Morbidity Associated With the Use of Intracranial Electrodes for Epilepsy Surgery

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ABSTRACT: ***Background:*** Invasive monitoring for the investigation of medically intractable epilepsy may be associated with undesirable morbidity. We performed a review of our recent experience to determine the incidence of major complications. ***Methods:*** We reviewed the clinical records of all patients who underwent invasive EEG monitoring at our institution between 2000 and 2004. ***Results:*** One-hundred and sixteen patients (57 males, 59 females) with a mean age of 32 years of age underwent intracranial placement of electrodes for epilepsy surgery investigation. Subdural strips were placed in 115 patients with a mean of eight strips per patient. Subdural grids were inserted in 11 patients and depth electrodes in five. Fourteen of the 15 patients with grids or depth electrodes also had strips. Coverage was unilateral in 37 patients and bilateral in 79 patients. Electrodes were placed over the frontal lobe in 78 cases, temporal in 93, parietal in 24, and occipital in 27 patients. The average duration of investigation was 12.3 days (range 3-29). The evaluation led to the performance of a surgical resection in 85 patients (74%). Complications were seen in four patients with subdural strips (3%), and in two patients with grids (13%), characterized by clinical infection, intracranial hemorrhage, aseptic meningitis, transient neurological deficits, and status epilepticus. Mortality was nil. ***Conclusions:*** In comparison with previously published literature on the topic, the major complication rate in this group of patients appears to be low.

RÉSUMÉ: Morbidité associée à l'utilisation d'électrodes intracrâniennes dans la chirurgie de l'épilepsie. ***Contexte:*** La surveillance effractive dans l'évaluation de l'épilepsie réfractaire au traitement médical pourrait être associée à une morbidité regrettable. Nous avons revu notre expérience récente pour déterminer l'incidence de complications majeures. ***Méthodes:*** Nous avons révisé le dossier clinique de tous les patients qui ont subi une surveillance ÉEG effractive dans notre institution entre 2000 et 2004. ***Résultats:*** On a implanté des électrodes intracrâniennes dans le cadre d'une évaluation pour chirurgie de l'épilepsie chez cent seize patients (57 hommes et 59 femmes) dont l'âge moyen était de 32 ans. Des électrodes sous-duales ont été placées chez 115 patients, soit en moyenne 8 électrodes par patient. Une grille d'électrodes sous-durales a été placée chez 11 patients et des électrodes profondes chez 5 patients. Quatorze des 15 patients avec une grille d'électrodes ou des électrodes profondes avaient également des électrodes en bandes. Le champ d'application était unilatéral chez 37 patients et bilatéral chez 79 patients. Les électrodes étaient placées au lobe frontal chez 78 patients, au lobe temporal chez 93, au lobe pariétal chez 24 et au lobe occipital chez 27. La durée moyenne de l'évaluation était de 12,3 jours (écart de 3 à 29 jours). L'évaluation a mené à une résection chirurgicale chez 85 patients (74%). Quatre patients qui avaient des bandes sous-durales (3%) et deux patients qui avaient des grilles (13%) ont présenté des complications, soit une infection clinique, une hémorragie intracrânienne, une méningite aseptique, des déficits neurologiques transitoires et un état de mal épileptique. Il n'y a eu aucun décès. ***Conclusion:*** Le taux de complications majeures chez ce groupe de patients semble bas comparé à ce qu'on retrouve dans la littérature sur ce sujet.

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The goal of diagnosis and treatment of patients with medically intractable epilepsy is complete seizure freedom. For that reason, patients may be considered for surgical therapy and undergo presurgical evaluation. Epilepsy surgery is based on the principle that resection of an epileptogenic focus can result in seizure freedom.

When a standard presurgical evaluation (consisting of video-EEG, MRI, functional neuroimaging and neuropsychological assessment), cannot identify the epileptogenic focus, invasive intracranial electrodes are often required to help with localization. The main purpose of intracranial recording is to further delineate the area of onset and early propagation of a seizure. For these purposes, coverage of large areas of the brain placed through a craniotomy or bilateral craniotomies is required.

The use of intracranial electrodes has become more frequent in the last two to three decades.[1-5] Invasive monitoring rates in

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adult epilepsy centers ranges from 25 to 50%.[6] The use of intracranial recordings does not lack potential complications, even though invasive recordings provide much more sensitive information than scalp recordings.

The chronic implantation of electrodes carries the risk of mass effect, hemorrhage, and infection. It is desirable, then, to limit the number of studies and electrodes possible without compromising the ability to gain sufficient information for subsequent surgery.[7]

The purpose of this study was to identify the presence of major complications related to the use of any type of intracranial placed electrodes for epilepsy surgery evaluation, analyzing the experience at London Health Sciences Centre.

Materials and Methods

Patient population

All patients consecutively admitted to the London Health Sciences Centre Epilepsy Unit, between January 2000 and July 2004 for intracranial placement of electrodes for epilepsy surgery evaluation were included.

Electrode placement

Subdural strips are the most common form of invasive recording used at our institution. Prior to August 2003, all electrodes were manufactured "in-house." Since January of 2004 we have been using Ad-Tech® Subdural Strip Electrodes (Ad-Tech Medical Instrumentation Corporation, Racine, WI). After the scalp is completely shaved and thoroughly prepped, the head is placed in a neutral position, flexed forward and supported by the neck and occiput by a hardening suction "beanbag". This allows for access to the entire vertex and facilitates bilateral placements. The strips are placed through one or several burr holes depending on the coverage desired. For unilateral temporal (mesial and lateral), occipital (mesial and lateral) as well as lateral parietal placements, a single burr hole is placed just superior to the transverse sinus immediately posterior to the mastoid process. In frontal (lateral, mesial and orbitofrontal) placements the hole is placed 1-2 cm anterior to the coronal suture, slightly lateral of the midline. Rarely, posterior midline holes are required to place mesial parietal electrodes or to augment supplementary motor area coverage. Electrodes are

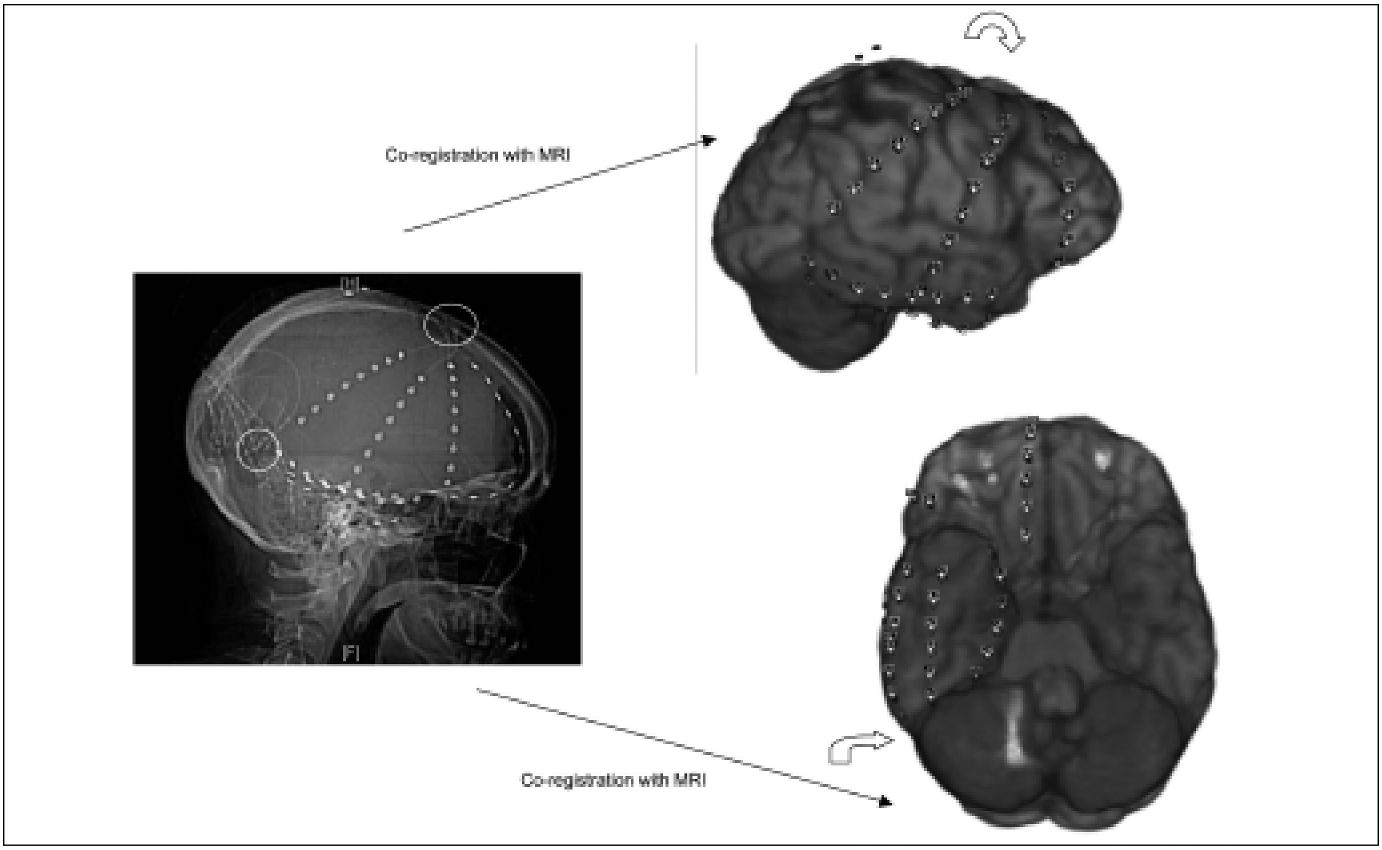

Figure: *The picture shows the results of co-registration (fusion) of a pre-operative T1-spoiled gradient-recalled MRI to a post-operative CT scan using a volumetric mutual information algorithm (Atamai, Inc., London, Ontario). On the left of the figure, a post-operative X-RAY shows the strips of electrodes, with 2 white circles indicating the areas of the burr holes. The figure on the right is the result of the co-registration. The open arrows show the areas where the burr holes were located. The view after the co-registration is a tri-dimensional picture; here we show a view from the right side and from below. This particular case had right hemispheric and right mesial temporal onset of seizures on scalp recordings, with evidence of right mesial temporal sclerosis on structural MRI. Subsequent evaluation with subdural electrodes revealed a right mesial temporal onset.*

introduced in the subdural space and, using fluoroscopy, are guided to the desired location. Electrodes can often be guided great distances from the entry sites if needed. For example, the orbitofrontal surface is usually reached by a strip placed though the pre-coronal burr hole and guided around the frontal pole inferiorly. The electrodes are tunneled out through a separate incision placed at a distance from the entry site and are sutured in place. When necessary, different sizes of subdural grids are inserted by craniotomy. Often, subdural strips are placed though the craniotomy at the same time. Depth electrodes, which are infrequently utilized at our institution, are placed using a Leksell stereotactic frame and tunneled to separate exit sites.

Since 2003, the placement of all electrodes has been post-operatively confirmed by fusing a pre-operative T1-spoiled gradient-recalled (SPGR) - MRI to a post-operative CT scan using a volumetric mutual information algorithm (Atamai Inc., London, Ontario, Canada) (See Figure).

At the end of the investigations, the subdural and depth electrodes are removed at the bedside. Grids are removed in the operating room.

Prophylactic antibiotics and dexamethasone are used in all cases. The exact timing and doses of the medications differs slightly between the two epilepsy surgeons (DS & AP). Both surgeons administer 1 gram of intravenous (IV) cefazolin one hour prior to surgery. One surgeon (DS) continues cefazolin 1 gram IV every eight hours for three doses and the other (AP) does not administer any postoperative antibiotics. Antibiotics are not given after 24 hours by either surgeon regardless of the length of implantation. Ten milligrams of IV dexamethasone is administered to all patients prior to surgery. After surgery, the steroids are tapered over 48 (AP) or 96 (DS) hours.

Data recording

After a retrospective review of patients' charts, a database was created that included the following independent variables: age of patient, gender, and days of evaluation with intracranial electrodes. Regarding intracranial coverage, the variables used were: type of intracranial electrodes (depths electrodes, grids, strips or lines), number of lines or strips, number of grids, lobes covered, number of lobes covered with electrodes, and if it was a bilateral or unilateral coverage.

The occurrence of complications was tabulated as follows: infections, intracranial bleeding (subdural, epidural, or intracranial), presence of status epilepticus or seizures, and others. Outcome of investigation was annotated as well.

Data analysis

All descriptive analyses were performed using MS Excel 2003® (Microsoft Corporation, Redmond, WA). Logistic regression analysis was used to investigate the relationship between the occurrence of complications and the various independent variables listed above, with potential confounders controlled. Two sets of logistic regression models were generated to estimate odds ratios for the occurrence of complications with intracranially placed electrodes. The first

Table 1: Clinical characteristics of the six patients with complications

Patient	Gender	Age	Number of strips	Grids	Days of implantation	Coverage	Complication	Localization of epilepsy onset	Treatment	Clinical results	Follow-up months
1	M	17	5	No	10	Left: Mesial temporal Inferior lateral temporal Superior lateral temporal Posterior orbital frontal Anterior orbital frontal	Left thalamic hemorrhage	Left mesial Temporal (hippocampal sclerosis)	ATL	Ia	7
2	F	23	6	No	14	*Left*: Mesial temporal Inferior lateral temporal Medial lateral temporal Superior lateral temporal Posterior lateral temporal	aseptic meningitis	Left mesial temporal (hippocampal sclerosis)	ATL	Ia	1
3	F	53	6	7 X 8 electrodes	7	*Right*: Mesial temporal Superior orbitofrontal Inferior orbitofrontal Medial Frontal convexity Inferior Frontal convexity (opercular) Superior frontal convexity	Epidural hematoma	Right Frontal (cortical dysplasia)	corticectomy	Ia	14
4	M	61	6	No	14	*Right and Left:* Mesial temporal (two) Lateral temporal	Left third nerve palsy Meningitis	Right mesial temporal (hippocampal sclerosis)	ATL	Ia	8
5	F	63	9	No	4	*Right*: orbitofrontal parietal and frontal convexity Inf and sup lateral temporal	Intraparenchymal hemorrhage	Right hemisphere (oligodendroglioma)	No surgery	n/a	n/a
6	F	21	10	7 X 4 electrodes	21	*Right*: mesial occipital Lateral occipital Mesial temporal Posterior lateral temporal	Status epilepticus	Right occipital	No surgery	n/a	n/a

ATL: Anterior Tempora Lobectomy , n/a:Not applicable, Ia: engel's classification

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model incorporated only the occurrence of a complication as the independent variable and generated unadjusted odds ratios. The second set included all variables described in the previous section. Statistics were computed with SAS v 9.0 for Windows® (SAS, Cary, NC).

Results

A total of 116 patients (57 males, 59 females) with a mean age of 32 years (range: 9-65), underwent intracranial placement of electrodes for epilepsy surgery investigation. Subdural strips were placed in 115 patients. A mean of 8 strips were placed in each case with a range of 1 to 17 lines or strips per patient. Grids were inserted in eleven patients and depth electrodes in five. Subdural strips were used exclusively in 100 patients, grid and strips in 10 patients, depth and strips in 5 patients, and one patient had a grid only.

Thirty seven patients received unilateral coverage, while 79 had bilateral coverage. Electrodes were placed over the frontal lobe in 78 cases, temporal in 93, parietal in 24, and occipital in 27 patients. The average duration of investigation was 12.3 days (range: 3-29 days). Evaluation allowed the performance of surgical resection in 85 patients (74%).

Complications were seen in only four patients with subdural strips (3%) and in two patients with subdural grids (13%), characterized by clinical infection, intracranial hemorrhage, aseptic meningitis, transient neurological deficits, and status epilepticus (see Tables 1 and 2). No complications were seen with depth electrodes.

The diagnosis of these complications was obtained from the review of the medical records. The presence of neurological deficits was identified by neurological exam; the diagnosis of infection was characterized by a clinical picture of fever, meningismus, and a compatible cerebrospinal fluid. Aseptic meningitis was diagnosed in a patient with severe headache, not improving with the usual analgesic treatment, with meningismus, and a cerebrospinal fluid not revealing infection. Status epilepticus was diagnosed based on clinical and electroencephalographic findings, which improved after removal of the grid, and without evidence of bleeding or any other structural damage by neuroimaging. Intracranial hemorrhage was diagnosed with neuroimaging studies.

Logistic regression results are shown in Table 3. The first column (model 1) presents unadjusted odds ratios for the occurrence of complications; while the second one represented the multivariate logistic regressions that controlled for all independent variables (model 2). The analysis did not find association between the possible explanatory variables and the occurrence of complications.

Discussion

The importance of invasive, presurgical evaluation of certain causes of intractable epilepsy has been well established,[2,8,9] and the use of intracranial electrodes goes back to 50 years ago, when Penfield and Jasper[10] reported the technique as an intraoperative measure.

Little has been published concerning morbidity and mortality associated with craniotomies for intracranial electrodes, and the rates have been reported to be as high as 7.9%.[1,11,12] A common finding has been that the longer the duration and the higher the number of electrodes used, the higher the chances of complications, infection being the most common.

In our experience, the rate is low as presented in this study, and was characterized by the presence mixed clinical presentations. In the patients evaluated with subdural strips, the complication rate was only 3%, which indicates that the placement of such electrodes can be a low risk procedure in expert hands. Although the number of grids in this series is low, the complication rate for these electrodes seemed to be higher, although this did not reach statistical significance. Nonetheless, it is our preference to use strips alone in the majority of patients. The small number of cases with depth electrodes does not allow us to make conclusions in regards to the safety placement of this particular type of electrode.

In the regression analysis, gender, age of patient, number of lines or electrodes, number of days with intracranial electrodes,

Table 2: Complications seen during presurgical evaluation in patients with intracranially placed electrodes

Complications	Number of Patients
Intracranial hemorrhage	2
Infection (meningitis)	1
Status Epilepticus	1
Aseptic meningitis	1
Transient neurological deficits	1

Table 3: Summary of logistic regression analysis (Odds Ratios and their 95% confidence intervals)

	Univariate	Multivariate
Age		
Less than 25 years	Reference	Reference
25-34 years	1.4 (0.3-6.0)	2.7 (0.5-15.8)
Older than 34 years	0.3 (0.1-3.1)	0.3 (01-3.6)
Number of lines (strips)		
Less than 7	Reference	Reference
7-9	0.3 (0.1-1.8)	0.3 (0.1-1.8)
More than 9	0.5 (0.1-2.6)	0.7 (0.1-4.4)
Time of evaluation (days)		
Less than 8	Reference	Reference
8-14	0.5 (0.1-2.1)	0.4 (0.1-2.0)
More than 14	0.2 (0.1-2.1)	0.2 (0.1-2.4)
Gender		
Male	0.5 (0.1-1.9)	0.5 (0.1-2.2)

and number of lobes covered were not associated with the presence of complications. Thus our study, in contrast to previous findings presented in the literature, found minimal complications when subdural strips are used and no relation to these factors already mentioned.

Possible explanations for our findings may include the use of perioperative dexamethasone and antibiotic coverage, although we do not continue antibiotics beyond 24 hours after surgery Also, the low complication rate seen with subdural lines or strips may be related to the fact that a strip of electrodes does not cover a great area of cerebral cortex, and even though many of them can be placed closed together, there will be always a "free space" in between, minimizing any local mass effect produced by the electrodes. The high rate of infection (7.9%) found in a previous investigation,[11] was most likely related to the design of that particular study. The prospective nature of it as well as the dedicated search for infection, in some of the cases asymptomatic, likely increased the rate.

The main limitation of the current study is its retrospective nature as well as the fact that the diagnosis of a complication was obtained from the information registered in the chart, which could have introduced some collection bias. However, the findings using this methodology are more likely to reflect what are felt to be clinically significant complications requiring some type of intervention.

In summary, the major complication rate of telemetry using intracranial subdural strip electrodes appears to be quite low. Although it would appear that the complication rate from grids is higher, too few patients underwent grid placement to make a valid comparison.

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