FULL-LENGTH ORIGINAL RESEARCH

Utility of foramen ovale electrodes in mesial temporal lobe epilepsy

*[1]Sameer A. Sheth, †[1]Joshua P. Aronson, ‡Mouhsin M. Shafi, †H. Wesley Phillips, §Naymee Velez-Ruiz, †Brian P. Walcott, †Churl-Su Kwon, †Matthew K. Mian, ¶Andrew R. Dykstra, ¶Andrew Cole, and †Emad N. Eskandar

Epilepsia, 55(5):713–724, 2014
doi: 10.1111/epi.12571

Sameer A. Sheth is Assistant Professor of Neurosurgery at Columbia University Medical Center in New York.

Summary

Objectives: **To determine the ability of foramen ovale electrodes (FOEs) to localize epileptogenic foci after inconclusive noninvasive investigations in patients with suspected mesial temporal lobe epilepsy (MTLE).**

Methods: **We identified patients with medically intractable epilepsy who had undergone FOE investigation for initial invasive monitoring at our institution between 2005 and 2012. Indications for initiating FOE investigation were grouped into four categories: (1) bilateral anterior temporal ictal activity on scalp electroencephalography (EEG), (2) unclear laterality of scalp EEG onset due to muscle artifact or significant delay following clinical manifestation, (3) discordance between ictal and interictal discharges, and (4) investigation of a specific anatomic abnormality or competing putative focus. The FOE investigation was classified as informative if it provided sufficient evidence to make a treatment decision.**

Results: **Forty-two consecutive patients underwent FOE investigation, which was informative in 38 patients (90.5%). Of these 38 patients, 24 were determined to be appropriate candidates for resective surgery. Five were localized sufficiently for surgery, but were considered high risk for verbal memory deficit, and nine were deemed poor surgical candidates because of bilateral ictal origins. The remaining 4 of 42 patients had inconclusive FOE studies and were referred for further invasive investigation. Of the 18 patients who underwent resective surgery, 13 (72%) were seizure-free (Engel class I) at last follow-up (mean 22.5 months).**

Significance: **More than 90% of our 42 FOE studies provided sufficient evidence to render treatment decisions. When undertaken with an appropriate hypothesis, FOE investigations are a minimally invasive and efficacious means for evaluating patients with suspected MTLE after an inconclusive noninvasive investigation.**

KEY WORDS: **Foramen ovale, Depth electrodes, Epilepsy, Mesial temporal sclerosis.**

The incidence of epilepsy in developed countries is approximately 40–50 per 100,000 person-years.[1,2] Despite advances in our understanding of the pathophysiology of seizures and pharmacologic strategies to control them, intractability still affects up to one third of patients with epilepsy.[3] Temporal lobe epilepsy (TLE) is the most common form of intractable epilepsy, but it is also highly amenable to surgical intervention.[4–9] Given the high success rate of resective surgery, it is important to identify surgical candidates. Ictal electroencephalography (EEG) in combination with video monitoring has a high diagnostic yield for

Accepted January 23, 2014; Early View publication March 7, 2014.
*Department of Neurosurgery, Columbia University Medical Center, New York Presbyterian Hospital, New York, New York, U.S.A.; †Department of Neurosurgery, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, U.S.A.; ‡Division of Epilepsy, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, U.S.A.; §Department of Neurology, Emory University School of Medicine, Atlanta, Georgia, U.S.A.; and ¶Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, U.S.A.
[1]Contributed equally.
Address correspondence to Sameer A. Sheth, Neurological Institute, 4th floor, 710 W. 168th Street, New York, NY 10032, U.S.A. E-mail: sheth@post.harvard.edu

Wiley Periodicals, Inc.

localizing the epileptogenic zone, especially in TLE. However, because of variable propagation patterns, up to one third of patients are not sufficiently localized following scalp EEG.[10] Factors contributing to difficulties in conclusively identifying the ictal focus include bilateral ictal or interictal discharges and muscle artifact. Significant discordance between scalp EEG findings and neuroimaging abnormalities may also introduce substantial uncertainty into the localization of the seizure focus.

Invasive EEG may be considered if preliminary noninvasive investigations are indeterminate. There are various options for the placement of invasive electrodes—including intracerebral depth, subdural, epidural, and foramen ovale—each with a distinct profile of advantages and drawbacks. Intracranial electrodes offer higher signal-to-noise ratios, less muscle artifact, and less distortion by intervening brain, bone, and scalp.[11]

Foramen ovale electrodes (FOEs), developed in the 1980s,[12] are particularly useful in the presurgical evaluation of mesial TLE. The deep contacts of FOE lie within the ambient cistern adjacent to the mesial temporal lobe, thus providing an attractive option for investigating a putative mesial temporal source. Compared to depth electrodes, FOEs are less invasive and are placed through a natural aperture in the skull. In addition, they permit simultaneous scalp EEG recordings. Although many centers in Europe utilize FOEs routinely,[13] they are relatively rarely used in the United States.[14]

We have been using FOE recordings at our institution when the noninvasive investigation is inconclusive but generates a hypothesis requiring an intracranial investigation focused on the temporal lobe. Sampling bias inherent to a focused intracranial investigation such as FOE recordings makes it essential to select appropriate patients and initiate the investigation with a clearly testable hypothesis. We present our experience describing the utility of FOE investigations as a means to investigate such patients in a minimally invasive manner. We paid particular attention to identifying the hypothesis being tested by each investigation, and determining whether the results of the recording resolved the preexisting hypothesis.

Methods

Study population

This study was approved by the Massachusetts General Hospital Institutional Review Board. We retrospectively reviewed the records of all patients who underwent intracranial EEG investigation with FOE as an initial invasive monitoring procedure between 2005 and 2012. General criteria for FOE recordings included a suspected diagnosis of partial epilepsy with presumed temporal lobe onset in which history, imaging, noninvasive scalp EEG, and neuropsychological testing were not able to conclusively determine the ictal focus.

FOE placement procedure

After obtaining informed surgical consent, general endotracheal anesthesia was induced. The patient was positioned supine, with the neck extended slightly and the head turned away from the initial insertion side. The fluoroscope C-arm was angled approximately 45 degrees from vertical to demonstrate the foramen ovale. The foramen was seen lateral to the pterygoid plate, medial to the ramus of the mandible, superimposed on the petrous ridge. The approach was therefore essentially identical to that used for trigeminal radiofrequency rhizotomy or glycerol injection procedures.

Both cheeks were prepped with a chlorhexidine solution. Sterile towels were used to drape the circumference of the face. Using fluoroscopy, the foramen ovale was identified, and the patient's head was gently mobilized from side to side to provide an optimal view. Lidocaine 1% was injected into the cheek, approximately 2.5 cm lateral to the labial fissure. A 16-gauge needle was used to pierce the skin. Subsequently a 10-cm needle (Ad-Tech, Racine, WI, U.S.A.) was advanced through the skin toward the foramen ovale, using fluoroscopy to adjust the trajectory as necessary. Particular attention was paid to avoid transgressing the buccal mucosa.

The needle was passed through the foramen ovale, with tactile feedback guiding passage through soft tissue compared to the surrounding skull base. Once the needle was through the foramen, a lateral fluoroscopic image was obtained to confirm positioning. The needle was placed so its tip was approximately 2 mm anterior to the clival line. The stylet was then withdrawn. Under fluoroscopic guidance, a four-contact electrode (Ad-Tech) was gradually advanced through the needle and positioned so that all four contacts were beyond the tip of the needle. If resistance was encountered, the electrode was withdrawn, the needle was advanced 1 mm, and another attempt was made. This process was repeated until the needle was 2 mm posterior to the clival line and advanced no further. If the electrode still failed to pass, the needle was withdrawn completely and repositioned, usually more laterally. Although there may be some patients in whom the anatomy is simply not favorable, and generally the recommended approach is to abandon the procedure rather than risk a vascular or neurologic injury, this obstacle was not encountered in our population.

A final lateral fluoroscopic image was obtained with the electrode in position. The needle was then carefully removed, and the electrode was secured to the cheek using 0 silk sutures. The procedure was then repeated on the opposite side. Final anteroposterior and lateral fluoroscopic images were obtained after placement of the electrodes demonstrating both electrodes in position (Fig. 1A). A sterile dressing was placed over the electrode exit sites.

The patient was then awakened from general anesthesia. After confirmation of baseline neurologic function, the

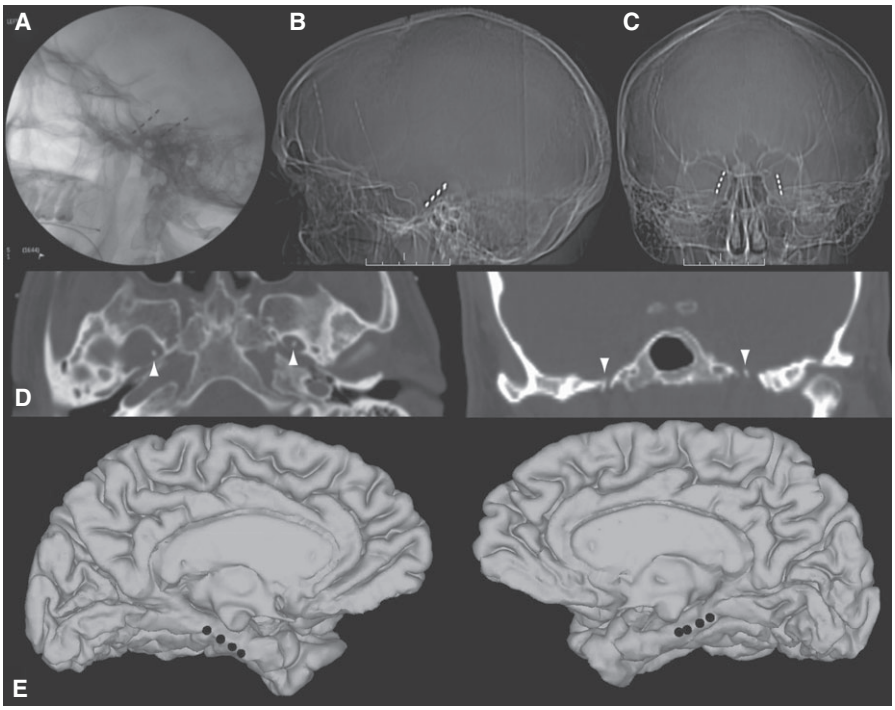

Figure 1.
Foramen ovale electrode (FOE) placement and position. (**A**) Intraoperative lateral oblique fluoroscopic image obtained after placement of bilateral FOE. (**B**, **C**) Postoperative CT scan lateral (**B**) and anteroposterior (**C**) scout images showing FOE position. (**D**) Axial and coronal CT scan images at the level of the foramen ovale showing the electrode passing through the foramen (arrowheads). (**E**) A representative patient's postoperative CT scan was co-registered to the preoperative MRI to visualize the position of the FOE contacts using a method described previously.[22] The contacts (black circles) are displayed superimposed on the MRI surface extraction and lie along the mesial temporal lobe.

patient was observed in the postanesthesia recovery room for 1 h. We then obtained a computerized tomography (CT) scan (Fig. 1B–D), and the patient was taken to the epilepsy monitoring unit for observation, where scalp EEG leads may also be placed. Antiepileptic drugs (AEDs) were continued at home dosage initially, and gradually weaned while observing for seizures with video and EEG surveillance. Antibiotics with gram-positive and gram-negative coverage, typically vancomycin and ceftriaxone, were continued while the FOEs were in place. In most circumstances, we allowed FOEs to remain in place for a maximum of 2 weeks.

At the conclusion of the investigation, FOEs were removed at the patient's bedside, with prophylactic anticoagulation withheld on the morning of removal. The silk securing stitches were released, and the electrodes were gently withdrawn. The patient was closely observed over the next hour for development of increasing headache or neurologic deficit.

Analysis

We identified the hypothesis being tested for each FOE investigation based on the Epilepsy Multi-Disciplinary Conference note detailing the discussion following each patient's noninvasive investigation. Indications for initiating FOE investigations were grouped into four categories: (1) bilateral anterior temporal ictal activity on scalp EEG, (2) unclear laterality of scalp EEG onset due to muscle artifact or significant delay or absence following clinical manifestation, (3) discordance between ictal and interictal discharges, and (4) investigation of a specific anatomical abnormality or competing putative focus.

Our principal outcome measure was whether the FOE recordings provided sufficient information to disambiguate the investigation and enable the generation of a treatment plan. We therefore classified the FOE investigation for each patient as definitive if a treatment recommendation was formulated at its conclusion. Definitive investigations included those that lateralized to a unilateral mesial temporal lobe. These either resulted in recommendations for resective surgery (anterior temporal lobectomy [ATL] including amygdalohippocampectomy or lesionectomy), or conservative management if other aspects of the investigation (neuropsychological testing, Wada test, functional magnetic resonance imaging [fMRI]) suggested that resective surgery carried a high risk of postoperative verbal memory decline.

Definitive investigations also included those cases in which the FOE confirmed unequivocally that seizures originated independently from the left and right temporal lobes with approximately equal frequency. In these symmetric, independent, bilateral onset cases, patients were deemed inappropriate for resective surgery, and the investigation was concluded. However, a significant asymmetry in the number of seizures clearly starting from each side, or confirmation that the clinically morbid seizures all originated from one hemisphere, often led to a recommendation for a palliative resection.

Cases in which the FOE investigation failed to answer the preoperative hypothesis and generate a treatment plan (e.g., definitively determine whether the patient is a resective candidate) were considered noninformative. These cases required further invasive recordings with intracerebral depth electrodes.

Results

A total of 42 consecutive patients with medically intractable epilepsy underwent FOE investigation at our institution between 2005 and 2012. All were AED refractory and had noninvasive investigations including MRI, positron emission tomography (PET), video-EEG, and neuropsychiatric assessment that suggested anterior temporal epilepsy, but without sufficiently confident lateralization or localization to arrive at a treatment decision. Twenty-four patients were men, with a mean age (±standard deviation, SD) of 38.3 ± 13.7 years (range 10–65 years), and mean epilepsy duration of 18.6 ± 14.6 years (range 1–53 years). A summary of the demographics of these patients, along with imaging findings and details of their FOE investigation, is provided in Table 1. Categorical reasons for initiating the FOE investigation and the final decision after the investigation are shown in Figure 2.

Bilateral scalp ictal activity

Bilateral anterior temporal ictal activity on prior scalp EEG recordings was the most common reason for initiating an FOE investigation, with 20 patients (47.6%) in this group. In 13 of these 20 patients, FOE recordings successfully lateralized the epileptogenic zone, and an ATL was recommended in 10. In the three patients not recommended for ATL (Table 1; patients 1, 6, and 7), FOE recordings clearly implicated the left mesial temporal lobe, but other data including neuropsychological assessment, fMRI, and Wada testing indicated a high risk for postoperative verbal memory deficits. In consultation with the epilepsy team, patient, and family, resective surgery was therefore not offered in these three patients. In addition, 6 of 20 patients showed bilateral ictal activity on FOE recordings, and were deemed poor surgical candidates.

In one patient (Table 1, patient 18), all 13 seizures captured with FOE recordings showed a preceding low-amplitude beta-frequency run of epileptiform activity from the right mesial temporal lobe. However, the MRI suggested sclerosis in the left mesial temporal lobe, and a PET study showed left temporal hypometabolism. Given the discordance between the imaging and FOE results, bilateral frontal and temporal depth electrodes were recommended to better delineate the epileptogenic zone.

Thus, 19 (95.0%) of 20 patients with bilateral anterior temporal ictal activity on previous scalp EEG had informative FOE recordings that enabled conclusion of their surgical candidacy evaluation, whereas only one of the 20 patients required further invasive investigation.

Unclear laterality due to artifact, delay, or minimal scalp EEG correlate

In 11 patients (26.2%), FOE investigation was initiated because the electrographic origin of the seizures was unclear on previous scalp recordings, due to either obscuring muscle artifact or a significantly delayed or absent EEG correlate for each seizure. In nine of these patients, FOE recordings identified a clear mesial temporal origin, and seven were referred for resective surgery. In one of the patients not referred for surgery (Table 1, patient 4), scalp EEG (acquired simultaneously with FOEs) during the seizure showed only some irregular left temporal delta/theta slowing, beginning 10–15 s after seizure onset. In contrast, FOEs clearly localized a definitive left mesial temporal focus (Fig. 3), but the risk of postoperative verbal memory decline precluded resective surgery. In the other (Table 1, patient 35), FOEs demonstrated left > right interictal epileptiform activity with left-sided ictal onsets, but there was poor correlation with clinical symptoms, and palliative left ATL was considered too high risk for neurologic deficit given uncertain benefit.

One patient (Table 1, patient 38) had bilateral independent ictal origins and was deemed not to be a surgical candidate. In one patient (Table 1, patient 30), the absence of temporal lobe epileptiform activity on FOE resulted in further invasive investigation.

Thus, in 10 (90.1%) of 11 patients whose noninvasive investigation was obscured by muscle artifact or delayed or absent EEG correlate, FOEs were able to provide sufficient information to initiate a treatment plan, whereas one patient required further invasive investigation.

Interictal/ictal discordance

Discordance on prior scalp EEG between interictal and ictal epileptiform activity was the reason for initiating FOE investigations in six patients (14.3%). FOE recordings showed a clear unilateral mesial temporal locus in four patients, each of whom was recommended for ATL. As an illustrative example, one of these (Table 1, patient 21) is depicted in Figure 4. On scalp EEG (acquired simultaneously with FOEs), this patient had a bilaterally synchronous seizure onset with a right-sided predominance, but had L > R interictal discharges. With FOE, a unilateral left temporal seizure onset is clearly visible more than 30 s before the scalp EEG onset. In one patient (Table 1, patient 31) FOE revealed bilateral mesial temporal ictal onsets, and the patient was considered ineligible for resective surgery. No clear mesial temporal ictal onset was seen on FOE in one patient (Table 1, patient 9), who required bilateral depth electrodes for further invasive investigation. Thus FOE recordings provided conclusive information in five of six patients with interictal/ictal discordance on prior scalp EEG.

Investigate a competing putative focus

Five patients (11.9%) underwent FOE investigation because the previous scalp EEG was suggestive of an anterior temporal source, but imaging demonstrated an additional putative epileptogenic focus. Three patients (Table 1; patients 15, 29, and 36) had a clear resective surgical plan

Table 1. Patient characteristics and FOE investigation motivation and outcome

Pt no.	Age	Epilepsy duration (years)	Sex	Sz freq (per month)	MRI[a]	PET[b]	FOE motivation[c]	FOE outcome	Treatment decision	Follow-up duration (months)	Surgical outcome
1	49	34	M	2	L	R	Bilateral ictal scalp (1)	L ictal onset	Conservative (risk to verbal memory)		
2	47	29	M	2	R > L	R > L	Bilateral ictal scalp (1)	R ictal onset	R ATL	70	III
3	38	36	M	6	R	R	Bilateral ictal scalp (1)	Bilateral ictal onset	Not surgical candidate		
4	31	17	M	3	L	L	Delayed EEG correlate (2)	L ictal onset	Conservative (risk to verbal memory)		
5	46	3	M	10		R > L	Bilateral ictal scalp (1)	R ictal onset	R ATL	71	I
6	55	38	F	1	L	L	Bilateral ictal scalp (1)	L ictal onset	Conservative (risk to verbal memory)		
7	52	22	M	12	R > L	L	Bilateral ictal scalp (1)	L ictal onset	Conservative (risk to verbal memory)		
8	19	6	F	12	Neither	L	Temporal vs. occipital focus (4)	Multifocal	Not surgical candidate		
9	64	4	F	4	L	L	Interictal/ictal discordance (3)	No temporal ictal onset	Further invasive investigation		
10	53	53	M	16	R	R	Delayed EEG correlate (2)	R ictal onset	R ATL	32	I
11	19	2	F	12	Bilat	R	Bilateral ictal scalp (1)	R ictal onset	R ATL	21	I
12	19	7	F	8	Neither	L > R	Bilateral ictal scalp (1)	Bilateral ictal onset	Not surgical candidate		
13	36	29	F	2	L	R	Bilateral ictal scalp (1)	R ictal onset	R ATL offered, patient declined		
14	27	17	F	3	L	L	Delayed EEG correlate (2)	L ictal onset	L ATL	18	I
15	30	14	M	22	R	Neither	Investigate residual lesion (4)	R ictal onset	R ATL offered, patient declined		
16	52	40	M	10	L	L	Bilateral ictal scalp (1)	L ictal onset	L ATL offered, patient declined		
17	33	9	M	30	L	L	Muscle artifact (2)	L ictal onset	L ATL	28	I
18	33	32	F	135	L	L	Bilateral ictal scalp (1)	R ictal onset	Further invasive investigation		
19	32	10	M	2	L	L	Bilateral ictal scalp (1)	L ictal onset	L ATL	30	I
20	39	20	F	30	Neither	L	Bilateral ictal scalp (1)	R ictal onset	R ATL	15	III
21	45	15	M	16	L	L	Interictal/ictal discordance (3)	L ictal onset	L ATL	Lost to f/u	
22	32	13	M	75	Bilat	R > L	Bilateral ictal scalp (1)	L ictal onset	L ATL	13	II
23	65	7	M	12	Bilat	Neither	Bilateral ictal scalp (1)	Bilateral ictal onset	Not surgical candidate		
24	23	23	F	75	L	Neither	Investigate residual dysplasia (4)	Bilateral ictal onset	Further invasive investigation		
25	33	15	F	75	L	L	Absent EEG correlate (2)	L ictal onset	L ATL	13	I
26	27	3	F	1–30	Bilat	L	Delayed EEG correlate (2)	R ictal onset	R ATL offered, deceased prior to surgery		
27	46	46	M	2	R	L > R	Interictal/ictal discordance (3)	R ictal onset	R ATL	7	II
28	40	24	F	1	Neither	Bilat	Interictal/ictal discordance (3)	R ictal onset	R ATL	15	I
29	57	38	M	2–3	Bilat	L	Interrogate competing lesion (4)	R ictal onset	R ATL	5	I
30	33	1	M	0.25	R	R	Delayed EEG correlate (2)	No temporal ictal onset	Further invasive investigation		
31	10	5	M	6	Bilat		Interictal/ictal discordance (3)	L ictal onset	Not surgical candidate		
32	26	11	M	4	Neither	L	Delayed EEG correlate (2)	L ictal onset	L ATL	Lost to f/u	
33	57	42	M	2	Neither	Bilat	Bilateral ictal scalp (1)	Bilateral ictal onset	Not surgical candidate		
34	35	29	F	30	L	L	Delayed EEG correlate (2)	L ictal onset	L ATL	29	IV
35	41	6	M	8	Neither	Neither	Delayed EEG correlate (2)	L ictal onset	Conservative (risk to verbal memory)		
36	44	2	F	30	R		Competing lesional focus (4)	No clear mesial temp activity	R lesionectomy only (cavernoma)	1	I
37	55	5	F	20	R	R	Bilateral ictal scalp (1)	R ictal onset	R ATL	31	I
38	41	41	M	10	Neither	R	Delayed EEG correlate (2)	Bilateral ictal onset	Not surgical candidate		
39	31	16	F	2	L	L	Bilateral ictal scalp (1)	Bilateral ictal onset	Not surgical candidate		
40	57	9	F	42	L	L	Bilateral ictal scalp (1)	Bilateral ictal onset	Not surgical candidate		
41	21	5	M	2	Bilat	L	Interictal/ictal discordance (3)	L ictal onset	L ATL	4	I
42	16	2	F	5	R	R > L	Bilateral ictal scalp (1)	R ictal onset	R ATL	2	I

[a]L (left), R (right) or Bilat (bilateral) indicates laterality of pathology (mesial temporal sclerosis or lesion) seen on MRI; Neither indicates no pathology noted.
[b]L (left), R (right) or Bilat (bilateral) indicates laterality of temporal hypometabolism seen on interictal PET; Neither indicates no hypometabolism noted.
[c]Parentheses indicate motivation grouping per categories in text and Figure 2.

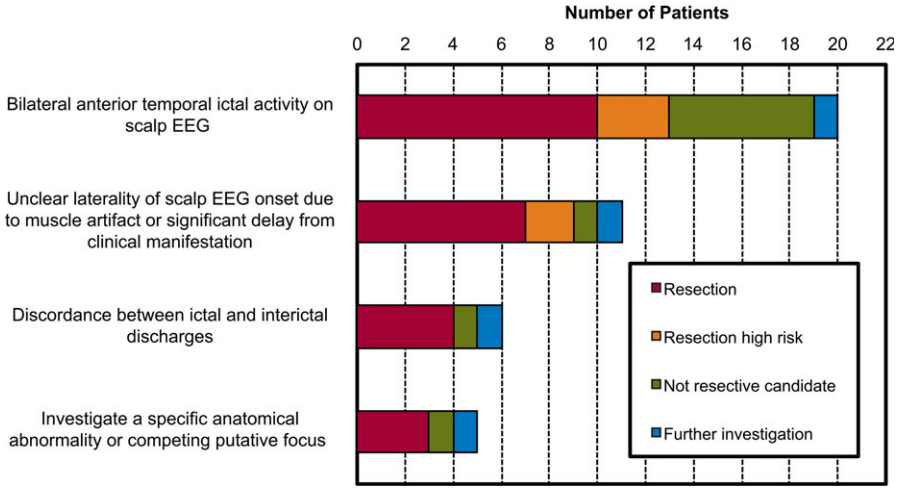

Figure 2.
Indications and outcomes of FOE investigation. Bars are grouped according to the four categorical reasons for initiating the FOE investigations. Within each category, red indicates a decision for resective surgery. Orange indicates patients in whom the FOE investigation localized seizure onset to a unilateral temporal lobe, but who were treated nonsurgically because of a concern for verbal memory deficit following resective surgery. Green indicates patients in whom the FOE investigation detected bitemporal foci who were therefore not surgical candidates. Blue indicates FOE investigations that could not disambiguate the ictal focus, necessitating further invasive investigation. Conclusive FOE investigations are therefore denoted by red, orange, and green.

formulated based on FOE recordings. A fourth (Table 1, patient 8) presented with temporal and occipital epileptiform activity on scalp EEG, an equivocal MRI, and a PET scan showing left temporal hypometabolism. FOE recordings revealed bilateral epileptiform activity independent of the occipital discharges on simultaneous scalp EEG, and the patient was not offered resective surgery.

One patient (Table 1, patient 24) had a residual left orbitofrontal cortical dysplasia, but ambiguous scalp EEG and uninformative imaging. Subsequent FOE recordings captured five seizures from the right, and two simultaneous bilateral seizures. Given this discordance and the possibility of a nonmesial temporal focus, a bilateral depth electrode investigation was recommended for further investigation.

Thus of these five patients, FOE provided conclusive information in four of five.

Population summary

In the 42 total patients in this series in whom a thorough noninvasive investigation was unable to localize the epileptogenic zone, FOE investigation provided informative data in 38 patients (90.5%) that led to the generation of a definitive treatment plan (Fig. 2). Of these 38 patients in whom the FOE investigation was informative, 24 were recommended for resective surgery, 5 were localized but not offered resective surgery due to concern for verbal memory deficit, and 9 were deemed inoperative due to independent multifocality. In the remaining 4 of the total 42 patients, FOE recordings were insufficient to localize the ictal focus, and further invasive investigation was recommended.

Of the 24 patients recommended for resective surgery, 18 underwent resective procedures (17 ATL, one lesionectomy). Of the remaining six patients, three declined surgery due to concern for risk of complications (despite counseling prior to initiation of the FOE investigation), two were lost to follow-up, and one patient died prior to surgery (SUDEP; sudden unexplained death in epilepsy). Thirteen (72%) of the patients who underwent surgical resection were seizure-free (Engel class I) at last follow-up (mean ± standard deviation 22.5 ± 20.3 months; range 1–71 months). Two patients (11%) were Engel class II, two were Engel class III, and one (6%) was Engel class IV.

Analysis by imaging/EEG discordance

An alternative perspective for considering these results is to focus on MRI findings and their potential discordance with EEG data. We therefore recategorized the patients according to these criteria in Table 2. The first category (type A) included patients in whom the MRI demonstrated a unilateral lesion, but there was significant discordance with scalp EEG (e.g., contralateral, contralateral predominant, or bilateral symmetric interictal epileptiform activity). The second category (type B) cases were similar to type A in terms of the presence of a unilateral lesion, but the discordance with EEG was less pronounced (e.g., infrequent or vague interictal discharges, bilateral but ipsilateral predominant interictal discharges, or ictal/interictal EEG discordance). Type C patients had a normal or nearly normal MRI (typically read as normal by radiology, but considered suggestive

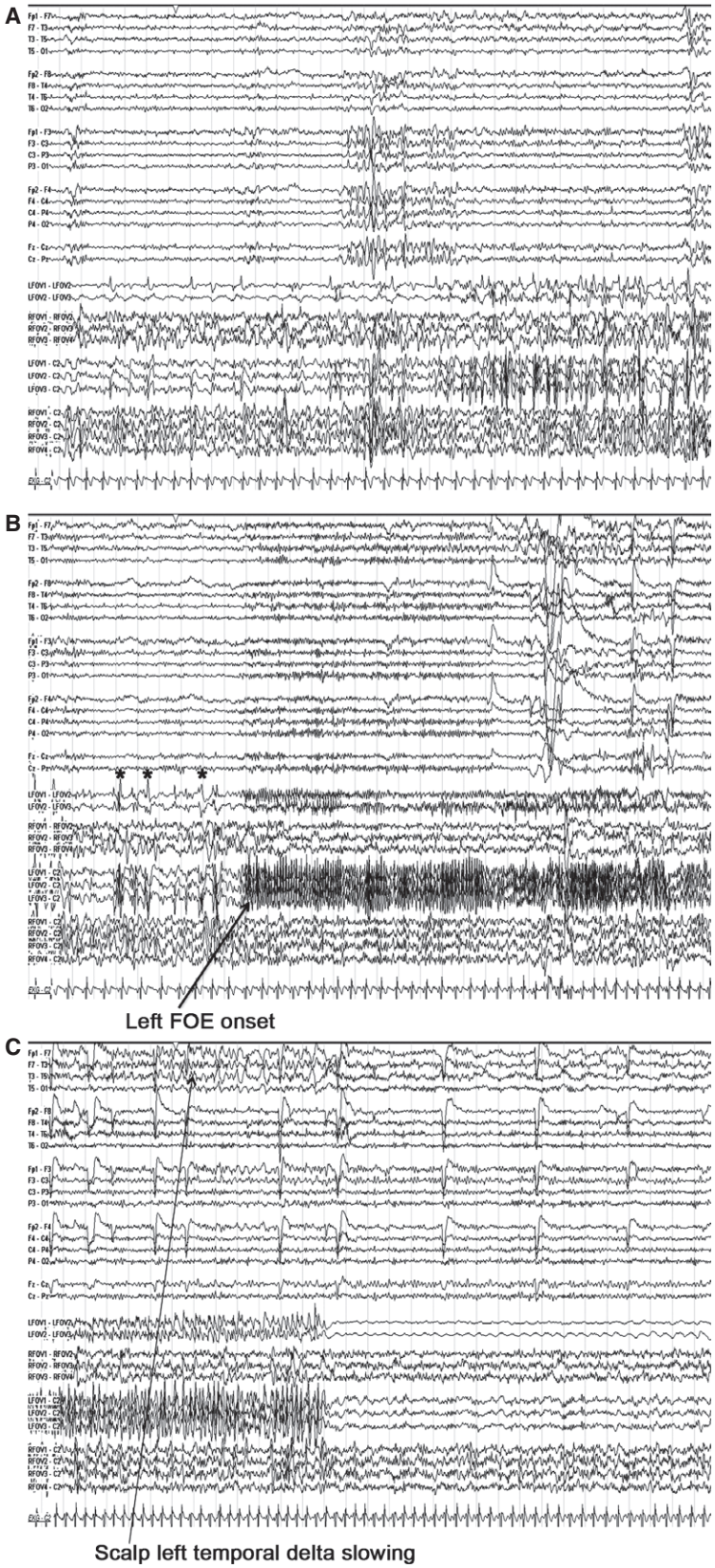

Figure 3.
FOEs reveal a definite left temporal seizure onset in a patient (Table 1, patient 4) with very subtle scalp electrode changes. (**A**) FOEs show frequent left mesial temporal interictal epileptiform discharges (asterisks), but the scalp EEG shows only some irregular slowing. (**B**, **C**) A typical seizure (nota bene: panels **B** and **C** are continuous). The seizure begins with the onset of clear 8–10 Hz rhythmic spiking in the left FOE, without scalp EEG correlate (arrow, panel **B**). The first scalp change occurs approximately 15 s later, with some left temporal delta/theta slowing, which is present irregularly throughout the rest of the seizure (e.g., arrow, panel **C**), but without clear buildup or rhythmic evolution.
Epilepsia © ILAE

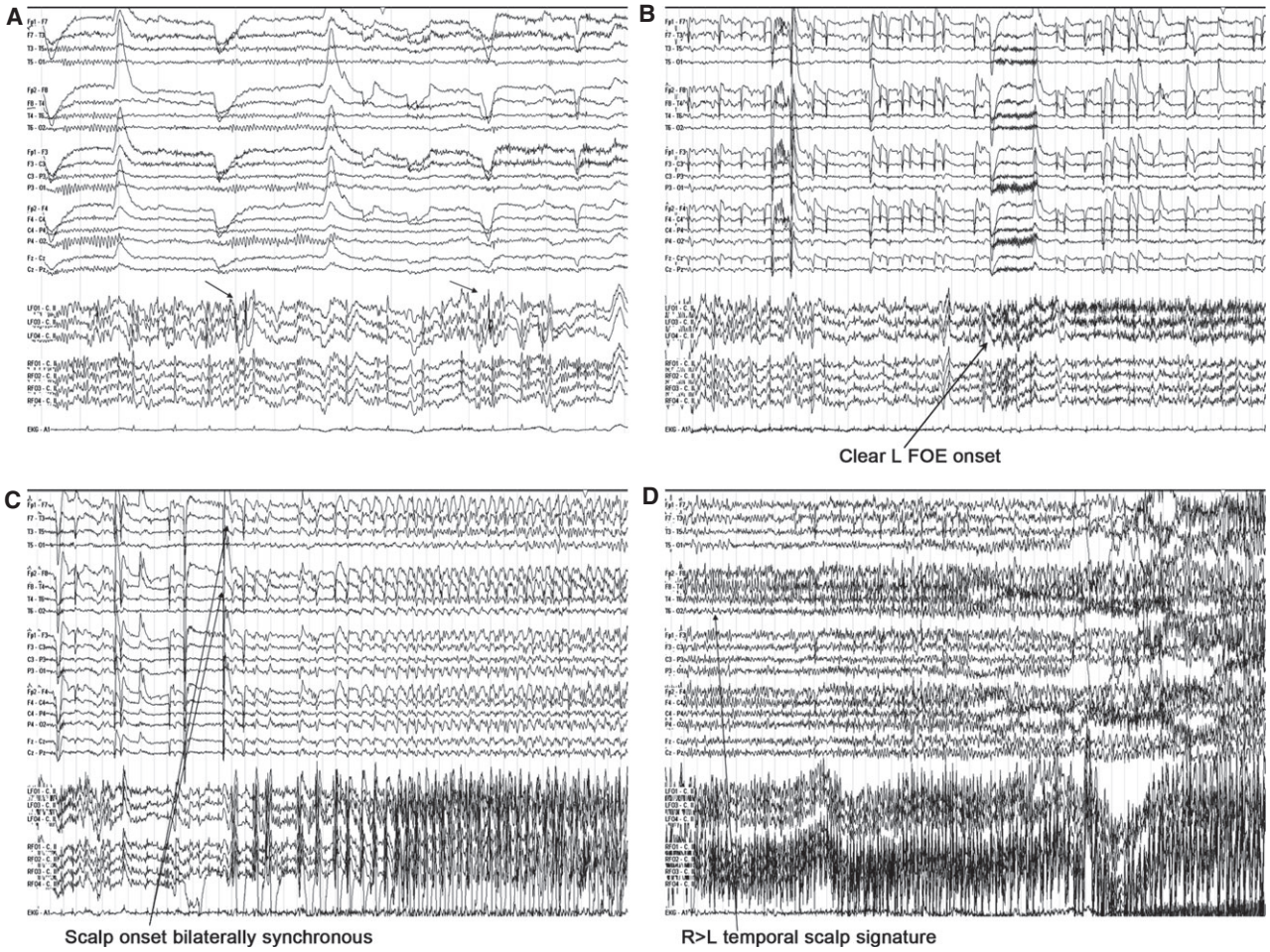

Figure 4.

FOEs reveal a clear left temporal seizure onset in a patient (Table 1, patient 21) with left temporal interictal discharges but delayed predominantly right temporal scalp EEG seizure onsets. (**A**) Left FOE demonstrates frequent interictal discharges without scalp representation (arrows). (**B**–**D**) EEG findings during a typical seizure (NB: panels **B**–**D** are continuous). The first ictal change consists of the onset of rhythmic low-voltage 13–18 Hz activity in the left FOE (arrow, panel **B**), without scalp correlate. (The EEG activity seen in the posterior leads at that time is alpha activity resulting from eye closure.) The first ictal scalp change occurs approximately 35 s later, with the development of rhythmic theta/delta slowing in the bilateral temporal leads (arrow, panel **C**). This slowing subsequently evolves into rhythmic spiking activity, more prominent in the right temporal leads (arrow, panel **D**). By this time, ictal activity is also more prominent in the right FOE (next to bottom trace).

by the epilepsy committee), and type D patients had bilateral abnormalities.

Of the six type A patients, all six had informative FOE investigations (four proceeded to temporal lobectomy, one was considered high risk, and one was not a surgical candidate due to bilateral independent onset). Of the 13 type B patients, 10 had informative investigations (8 were offered resections and 2 were considered high risk). The three remaining type B patients required further invasive investigation. Of the 13 type C patients, 12 had informative investigations (proceeded to temporal lobectomy, one was considered high risk, and 5 were not surgical candidates). The single remaining Type C patient required a further invasive investigation. Of the 10 type D patients, all 10 had informative FOE investigations (6 were offered resections, one was considered high risk, and 3 were not surgical candidates).

Twenty patients had MRI findings that had some degree of discordance with eventually obtained FOE data. These included patients with MRIs that were normal or nearly normal (type C) in whom FOE recordings identified a unilateral focus (numbers 28, 32, and 35) or bilateral foci (numbers 8, 12, 33, 38, and 40). Other examples of discrepancies were patients with MRIs showing bilateral abnormalities (type D) with unilateral seizure foci (numbers 2, 7, 11, 13, 26, 29, 31, and 41). The final type of discordance was the

Table 2. Patient characteristics and FOE investigation categorized by imaging and scalp EEG

Pt no.	Type	MRI	PET	Scalp interictal	Reason for FOE	FOE outcome	Decision	Follow-up duration (months)	Surgical outcome
3	A	R MTS	R	L occasional	Bilateral ictal scalp	Bilateral ictal onset	Not surgical candidate		
4	A	L MTS	L	Bilat slowing	Absent EEG correlate	L ictal onset	Conservative (risk to verbal memory)		
20	A	L MT abnormality	L	Bilat (R > L 6:1)	Bilateral ictal scalp	R ictal onset	R ATL	15	III
22	A	L MT mild fullness	R > L	Bilat (R > L 3:1)	Bilateral ictal scalp	L ictal onset	L ATL	13	II
34	A	L MTS	L	Bilat frontal slowing	Delayed EEG correlate	L ictal onset	L ATL	29	IV
42	A	R anterior temporal FLAIR bright	R > L	Bilat	Bilateral ictal scalp	R ictal onset	R ATL	2	I
1	B	L MTS	R	Bilat (L > R 2:1)	Bilateral ictal scalp	L ictal onset	Conservative (risk to verbal memory)		
6	B	L MTS	L	Bilat (L > R)	Bilateral ictal scalp	L ictal onset	Conservative (risk to verbal memory)		
10	B	R MTS	R	Bilat intermittent (R > L 3:1)	Delayed EEG correlate	R ictal onset	R ATL	32	I
14	B	L MTS	L	Bilat (L > R)	Delayed EEG correlate	L ictal onset	L ATL	18	I
15	B	R residual lesion	Neither	R slowing	Investigate residual lesion	R ictal onset	R ATL, patient declined		
16	B	L MTS	L	Bilat (L > R)	Bilateral ictal scalp	L ictal onset	L ATL, patient declined		
18	B	L MTS	L	Bilat (L > R)	Bilateral ictal scalp	R ictal onset	Further invasive investigation		
21	B	L MTS	L	L	Interictal/ictal discordance	L ictal onset	L ATL	Lost to f/u	
24	B	L residual lesion	Neither	Bilat (L > R)	Investigate residual dysplasia	Bilateral ictal onset	Further invasive investigation		
25	B	L MTS	L	L occasional	Absent EEG correlate	L ictal onset	L ATL	13	I
27	B	R gliosis	L > R	Bilat (R > L 2:1)	Interictal/ictal discordance	R ictal onset	R ATL	7	II
30	B	R parietotemporal encephalomalacia	R	R	Delayed EEG correlate	No temporal ictal onset	Further invasive investigation		
36	B	R cavernoma, R HC slightly smaller		R rare	Investigate mesial temp involvement	No clear mesial temporal activity	R lesionectomy only (cavernoma)	1	I
5	C		R > L	Bilat	Bilateral ictal scalp	R ictal onset	R ATL	71	I
8	C	Normal	L	R intermittent	Temporal vs. occipital focus	Multifocal	Not surgical candidate		
9	C	Subtle L MT abnormal signal	L	L intermittent	Interictal/ictal discordance	No temporal ictal onset	Further invasive investigation		
12	C	Normal	L > R	Bilat slowing	Bilateral ictal scalp	Bilateral ictal onset	Not surgical candidate		
17	C	Subtle L MT abnormal signal	L	L	Muscle artifact	L ictal onset	L ATL	28	I
19	C	Subtle FLAIR brightness in L HC	L	L	Bilateral ictal scalp	L ictal onset	L ATL	30	I
28	C	Normal	Bilat	Bilat (L > R)	Interictal/ictal discordance	R ictal onset	R ATL	15	I
32	C	Normal	L	L	Delayed EEG correlate	L ictal onset	L ATL	Lost to f/u	
33	C	Normal	Bilat	Bilat (L = R)	Bilateral ictal scalp	Bilateral ictal onset	Not surgical candidate		
35	C	Normal	Neither	L intermittent	Absent EEG correlate	L ictal onset	Conservative (risk to verbal memory)		
37	C	Subtle R MT abnormal signal	R	R	Bilateral ictal scalp	R ictal onset	R ATL	31	I
38	C	Normal	R	L	Delayed EEG correlate	Bilateral ictal onset	Not surgical candidate		
40	C		L	Bilat (L > R)	Bilateral ictal scalp	Bilateral ictal onset	Not surgical candidate		

Continued

Epilepsia, 55(5):713–724, 2014
doi: 10.1111/epi.12571

Table 2. Continued.

Pt no.	Type	MRI	PET	Scalp interictal	Reason for FOE	FOE outcome	Decision	Follow-up duration (months)	Surgical outcome
		Subtle FLAIR brightness in L HC							
2	D	Bilat (R > L) MTS	R > L	Bilat (R > L)	Bilateral ictal scalp	R ictal onset	R ATL	70	III
7	D	Bilat (R > L) MTS	L	Bilat rare	Bilateral ictal scalp	L ictal onset	Conservative (risk to verbal memory)		
11	D	Bilat atrophy	R	Bilat (R > L)	Bilateral ictal scalp	R ictal onset	R ATL	21	I
13	D	Bilat (L HC smaller, R HC brighter FLAIR)	R	R intermittent	Bilateral ictal scalp	R ictal onset	R ATL, patient declined		
23	D	Bilat atrophy	Neither	Bilat (L > R)	Bilateral ictal scalp	Bilateral ictal onset	Not surgical candidate		
26	D	Bilat atrophy	L	Bilat	Delayed EEG correlate	R ictal onset	R ATL, deceased prior to surgery		
29	D	Bilat (R MTS, L temporal encephalomalacia)	L	R	Interrogate competing lesion	R ictal onset	R ATL	5	I
31	D	Bilat multiple cortical tubers		L	Interictal/ictal discordance	L ictal onset	Not surgical candidate		
39	D	Bilat MTS (L > R)	L	Bilat (L > R)	Bilateral ictal scalp	Bilateral ictal onset	Not surgical candidate		
41	D	Bilat scattered T2 prolongations	L	Bilat (L > R)	Interictal/ictal discordance	L ictal onset	L ATL	4	I

group with unilateral MRI lesions with bilateral (numbers 3 and 24) or even contralateral (numbers 18 and 20) seizure onset.

Complications

Short-term complications occurred in two patients (4.8%). One patient developed a sudden headache without neurologic sequelae following bedside FOE removal. An immediate noncontrast CT scan demonstrated a small amount of subarachnoid hemorrhage in the ambient cisterns. The patient was managed conservatively and recovered to baseline over the next day with no further complications. One patient had persistent jaw pain following FOE insertion that resolved when the electrodes were removed. There were no permanent complications. No patients developed infection, and no patients had to return to the operating room for electrode repositioning following initial placement.

Discussion

In this consecutive series of 42 patients with anterior temporal seizures and inconclusive noninvasive studies, we obtained information sufficient to generate a definitive treatment plan in 38 (90.5%) with FOE investigation.

FOE recordings offer several advantages as a minimally invasive means of intracranial investigation. They can provide detailed neurophysiologic data about seizures emanating from the mesial temporal lobe, with a signal-to-noise ratio that is favorable to scalp electrodes.[9,12] Indeed, many epileptiform discharges identified with FOE recordings are not detectable extracranially,[15] although it is unclear whether intracranially recorded mesial temporal epileptiform discharges have the same significance as discharges visible on scalp EEG. Similarly, focal seizure onset can be identified on FOE recordings several seconds before electrical changes are seen on the scalp.[16] In addition, FOEs are inserted through a natural aperture in the skull and thus do not disrupt its conductive properties. Furthermore, FOE placement is generally well tolerated and associated with fewer complications than subdural grids and strips.[17] Nevertheless, FOEs are somewhat invasive and are most appropriately used to test specific hypotheses.

One of the most common clinical scenarios in the investigation of temporal seizures is distinguishing between bitemporal and unilateral onset. In the largest study to date, Alarcon et al.[13] examined 314 seizures from 110 patients. Although 67.2% of seizures showed bilateral onset on scalp EEG, only 27.7% were bilateral on FOE investigation. This discrepancy suggests that ictal propagation patterns can frequently make unilateral temporal seizures appear bilateral on scalp EEG. Our series demonstrates the capability of FOE investigations in lateralizing apparent bilateral mesiotemporal lobe onset seizures seen on scalp EEG (Fig. 4), allowing for a more accurate presurgical evaluation.

Another indication for FOEs is in resolving seizures whose laterality on scalp EEG is unclear either due to muscle artifact or a delayed or absent electrographic correlate (Figs 3 and 4). Bypassing signal attenuation and artifact from the skull, muscle, and scalp is an important advantage of FOE recordings.[18] Others have similarly found an improvement in seizure onset detection due to reduction of such artifacts.[13]

Discordance in laterality between ictal and interictal discharges is a recognized, albeit infrequent, characteristic of scalp EEG.[19] When present, this discordance can cast doubt on the presurgical evaluation. FOE recordings can successfully resolve this discrepancy, as we observed in five of six cases.

Advances in neuroimaging—particularly MRI—over the past several years have transformed the presurgical epilepsy evaluation, allowing us to resolve even subtle structural abnormalities. This improved resolution can complicate the presurgical evaluation, however, when it demonstrates a subtle anatomic abnormality in a region discordant with one implicated by scalp EEG. To highlight the relationship between imaging and scalp EEG findings, we categorized our patients based on MRI and scalp interictal (and ictal) characteristics (Table 2). As expected by the fact that these patients required intracranial recordings, there were no patients with clear concordance between these measures. Given this lack of concordance, patients could have been considered for intracranial investigation or dismissed from surgical candidacy. In these cases, we felt that there was sufficient information to consider a mesial temporal hypothesis and utilize FOEs rather than intracerebral electrodes. As demonstrated, this approach was successful in 38 of 42 cases. We therefore advocate considering FOE recordings as a less invasive option when an appropriate hypothesis can be formulated from noninvasive data.

Described complications related to FOE placement or removal include hemorrhage, hypoesthesia, and infection.[20] In a previous study of 331 bilateral FOE implantations, 1.81% of cases resulted in serious complications such as hemorrhage.[17] Our series of 42 patients demonstrated a similarly low complication rate, with one self-limited subarachnoid hemorrhage, and one minor complication of jaw pain.

An important limitation of this study is the lack of an established gold standard regarding the ictal origin. One could argue that the electrophysiologic gold standard is the identification of individual neurons evidencing hypersynchronous firing.[21] On the other hand, the clinical gold standard could be defined as freedom from seizures following resection. Thus patients in this series who were unilaterally localized by FOE but who either did not undergo resective surgery or who were not completely seizure-free postoperatively may have been incorrectly localized. Conversely, patients deemed bilateral and therefore not offered surgery may in fact have been unilateral and inappropriately removed from surgical consideration. These potential false positives and false negatives place a limit, albeit of unknown size, on the utility of FOE recordings.

Conclusions

A number of circumstances can cast ambiguity over the presurgical evaluation of patients with epilepsy. FOE recordings offer greater sensitivity and earlier detection of ictal mesial temporal epileptiform activity than scalp recordings, and they bypass muscle artifact, can be combined with scalp recordings, and have a low complication rate. Intracranial investigation in a substantial proportion of patients with unclear, bilateral, or delayed electrographic seizures on scalp recordings, or with discordance between scalp EEG and imaging, will in fact reveal a focal onset, making them potential candidates for resective surgery. In our series, when FOEs were employed to test specific hypotheses, they enabled the generation of a definitive treatment plan in 90.5% of patients. Seventy-two percent of patients who went on to resective surgery following FOE investigations were seizure-free (Engel class I) at last follow-up postoperatively.

Acknowledgments

MMS is supported by a KL2 Medical Research Investigator Training (MeRIT) award from Harvard Catalyst, The Harvard Clinical and Translational Science Center (National Center for Research Resources and National Center for Advancing Translational Sciences, National Institutes of Health (NIH) Award 8KL2TR000168-05).

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References

1. Banerjee PN, Hauser WA. Incidence and prevalence. In Engel J Jr., Pedley TA, Aicardi J, Dichter MA, Mosh S, Perucca E, Trimble M. (Eds) *Epilepsy: a comprehensive textbook*. Philadelphia, PA: Lippincott Williams & Wilkins, 2007: 45–56.
2. Kotsopoulos IA, van Merode T, Kessels FG, et al. Systematic review and meta-analysis of incidence studies of epilepsy and unprovoked seizures. *Epilepsia* 2002;43:1402–1409.
3. Berg AT, Vickrey BG, Testa FM, et al. How long does it take for epilepsy to become intractable? A prospective investigation. *Ann Neurol* 2006;60:73–79.
4. Berg AT, Walczak T, Hirsch LJ, et al. Multivariable prediction of seizure outcome one year after resective epilepsy surgery: development of a model with independent validation. *Epilepsy Res* 1998;29:185–194.
5. Cohen-Gadol AA, Wilhelmi BG, Collignon F, et al. Long-term outcome of epilepsy surgery among 399 patients with nonlesional seizure foci including mesial temporal lobe sclerosis. *J Neurosurg* 2006;104:513–524.
6. Elliott RE, Bollo RJ, Berliner JL, et al. Anterior temporal lobectomy with amygdalohippocampectomy for mesial temporal sclerosis: predictors of long-term seizure control. *J Neurosurg* 2013;119:261–272.

7. Engel J Jr, McDermott MP, Wiebe S, et al. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. *JAMA* 2012;307:922–930.
8. Schramm J, Lehmann TN, Zentner J, et al. Randomized controlled trial of 2.5-cm versus 3.5-cm mesial temporal resection in temporal lobe epilepsy–part 1: intent-to-treat analysis. *Acta Neurochir (Wien)* 2011;153:209–219.
9. Wieser HG, Schwarz U. Topography of foramen ovale electrodes by 3D image reconstruction. *Clin Neurophysiol* 2001;112:2053–2056.
10. Foldvary N, Klem G, Hammel J, et al. The localizing value of ictal EEG in focal epilepsy. *Neurology* 2001;57:2022–2028.
11. Yuan J, Chen Y, Hirsch E. Intracranial electrodes in the presurgical evaluation of epilepsy. *Neurol Sci* 2012;33:723–729.
12. Wieser HG, Elger CE, Stodieck SR. The 'foramen ovale electrode': a new recording method for the preoperative evaluation of patients suffering from mesio-basal temporal lobe epilepsy. *Electroencephalogr Clin Neurophysiol* 1985;61:314–322.
13. Alarcon G, Kissani N, Dad M, et al. Lateralizing and localizing values of ictal onset recorded on the scalp: evidence from simultaneous recordings with intracranial foramen ovale electrodes. *Epilepsia* 2001;42:1426–1437.
14. Carter DA, Lassiter AT, Brown JA. Cost-efficient localization of seizures of mesiotemporal onset with foramen-ovale electrodes. *Neurol Res* 1998;20:153–160.
15. Fernandez Torre JL, Alarcon G, Binnie CD, et al. Comparison of sphenoidal, foramen ovale and anterior temporal placements for detecting interictal epileptiform discharges in presurgical assessment for temporal lobe epilepsy. *Clin Neurophysiol* 1999;110: 895–904.
16. Kissani N, Alarcon G, Dad M, et al. Sensitivity of recordings at sphenoidal electrode site for detecting seizure onset: evidence from scalp, superficial and deep foramen ovale recordings. *Clin Neurophysiol* 2001;112:232–240.
17. Pastor J, Sola RG, Hernando-Requejo V, et al. Morbidity associated with the use of foramen ovale electrodes. *Epilepsia* 2008;49: 464–469.
18. Karakis I, Velez-Ruiz N, Pathmanathan JS, et al. Foramen ovale electrodes in the evaluation of epilepsy surgery: conventional and unconventional uses. *Epilepsy Behav* 2011;22:247–254.
19. Cendes F, Li LM, Watson C, et al. Is ictal recording mandatory in temporal lobe epilepsy? Not when the interictal electroencephalogram and hippocampal atrophy coincide. *Arch Neurol* 2000;57:497–500.
20. Steude U, Stodieck S, Schmiedek P. Multiple contact foramen ovale electrode in the presurgical evaluation of epileptic patients for selective amygdala-hippocampectomy. *Acta Neurochir Suppl (Wien)* 1993;58:193–194.
21. Schevon CA, Weiss SA, McKhann G Jr, et al. Evidence of an inhibitory restraint of seizure activity in humans. *Nat Commun* 2012;3:1060.
22. Dykstra AR, Chan AM, Quinn BT, et al. Individualized localization and cortical surface-based registration of intracranial electrodes. *Neuroimage* 2012;59:3563–3570.