Intraoperative Seizures in Awake Craniotomy for Perirolandic Glioma Resections That Undergo Cortical Mapping

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Abstract

Background Perirolandic motor area gliomas present invasive eloquent region tumors within the precentral gyrus that are difficult to resect without causing neurologic deficits.

Study Aims This study evaluates the role of awake craniotomy and motor mapping on neurologic outcome and extent of resection (EOR) of tumor in the perirolandic motor region. It also analyzes preoperative risk factors for intraoperative seizures.

Methods We evaluated 57 patients who underwent an awake craniotomy for a perirolandic motor area eloquent region glioma. Patients who had positive mapping (PM) or intraoperative identification of motor regions in the cortex using direct cortical stimulation were compared with patients with no positive motor mapping following direct cortical stimulation and negative mapping (NM). Preoperative risks, intraoperative seizures, perioperative outcomes, tumor characteristics, and EOR were also compared. A logistic regression model was used to evaluate the predictors for intraoperative seizures in this patient cohort.

Results Overall, 33 patients were in the PM cohort; 24 were in the NM cohort. Our study showed an 8.8% incidence of intraoperative seizures during cortical and subcortical mapping for awake craniotomies in the perirolandic motor area, none of which aborted the case. PM patients had significantly more intraoperative and postoperative seizures (15.5% and 30.3%, respectively) compared with the NM patients (0% and 8.3%, respectively; $p = 0.046$ and 0.044). New transient postoperative motor deficits were found more often in the PM group (51.5%) versus the NM group (12.5%; $p = 0.002$). A univariate logistic regression showed that PM (odds ratio [OR]: 1.16; 95% confidence interval [CI], 1.01–1.34; $p = 0.035$) and preoperative tumor volume (OR: 0.998; 95% CI, 0.996–0.999; $p = 0.049$) were significant predictors for intraoperative seizures in patients with perirolandic gliomas.

Conclusion Awake craniotomies in the perirolandic motor region can be safely performed with a similar incidence of intraoperative seizures as reported for the language cortex. PM in this region may increase the likelihood of perioperative seizures or motor deficits compared with NM. Craniotomies that minimize cortical exposure for perirolandic gliomas that may not localize motor regions can still allow for extensive tumor resection with a good postoperative outcome.

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Introduction

A craniotomy with intraoperative cortical and subcortical mapping allows for the resection of intrinsic lesions in or adjacent to the eloquent cortex that were once considered inoperable.[1–3] This ability becomes more important in gliomas where functional white matter is found within the tumor bulk.[4,5] Although diagnostic imaging allows for an improved understanding of tumor margins, this method alone is not reliable to distinguish tumor from functional motor or language areas accurately, and it can show false-positive and false-negative eloquent regions on functional magnetic resonance imaging (fMRI).[6–8] Cortical and subcortical stimulation provides intraoperative functional mapping in real time that can identify eloquent areas that need to be protected during surgery. The precision available with cortical/subcortical mapping and intraoperative monitoring allows for a successful tumor resection with limited damage to the surrounding functional cortex.[9]

An awake craniotomy (AC) adds to cortical mapping by allowing the surgeon to monitor the patient's intraoperative clinical responses that correspond to the stimulation. However, awake craniotomies were reported to risk causing stimulation-induced intraoperative seizures (IOSs) from cortical stimulation that can lead to an aborted operation.[10–13] In addition, the perirolandic cortical region, involving the motor area, was reported to have a higher incidence of IOSs during tumor resections in awake craniotomies compared with other areas.[10,12,14] IOSs can complicate cortical mapping by making it difficult to monitor the functionality of an awake patient.[12] This causes many surgeons to reserve an AC exclusively for lesions within the language cortex.

Regarding cortical mapping, previous studies reported that the functional cortex must be identified and spared before proceeding with tumor resection in an AC.[15–19] However, positive stimulation of eloquent areas is not always feasible in minimally invasive ACs that expose the tumor and limited amounts of the adjacent cortical areas. It is still unclear whether complete cortical mapping that requires an extensive craniotomy is mandatory to reduce the number of postoperative deficits.[17,19–23] Additionally, whether negative mapping (NM) causes an increase in postoperative deficits remains uncertain.

In this study, we analyzed the effect of positive or negative cortical mapping on postoperative neurologic outcomes and extent of resection (EOR) in the perirolandic region during an AC, which to our knowledge is the first time this analysis has been presented in the literature for this specific cortical region. We also report the incidence of IOSs in ACs for perirolandic motor area gliomas and evaluate preoperative predictors for IOSs.

Method and Materials

Patient Population

Between August 2005 and August 2016, 57 patients had an AC for the resection of a perirolandic motor area glioma with the use of intraoperative motor mapping by the senior surgeon (A.Q.H.) at a single institution. All patients had a hemispheric glioma located within the primary motor cortex that required awake motor mapping before tumor resection. Patients who had motor function identified with intraoperative direct cortical stimulation were considered the positive mapping (PM) group; patients who underwent intraoperative direct cortical stimulation but no motor response occurred were the negative mapping (NM) group. The patient's preoperative risk factors, symptoms, EOR, postoperative complications, and cortical mapping outcomes were collected.

Preoperative Preparation

Patients were selected by the senior surgeon, and a physical examination with cognitive testing was conducted to determine whether the patient was appropriate for an AC. The patient was fully informed about the specific operative procedure as well as the risks and benefits. A preoperative MRI with diffusion tensor imaging (DTI) and confirmation of tumor involvement with the primary motor cortex by a neurosurgeon and radiologist blinded to the patient cohort was obtained. All patients, whether they had a preoperative seizure or not, were treated with preoperative antiepileptic loading doses before surgery with intravenous levetiracetam (500–1,000 mg) or fosphenytoin (15–20 mg/kg).

Operative Procedure

All cases were conducted with the assistance of an experienced neuroanesthesiologist, and the preoperative goal for surgery was a safe gross total resection. Before the operation the patient received premedication of 2 mg midazolam and 50 µg fentanyl. A scalp block was administered using 0.5% Marcaine with epinephrine (1:200,000 ratio) along the pin sites (for the supraorbital, auriculotemporal, and occipital nerves bilaterally). Patients received neuromonitoring with somatosensory evoked potentials (SSEPs) and an electroencephalogram (EEG), in addition to direct cortical stimulation. During surgery, sedation was maintained using propofol (up to 100 µg/kg/min) or dexmedetomidine (up to 0.2–0.7 µg/kg/min). Surgical navigation (VectorVision; Brainlab, Munich, Germany) was used to tailor the craniotomy to the lesion size and location.

The craniotomy allowed for exposure of the lesion as well as an additional 1 to 3 cm of cortex around the lesion to allow for intraoperative mapping. The dura was infiltrated using a tuberculin syringe loaded with Marcaine/epinephrine local anesthetic between the dural leaflets. Before opening the dura, the patient was awakened to participate in neurologic testing. A strip electrode was placed under the dura at the cortical areas of interest to monitor for afterdischarges. An Ojemann cortical stimulator (Integra LifeSciences Corp., Plainsboro Township, New Jersey, United States) was used for cortical stimulation. Stimulation current intensity started at 2 mA and was increased by 0.5-mA increments to as high as 6 mA, until afterdischarges or a clinical response was seen. The Ojemann stimulator delivered biphasic waves at 50 Hz for a pulse phase duration of 0.5 ms as previously reported.[24,25] The stimulation was applied to a given area for 2 to 3 seconds.

The neurologic tests were performed during the cortical and subcortical stimulation, as well as during the tumor resection. Several batteries of paradigms were used to test the patient's performance intraoperatively, and the selection of the tasks

depended on the region of interest. To test gross and fine motor skills during motor/premotor cortical stimulation, the patient or anesthesiologist reported any face, arm, or leg movement or lack of movement. Involuntary or deficient motor function during stimulation was considered PM. NM was described when no positive stimulation response was seen at the indicated site. An EEG was used to record afterdischarges to monitor for any seizures occurring during stimulation.

Intraoperative Seizure Management
Any IOS occurring during surgery was determined by the anesthesiologist, surgeon, or electrophysiologic monitoring. If an IOS occurred, stimulation was stopped and cold saline irrigation was poured over the cortex. Sedatives were avoided to continue clinical assessment while conducting functional mapping. Stimulation ceased until the patient was able to regain speech and motor function. In cases where seizures persisted, additional intravenous levetiracetam and/or midazolam were administered to stop the seizure.

Postoperative Management
After surgery, patients with no preoperative seizure history and no postoperative seizures received 14 days of postoperative antiepileptics (levetiracetam 500–1,500 mg twice/day). Patients with a preoperative seizure history or intra/postoperative seizures had their antiepileptics managed in conjunction with a neurologist for > 14 days. Patients were assessed for postoperative complications immediately following surgery, at the 1-month and 6-month follow-up visit, and then annually. Transient neurologic deficits were considered new or worsening deficits following surgery that resolved before the 6-month follow-up visit. Duration of a deficit was considered the length of time from surgery to the outpatient clinic/emergency department visit at which the patient was noted to no longer have a postoperative deficit. Permanent deficits were defined as those that did not improve beyond the 6-month follow-up clinic visit. Cognitive deficits were considered new-onset postoperative attention, memory, decision making, planning, or reasoning deficits reported by the patient following surgery.

Tumor Volume Analysis
MRI was performed to obtain preoperative tumor volume. Axial cuts, 1.5 to 3 mm thick, were used to determine the cross-sectional areas of the tumor using either T1-weighted with contrast or T2-weighted MRIs. OsiriX software (Pixmeo; http://pixmeo.com) was used to calculate the tumor volume based on the axial cuts as previously described.[26–28] A similar technique was used to calculate postoperative tumor volume. Tumor identification on MRI was conducted by a clinician blinded to the patient outcomes. EOR was calculated by (preoperative and postoperative tumor volume)/preoperative tumor volume.

Preoperative peritumoral edema volume was assessed using a T2 fluid-attenuated inversion recovery MRI by determining the cross-sectional area of the edema on axial cuts, 1.5 to 3 mm thick. OsiriX was used to calculate the total volume of the edema and tumor combination, based on the sum of the axial cuts. This volume was then subtracted from the preoperative tumor volume to calculate the total volume of peritumoral edema.

Statistical Analysis
Univariate statistical analyses were used to evaluate the data. For parametric variables, means and standard deviations were used; for nonparametric variables, median and range were used. Two parametric variables were compared using a Student t test; nonparametric comparisons were done with a Mann-Whitney U test. Categorical comparisons were performed using a Pearson chi-square test. A type I error-rate threshold of $\alpha = 0.05$ was used to establish significant difference. A logistic regression was used to assess for significant predictors of IOS. Significant variables of the univariate model were then assessed in the multivariate logistic regression model. SPSS statistical software v.23.0.0 (IBM Corp., Armonk, New York, United States) was used for all statistical analysis. A biostatistician (Y.L.) conducted the statistical analysis. The study was approved by the institutional review board.

Results

Patient and Tumor Characteristics
Fifty-seven patients with perirolandic motor region glioma underwent an AC between August 2005 and August 2016. Of these patients, 33 patients (57.9%) had PM, and 24 patients (42.1%) had NM. The mean age of PM patients was 49.1 years; mean age of the NM group was 51.3 years ($p = 0.319$). Men made up 48.5% of the PM population and 50% of the NM population ($p = 0.910$). Preoperative symptoms most often presented were headaches (45.5% PM group, 41.7% NM group; $p = 0.776$), followed by motor deficits (42.4% PM group, 41.7% NM group; $p = 0.954$).

The preoperative tumor volume for the PM group was 30.7 cm^3 and for the NM group was 30.1 cm^3 ($p = 0.949$). Peritumoral edema, found on preoperative imaging, was 22.0 cm^3 in the PM group and 20.6 cm^3 in the NM group ($p = 0.809$). Postoperative residual tumor was 4.5 cm^3 and 4.2 cm^3 in the PM and NM groups, respectively ($p = 0.605$). The EOR for the PM and NM patients was 87.8% and 92.4%, respectively ($p = 0.234$; ►**Table 1**).

Intraoperative Characteristics
The median current intensity for the direct cortical/subcortical stimulation was 3.75 mA (range: 2–6 mA) for the PM group and 4.0 mA (range: 2–6 mA) for the NM patient population ($p = 0.176$). For the PM group, stimulation-induced movements or cessation of voluntary movements were found at a median current intensity of 3.75 mA for both cortical and subcortical stimulation. IOSs were induced at a median current of 4.5 mA (range: 2–6 mA). All stimulation-induced seizures followed cortical stimulation, and none were seen during subcortical stimulation. No cases in either group were aborted. Of the 33 PM patients, 20 patients experienced stimulation-induced cessation of voluntary movement, 10 patients experienced stimulation-induced involuntary movement, and 3 experienced a combination of the two.

Table 1 Demographic characteristics of 57 patients undergoing brain stimulation for resection of perirolandic eloquent region gliomas

	Intraoperative seizures		
Characteristic	Positive ($n = 33$)	Negative ($n = 24$)	p
Age, mean (SD)	49.1 (13.6)	51.3 (9.8)	0.319
Male sex, n (%)	16 (48.5)	12 (50.0)	0.910
KPS, mean (SD)	89.3 (10.5)	90.9 (7.0)	0.580
Preoperative symptoms, n (%)			
Headaches	15 (45.5)	10 (41.7)	0.776
Motor deficits	14 (42.4)	10 (41.7)	0.954
Seizures	11 (33.3)	7 (29.2)	0.738
Sensory deficits	5 (15.2)	4 (16.7)	0.877
Confusion	2 (5.9)	1 (4.2)	0.752
Nausea/Vomiting	1 (3.0)	1 (4.2)	0.818
Pathology, n (%)			
High-grade glioma			0.931
Glioblastoma multiforme	16 (48.5)	11 (45.8)	
Astrocytoma, III	6 (18.2)	4 (16.7)	
Oligodendroglioma, III	2 (6.1)	2 (8.3)	
Low-grade glioma			0.807
Astrocytoma, II	6 (18.2)	5 (20.8)	
Oligodendroglioma, II	3 (9.1)	2 (8.3)	
Tumor volume, mean (SD)			
Preoperative tumor volume, cm^3	30.7 (14.1)	30.1 (12.4)	0.949
Preoperative peritumoral edema volume, cm^3	22.0 (20.2)	20.6 (14.8)	0.809
Residual tumor volume, cm^3	4.5 (8.6)	4.2 (6.4)	0.605
EOR, overall (%)	87.8 (7.1)	92.4 (9.4)	0.234
High-grade glioma, EOR (%)	85.7 (9.4)	90.7 (10.2)	0.287
Low-grade glioma, EOR (%)	90.8 (10.4)	97.0 (5.2)	0.479

Abbreviations: EOR, extent of resection; KPS, Karnofsky Performance Status; SD, standard deviation.

Five patients from the PM group experienced IOSs during the stimulation of the motor cortex. For three of the cases, cold saline irrigation was used to stop the seizure, and for two cases, where the seizures were intractable to the irrigation, patients were treated with additional intravenous levetiracetam or midazolam. No patients needed to be converted to surgery under general anesthesia as a result of intractable seizures. No IOSs occurred with NM ($p = 0.046$).

Postoperative Characteristics

Postoperative seizures were seen in 30.3% of the PM group and 8.3% of the NM group ($p = 0.044$). New motor deficits were seen in 51.5% of the PM group and 12.5% of the NM

Table 2 Characteristics of 57 patients undergoing brain stimulation for resection of perirolandic eloquent region gliomas by positive versus negative mapping

	Mapping		
Characteristic	Positive ($n = 33$)	Negative ($n = 24$)	p
Postoperative KPS, mean (SD)	83.5 (15.5)	85.3 (14.4)	0.194
Intraoperative seizures, n (%)	5 (15.2)	0 (0.0)	**0.046**
Postoperative seizures, n (%)	10 (30.3)	2 (8.3)	**0.044**
New motor deficit, n (%)	17 (51.5)	3 (12.5)	**0.002**
Transient deficit	14 (42.4)	3 (12.5)	**0.015**
Duration of deficit, mo, mean (SD)	1.1 (0.8)	0.6 (0.1)	0.123
Permanent deficit	3 (9.1)	0 (0.0)	0.129
New sensory deficit, n (%)	1 (3.0)	0 (0.0)	0.390
New cognitive deficit, n (%)	3 (9.1)	1 (4.2)	0.472
Discharge status			**0.033**
Home, n (%)	17 (51.5)	19 (79.2)	
Rehabilitation, n (%)	16 (48.5)	5 (20.8)	
Length of stay, d, mean (SD)	4.0 (2.6)	3.1 (1.5)	0.169

Abbreviation: KPS, Karnofsky Performance Status; SD, standard deviation.
Note: The boldface indicates significance ($p < 0.05$).

group ($p = 0.002$). The incidence of transient motor deficits in the PM group was 42.4% compared with the NM group (12.5%) ($p = 0.015$). Permanent motor deficits were seen in 9.1% of PM patients and none of the NM patients ($p = 0.129$).

Patients in the PM group had a similar length of stay with a mean of 4.0 days versus 3.1 days for the NM group ($p = 0.169$). Fewer patients in the PM group (51.5%) were discharged home following surgery compared with the NM group (79.2%; $p = 0.033$; ►**Table 2**).

Predictors of Intraoperative Seizures

A logistic regression was conducted to evaluate factors that might predict an IOS during an AC for a perirolandic glioma. Exploratory univariate analysis revealed that positive cortical mapping ($p = 0.035$) and preoperative tumor volume ($p = 0.049$) were significant predictors of IOSs (►**Table 3**). A multivariate logistic regression incorporating these two variables did not show significance for either the positive cortical mapping ($p = 0.132$) or preoperative tumor volume ($p = 0.190$).

Discussion

We evaluated the role of motor mapping on perioperative outcomes and EOR and analyzed the preoperative risk factors for IOSs in awake craniotomies for perirolandic motor area

Table 3 Univariate logistic regression model assessing independent predictors for intraoperative seizures in patients with perirolandic gliomas undergoing an awake craniotomy

Variable	Odds ratio	95% CI	p
Positive cortical mapping	1.16	1.01–1.34	**0.035**
Preoperative tumor volume	0.998	0.996–0.999	**0.049**
Age	1.00	0.99–1.01	NS
Sex	0.945	0.817–1.09	NS
Preoperative seizure history	1.06	0.91–1.23	NS
Preoperative peritumoral edema	1.00	0.99–1.01	NS
Preoperative KPS	1.00	0.99–1.01	NS
Low-grade glioma	0.91	0.73–1.12	NS
Preoperative antiepileptic drug	0.89	0.74–1.07	NS

Abbreviations: CI, confidence interval; KPS, Karnofsky Performance Status; NS, not significant.
Note: The boldface indicates significance ($p < 0.05$).

gliomas. The study provides new insight into our understanding about the AC in the perirolandic motor area regarding IOSs and cortical mapping. Our findings suggest that for cortical mapping in the perirolandic motor region, NM allows for a similar extent of glioma resection as PM while causing fewer postoperative seizures and fewer new motor deficits compared with PM. We also show that PM and preoperative tumor volume may play a role in predicting IOSs for perirolandic gliomas.

Intraoperative Seizures

In the literature, the incidence of IOSs during an AC for all cortical regions were reported to range from 3.4% to 20% of cases.[1,10,12,13,29,30] Our study showed five patients (8.8%) undergoing an AC for perirolandic motor area gliomas with an IOS that is well within the range of what was previously reported. Given that perirolandic lesions previously were reported to have high rates of IOSs, our study shows an incidence of IOSs in the perirolandic region that is similar to rates reported for ACs in the language cortex.[10,12,14]

Szelényi et al showed a correlation between IOS and the intensity of the cortical stimulation current, length of cortical stimulation, and repetitive cortical stimulation.[31] In our experience, duration of stimulation lasted 2 to 3 seconds, and cortical stimulation occurred up to three times at a given location. The cortical stimulation intensity showed no significant difference between the PM and NM group. Median stimulation current was 3.75 mA and 4.0 mA for the PM and NM group, respectively. Other studies showed upper limit cortical stimulation intensities from 4 to 10 mA.[1,10–12] In an attempt to minimize the cortical stimulator intensity, when possible, we used the nearby eloquent cortical regions to establish the lowest possible current intensity that would provide PM on the cortex. We then kept the same intensity

setting for the remaining cortical and subcortical stimulation. Boetto et al[1] showed that this stimulation strategy can effectively stimulate cortical and subsequent subcortical regions without needing to alter the current intensity.

IOSs were shown to lead to aborted awake craniotomies in 0.4 to 18% of cases.[11–13] Our study did not have any aborted cases or conversions to surgery under general anesthesia due to IOS. This success with AC cases is partially due to the coordinated team management for IOS. Cold irrigation was prepared preoperatively and available close to the operative field, antiepileptics were optimized during the case in coordination with neuroanesthesiology, and ancillary staff/neuromonitoring technicians continuously monitored the patient for early signs of seizure activity.

Preoperative Predictors for Intraoperative Seizures

Preoperative seizure or epilepsy history was reported to correlate with IOSs, with patients who have preoperative seizures considered to have an increased susceptibility for intraoperative or postoperative seizures.[12] In our series, however, we did not find a correlation between preoperative seizures and the incidence of IOSs in our logistic regression model ($p = 0.471$). For our cohort, regardless of preoperative seizure history, all patients undergoing an AC had an antiepileptic drug preoperatively, and they followed a postoperative course of levetiracetam for at least 14 days. We suspect that this perioperative course of prophylactic antiepileptics helped prevent intra/postoperative seizures in some patients, although the literature still varies on the efficacy of postoperative antiepileptic drugs.[32]

Skardelly et al[33] associated increased preoperative peritumoral edema for gliomas with an increased likelihood of perioperative seizures. To see whether this applied to IOSs, we used our volumetric calculation program to evaluate preoperative edema for the perirolandic gliomas and found that the extent of peritumoral edema did not serve as a preoperative predictor. Our univariate logistic regression identified PM and preoperative tumor size as predictors of IOSs. The trend for our cohort revealed that patients with smaller gliomas had a higher likelihood of an IOS, although both PM and tumor size were not found to be significant predictors in the multivariate analysis. We suspect that smaller lesions have more cortical/subcortical area exposed around it that allows for increased cortical stimulation to those areas that may lead to an increased likelihood for IOS. Further studies evaluating surface area and volume ratios between the cortex and tumor are needed to confirm this hypothesis.

Cortical Mapping

One way to reduce IOSs may stem from an evaluation of cortical mapping. Few studies have compared the results of cortical mapping with IOS and postoperative neurologic outcome.[9,34] The rates of PM for awake craniotomies vary in the literature from 30% to 100%.[9,19,34–37] Our series identified eloquent cortex in 58% of cases. Our surgical strategy for cortical stimulation involves making a craniotomy wide enough to encompass the lesion of interest as well as the adjacent cortical areas, but not too extensive to expose

vast cortex for the sole purpose of cortical stimulation, which may account for some of our NM occurrences. Preoperative aids such as fMRI and DTI assist in locating eloquent regions. However, fMRI mapping was shown to be compromised at the tumor margins and around normal vascular anatomy, in addition to false-negative and false-positive eloquent region findings on imaging.[38–40] In addition, slow-growing gliomas can alter the location of functional tissue, making it difficult to identify cortical eloquence intraoperatively.[41,42] This would cause cortical regions that look eloquent based on a preoperative fMRI or DTI not necessarily to be functional tissue during cortical stimulation.

Additionally, patients in our cohort received cortical stimulation via a bipolar electrode. This allows for localized current flow at the site of interest that can often stimulate larger amounts of brain tissue than a monopolar electrode.[43] Monopolar electrodes, with one electrode at the site of interest and a distant reference electrode located on noneloquent cortex, provide a similar ability as the bipolar electrode to elicit a stimulation-induced clinical response, but often requires a higher stimulation intensity to achieve this clinical response compared with the bipolar electrode.[44] The monopolar electrodes were also shown to produce fewer afterdischarges than bipolar electrodes during cortical stimulation and may offer an additional technique for conducting awake craniotomies that may reduce IOS occurrence.[44]

Identification of the eloquent cortex via brain mapping in our study was associated with a worse neurologic outcome in the form of new motor deficits. We found that most (82.4%) of these new deficits in the PM group were transient and resolved over 1.1 months; 17.6% of these new deficits were permanent. Although PM is an important part of direct cortical stimulation that allows a surgeon to detect eloquent cortex near a tumor, it also indicates a higher risk for causing damage to functional brain that can occur with resecting a tumor at its margins. NM, in contrast, appeared to identify adequately the perirolandic regions of the cortex that were safe for resection and led to no permanent postoperative motor deficits. However, transient motor deficits were seen in three patients (12.5%) in the NM group, which could have resulted from current stimulation that was possibly at too low a setting to be able to identify an eloquent motor region.

Previous studies also showed worsened postoperative outcomes after PM. Haglund et al[19] showed a lower incidence of language deficits in glioma resections when the resection took place at a negatively mapped cortical region that was 1 cm from the nearest eloquent location. In those patients with PM, 19% had worsened neurologic language deficits.[19] In the immediate postoperative period, Kim et al[9] reported that 43% of patients with PM had worsened deficits; 23% of the NM group had worsened deficits. At the 1-month follow-up, 21% of PM patients and 9% of NM patients had worsened neurologic deficits.[9]

In our study, the PM group showed a greater number of postoperative seizures (30.3%) compared with the NM group that had two patients (8.3%) with postoperative seizures ($p = 0.044$). Sanai et al[34] evaluated 250 patients who had language mapping to resect gliomas in negatively mapped sites who showed no postoperative seizure occurrences. Our study found that with higher incidences of postoperative seizures and motor deficits, patients in the PM group were more likely to be discharged from the hospital to rehabilitation instead of home. This additional need for a health care facility following hospitalization adds to the overall health cost to the patient.[45]

Extent of Resection

EOR in glioma surgery was shown to have a direct correlation with patient survival.[16,46–49] Pursuing a lesion intraoperatively until positive stimulation occurs helped maximize a tumor resection until eloquent areas are encountered.[17,21,41,50,51] In our study, the EOR of the PM group (87.8%) was similar to the NM group (92.4%). Although our general practice is not to pursue resection of tumor components aggressively that are invading into positively mapped cortical/subcortical regions, our study did not find a significant difference in the EOR between positively and negatively mapped groups. With patient safety our top priority during surgery, for some NM patients who required additional deep subcortical tumor resection in areas considered eloquent on neuronavigation where visual and tactile differences between tumor and normal brain could not be determined, it would often lead to ending the resection, which may have accounted for the residual tumors in the NM group.

EOR was also limited by PM in our cohort. For the NM mapping group for low-grade glioma patients, one patient (14.3%) had residual tumor. For the NM group for high-grade glioma patients, three patients (17.6%) had residual tumor. The PM patients who experienced an IOS had an EOR of 59.1%, a significant difference from the NM group ($p = 0.04$). This result shows that better resections were performed in patients who did not experience IOMs. We suspect that when a patient experienced an IOS and was treated with cold irrigation or antiepileptic medications, the patient's ability to follow commands declined, due to the seizure therapy or development of transient motor deficits from a postictal state that compromised the surgeon's capacity to map out eloquent regions adequately. During these situations, the surgeon could not pursue an aggressive resection, which most likely led to a less thorough surgical debulking.

Previous studies reported utilizing a smaller craniotomy and emphasized the value of NM, where eloquent regions are not necessarily identified before tumor resection.[9,34] It is unclear whether this type of NM strategy can be dangerous if false negatives are produced from inadequate cortical stimulation intensity. Although we also try to limit the size of the craniotomy, we expose a portion of the adjacent cortex to attempt to identify proximal eloquent regions as well as using the cortical strip electrode to locate the motor strip and evaluate for afterdischarges. Our maximum cortical stimulation intensity may also go as high as 6 mA during NM to decrease the risk for false negatives, although these higher intensities can make a patient susceptible to an IOS.

Given the similar EOR between the PM and NM group, in our experience, a wide craniotomy allowing for complete cortical mapping does not appear necessary to improve the EOR. In addition, the extra exposed normal cortex is at risk of

being damaged during the craniotomy or dural exposure process. Future studies may look at cortical stimulation using subdural strip electrodes to determine whether this form of PM, without the additional cortical exposure, may cause increased risk for IOSs. Cortical mapping remains an important aspect of the AC, and a thorough mapping of the involved cortical/subcortical areas is vital for these cases.

Limitations

This study is based on the experience of a single surgeon and could provide a source of bias. Limitations inherent to a retrospective study are also found in this study. This study does not account for certain changes in technique and management for ACs that evolved over the 11-year experience. Although the cortical stimulation method and EEG monitoring remained the same throughout our cohort, advances in neuronavigation technology and surgeon experience may also play a role in outcomes. Motor mapping with electromyography was also shown to be more sensitive than visual observation for evaluating motor response and may allow for an improved assessment of positive and negative motor mapping in future studies.[52] We previously showed similar perioperative outcomes when using cortical mapping during craniotomies for brain tumors between awake craniotomies and asleep craniotomies with electromyelogram.[53] Our study evaluates intraoperative cortical mapping and its relationship with IOS and EOR; however, further work evaluating cortical mapping in conjunction with other intraoperative monitoring techniques (i.e., SSEP, motor evoked potential, ultrasound, 5-aminolevulinic acid) will help further improve the treatment of eloquent region gliomas.

Conclusion

Our study shows that an AC can be performed in the perirolandic motor area safely, with comparable rates of IOSs to what was reported in the literature for similar awake surgeries in the language cortex. Positive cortical mapping in this region was found to have increased perioperative seizures and motor deficits compared with NM. Our study suggests that craniotomies minimizing cortical exposure for perirolandic gliomas that may not localize motor regions and follow thorough cortical stimulation can still allow for EOR of tumor with good postoperative outcomes.

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