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Intracranial recordings for non-lesional mesiotemporal epilepsy? Almost always, but not quite always



Resective epilepsy surgery is standard of care and the only curative treatment for drug-resistant focal epilepsy. Among epilepsy surgeries, mesiotemporal lobe resection for unilateral temporal lobe epilepsy (TLE) in patients with mesiotemporal sclerosis (MTS), has been shown to have the best long-term seizure-free outcome with 60–80% seizure-free rates [1–3].

“Bilateral” mesiotemporal lobe epilepsy is difficult to define, and is best viewed as a continuum that has various degrees. The degree of “bilaterality” is a quantitative or a graded variable, and not a qualitative “yes/no” or binary variable. “True” unilateral disease would be a patient with zero evidence of contralateral involvement (by any measure: electrographic, structural imaging, or function), 100% seizure onset from one hippocampus, and a seizure free outcome after mesiotemporal resection. At the other end of the spectrum, “true” bilateral temporal lobe epilepsy could be defined as a patient with exactly 50% seizures arising from left and right mesiotemporal structures independently on intracranial recording. Those two extremes are obviously theoretical, and in clinical practice, most patients fall somewhere in between. There are multiple variables: semiology, interictal and ictal scalp EEG findings, interictal and ictal intracranial EEG findings, structural neuroimaging, functional neuroimaging and neuropsychology (including Wada testing).

In the study by Perven et al. [4, this issue], all patients with non-lesional mesial TLE and unilateral pre-implantation hypothesis underwent bilateral invasive evaluation. They found that 4 of 28 patients (14%) had independent bitemporal seizures on invasive intracranial recording. Based on their findings, the authors propose that *all* patients with non-lesional mesial temporal lobe epilepsy require bilateral intracranial EEG prior to considering mesial temporal lobe resection, even if non-invasive evaluation data point to a unilateral seizure focus. Patients in the “non-lesional” group in this study had negative MRI *and* negative PET and that is a particularly challenging population, but we would argue that strictly speaking, PET is a functional neuroimaging modality and “non-lesional” should only refer to anatomy (MRI).

In the evaluation of the four “non-lesional” patients, several important pre-surgical tests were not performed: MEG (3 patients), Wada (3 patients), fMRI (2 patients), neuropsychological evaluation (1 patient), and ictal SPECT (no patients). We would argue that if any of those were strongly localizing to the same hippocampus, intracranial recordings might not be needed.

While we agree that non-lesional cases will *almost always* require intracranial monitoring to rule out bilateral temporal disease prior to surgical resection, this should not be a universal rigid rule, and must be individualized. Every patient’s situation is differ-

ent and there are many variables, with an indefinite number of possibilities. For example, even in patients with bilateral disease, all seizures may not be equally disabling. One side may be responsible for clinical disabling seizures (that may generalize) while the other side may be mostly subclinical. Because of so many variables, each patient is unique and should be individualized. In addition to patients with negative MRI, to some degree the same discussion applies to patients with bilateral MTS on MRI. In addition, pre-surgical data that are conflicting rather than neutral may themselves indicate bilateral disease.

Another important (and new) question is: If intracranial recordings are needed, is there a role for traditional intracranial EEG (short sampling), or should it be replaced by “chronic ambulatory electrocorticography” with the RNS system (longer sample and treatment)?

RNS allows intracranial EEG recording for long periods providing more accurate data based on a larger sample of recording than what can be obtained during video-EEG monitoring in an epilepsy monitoring unit (EMU). It has been shown that the average time to capture an electrographic contralateral seizure in a patient with suspected bilateral seizures was 41.6 days, far longer than an average EMU stay [5]. Seizures may cluster and alternate onset between sides after weeks to months [6]. Typical video-EEG recording sessions during an EMU hospital stay, whether scalp or intracranial, may falsely lateralize the seizure onset zone due to short sampling time window.

RNS does not exclude the option of a resective surgery in the future. It provides reliable information to be used prior to a “destructive” procedure, while in the meantime, it provides treatment. In a recent study [6], 16% of patients treated with RNS using bilateral MTL leads for suspected bilateral MTL epilepsy subsequently underwent MTL resection, one third of whom had exclusively unilateral electrographic mesial temporal lobe (MTL) seizures recorded over two years prior to resection. Another study showed that 16% of 82 patients implanted with bilateral MTL leads had only unilateral electrographic seizures after an average of 4.6 years [5].

While RNS may now be preferred over short-term intracranial EEG in this situation, it has its limitations. RNS system is not widely available worldwide, and is currently only available in the US. It is expensive and requires close follow-up with compliant and cooperative patients who are reliable in uploading data. It has limited storage capacity and does not have video to differentiate clinical from electrographic seizures. While the RNS system has the advantage of recording data over a prolonged period, it has limited spatial coverage (to only eight electrodes and four channels), as opposed to intracranial monitoring, which typically provides

broader coverage but for a short period of time. In other words, RNS is better in time but limited in space, while traditional intracranial EEG is better in space but limited in time.

Where RNS is not the preferred option or is not available, “traditional” short-term intracranial EEG (frequently stereo-EEG) remains the best option. The 80% predominance on one side has been a general consensus, but how many seizures should this be based on remains an unanswered question.

Ethical statement

The authors confirm compliance with all relevant ethical regulations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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