Current Literature
In Clinical Science

Difficult-to-Localize Intractable Focal Epilepsy: An “In-Depth” Look

Stereoencephalography in the “Difficult to Localize” Refractory Focal Epilepsy: Early Experience From a North American Epilepsy Center.

PURPOSE: Stereo-encephalography (SEEG) enables precise recordings from deep cortical structures, multiple noncontiguous lobes, as well as bilateral explorations while avoiding large craniotomies. Despite a long reported successful record, its application in the United States has not been widely adopted. We report on our initial experience with the SEEG methodology in the extraoperative mapping of refractory focal epilepsy in patients who were not considered optimal surgical candidates for other methods of invasive monitoring. We focused on the applied surgical technique and its utility and efficacy in this subgroup of patients. METHODS: Between March 2009 and May 2011, 100 patients with the diagnosis of medically refractory focal epilepsy who were not considered optimal candidates for subdural grids and strips placement underwent SEEG implantation at Cleveland Clinic Epilepsy Center. Demographics, noninvasive clinical data, number and location of implanted electrodes, electrophysiologic localization of the epileptic zone, complications, and short-term seizure outcome after resection were prospectively collected and analyzed. KEY FINDINGS: Mean age was 32 years (range 5-68 years); 54 were male and 46 female. The mean follow-up after resection was 15 months. In total, 1,310 electrodes were implanted. Analyses of the SEEG recordings resulted in the electrographic localization of the epileptogenic focus in 96 patients. In the group of 75 patients who underwent resection, only 53 had at least 12 months follow-up. From this group, 33 patients (62.3%) were seizure-free at the end of the follow-up period. The presence of abnormal pathologic finding was strongly associated with postoperative seizure control (p = 0.005). The risk of hemorrhagic complications per electrode was 0.2%. SIGNIFICANCE: In patients who are not considered to be ideal candidates for subdural grids and strips implantation, the SEEG methodology is a safe, useful and reliable alternative option for invasive monitoring in patients with refractory focal epilepsy, providing an additional mean for seizure localization and control in a “difficult to localize” subgroup of patients.

Commentary
Monitoring with intracranial electrodes is the gold standard for identification of seizure-onset zones and mapping of eloquent cortex in patients with intractable focal epilepsy. Electrode implantation is guided by hypotheses about localization of the epileptogenic zones that are based on assessment of seizure semiology, interictal and ictal scalp-EEG, functional and anatomic neuroimaging, and neuropsychological testing. Optimal monitoring may be done with depth electrodes if the presumed epileptic focus is deep, and with subdural electrodes if the focus is superficial and if precise, systematic cortical mapping is needed. However, the trends in Europe and the United States over the past several decades have been to use stereoelectroencephalography (SEEG) and subdural electrode monitoring, respectively, as primary methods for evaluation of intractable epilepsy, regardless of the presurgical hypotheses.

The history of SEEG dates back to 1957, when Jean Talairach built a coordinate system using the anterior and posterior commissures as landmarks and generated a stereotactic atlas of deep brain nuclei. Jean Bancaud soon realized the potential use of stereotactic surgery in localizing epileptic brain regions in three dimensions. Bancaud and Talairach devoted an operating room to stereotactic neurosurgery in 1959, and coined the term stereoelectroencephalography (SEEG) in 1962 (1). Electrodes are implanted stereotactically, targeting areas within and around epileptogenic lesions and areas suspected to be part of the seizure network, thus helping to identify the ictal onset zone and areas of interictal spiking (2). In some European centers, SEEG has been used for evaluation of any intractable epilepsy, including situations when language mapping may be necessary such as in the Sylvian areas (3). Soon afterwards, the use of SEEG became part of the surgical evaluation of intractable epilepsy in the Montréal Neurological Institute (4), but its introduction to the United States was slower,

Epilepsy Currents, Vol. 13, No. 2 (March/April) 2013 pp. 88–89 © American Epilepsy Society
OPEN ACCESS Freely available online
where the use of subdural electrodes saw more proliferation across the years. In the United States, depth electrodes have been used primarily to record from the mesial temporal structures. Of note, Sperling and O’Connor compared depth with subdural electrodes in temporal lobe epilepsy and found that the ictal discharges were detected initially by depth electrodes before they propagated to subdural electrodes (5).

Gonzalez-Martinez et al. report their recent experience with SEEG at the Cleveland Clinic. Between 2009 and 2011, they implanted 1,310 electrode arrays in 100 patients, including 17 children, who were not ideal candidates for subdural electrode monitoring. The 100 patients included 39 with focal MRI abnormality and 27 who have had prior epilepsy surgery, including subdural monitoring or surgical resection. Forty patients underwent bilateral SEEG implantation. Indications for SEEG use included targeting deep regions, such as the mesial temporal structures, insula, or cingulate gyrus; subjects who failed prior subdural monitoring; bihemispheric implantation for lateralization or localization of the epileptic focus; and nonlesional cases where multiple locations within a network, such as the limbic system, needed to be sampled as suggested by the seizure semiology.

SEEG monitoring allowed localization of the epileptic focus in 96 patients, of whom 75 patients underwent resection. The authors appropriately excluded acute postoperative seizures for up to 1 week after surgery from the classification of the surgical outcome, included patients who had at least 1 year of follow-up, and defined seizure freedom as absence of all kinds of seizures including auras. Only 53 patients completed 1 year follow-up, including 28 nonlesional patients and 22 with temporal lobe epilepsy. Of the 53 subjects, 33 (62.3%) were seizure free. Complications occurred in 3 patients of the 100, including intraparenchymal hemorrhage in two patients and subdural hemorrhage in one. Each of these complications occurred with one electrode per subject, making the overall risk of complications per electrode 0.2%. As regards surgical outcome, the authors found that the absence of histopathological abnormalities in the resected tissue, but not nonlesional or extratemporal epilepsy, was associated with poor surgical outcome. Of interest, the authors also used SEEG for functional mapping, but they did not report the results. They had an impression that SEEG-guided resections may be smaller than resections determined through subdural monitoring, suggesting more specificity of identification of the epileptic focus by SEEG. They also argued that their method may be safer than the traditional SEEG implantation methods described by European authors.

Subdural electrode monitoring has high spatial resolution of the superficial cortex, which constitutes only a small subset of the cerebral cortex as it facilitates systematic mapping of the superficial cortex, SEEG allows mapping of the depth of the sulci, white matter, and deep brain structures (6). Thus, SEEG allows for studying neuronal networks involved in seizure generation and propagation as well as those important for cognitive or behavioral functions.

A particularly interesting indication of SEEG is in nonlesional patients whose presurgical evaluation suggests involvement of a network, such as the limbic system. In such cases, multiple targets within the same network may be sampled by SEEG to improve accuracy of detecting seizure focus and, consequently, the surgical outcome, which is historically inferior in nonlesional epilepsy than in patients with MRI abnormalities. For example, in patients whose seizure semiology and scalp EEG are consistent with temporal lobe epilepsy, SEEG sampling of the mesial temporal structures as well as areas that have known connectivity with the temporal lobe, such as the posterior cingulate gyrus, the basal temporal cortex, the orbitofrontal cortex, and insula, among others, may help rule out extratemporal seizure onset in a clinically silent region with secondary propagation to the mesial temporal structures (7).

SEEG appears to be a safe procedure with an acceptable rate of surgical risks. It has evolved over the years owing to the introduction of magnetic resonance imaging in the evaluation of patients with epilepsy, and to advanced software that provides accurate coordinates for stereotactic implantation of desired brain targets, and efficiently performs reliable superimposition of cerebral angiograms and brain MRI facilitating avoiding blood vessels during implantation. It would be exciting to see more centers in the United States using SEEG in conjunction with subdural electrode monitoring, as optimal monitoring should be considered with either or both methods depending on the presurgical hypothesis about localization of the epileptogenic zone.

by Mohamad Z. Koubeissi, MD

References

American Epilepsy Society

Epilepsy Currents Journal

Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in four parts.

1. Identifying information.
   Enter your full name. If you are NOT the main contributing author, please check the box “no” and enter the name of the main contributing author in the space that appears. Provide the requested manuscript information.

2. The work under consideration for publication.
   This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking “No” means that you did the work without receiving any financial support from any third party – that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check “Yes”. Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

3. Relevant financial activities outside the submitted work.
   This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. For example, if your article is about testing an epidermal growth factor receptor (DGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

   Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work’s sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

   For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Other relationships
   Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.
Section #1 Identifying Information

1. Today’s Date: 6/12/2012

2. First Name Mohamad Last Name Koubeissi Degree MD

3. Are you the Main Assigned Author? ☐ Yes ☐ No

If no, enter your name as co-author:

4. Manuscript/Article Title: Difficult-to-Localize Intractable Focal Epilepsy: An “In-Depth” Look

5. Journal Issue you are submitting for: 13.2

Section #2 The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

<table>
<thead>
<tr>
<th>Type</th>
<th>No</th>
<th>Money Paid to You</th>
<th>Money to Your Institution*</th>
<th>Name of Entity</th>
<th>Comments**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Grant</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Consulting fee or honorarium</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Support for travel to meetings for the study or other purposes</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Fees for participating in review activities such as data monitoring boards, statistical analysis, end point committees, and the like</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Payment for writing or reviewing the manuscript</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Provision of writing assistance, medicines, equipment, or administrative support.</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Other</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This means money that your institution received for your efforts on this study.
** Use this section to provide any needed explanation.
Section #3 Relevant financial activities outside the submitted work.
Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the “Add” box. You should report relationships that were present during the 36 months prior to submission.

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

<table>
<thead>
<tr>
<th>Type of relationship (in alphabetical order)</th>
<th>No</th>
<th>Money Paid to You</th>
<th>Money to Your Institution*</th>
<th>Name of Entity</th>
<th>Comments**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Board membership</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Consultancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Employment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Expert testimony</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Grants/grants pending</td>
<td></td>
<td></td>
<td>The authors is a Spitz scholar and has received Grants from the Coulter Foundation and Medtronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Payment for lectures including service on speakers bureaus</td>
<td></td>
<td>From UCB, Cyberonics and Pfizer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Payment for manuscript preparation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Patents (planned, pending or issued)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Royalties</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Payment for development of educational presentations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Stock/stock options</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Travel/accommodations/meeting expenses unrelated to activities listed.**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Other (err on the side of full disclosure)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Section #4 Other relationships
Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

☑ No other relationships/conditions/circumstances that present a potential conflict of interest.
☐ Yes, the following relationships/conditions/circumstances are present:

Thank you for your assistance.

Epilepsy Currents Editorial Board