Merging Tradition with Innovation: Intraoperative Corticography and 7 Tesla Magnetic Resonance Imaging Sparing Chronic Intracranial Electrode Implantation in “Non-Lesional” Epilepsy Surgery

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Abstract

The practice of epilepsy surgery has largely shifted from invasive investigations with chronic intracranial electrodes to high resolution imaging modalities that may delineate the epileptogenic zone in a non-invasive manner. Nevertheless, non-lesional cases, particularly due to extratemporal cryptic pathology, still pose a major challenge. Here we describe the value of combining traditional electrocorticography with the innovation of 7 Tesla magnetic resonance imaging for the detection of a focal cortical dysplasia and thereby sparing the need for further invasive investigation with chronic intracranial electrodes. We conclude that, especially for extratemporal malformations of cortical development, the use of electrocorticography guided by higher resolution magnetic resonance imaging may effectively delineate the epileptogenic zone and define appropriate resection margins. This highlights the importance of a multidisciplinary approach and of combined neurophysiologic and imaging techniques in contemporary epilepsy surgery.

Introduction

Refractory epilepsy in the setting of negative conventional radiological evaluation is often due to subtle focal cortical dysplasias (FCDs). It remains a great challenge for contemporary epilepsy surgery, particularly in extratemporal cases, where the semiological presentation and the scalp EEG recordings are variable and frequently misleading. Many of these cases end up being implanted with chronic subdural electrodes. Here we report the value of combining higher resolution magnetic resonance imaging (MRI) with intraoperative electrocorticography (ECoG) in obviating the need for additional investigation, with favorable surgical outcome.

Case Report

A 27-year-old, right-handed woman with intractable epilepsy was referred for pre-surgical evaluation. Seizures began at age 10. Initially attacks consisted of generalized tonic-clonic seizures without warning or lateralizing features. Between ages 15-18, complex partial seizures with right arm clonic activity and version to the right became apparent. At age 18, seizures with no aura, expressive aphasia, impaired consciousness and rocking automatisms emerged and became her sole seizure type, occurring several times each week.

Pregnancy, delivery and early development were normal. She had mild learning disabilities identified by age 7 that necessitated special education. Her seizures have been refractory to 7 prior antiepileptic medications administered singly and in combination. On referral she was taking high doses of lamotrigine, levetiracetam and benzodiazepines.

Clinical examination showed a Montreal Cognitive Assessment score of 21 out of 30 characterized primarily by frontal lobe cognitive deficits. She scored low on the Beck’s depression inventory and borderline on the Beck’s anxiety inventory (21). Her examination was otherwise non lateralizing.

On initial investigation a 3-Tesla MRI of her brain was unremarkable. 18-FDG-PET scan failed to show focal hypometabolism. Scalp recordings showed frequent paroxysms of spikes, polyspikes and spike-wave discharges with a widespread, bilateral, frontocentral distribution and a consistent left frontal amplitude predominance (Figure 1). At least 12 brief clinical events were captured, during which the patient had an acute sense of fear, ictal aphasia, claspmg of her hands, rocking back and forth and rapid recovery with recollection of half of them. During those events the patient’s EEG showed generalized attenuations with muscle artifact but no clear lead in scalp EEG changes. Neuropsychological evaluation reported borderline to low average intellectual profile with weakness in processing speed, abstract thinking, spatial attention and confrontation naming with intact verbal and visual memory. A magnetoencephalogram (MEG) showed frequent spikes in the frontotemporal sensors, some bilaterally and some lateralized to the left. In combination with a functional MRI she was identified as left hemispheric dominant for language.

The patient was readmitted for depth electrode investigation, which was performed with 5 orthogonal depth electrodes on each side, placed in the orbitofrontal, prefrontal, premotor, cingulate and anterior temporal regions (Figure 2). Recordings showed frequent...
focal spikes, spike and wave complexes and polyspikes originating mainly from the deep contacts of the left prefrontal depth electrode (LPF 1), at times in isolated runs and at other times propagating to the deep contacts of the left premotor depth electrode (LPM 1 to 3) and the deep/middle contacts of the left cingulate electrode (LCG 1 to 6). Less common independent focal spikes were seen from the other depth electrodes contacts in the left hemisphere, however, the left premotor electrode (particularly contacts LPM 2 to 3) became the most active electrode interictally after the occurrence of the seizures. There was significant activation of the interictal activity during drowsiness and sleep. Approximately 40 seizures were recorded, particularly in drowsiness and sleep. They were of brief duration, typically less than 30 seconds and were clinically stereotyped, consisting of partial loss of consciousness, speech arrest, and wringing movements of both upper extremities, bilateral shoulder shrugging and occasional sitting up in bed, typical for the patient’s habitual events. Rare electrographic events had no visible behavioral correlate. Electrocgraphically, all seizures were characterized by interruption of the baseline abundant
interictal epileptiform activity followed by a widespread, high-frequency rhythmic activity that had a good representation in all depth electrodes bilaterally but appeared of higher amplitude of the left premotor depth electrode (particularly LPM 3 to 4) with spread to the adjacent to it left cingulate and left prefrontal depth electrodes (Figure 3). The scalp EEG showed similar pattern of widespread, high-frequency rhythmic activity, maximal frontocentrally. Prior to explantation of the electrodes, direct stimulation was performed which failed to reproduce the patient’s clinical seizures despite stimulating several regions. At this juncture, it was apparent that the phase II investigation lateralized the patient’s epilepsy to the left and localized it to the frontal lobe but it did not manage to pinpoint the extent or margins of the epileptogenic zone.

With the knowledge of the depth recordings in mind and thanks to its higher resolution a 7 Tesla MRI identified a subtle loss of gray-white matter differentiation along the medial aspect of the left superior frontal gyrus, associated with mildly increased T2 signal in the adjacent subcortical white matter (Figure 4). That became more apparent in further quantitative analysis of extent in the white matter blurring (Figure 5). It was therefore decided to investigate that region with intraoperative electrocorticography (ECoG) and if it localized

![Figure 3](image3.png)

**Figure 3:** Ictal depth electrode recording showing interruption of the baseline abundant interictal epileptiform activity followed by a widespread, high-frequency rhythmic activity with a good representation in all depth electrodes bilaterally, maximal at the left premotor depth electrode and the adjacent to it left cingulate and left prefrontal depth electrodes. Settings: Bipolar montage, low pass filter 1Hz, high pass filter 70Hz, sensitivity 100uV.

![Figure 4](image4.png)

**Figure 4:** Coronal view of 7 Tesla MRI (FLASH susceptibility weighted T2*, 330 micron in-plane resolution 1mm thick) showing a subtle loss of gray-white matter differentiation along the medial aspect of the left superior frontal gyrus, associated with mildly increased T2 signal in the adjacent subcortical white matter (green arrow).
the previously seen epileptiform abnormalities to a specific region, to proceed with an ECoG guided resection. Otherwise, a chronic implantation with a grid in left frontal lateral convexity would be performed.

The intraoperative electrocorticography was performed with a special reformatted 64 contact grid over the left lateral frontal convexity with the anterior-superior corner of the grid represented by contact 1, 2 and 9 and the superior-inferior corner of the grid represented by contacts 7, 8 and 16 (Figure 6). Frequent brief bursts of polyspikes were present and well localized at contact 1, 2, 9 and 10 (Figure 7). These organized in runs up to 15 seconds and were further activated with administration of 30 mcg/kg of alfentanil, evolving into brief electrographic seizures. The electrographic signature of that region as recorded by ECoG resembled well the morphology of the seizure onset as recorded by invasive recordings. Yet it was significantly more focal, consistent with the provisional diagnosis of focal cortical dysplasia and was confirmatory of the epileptogenic focus. Thus, chronic implantation with a grid of intracranial electrodes was evaded.

After identification of the regions showing increased excitability motor mapping was performed. The first part of this consisted in central sulcus localization using the median cortical SSEPs phase reversal technique. An 8 contact strip was used, placed across and perpendicular to the presumed location of the central sulcus, at the level of the hand area on the lateral convexity, with contact 1 most posterior. Phase reversal was identified between contact 5 (precentral) and 3 (postcentral) (Figure 8). Subsequently direct cortical electrical stimulation was performed with currents ranging from 2-8mA using multipulse train technique through a handheld monopolar stimulating electrode. The threshold for the motor strip was considered at 7mA, when muscle motor evoked potentials (MEPs) were obtained in the contralateral hand muscles. No after-discharges or seizures were triggered. Consequently, the motor strip was identified posteriorly for the resection target recognized by ECoG. After resection was performed, the post-resection ECoG showed dramatic resolution of the epileptiform activity (Figure 9). Rare residual sharps were present at the border of the inferior frontal gyrus and these regions were not resected further given their proximity with the Broca’s area.

The patient tolerated the procedure well without any postoperative deficits. Postoperative MRI showed expected post-resection changes (Figure 10). Pathological analysis of the surgical resection specimen was consistent with cerebral cortex with focal neuronal clustering, large dysmorphic neurons, and balloon cells, with numerous neurons in the white matter and disrupted radial and laminar architecture of the cortex. These findings confirmed the diagnosis of a focal cortical dysplasia type IIb. Nine months postoperatively, the patient has sustained only a single seizure.

Discussion

Successful epilepsy surgery requires removal of both the epileptogenic lesion along with the surrounding epileptogenic zone [1].

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Figure 5: Quantitative analysis of the suspected area identified in the 7 T MRI showing the extent of the estimated region of abnormal white matter projected to surface in a sagittal, axial and coronal view (red region).

Figure 6: Schematic representation of the 64 contact grid layout used for the intraoperative electrocorticography over the left lateral frontal convexity. The anterior-superior corner of the grid was represented by contact 1, 2 and 9 and the superior-inferior corner of the grid was represented by contacts 7, 8 and 16.
Figure 7: Pre-resection intraoperative electrocorticography showing frequent brief bursts of polyspikes better localized at contact 1, 2, 9 and 10 that organized in runs up to 15 seconds (highlighted contacts). The electrographic signature of that region was consistent with the provisional diagnosis of focal cortical dysplasia and was confirmatory of the epileptogenic focus.

Figure 8: Central sulcus localization using the median cortical SSEPs phase reversal technique. An 8 contact strip was used, placed across the presumed location of the central sulcus with contact 1 most posterior. Phase reversal was identified between contact 5 (precentral) and 3 (postcentral).
Figure 9: Post-resection intraoperative electrocorticography showing dramatic resolution of the epileptiform activity. Rare residual sharps were present at the border of the inferior frontal gyrus and these regions were not resected further given their proximity with the Broca’s area.

Figure 10: Coronal FLAIR post-operative MRI showing encephalomalacia of the left superior parasagittal frontal cortex, correlating with the resection cavity. A crescentic, non-enhancing, extra-axial subdural collection along the left frontal-parietal convexity deep to the craniotomy site was also seen, related to operative changes.

However structural lesions are associated with zones of epileptogenesis in neighboring and remote areas of the brain [1]. The detection of the epileptogenic zone solely through scalp EEG recordings may be problematic due to the complex anatomy of the various regions, deep or restricted foci, rapid propagation or contamination from muscle and movement artifacts [2]. Therefore, intra- or extraoperative subdural recordings may be required for further localization.

Intraoperative corticography was established as a cornerstone of epilepsy surgery in early 1950s by Penfield and Jasper [3]. It offers flexible positioning of recording electrodes pre- and post-resection and provides also the opportunity for direct stimulation for seizure reproduction and cortical mapping without the risks associated with chronic implantation of subdural electrodes [4]. Corticography is limited by the time constraints of an operation, the common inability to capture seizures, the widespread and often propagating distribution of the interictal activity and the effect of the concurrently used anesthetic medication [4]. Despite its long history, the utility of intraoperative electrocorticography remains controversial [5].

In temporal lobe epilepsy, ECoG has been used to determine the boundaries of the epileptogenic zone and hence, guide the extent of the resection. Most studies failed to show a reliable predictive value of ECoG in surgical outcome of anatomically standardized anterior temporal lobectomies [6]. However, significant controversy exists regarding the extent of hippocampal resection posteriorly and other investigators identified a role for ECoG in answering that question [7].
Extratemporal lobe epilepsy is a more heterogeneous group that poses several challenges in the quest for the epileptogenic zone [8]. The semiology is variable, the epileptogenic zone is frequently broad and may coexist with hippocampal sclerosis (“dual pathology”), the interictal and ictal patterns multifocal, absent and occasional misleading and the imaging studies often unrevealing [8]. Most of the literature pertaining on the use of ECoG in extratemporal epilepsy stems from lesional cases [9-12], although prospective studies are lacking [13]. For non lesionalextratemporal resections the data is sparse [14]. The existing data failed to show a clear relationship between the extent of epileptogenic tissue resected and the seizure outcome [10,15].

Cortical dysplasias along with tumors constitute the majority of extratemporal epilepsy causes [16]. They are often associated with characteristic electrographic signatures consisting of repetitive electrographic seizures, repetitive bursting discharges and continuous or semi-continuousspiking [17]. The interictal pattern identified in ECoG can reliably reflect the interictal pattern of long term intracranial recordings and has good correlation with the ictal zone when the interictal discharges frequency exceeds 3 spikes/min [18]; a rate typically exceeded in FCDs. Despite the widespread evidence of cortical irritability, particularly among extratemporal cases of FCDs, the principal spike lobe and scalp-recorded seizure origin appear to correlate well with epileptogenesis [19]. Palmini et al. [17] showed favorable surgical outcome in 75% of patients with complete excision of the cortical tissue displaying epileptiform activity in the pre-resection ECoG [17]. Conversely, when epileptogenic tissue remained in situ as indicated by ECoG, the outcome was poor [17]. Therefore, ECoG appears to have a clearer indication in epilepsy surgery related to FCDs as illustrated also in our case.

The advent of modern neuroimaging modalities has revolutionized the practice of epilepsy surgery in the past decades, particularly for often subtle abnormalities such as FCDs. Radiological findings of FCDs include cortical thickening, loss of gray-white differentiation and increased T2/FLAIR and/or decreased T1 signal extending from the ependymal layer to the cortical surface, also known as the transmantle sign. Similarly focal hypoplasia, deep sulci with malformation in their depth, gyral broadening and white matter atrophy has been described [20]. Various MRI sequences with the potential to increase the yield for detection of FCDs have been reported including arterial spin labeling evaluating cerebral blood flow [21], susceptibility weighted imaging targeting iron deposition regions [22] and diffusion tensor imaging assessing the extent of white matter involvement associated with the dysplasia [23]. The detection of subclinical abnormal gyration patterns using specialized software [24] or automated lesion detection methods such as voxel-based morphometry [20] have also been implemented. The use of MEG [25] and FDG-PET co-registered with MRI [26] have also been proposed as sensitive tools to assist in the detection of type IIIB FCDs.

Optimizing image quality is essential for the identification of focal FCDs. One approach to improving the signal-to-noise ratio is to use of phased array surface coils with larger arrays [27]. Another approach is to employ higher field strength magnets, including 3T and now 7T MRI machines [27]. We have noticed significant improvement with those two techniques, as also depicted in the case reported herein.

Conclusion

Subtle focal cortical dysplasias are often the culprit of “non lesional” intractable epilepsy. For these cases the ability to delineate and fully resect the entire dysplastic cortex is the most powerful predictor of good surgical outcome [28]. Merging traditional techniques such as ECoG and modern neuroimaging modalities such as 7 Tesla MRI can complement each other in this endeavor and spare the need for more invasive recordings with chronically implanted subdural electrodes.

References


