neocortical temporal dysplasia. In 12 patients histologically proven to have that association, and who underwent simultaneous invasive recordings, mutual ictogenic roles of both pathologies could be identified.¹⁴ Nevertheless, Usui et al¹⁵ could not decisively answer the question of whether the amygdalo-hippocampal complex (AHC) should be removed when surgical treatment of lesional lateral temporal epilepsy is being carried out. Invasively recorded interictal spikes arising from the AHC were detected in all their patients. Four of the fifteen patients achieved Engel's class I outcome although their hippocampi were left intact. Moreover, 47% showed independent ictal discharges from the AHC. The proposed theory of "secondary epileptogenesis" might give a broad explanation for their observations but it does not solve the clinical dilemma in practice.

Epileptogenic zone versus cortical eloquence. The ability to stimulate brain cortices through the implanted intracranial electrodes offers the advantage of verifying the exact location of eloquence. In case of possible overlapping between the epileptogenic zone and indispensable critical areas, subdural grids can help maximize the extent of resection without causing permanent neurological damage.¹⁶ Essential language sites are still best mapped by electrical stimulation of the cortex.¹⁷ Spatial resolution of reorganized cortical areas by virtue of neural plasticity is an anatomical challenge that can be successfully handled with the aid of electrical stimulation mapping (ESM).¹⁸

Different types of intracranial electrodes. Foramen ovale electrodes. Also called the semi-invasive approach, is carried out by inserting an electrode through the foramen ovale and this enables recording from the mesial temporal area. These electrodes are superior to scalp and sphenoidal ones. The data obtained by foramen ovale electrodes are limited for confirmation of the mesiobasal origin of seizures and lateralization. That could be achieved in 60% of cases where scalp-sphenoidal electrodes failed to lateralize the origin of mesial temporal seizures. Furthermore, postsurgical outcome was comparable to that recorded for mesial temporal lobe epilepsy (MTLE) surgery.¹⁹ Foramen ovale electrodes are associated with a reasonable rate of complications (6.6%).²⁰ It can rarely serve as a stand-alone depth recording modality and usually is supplemented by other intracranial recording techniques.

Epidural electrodes. The epidural electrodes may have, at least theoretically speaking, less morbidity than the subdural ones although they have the same indications. There are different types of epidural electrodes (pegs, screws, strips, or grids). They can be considered as an intermediate option that might ultimately lead to either cessation of investigation due to the widespread epileptic activities or proceeding with more invasive modalities

such as depth or subdural electrodes. Sometimes, they suffice, and a resective procedure can be planned depending on their yield.²¹

Subdural electrodes. Subdural and depth electrodes are the most commonly used for invasive intracranial recordings. Subdural electrodes may be one of 2 main types; strips or grids. Subdural strips are usually arrayed in a single row of 4-8 contacts, and their use is illustrated in **Figure 1**. Grids consist of 2 or more rows paralleled

in a rectangular or square fashion. Here, the number of contacts ranges from 16-64. Multiple variations are available in the market to best match the clinical needs. The flexibility of the material in which the electrodes are embedded is of paramount importance. Flexible strips and grids can provide the best material-brain interface for optimal recording. Burr holes versus craniotomies can be used for insertion of the strips and grids.²² It is common to get both types of subdural electrodes implanted in a single craniotomy so a large area of the

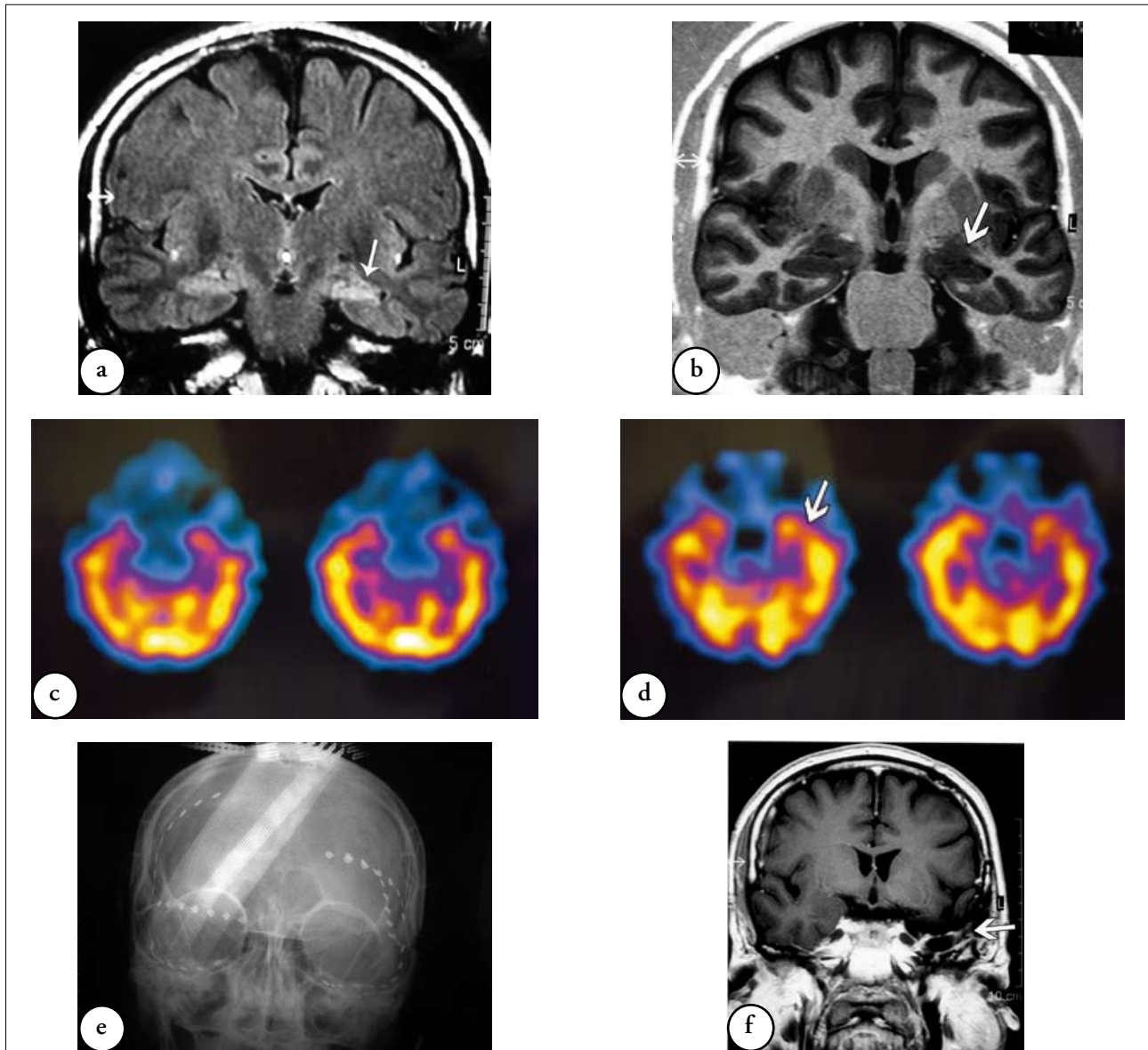


Figure 1 - A 44-year-old man with hypomotor non-lateralizing complex partial seizure semiology and right temporal rhythmic theta and α activity on video-EEG. a) Coronal Flair MRI section showing high signal in the left hippocampus suggestive but inconclusive of left mesial temporal sclerosis (arrow). b) Inversion recovery coronal MRI section showing slightly smaller left hippocampus (arrow). c) Inter-ictal SPECT scan. d) Ictal SPECT scan showing increased uptake in the left mesial temporal region when compared to the inter-ictal study (arrow). e) Upon forming the working hypothesis, bilateral subdural strip electrodes were placed as shown in this anteroposterior skull x-ray. f) Post operative coronal MRI image demonstrating resection of the left mesial structures (arrow). The patient became seizure free.

brain is covered as illustrated in Figure 2. All measures that may reduce the rate of infections should be respected. For example, a good dressing needs to be applied taking into account the common problem of CSF leak that may accompany patients throughout their stay in the epilepsy monitoring unit. Subcutaneous tunneling of the wires and exteriorization through separate incisions may decrease the incidence of CSF leak. All antiepileptics are usually discontinued except in special cases. Five-ten days of continuous EEG recordings are usually sufficient to define the cortical area that needs to be extirpated. The resection may then be carried out through a craniotomy that involves the same burr holes or the previous craniotomy. A successful mission of subdural electrodes is dependent on a critical and thorough analysis of the

data obtained by virtue of noninvasive and sometimes also by semi-invasive recording tools. Once implanted, the strip or grid cannot get any hint from its vicinity not encompassed by the relatively small recording area. Shifting from surface scalp EEG to the invasive one is similar to the camera zoom-in where you better see at higher magnification at the expense of losing vision at the periphery.

Cortical mapping may also be performed via the subdural grid. In order to get an accurate cortical map, cautious interpretation of the clinical responses elicited by pure electrode stimulation should be carried out. The responses related to confined cortical activation should be discriminated from those due to afterdischarges. Thus, subdural electrodes provide the epileptologist

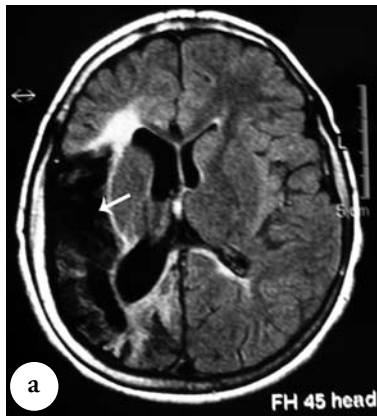
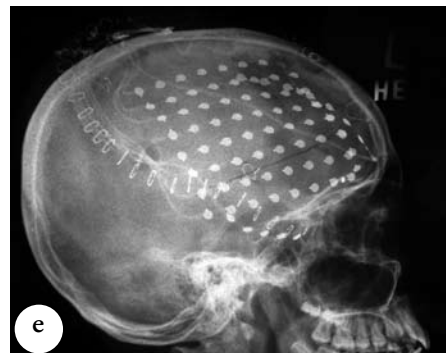
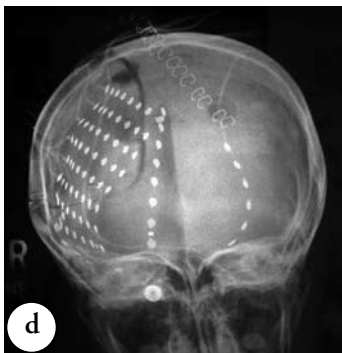
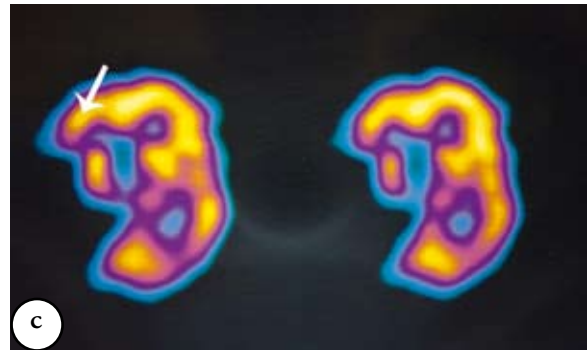
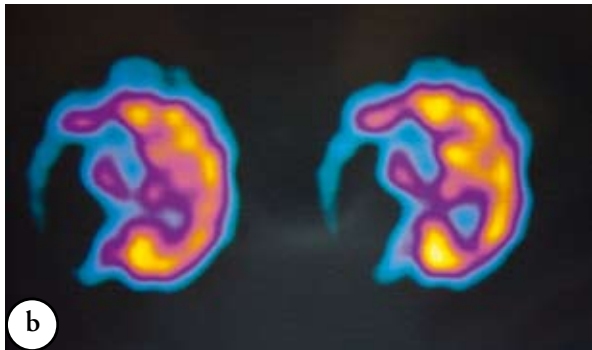


Figure 2 - A 13-year-old boy with a history of meningoencephalitis and right middle cerebral artery (MCA) infarct in early childhood causing intractable seizures of probable right frontal origin, but no significant functional impairment of the arm and leg. a) Axial flair image showing the extensive area of encephalomalacia in the right hemisphere following MCA territory infarct (arrow). b) Interictal SPECT scan. c) Ictal SPECT scan showing hyperintensity in the fronto-polar regions bilaterally and anterior to the area of encephalomalacia when compared to the inter-ictal study (arrow). d) Anteroposterior skull x-ray showing the large grid and 2 strips placed at surgery. e) Lateral skull x-ray demonstrating the grid.



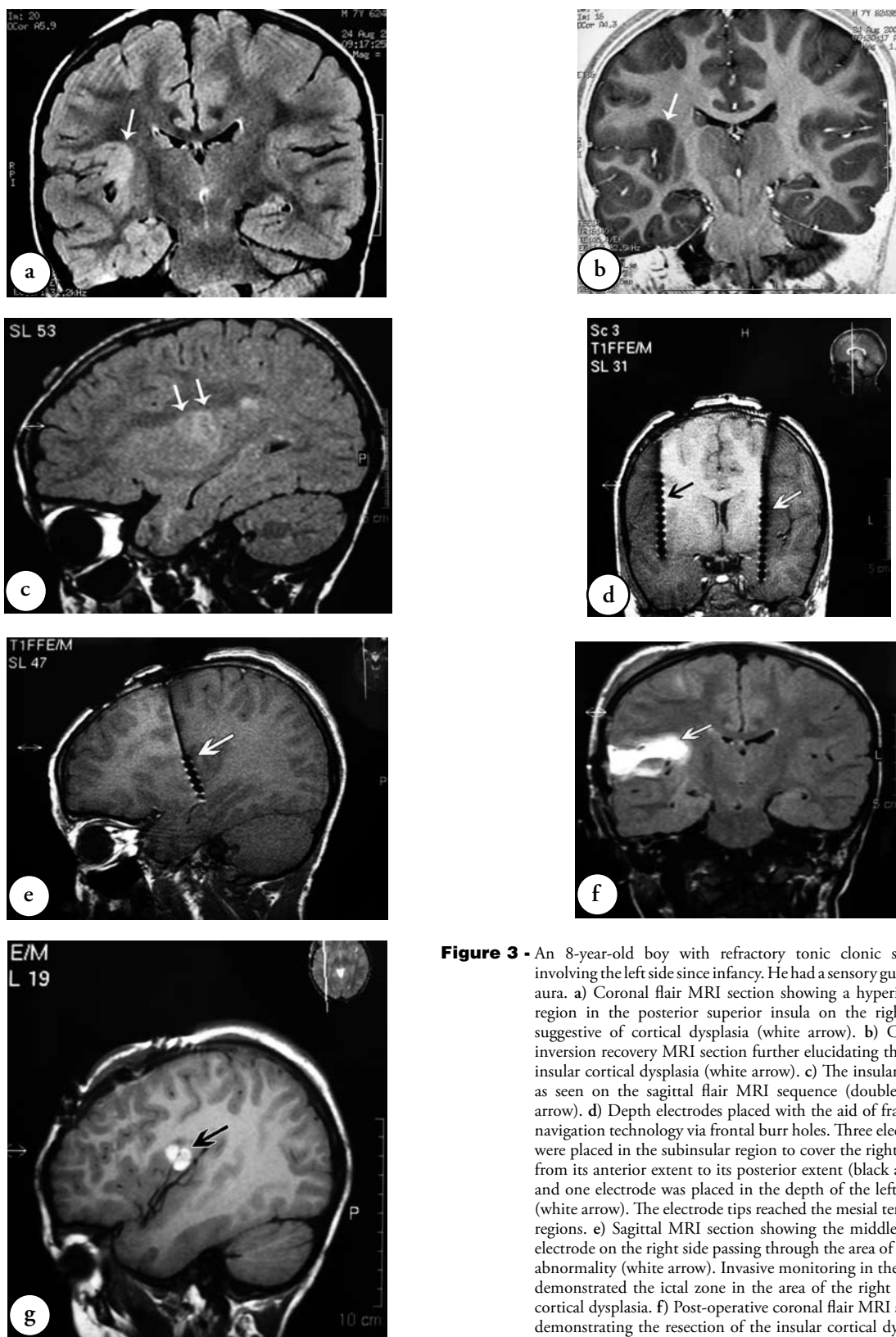


Figure 3 - An 8-year-old boy with refractory tonic clonic seizures involving the left side since infancy. He had a sensory gustatory aura. **a**) Coronal flair MRI section showing a hyperintense region in the posterior superior insula on the right side suggestive of cortical dysplasia (white arrow). **b**) Coronal inversion recovery MRI section further elucidating the right insular cortical dysplasia (white arrow). **c**) The insular lesion as seen on the sagittal flair MRI sequence (double white arrow). **d**) Depth electrodes placed with the aid of frameless navigation technology via frontal burr holes. Three electrodes were placed in the subinsular region to cover the right insula from its anterior extent to its posterior extent (black arrow), and one electrode was placed in the depth of the left insula (white arrow). The electrode tips reached the mesial temporal regions. **e**) Sagittal MRI section showing the middle depth electrode on the right side passing through the area of insular abnormality (white arrow). Invasive monitoring in the EMU demonstrated the ictal zone in the area of the right insular cortical dysplasia. **f**) Post-operative coronal flair MRI section demonstrating the resection of the insular cortical dysplasia performed with the navigation-assisted technique (white arrow). **g**) Sagittal MRI section showing the focal resection (black arrow). The patient is seizure free at last follow up.

with a mapping tool of high credibility that can bring the postsurgical neurological deficit to a minimum.

Intraoperative electrocorticography (ECoG). Also called acute ECoG to differentiate it from recordings obtained via chronically implanted subdural electrodes. Albeit it does not add significant morbidities to the epilepsy surgery, it provides only information on the extent of the irritative zone. In other words, interictal activities are detected by this means. Thus, the operator will not be provided with data regarding the epileptogenic zone, ictal onset zone, and the functional maps of the brain.¹ Currently, the main role of intraoperative ECoG is to guide the neocortical resection in cases of extratemporal epilepsy.^{4,23} Resection of a neocortical tumor (for example, dysembryoplastic neuroepithelial tumor) may lead to disappearance of surrounding spikes, thus, unnecessary cortical resection is avoided.²⁴ With a small series of patients with unilateral MTL surgery, Oliveira et al²⁵ tried to establish some prognostic parameters derived from intraoperative ECoG. However, the poor statistical power of their results disturbed the yield of the meticulous stepwise recordings carried out during surgery. This strategy has been abandoned in most centers treating such cases, since residual spikes were not associated with poor outcome.²⁶

Depth electrodes. Depth electrodes can record from buried cortex (namely, hippocampus, insula). Subdural recordings cannot immediately detect signals originating from those structures. However, the EEG obtained by the multi-contact depth electrode arrays has limited spatial sampling. Stereotactic techniques used for implantation can provide a precise targeting method. Nevertheless, detection of seizure onset at certain points using stereotactic depth EEG (SEEG) is not a guarantee that the ictal zone is not elsewhere, and what we get is only epileptiform discharges propagating from a distance.

The insertion planes are mainly orthogonal and parasagittal. The SEEG, described by Talairach and Bancaud²⁷ was basically planned using both MRI and angiography in addition to a stereotactic brain atlas aiming at targets in the coronal plane. The technique efficacy was confirmed in many clinical studies.²⁸ However, other techniques have been reported using different stereotactic frames and employing the parasagittal planes in the implanted electrodes maps. Afif et al²⁹ described the oblique approach to the insular region and the advantages it has over the orthogonally implanted electrodes. More contacts using a single electrode, the ability to explore a wider insular region in an anatomic and spatial fashion, and the reliability of recordings are the main benefits gained from that technical nuance illustrated by one of our patients with deep insular cortical dysplasia in Figure 3. As long as the suspicion goes around cortical areas amenable to subdural electrodes, epilepsy surgeons tend to look at

depth electrodes as a second option. Nowadays, the most common indication for depth electrodes is non-lateralizing MTS where both mesial temporal lobes need to be sampled. Dual recordings can lateralize the seizures; confirm the existence of bilateral ictal onset zones in certain cases, and calculate the interhemispheric propagation time.³⁰ Nevertheless, Eisenschenk et al³¹ found that properly placed mesial subtemporal subdural strips medial to the collateral sulcus could lateralize all seizures when their recordings were interpreted alone. This was illustrated earlier in Figure 1, where the patient had MTS with false lateralization on non-invasive EEG monitoring.

Complications. Invasive diagnostic methods always carry a higher morbidity rate in comparison to non-invasive ones. This rule extends to the intracranial EEG recording tools. Extra-axial hematomas may complicate the course of subdural electrode implantation. In their clinical series, Fountas et al³² reported postoperative epidural (EDH) hematomas in 1.6%, and subdural (SDH) in 1.1% of their patients. In fact, the incidence of EDH ranges between 0-2.5%, and 0-14% for the SDH when clinical series are reviewed. According to the rule of Monroe-Kellie,³³ the subdural implant (grid, strip) is not easily affordable in the closed skull. Hence, increased intracranial pressure (ICP) may first come to mind as a sequela of the “space occupying” subdural body, causing disturbance in the homeostasis of ICP. Incited by a single catastrophe related to an underdiagnosed fatal intracranial hypertension (ICH), Shah et al³⁴ insisted on using ICP monitors in all cases of subdural grid recordings. They encountered an elevated baseline ICP compared with the values expected for age. Moreover, they suggested that epileptic activity per se can lead to elevation of ICP in children. One of the 2 mortalities that occurred in the series of Fountas et al³¹ was the result of malignant brain edema that went out of control. Although rare, morbidities relating to intracranial hypertension in the context of subdural electrode implantation are serious enough to render medical awareness of utmost sensitivity. Prophylactic administration of dexamethasone could decrease cerebral edema and its consequences in pediatric patients undergoing invasive intracranial monitoring.³⁵

The risk of hemorrhage after stereotactic electrodes placement ranges from 0.6-2.1%. From a total of 567 stereotactically inserted electrodes for different diagnoses, 274 electrodes were instilled in the context of SEEG for epilepsy localization. The risk of symptomatic ICH was 1.2%. Only one hemorrhage occurred after a hippocampal depth electrode was inserted. Hypertension was the most significant risk factor for ICH.³⁶ Morbidity relating to infections range from 0-12% when different series are reviewed.³⁷ By following meticulous techniques in dural closure, electrode subcutaneous tunneling, purse ring sutures, and heavy

dressings, we have not encountered any complications in our series of patients who were subjected to invasive monitoring.

The future. The noninvasive localization of brain regions involved in the initiation and propagation of epileptic activities is the ultimate goal of many current clinical research studies. Moreover, the obtained findings of those new diagnostic tools may revolutionize the concepts of epileptic syndromes. For instance, dense array EEG holds the promise to maximize the yield of scalp recordings by improving the spatio-temporal resolution of EEG, and it may also lead to new theories on epilepsy circuitries and consciousness (namely, corticothalamic and corticolimbic circuits).³⁸ The complementary effect provided by combining EEG recordings and fMRI scanning may shed light on the spectrum of cortical involvement in the network topology of seizures.³⁹ Advances are not exclusive to noninvasive methods, as the available sophisticated computing software is dictating modified epileptic networks, observations and therapeutic targets when applied to the intracranial recordings.⁴⁰ Cortical stimulation by chronically implanted subdural electrodes is being involved in more than eloquence maps construction. In some centers, a cortico-cortical evoked potential study is included in the presurgical invasive investigation in order to track the functional connectivity and to understand the ictal semiology.⁴¹ Further expansion of the cortical recordings and stimulation legacy will provide us with better insights into the prognostication of epilepsy surgery and will broaden our view of the whole brain function.

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