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Functional Cortical Mapping Using Subdural Grid Electrodes in Patients with Low-Grade Gliomas Presenting with Seizure

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Functional stimulation mapping with subdural electrode arrays to define eloquent cortex is a standard technique in epilepsy surgery. Before tumors in eloquent regions of the brain are resected, epilepsy surgeons may use this technique as an alternative to awake craniotomy for mapping. We performed detailed functional mapping in 18 patients with low-grade gliomas before they underwent resection. All patients harboring tumors with abnormal enhancement underwent complete resection of the abnormality. The region of T2-weighted abnormality was resected completely in 5 (28%) patients and almost completely in 4 (22%). The most common complication was subdural fluid collection after grid placement. All patients achieved a good outcome at 1 year. Subdural cortical mapping allowed aggressive tumor cytoreduction and was associated with an acceptable rate of neurological morbidity. However, the overall morbidity rate was higher and duration of hospitalization was longer compared to those associated with other tumor mapping methods.

Key Words: brain mapping, cortical stimulation, primary brain tumor, subdural grid electrodes

Abbreviations Used: CT, computed tomography, MR, magnetic resonance; mRS, modified Rankin Scale; WHO, World Health Organization

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Primary low-grade brain tumors in eloquent cortex are challenging lesions to resect. The margin between infiltrating tumor and normal white matter is often indistinct, and their removal risks significant postoperative disability. Several mapping techniques have been developed to limit postoperative neurological morbidity while optimizing the extent of resection. These techniques include intraoperative direct cortical stimulation in awake patients, functional magnetic resonance imaging, magnetoencephalography, and functional mapping with subdural cortical electrode arrays.^{2,4-8} Intraoperative awake stimulation has emerged as the gold standard for resection of these lesions because of the low incidence of postoperative deficits and the ability to map subcortical white matter tracts.^{3,9} However, not all eligible patients are able to undergo awake craniotomy because of the surgeon's or patient's preference or because the institutional expertise needed for mapping is lacking.

We hypothesized that we could leverage our epilepsy experience to develop an alternative to awake mapping using subdural electrode arrays. Subdural arrays are a standard tool in epilepsy surgery for refining seizure localization and mapping functional cortex before lesionectomy. In this new application, the mapping information is used to identify functional gyri, thereby defining a corridor into the tumor and determining which gyri are safe to resect. To assess the utility of and complications associated with this strategy, we reviewed our experience in 18 patients presenting with first-time seizure

related to an intrinsic brain tumor located near eloquent cortex.

Methods

Between 1999 and July 2006, 18 consecutive patients (10 females, 8 males; mean age, 30 years; age range, 18–44 years) presenting with seizure with a primary low-grade (i.e., WHO grade I and II) brain tumor underwent subdural grid implantation and functional mapping followed by tumor resection. Indications for subdural grid mapping included the presence of a suspected low-grade tumor adjacent to or within eloquent cortex, good functional status with the ability to participate in the mapping process, and the recommendation from a weekly, multidisciplinary treatment planning conference. Only patients with a pathologically confirmed diagnosis of a low-grade intrinsic brain tumor are included in the present analysis. This study was approved by the Institutional Review Board of St. Joseph's Hospital and Medical Center.

The tumor was located in the left frontal lobe in six patients, in the right frontal lobe in two patients, in the left temporal lobe in four patients, in the left frontotemporal region in one patient, in the left parietal lobe in three patients, in the right parietal lobe in one patient, and in the left insula in one patient. All tumors were low grade (i.e., WHO grade I or II). Three patients had an oligodendroglioma, eight had an astrocytoma, three had an oligoastrocytoma, three had a ganglioglioma, and one had a juvenile pilocytic astrocytoma (Table 1). All patients presented with seizure.

Mapping and Tumor Resection

In the first stage, a modest-sized craniotomy was individually tailored centered over the lesion while the patient was under general anesthesia. Grids (Ad-Tech Medical Instrument Corp., Racine, WI) were slipped beneath the bone edges into the subdural space to cover the cortical region of interest. Mapping was undertaken in the epilepsy monitoring unit where patients underwent

video-electrocorticography. Grid-stimulation studies were performed in sessions using a Grass Model S12 Isolated Biphasic Stimulator (Astro-Med, Inc., West Warwick, RI). The peak current setting was used to test for sensory phenomena; cessation of motor function of the tongue, hand, and foot; and muscle twitches. Electrode pairs also were tested for the patient's ability to perform selected neuropsychological tests during cortical stimulation. Language domains mapped included reading, naming, and comprehension.

The goal of functional mapping was to determine safe cortical borders of resection by identifying gyri with eloquent function. Resection of the cortical surface of tumor proceeded from gyrus to gyrus, respecting pial borders. Wherever tumor appeared to infiltrate gyri containing no eloquent function, the tumor was resected along with a margin of normal-appearing brain tissue extending to the pial border of adjacent sulci. Gyri containing eloquent function were spared, even if imaging abnormalities indicated involvement of tumor.

Once the cortical borders of the resection were determined in this manner, the tumor was debulked internally. The margin of resection along the tumor's interface with the deep and subcortical white matter was determined by the extent of abnormalities evident on MR imaging and by visual inspection. Complete resection of regions with abnormal enhancement was the first priority, and resection of areas of T2-weighted hyperintensity was the second priority. The aim of surgery was tumor resection, not seizure control.

Outcome Analysis

The functional status of patients was estimated by the modified Rankin Scale (mRS). Minor neurological morbidity was defined as an mRS of 2 or better, and major morbidity was defined as an mRS score of 3 or worse. Permanent deficits were defined as those present 1 year after surgery.⁵

Tumor and residual volumes were estimated by calculating the volume of a modified ellipsoid shape (length x width

x thickness/2) on MR images obtained within 48 hours of surgery. Degree of resection was stratified based on reduction in the extent of T2-weighted abnormality according to published methods: 100% (complete), > 90% (near complete), and 50 to 90% (subtotal).⁷ Reduction in the abnormal enhancement was also tabulated.

Results

Mapping Results and Surgical Strategy

Useful mapping results were obtained in all patients. Domains mapped included motor function in 18 patients, sensory function in 6 patients, and language function in 14 patients (Table 1). The mean number of mapping sessions was 2.6 (range, 2 to 4 sessions). One patient was unable to complete her language-mapping objectives because of baseline dysphasia, but she was able to complete motor mapping. On two occasions, mapping sessions had to be terminated because seizure activity was induced by stimulation. In both patients, mapping was completed during subsequent sessions. The mean length of hospitalization was 9 days (range, 5 to 15 days).

In 10 patients the mapping data suggested that there was a sulcal margin between tumor and eloquent cortex. Therefore, complete resection of the region of abnormal enhancement and debulking of the region with T2-weighted signal change were planned. In the other 8 patients, mapping suggested that at least a portion of the tumor was located within eloquent cortex. In these cases, resection was limited to spare the eloquent gyri.

Operative strategy influenced the degree of cytoreduction. Regions of T2 weighted abnormality were completely or almost completely resected in 8 (80%) patients who had a sulcal margin between their tumor and functional cortex. In contrast, near complete resection was achieved in 1 patient (13%) whose tumor resided within functional cortex. Complete resection was achieved in all 13 patients with nodular or patchy en-

Table 1. Clinical Summary of 18 Patients with Low-Grade Tumors

Patient	Age/ Sex	Location	Tumor	Functions mapped	Estimated resection enhance- ment (%)	Estimated resection T2 abnormality	mRS			Interval to recurrence/ progression (yrs)
							At 1 yr	At last f/u	Interval (yrs)	
1	28/M	L temporal	oligodendro	Mo, S, La	100	subtotal	0	0	5	n/a
2	33/M	L frontal	astro	Mo, S, La	n/a	near complete	2	6	2.5	2
3	44/F	L parietal	JPA	Mo, La	100	subtotal	2	2	2	n/a
4	19/F	R frontal	ganglio	Mo	100	complete	0	0	3	n/a
5	32/M	L insula	astro	Mo, La	n/a	subtotal	0	6	2.5	2
6	37/F	L frontal	oligoastro	Mo, La	100	subtotal	0	0	1	n/a
7	31/M	L frontal	astro	Mo, La	100	subtotal	0	0	2	n/a
8	28/F	R frontal	oligoastro	Mo	100	subtotal	1	0	2	n/a
9	32/M	L parietal	astro	Mo, S, La	n/a	complete	2	0	3	n/a
10	34/F	L frontotemp	oligoastro	Mo, S, La	100	near complete	1	6	3	2.5
11	20/F	L frontal	astro	Mo, La	100	near complete	0	6 [†]	3	n/a
12	38/F	L frontal	astro	Mo, La	100	complete	1	0	6	n/a
13	37/M	L temporal	astro	Mo, La	100	subtotal	2	6	7	5
14	21/M	L parietal	ganglio	Mo, S	n/a	near complete	0	0	3	n/a
15	31/F	R parietal	astro	Mo, S	n/a	subtotal	2	2	1.5	n/a
16	41/F	L temporal	oligodendro	Mo, La	100	subtotal	1	6	7	5
17	18/F	L frontal	oligodendro	Mo, La	100	complete	1	1	2	n/a
18	21/M	L temporal	ganglio	Mo, La	100	complete	0	0	6	n/a

[†]death unrelated to tumor. mRS = modified Rankin Score, f/u = follow up, yrs = years, L = left, R = right, M = male, F = female, Mo = motor, La = language, S = sensory, JPA = juvenile pilocytic astrocytoma, oligodendro = oligodendroglioma, ganglio = ganglioglioma, oligoastro = oligoastrocytoma, astro = astrocytoma, n/a = not available.

hancement on preoperative MR imaging (Fig. 1).

Outcomes

At 1 year all patients had achieved a good outcome (Table 1). There were no cases of permanent major neurological morbidity. At 1 year, four (22%) patients had minor postoperative deficits attributable to surgery, two of which had resolved by long-term follow-up (*Patients 8 and 9*). Difficulty naming objects persisted in two patients with posterior temporal lesions (*Patients 13 and 16*). During the mean follow-up of 3.5 years, five (28%) patients experienced tumor progression or recurrence.

Perioperative complications after grid implantation included 2 patients (11%) with subdural fluid collections that accumulated in a delayed fashion (Days 2-5) and required evacuation to relieve mass effect. Mapping and tumor resection were completed successfully in both pa-

tients during the same hospitalization. One patient (6%) required a wound revision at 2 years for exposed bone.

Discussion

Patients with low-grade tumors within or near eloquent cortex are a therapeutic challenge. The technique of mapping using subdural grid electrodes was adapted from epilepsy surgery to address a group of patients who, because of patient, surgeon, or institutional resources, were not candidates for awake cortical stimulation during resection.

Our data and the work of others highlight the advantages and disadvantages of invasive cortical mapping with subdural grids. First, cortical grid stimulation mapping offers the opportunity for significant tumor cytoreduction with acceptable neurological morbidity. In their series of high-grade gliomas resected with the aid of subdural grid map-

ping, Kral et al. used larger craniotomies and obtained a 31% rate of gross total resection with no permanent disability.⁷ Second, reliable information can be obtained without the constraints of mapping in the operative suite. Occasionally, awake craniotomies are terminated because of seizure activity, airway concerns, or claustrophobia.⁸ If a seizure is induced during grid stimulation, mapping can be completed successfully during a follow-up session. Third, physicians can counsel their patients about specific, potential postoperative deficits based on the mapping data obtained preoperatively. Fourth, accomplishing functional mapping and tumor resection through the same modest-sized craniotomy centered over the lesion avoids a large bone flap. Fifth, our epilepsy experience and the work of Berger et al.¹ indicate that children may benefit from this technology because functional data can be obtained and verified outside the

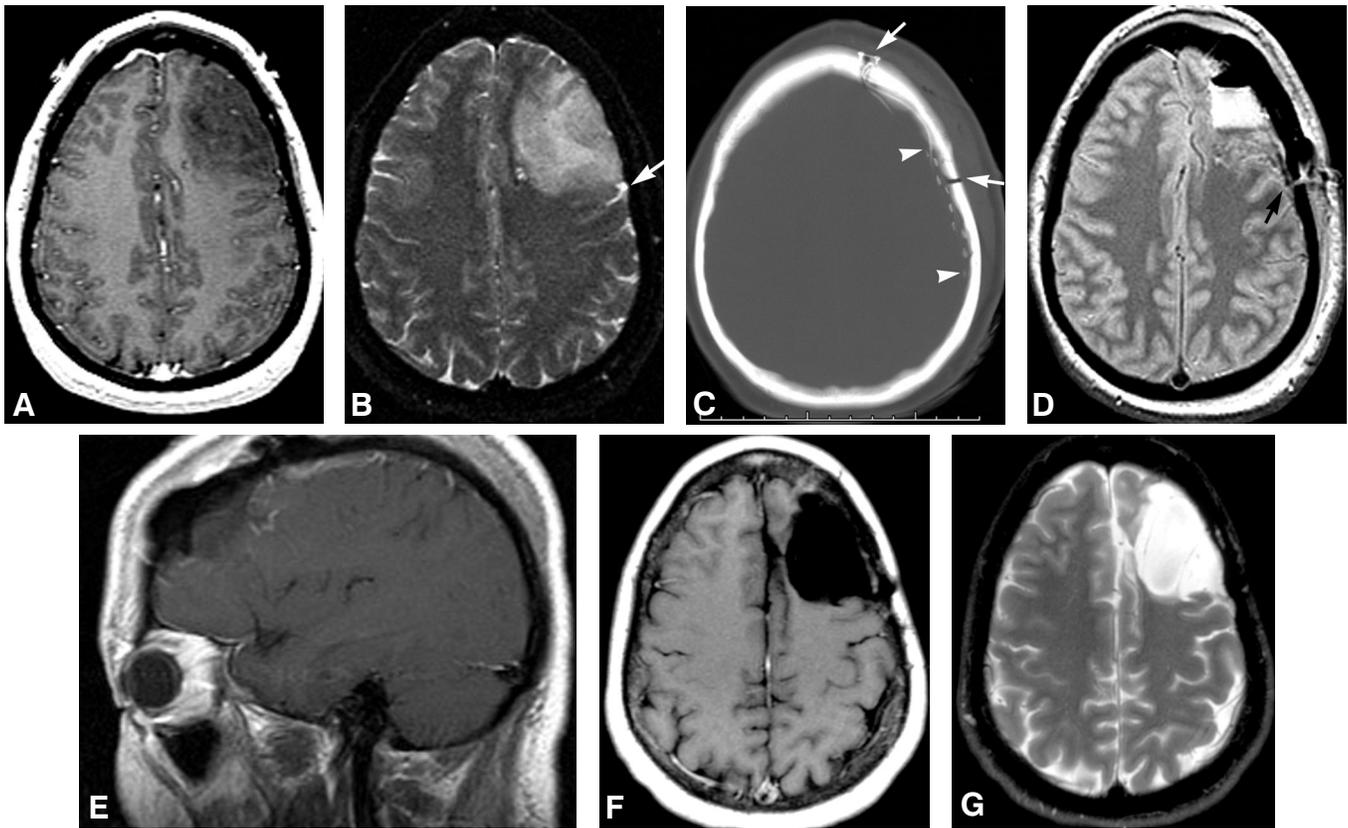


Figure 1. Patient 12. (A) Preoperative axial enhanced T1-weighted MR image shows a low-grade lesion in the left frontal lobe with patchy enhancement near Broca's area and the motor cortex in a 38-year-old woman. (B) Axial T2-weighted MR image shows a sulcus (*arrow*) at the posterior-inferior margin of the tumor. Mapping suggested that this sulcus was the margin between noneloquent and eloquent cortex. Resection proceeded to the sulcal margin. The functional cortex was spared, but the gyrus, which was partially infiltrated with tumor, was removed completely. (C) CT scan shows the position of a single 6 x 8 grid (*arrowheads*) placed over the posterior and inferior aspects of the lesion to map the boundaries of the motor and language cortices. Grids were slipped under the bone edges (*arrows*) to increase the mapping area without increasing the size of the bone flap. Immediate postoperative (D) axial T2-weighted and (E) enhanced T1-weighted sagittal MR images confirm sparing of the sulcal margin (*arrow*) as noted above the frontal operculum. Three-year follow-up enhanced axial (F) T1-weighted and (G) T2-weighted MR images show no tumor recurrence.

operative theater. Finally, this technique can easily be adopted by epilepsy surgeons because the technique is already part of their armamentarium.

Our experience also highlights the disadvantages of this strategy. First, only cortical mapping data can be obtained. The technique does not map the portion of a gyrus that is nestled in a sulcus or subcortical white matter pathways. Second, the resolution for mapping is limited by contact placement prefabricated at 1-cm intervals. Cortical stimulation with a probe may yield 5-mm sensitivity. Furthermore, grid mapping requires two craniotomies, two general anesthetics, and arguably a longer hospital stay to complete mapping. Finally, there is no real-time mapping feedback

to guide the extent of resection. We speculate that these limitations may explain the rate of neurological morbidity in our series. In two recent series using awake cortical stimulation, the rates of gross total resection were 25% to 30%.^{3,8} Furthermore, the rates of new postoperative deficits in language, motor, and sensory functions have ranged from 0% to 29%. We also noted several complications likely related to grid implantation, including subdural fluid collections and wound breakdown.

Conclusions

Our data demonstrate that cortical mapping using subdural grids to define eloquent cortex before tumor resection

offers the opportunity for significant tumor cytoreduction with an acceptable rate of neurological morbidity. However, the overall morbidity rate may be higher and hospital stays may be longer. In low-grade neoplasms where it can be difficult to determine the margin between tumor and normal white matter, functional mapping provides another tool for the surgeon to develop a preoperative resection strategy to minimize injury to eloquent cortex. Although this strategy requires a patient's cooperation during mapping sessions and tolerance of staged craniotomies, it may be an option for patients who would be unwilling or unable to participate in an awake craniotomy.

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