

Surgery after intracranial investigation with subdural electrodes in patients with drug-resistant focal epilepsy: outcome and complications

Roberta Morace · Giancarlo Di Gennaro ·
Angelo Picardi · Pier Paolo Quarato ·
Antonio Sparano · Addolorata Mascia ·
Giulio Nicolò Meldolesi · Liliana Graciela Grammaldo ·
Marco De Risi · Vincenzo Esposito

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Abstract Video–EEG monitoring with intracranial subdural electrodes is a useful assessment tool for the localization of the epileptogenic zone in patients with drug-resistant focal epilepsy. We aimed at assessing the morbidity related to electrode implantation and the surgical outcome in patients who underwent epilepsy surgery after intracranial EEG monitoring. All patients ($N=58$) admitted to our Epilepsy Surgery Centre for drug-resistant focal epilepsy who underwent resective surgery after intracranial monitoring with subdural electrodes and were followed up for at least 2 years were included in the study. Their mean age was 30.4 years (range 8–60 years), 25 (43 %) were female, and 44 (76 %) had a preoperatively detected structural lesion. The mean duration of invasive recording was 2.3 days

(range 1–14 days). Extraoperative ECoG allowed the identification of the epileptogenic focus in all cases. The temporal lobe was involved in 21 (36 %) patients, whereas extratemporal foci were identified in 24 (41 %) patients. Thirteen patients (23 %) had multilobar involvement. Functional brain mapping was performed in 15 (26 %) patients. Transient complications related to electrode implantation occurred in three patients. Among patients with evidence of lesion on preoperative MRI, lesionectomy alone was performed in 12 cases (27 %), while it was combined with tailored cortical resection in the remaining cases. Tailored cortical resection was also performed in patients without evidence of lesion on MRI. After resective surgery, transient neurological deficits occurred in five cases, while another patient experienced permanent lateral homonymous hemianopia. At the last follow-up observation, 34 (57 %) patients were seizure-free (Engel class I). This study suggests that invasive EEG recording with subdural electrodes may be useful and fairly safe for many candidates for epilepsy surgery.

R. Morace · G. Di Gennaro (✉) · P. P. Quarato · A. Sparano ·
A. Mascia · G. N. Meldolesi · L. G. Grammaldo · M. De Risi ·
V. Esposito
Epilepsy Surgery Unit, Department of Neurological Sciences,
IRCCS Neuromed,
86077 Pozzilli, Isernia, Italy
e-mail: gdigennaro@neuromed.it

A. Picardi
Center of Epidemiology, Surveillance and Health Promotion,
Italian National Institute of Health,
Rome, Italy

V. Esposito
Department of Neurosurgery, “La Sapienza” University,
Rome, Italy

G. N. Meldolesi
‘Neurone’ Foundation for Research in Neuropsychobiology and
Clinical Neurosciences,
Rome, Italy

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Introduction

About one fifth of patients with epilepsy suffer from medically intractable seizures [29]. These patients often have partial or localization-related epilepsy [14]. A substantial proportion of them may benefit from epilepsy surgery. While many patients with a discrete brain lesion or mesial temporal sclerosis can undergo surgery after non-invasive

investigations, other patients need intracranial EEG monitoring to identify the epileptogenic zone and possible eloquent areas that should be spared from resection. Intracranial EEG monitoring can be performed with depth electrodes and subdural electrodes, either alone or combined together. The former allows to explore sulci and internal portions of brain lesions [8], while the latter allows functional mapping and a larger coverage of neocortical structures [24].

Although 25–50 % of patients evaluated for epilepsy surgery undergo invasive EEG monitoring [34], relatively few data are available regarding technique, complications and outcome [1, 6, 9, 15, 16, 18, 22, 23, 25, 26, 33, 43, 45]. The present paper focuses on a series of 58 consecutive patients who underwent epilepsy surgery after EEG monitoring with subdural electrodes and were followed up for at least 2 years.

Methods

Participants All patients ($N=58$) with drug-resistant focal epilepsy who underwent resective surgery after intracranial monitoring with subdural electrodes and were followed up for at least 2 years at the Epilepsy Surgery Centre of the Neuromed-IRCCS Institute between 2003 and 2010 were included in the study. Their mean age was 30.4 ± 3.5 years (range 8–60 years), and 25 (43 %) were female.

Presurgical protocol All patients underwent a non-invasive diagnostic protocol described in detail elsewhere [28] that included a detailed seizure history, neurological examination, brain MRI scan (1.5 or 3 T, general electric system), neuropsychological assessment, psychiatric evaluation, and video–

EEG monitoring. Before electrode implantation, 3-T MRI volumetric sequences (T1-weighted FSPGR, slice thickness 1 mm) were also obtained before and after contrast administration. Neurological examination was abnormal in 17 cases (29 %). Eight patients (14 %) had mental retardation as measured by the Weschler Adult Intelligence Scale-R. In 44 patients (76 %), a structural lesion was preoperatively detected (focal cortical dysplasia in 14 cases, gliosis in 13 cases, low-grade tumor in 7 cases, mesial temporal sclerosis in 2 cases, cortical atrophy in 3 cases, cavernous hemangioma in 2 cases, and other lesions in 3 cases).

Electrode implantation Subdural electrodes (assembled in grids or strips) were implanted after craniotomy under general anesthesia to further delineate the epileptogenic zone and to perform cortical mapping of eloquent areas if needed. In each patient, the intracranial investigation strategy and electrode positioning were planned on the basis of the “suspected” epileptogenic zone, as defined by non-invasive presurgical evaluation discussed in a multidisciplinary case conference (Fig. 1). Depending on the preoperative planning, a variable number of flexible electrodes (with variable number of electrode contacts) were advanced subdurally in order to cover the exposed cortex. Overall, 59 grids and 122 strips were implanted, with a total of 3,343 and 891 contacts, respectively. Table 1 provides a detailed description of coverage and grid/strip size in each patient. To address the electrode placement over the desired cortical areas, three-dimensional MRI reconstructions were used in each patient (Fig. 2). In one patient, three depth electrodes with ten contacts each were also stereotactically implanted to explore the medial frontal lobe. Avascular trajectories were planned on the basis of preoperative MRI. After positioning of a Radionics CRW stereotactic frame, CT scans were obtained and fused with preoperative

Fig. 1 Example of planning of subdural electrodes implantation: mesial and dorsolateral frontal structures as well as mesial temporal structures constitute the target regions of this exploration

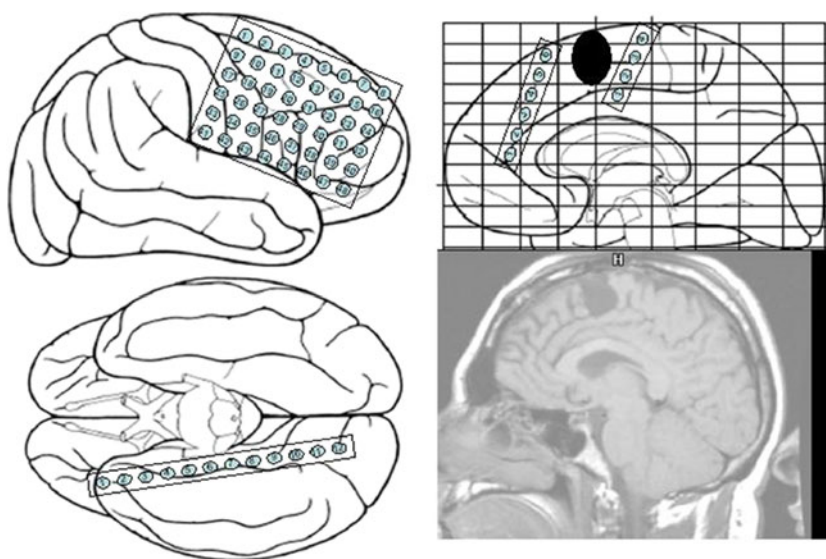


Table 1 Coverage and grid/strip size

Case number	Sex	Age at surgery	Coverage	Number of grids (contacts)	Number of strips (contacts)
1	F	37	TPOd (R)	1 (64)	2 (6+6)
2	M	37	TPOd (R)	1 (64)	–
3	M	32	TPOd (R)	1 (64)	–
4	M	27	Tm + TPOd (R)	1 (64)	1 (12)
5	F	38	FTd + Tm (R)	1 (64)	3 (12+6+4)
6	M	47	TPOd + Tm + Pm (R)	1 (48)	3 (10+8+8)
7	M	28	TPO + Tm (R)	1 (64)	1 (12)
8	M	22	TPO + Tm (L)	1 (64)	1 (12)
9	F	11	TPO + POm (R)	1 (48)	2 (4+4)
10	F	37	CTP + Tbm (R)	1 (48)	6 (8+8+8+6+6+12)
11	F	26	FC (L)	1 (48)	–
12	F	45	T (R)	1 (48)	–
13	M	17	FT + Fm (R)	1 (64)	3 (12+6+6)
14	F	24	FT + Fm + Tm (R)	1 (64)	4 (6+6+4+12)
15	M	22	TPO + Tm (R)	1 (64)	3 (6+6+12)
16	F	31	TPO + Tm (R)	1 (64)	1 (12)
17	M	12	Fm (L)	–	2 (6+6)
18	M	16	T + Tm (L)	1 (48)	1 (12)
19	F	8	F + Fm (R)	1 (48)	2 (6)
20	F	42	TPO + Tm (R)	1 (64)	1 (12)
21	M	36	F + Fm (R)	1 (64)	2 (6+6)
22	F	20	F + Fm(R)	1 (64)	4 (6+6+6+4)
23	M	40	TPO + Tm + Pm (R)	1 (64)	5 (6+6+6+8+12)
24	M	22	Td(L)	1 (48)	–
25	F	35	FTid + Tm (R)	1 (64)	4 (4+4+8+12)
26	F	14	TPOd (L)	1 (64)	–
27	M	12	FTd + Fm + Tm (L)	1 (64)	4 (12+4+4+4)
28	M	39	TPOd + FCd + Tm (R)	1 (64)	3 (12+6+6)
29	F	12	FTd + Fm + Tm (R)	1 (64)	4 (12+6+6+6)
30	M	27	TPOdm + Tm (L)	1 (64)	4 (12+6+6+6)
31	M	21	TPOd + POm + Tm (L)	2 (64+16)	2 (12+6)
32	M	28	TPOd + POm + Tm (R)	2 (64+8)	2(8+8)
33	M	42	TOd + Fdi (L)	1 (48)	3 (6+6+6)
34 ^a	M	32	Fdm (L)	1 (48)	4 (6+6+6+4)+3
35	M	35	Fdm (R)	1 (48)	3 (4+4+4)
36	M	42	TPOd + Fd (R)	1 (64)	4 (6+6+6+4)
37	M	38	FTdm (R)	1 (64)	5 (4+4+6+12+4)
38	F	42	Fd (L)	1 (64)	–
39	F	25	FCid (R)	1 (48)	3 (4+4+4)
40	M	48	Td (L)	1 (20)	–
41	M	20	FTdm (L)	1 (64)	4 (12+4+4+4)
42	M	33	TPO + Tm (L)	1 (64)	3 (12+4+4)
43	M	22	FCPm (L)	1 (16)	–
44	F	35	Ftd + Tm (L)	1 (64)	3 (12+4+4)
45	F	37	TPOd (R)	1 (48)	–
46	F	60	TPOd + Tm (R)	1 (64)	1 (4)
47	M	26	FTP + Tm (R)	1 (64)	2 (4+8)
48	M	17	Tdm (L)	1 (48)	1 (12)

Table 1 (continued)

Case number	Sex	Age at surgery	Coverage	Number of grids (contacts)	Number of strips (contacts)
49	F	35	TPO (R) Td	1 (64)	2 (6+6)
50	F	24	FTdm (R)	1 (64)	5 (4+4+4+4+12)
51	F	38	FT + Tm (R)	1 (64)	1 (12)
52	F	31	FTCd + Pm (L)	2 (64+8)	–
53	M	28	Fd (L)	1 (64)	–
54	M	49	TPOd + Tm (R)	1 (64)	1 (12)
55	F	40	CPd + Tm (R)	1 (64)	2 (12+4)
56	M	50	Tm (R)	–	1 (12)
57	M	23	CP (R)	1 (48)	–
58	F	41	TPOd (R)	1 (64)	2 (6+6)

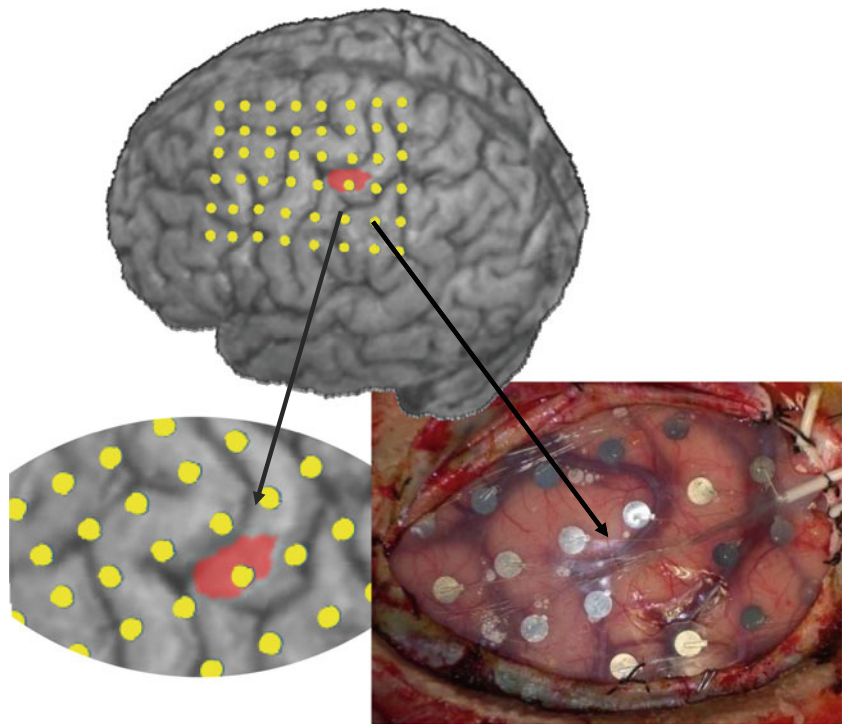
F female, *M* male, *T* temporal, *P* parietal, *O* occipital, *F* frontal, *C* central, *d* dorsolateral, *m* mesial, *i* insular, *L* left side, *R* right side

^aThis patient was also implanted with three depth electrodes (10–10–10)

MRI to obtain the stereotactic coordinates for each trajectory. Using a tool holder, the depth electrodes were subsequently implanted through a 1-cm burr hole. Before and after subdural electrode positioning, a digital photograph of the operatory field was taken. In some selected cases, contacts were then detected on post-implantation brain CT scans through a semi-automated procedure based on a MATLAB routine described in detail elsewhere [32]. Extraoperative video–ECoG recordings were performed in each patient’s room, with a 128-

channel Grass-Telefactor system with a sampling rate of 256 Hz. Bipolar and monopolar recordings of basic rhythms as well as interictal and ictal activity were analyzed. In some cases, adjunctive scalp electrodes were employed for sampling those brain regions that were not explored by intracranial electrodes. In all cases, video–ECoG monitoring was carried on until a number of seizures sufficient to allow the identification of the seizure onset zone was recorded. The mean duration of invasive monitoring was 2.3 days (range 1–14).

Fig. 2 Three-dimensional preoperative MRI reconstruction are used to address the electrodes placement over the desired cortical areas



Brain mapping In 15 patients in whom the epileptogenic zone was suspected to be close to or overlapping with eloquent area such as primary motor and language areas, functional mapping was also performed. Bipolar electrical stimulation was delivered on the explored cortex through the same subdural contacts used for invasive recordings. To exactly define the boundaries of functional areas, pairs of electrode contacts were progressively tested. Trains of 0.3 ms single pulses (interstimulus interval 16 ms) were delivered at 50 Hz. Intensities and train duration were different among cortical areas, ranging from 0.2 to 0.5 mA and 1 s duration for motor cortex to 5–15 mA and 2–8 s duration for language areas. In all cases, extraoperative cortical stimulation was performed in the patient's room during neurological evaluation, neuropsychological testing, and ECoG monitoring. Neuropsychological assessment for language required from 2 to 3 h and included naming, comprehension, counting and reading tasks, calculation, sentence completion, and writings tasks. When advised, resective strategies were tailored based on the invasive epileptological and functional mapping. Resections were performed under general anesthesia, with microsurgical technique. All patients underwent postoperative MRI. Neurological, EEG, and neuropsychological evaluations were repeated 1, 2, and 5 years after surgery. Seizure outcome was determined yearly according to Engel's classification [13].

Results

Invasive video-EEG monitoring Extraoperative ECoG allowed the identification of the epileptogenic focus in all cases. The temporal lobe was involved in 21 patients (36 %), whereas extratemporal foci were identified in 24 patients (41 %) (frontal in 16 cases, parietal in 4 cases, central in 3 cases, insular in 1 case). Thirteen patients (23 %) had multilobar involvement. The dominant hemisphere was involved in 20 patients (34 %). Among the 15 patients who underwent functional mapping, in 13 cases (87 %) the epileptic focus did not involve eloquent cortex. In one patient with a low-grade tumor arising in Broca's area, electrical cortical stimulation revealed a re-organization of language area in the adjacent cortex. In another patient with non-lesional left temporal epilepsy, the epileptogenic zone partially involved Wernicke's area; thus, a subtotal resection was planned based on the functional boundaries.

Complications related to subdural electrode positioning were brain edema in one patient and subdural hemorrhage in two patients. None of them experienced persistent neurological deficits. The patient who was implanted with both subdural and depth electrodes experienced no complications.

Resective surgery Among the 44 patients with evidence of lesion on preoperative MRI, the lesion was removed alone in 12 cases (27 %), while lesionectomy was combined with tailored cortical resection in 32 cases (73 %). Tailored cortical resection was also performed in 14 patients without evidence of lesion on MRI.

Postoperative transient neurological deficits occurred in five cases (dysphasia in three cases, sensorimotor deficits in the remaining two cases). Another patient experienced permanent lateral homonymous hemianopia. Postoperative MRI showed a gross total lesion removal in 41 of the 44 patients with symptomatic epilepsy (93 %). In the remaining three cases, the lesion was only partially removed. Histopathological findings together with preoperative MRI findings are reported in Table 2.

The mean duration of follow-up was 48 months (range 24–77). At the last follow-up observation, 34 patients (57 %) were seizure-free, whereas only three patients (5 %) did not experience any worthwhile improvement. Seizure outcome according to Engel's classification is detailed in Table 3.

Discussion

Intracranial electrode implantation represents an important assessment tool in candidates for epilepsy surgery, as non-invasive EEG recordings cannot adequately localize the epileptogenic zone in approximately 25 % of patients with refractory seizures [35]. Subdural electrodes have a relatively wide coverage with fairly uniform spacing and can be implanted over the cortical convexity, the basal neocortex, the mesial neocortex, or the interhemispheric neocortex [21]. On the other hand, depth electrodes may have a better view of some deep-seated dipoles, despite their markedly smaller sampling. Thus, they are used primarily to study deep structures such as the mesial temporal lobe [10, 36, 37,

Table 2 Histopathological findings compared to preoperative MRI

	Histology	Preoperative MRI
Focal cortical dysplasia	20	14
Gliosis	18	13
Low-grade tumors	8	7
Mesial temporal sclerosis	2	2
Cortical atrophy	0	3
Cavernous hemangioma	2	2
Other lesions	3	3
No lesion	5	14
Total number of patients	58	58

MRI magnetic resonance imaging

Table 3 Seizure outcome according to Engel's classification

Seizure outcome	N (%)
Class Ia	30 (52)
Class Ib	4 (5)
Class II	6 (14)
Class III	15 (24)
Class IV	3 (5)
Total number of patients	58 (100)

Class Ia free from seizures and auras, *Class Ib* only auras, *Class II* rare seizures, *Class III* worthwhile postoperative improvement, *Class IV* no worthwhile improvement

47]. The decision whether to use subdural electrodes alone, depth electrodes alone, or a combination of both types of electrodes depends mainly on the underlying pathology and suspected epilepsy type. According to current literature [2, 5, 19, 39], we implanted subdural grid electrodes alone in neocortical epilepsy or when the suspected epileptogenic zone was close to eloquent cortex. Combined subdural plus depth electrodes implantation was performed only in one patient, in order to assess the earlier involvement of medial frontal structures in the epileptogenic process as compared with neocortical regions.

Careful mapping of the irritative zone and ictal onset zone followed by complete surgical resection of the mapped epileptogenic zone was found to be associated with relatively good postoperative outcome [1, 17, 38]. In all our patients, the use of intracranial electrodes for extraoperative video-EEG monitoring allowed us to record one or more seizures. Even though intraoperative ECoG has been widely employed in tailoring cortical resections for epilepsy surgery [3, 4], this technique usually does not enable to detect the ictal onset zone because the amount of time for recording is relatively short.

While they allow functional mapping and provide large coverage of neocortical structures, subdural electrodes have also disadvantages, as they may exert a mass effect on the brain and there can be cerebrospinal fluid leakage through the openings in the dura. These openings may also favor the development of infection [20], especially when a high number of contacts are implanted [45]. In our series, no patient experienced permanent neurological sequelae, while three patients (5.2 %) had transient complications not requiring treatment. This relatively low proportion of complications related to electrode implantation is comparable with those reported by most other similar studies [1, 6, 15, 18, 22, 23, 25, 26, 33, 43].

Our seizure outcome was slightly less favorable (57 % in Engel's class I) as compared with those reported in the literature after standard temporal resections (60–90 % in Engel's class I), usually without invasive investigations

[13]. This is likely to ascribe to the high prevalence (64 %) of extratemporal lobe involvement in our series. In most studies, the percentage of success after extratemporal resections is 32–51 %, with better outcome in patients with detectable lesions [12, 40, 41, 44].

In our series, 12 of the 44 patients with symptomatic epilepsy underwent lesionectomy alone, while in the other patients, lesion removal was combined with tailored cortical resections, since invasive recordings demonstrated that the epileptogenic zone exceeded the boundaries of the epileptogenic lesion. In five of the 14 patients without detectable lesions on preoperative MRI, histopathological examination revealed malformations of cortical development. This finding confirmed the reported association between cortical dysplasia and epilepsy [27, 39].

In patients with epileptic focus suspected to be close to eloquent brain areas, good functional outcome was reported after intraoperative mapping under awake craniotomy [7, 11]. During intraoperative mapping, language and/or motor function is tested intermittently during the actual process of tumor resection under local anesthesia. Although it is widely considered to be the gold standard, particularly for language evaluation [7], awake craniotomy carries several disadvantages, including delayed operative time, patient discomfort, and less accuracy in neuropsychological assessment. In addition, cortical stimulation often elicits epileptiform afterdischarges, which can sometimes progress into seizures. This can delay or prevent functional mapping at some sites, particularly those closest to the seizure focus. In our series, extraoperative cortical stimulation allowed to identify the exact spatial relationship between epileptogenic focus and eloquent cortex in all cases. Also, continuous ECoG monitoring during cortical stimulation was useful in detecting afterdischarges, thus preventing stimulation-related seizures.

The role of fMRI as a possible substitute for neurophysiological methods in testing eloquent areas is still debated. There is a fairly high percentage (9 %) of false positive/negative results regarding language lateralization [46]. Also, the accurate cortical localization of higher functions such as writing or calculation is still a major problem [42]. Therefore, critical surgical decisions should not be based on this technique alone [30, 31].

In conclusion, our findings suggest that invasive EEG recording with subdural electrodes allows the identification of the epileptogenic zone and adequate functional brain mapping in most candidates for epilepsy surgery, with a relatively low incidence of complications.

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Comments

Steven G. Ojemann, Aurora, USA

Morace et al. report on 58 patients who underwent resective surgery at their Epilepsy Center following invasive monitoring. They detail the morbidity related to invasive monitoring and resective surgery and outcomes in terms of seizure control with a minimum follow-up of 2 years in this series.

Ictal intracranial EEG represents the definitive method for localizing an individual's ictal onset zone, and intracranial electrodes can overcome many of the limitations of scalp EEG, which include problems with volume conduction effects, difficulty identifying deeply located current sources, and problems with physiological artifacts. As the authors demonstrate, intracranial electrodes also provide the opportunity to perform electrical stimulation mapping of essential sites for critical functions such as language.

These advantages of invasive recordings potentially come at a price. Complications are well described in numerous articles cited by the authors, and their series further informs this literature. The authors report three complications related to electrode placement: one patient with brain edema and two with subdural hemorrhages. They do not report other types of complications such as wound infections, deeper infections, CSF leaks, or need for additional electrode placement or repositioning, which have been described in many of the other large series of invasive recording cited by the authors.

The authors cite one series in which complications were correlated with the number of contacts implanted, though others have failed to find such a correlation [1]. Insufficient coverage risks failure to adequately define the epileptic focus and potentially requires return to the operating room for additional electrode placement or repositioning in cases where ictal onset appears to arise outside of the covered area. Striking a balance between the questions of accuracy and safety requires judiciousness regarding when to employ intracranial monitoring and what territory one should monitor. These choices are best made in collaboration with an experienced, multi-disciplinary team taking into consideration multiple sources of data including evaluation of the ictal semiology, ictal electroencephalographic monitoring, high-resolution MR imaging, intracarotid amobarbital (Wada)

testing, neuropsychological measures, and sometimes additional imaging which has been shown to have clinical value, such as ictal single photon emission computed tomography or ¹⁸F-fluorodeoxyglucose and ¹¹C-flumazenil positron emission tomography. In cases of mesial temporal lobe epilepsy, when there is a high degree of concordance between these different measures of cerebral structure and ictal and interictal dysfunction, then good results have been obtained by proceeding to resection without first employing intracranial recording techniques [2].

With respect to mapping of essential sites for critical functions, the authors point out that mapping with subdural arrays can be performed over a longer time period and with greater patient comfort than one can typically achieve with intraoperative mapping. Intraoperative stimulation mapping, however, does offer the opportunity to assess function as the resection progresses and can often define the maximum extent of a resection that encroaches on an “eloquent” locus to a higher degree than extraoperative mapping can achieve. Intraoperative mapping also affords the opportunity to map subcortical white matter pathways when deeper resections are undertaken [3, 4]. Therefore, I would suggest that extraoperative and intraoperative mapping techniques each have advantages and disadvantages and can be used in a complementary manner.

Ablative or disconnective surgery for the treatment of epilepsy requires precise definition of the zone of ictal onset and precise definition of proximate or potentially overlapping sites that are essential for critical neurologic functions. In many cases, these zones and sites are associated with no structural features or abnormalities that can be defined with current imaging. Invasive recording and mapping techniques are therefore a fundamental part of the armamentarium of any center performing epilepsy surgery, and this article further informs the literature about the associated risks and benefits.

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Johannes Schramm, Bonn, Germany

The authors report on a medium-sized series of 58 cases who needed invasive presurgical evaluation with implanted strip and grid electrodes before epilepsy surgery. A minimum follow-up of 2 years is available. The array of diagnoses is a bit atypical with a high number of gliosis cases, an expected number of dysplasia cases, but only about 14 % tumors. In other series, tumors may account for 30–50 % of drug-resistant epilepsy cases.

The techniques used are pretty standard and well illustrated in the two figures. The tables provide detailed information about the electrodes that one can use, which may be pretty useful. This invasive evaluation allowed the authors to make a decision between those cases that needed lesionectomy alone compared to extended lesionectomy, i.e., lesionectomy combined with tailored cortical resection. The good coverage of recent references allows the reader to gain a good impression of this technique by reading the article or looking-up the references in addition.