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Circumferential sulcus-guided resection technique for improved outcomes of low-grade gliomas

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OBJECTIVE Many neurosurgeons resect nonenhancing low-grade gliomas (LGGs) by using an inside-out piecemeal resection (PMR) technique. At the authors' institution they have increasingly used a circumferential, perilesional, sulcus-guided resection (SGR) technique. This technique has not been well described and there are limited data on its effectiveness. The authors describe the SGR technique and assess the extent to which SGR correlates with extent of resection and neurological outcome.

METHODS The authors identified all patients with newly diagnosed LGGs who underwent resection at their institution over a 22-year period. Demographics, presenting symptoms, intraoperative data, method of resection (SGR or PMR), volumetric imaging data, and postoperative outcomes were obtained. Univariate analyses used ANOVA and Fisher's exact test. Multivariate analyses were performed using multivariate logistic regression.

RESULTS Newly diagnosed LGGs were resected in 519 patients, 208 (40%) using an SGR technique and 311 (60%) using a PMR technique. The median extent of resection in the SGR group was 84%, compared with 77% in the PMR group ($p = 0.019$). In multivariate analysis, SGR was independently associated with a higher rate of complete (100%) resection (27% vs 18%) (OR 1.7, 95% CI 1.1–2.6; $p = 0.03$). SGR was also associated with a statistical trend toward lower rates of postoperative neurological complications (11% vs 16%, $p = 0.09$). A subset analysis of tumors located specifically in eloquent brain demonstrated SGR to be as safe as PMR.

CONCLUSIONS The authors describe the SGR technique used to resect LGGs and show that SGR is independently associated with statistically significantly higher rates of complete resection, without an increase in neurological complications, than with PMR. SGR technique should be considered when resecting LGGs.

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KEYWORDS glioma; surgical resection; outcomes; en bloc resection; nonenhancing tumor; sulcus; extent of resection; oncology; surgical technique

Resection of low-grade gliomas (LGGs) can be technically challenging. Although LGGs are infiltrative,[1] several studies have shown that more extensive resection of the hyperintense abnormality observed on T2-weighted or FLAIR MRI results in improved survival compared with less extensive resection.[2–4] Given that diffuse gliomas often infiltrate functional brain, this oncological goal of maximal resection must be balanced by the goal of maintaining neurological function. Improvements in preoperative imaging, the development of computer-assisted methods that permit intraoperative identification of tumor borders, and awake mapping techniques[5–8] that identify the functionally important brain regions have all contributed to effective removal of LGGs. Indeed, many LGGs that were previously considered unresectable are now often resected.

Despite these advances, the ideal surgical technique for resecting LGGs has not been clearly defined, and there is little emphasis in the literature on the methods for removing these tumors. Most neurosurgeons remove LGGs by using an intralesional or piecemeal resection (PMR) technique in which the tumor is resected from the center toward the edges. This approach is often recommended because the resection remains within the tumor, avoiding

ABBREVIATIONS HR = hazard ratio; KPS = Karnofsky Performance Scale; LGG = low-grade glioma; OR = odds ratio; PMR = piecemeal resection; SGR = sulcus-guided resection.

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the surrounding healthy brain. In contrast, at our institution we have increasingly used a circumferential or sulcus-guided resection (SGR) technique, in which the edges of the tumor are defined at the beginning of the resection by using the surrounding sulci as a guide, and the tumor is resected circumferentially at its interface with the surrounding brain and sulci without ever entering the tumor core. This approach is consistent with principles of general surgical oncology, in which violating tumor margins is avoided. This SGR method is particularly applicable to LGGs, because LGGs rarely grow across sulci. Consequently, circumferential resections of LGGs can be achieved by exploiting the surrounding sulci as a guide to the borders of the tumor and performing transsulcal or subpial dissections of the surrounding sulci. With the SGR approach, intraoperative brain shift is significantly reduced compared with the PMR approach, because the walls of the tumor do not fall in on themselves as the tumor is dissected during SGR, rendering intraoperative image-guided navigation useful throughout the resection. Furthermore, the bottoms of the surrounding sulci often demarcate the deep portion of the tumor, or at least the interface between tumor and white matter is often best identified at this region, increasing the potential for a complete resection with SGR. Last, the blood supply to the tumor is identified early during SGR, resulting in a bloodless surgical field and preservation of the vessels that supply distal healthy brain.

Given these advantages, we hypothesized that SGR leads to greater extent of resection compared with PMR, without worsening neurological morbidity, in patients with LGG. To address this hypothesis, we compared the extent of resection and complications after SGR or PMR in a large cohort of patients with LGGs. Furthermore, we describe the SGR technique for LGGs in detail.

Methods

The institutional review board of The University of Texas MD Anderson Cancer Center approved the study. We retrospectively reviewed our prospective database to identify patients (n = 697) with LGGs who underwent initial resection at MD Anderson Cancer Center between June 1, 1993, and December 31, 2015. Only nonenhancing WHO grade II and III gliomas, which included astrocytomas and oligodendrogliomas, were included in the analysis. We included tumors that were hyperintense on T2-weighted or FLAIR MRI, with limited or no enhancement on T1-weighted MRI. We included only hemispheric glioma and excluded tumors in deep locations, the posterior fossa, or locations that might preclude an SGR technique, such as the ventricle, thalamus, or insula. Based on these criteria, 519 patients were included in the study. Preoperative data and intraoperative surgical methods were entered into the prospective database at the time of surgery by the treating physician. The following data were reviewed: demographics; presenting symptoms and Karnofsky Performance Scale (KPS) score; tumor volume pre- and postoperatively assessed using T1- and T2-weighted imaging; extent of resection (based on computerized volumetric analyses of pre- and postoperative MR images); extent of residual tumor; method of resection (SGR or PMR); type of anesthesia (awake or general); and postoperative neurological complications, seizures, and KPS score. The method of resection was noted by the neurosurgeons and entered into the database prospectively immediately after the procedure. The choice of resection method was based on surgical preference at the time of surgery, but the rationale behind this choice was not recorded in the database. We defined complete resection as 100% resection of all hyperintense disease observed on T2-weighted imaging. We dichotomized tumor locations as either in noneloquent cortex or in/near eloquent cortex based on previous publications from our institution.[9] Neurological complications, defined as new or worsening deficits that developed postoperatively, were recorded prospectively. Neurological complications that lasted beyond 30 days were considered long term.

Statistical Methods

The primary outcome was extent of resection, and the secondary outcome was neurological complications. Univariate analyses were performed using ANOVA for continuous variables and Fisher's exact test or chi-square test for categorical variables. All tests were 2-tailed. Multivariate analyses were performed using multivariate logistical regression; we planned a priori to include all variables with $p < 0.20$ in univariate analysis in subsequent multivariate analysis. Values were considered significant if $p \leq 0.05$. Odds ratios (ORs) and hazard ratios (HRs) are reported with 95% CIs. Overall survival time, defined as the time from the date of diagnosis to the date of death, was estimated using the Kaplan–Meier method. Cox regression survival analysis was applied to estimate HRs and their 95% CIs. Data were analyzed using SPSS version 23.0 software (IBM SPSS, Inc.).

Description of Circumferential Sulcus-Guided Surgical Technique

The SGR technique is based on the observation that LGGs in general do not cross sulci, and when they invade a neighboring gyrus they are likely to do so by following the short U-fibers. As a result, the boundaries of LGGs can be defined largely by the sulci that surround the hyperintense tumor as seen on FLAIR/T2-weighted MRI. The SGR technique leverages this concept by resecting the tumor circumferentially using the sulci as the guide to the edges of the tumor. Specifically, resection proceeds by dissecting down the sulci along the pia or by opening the sulci that surround the tumor (Figs. 1 and 2). Once at the base of the sulcus, the interface between tumor and white matter is identified, and the bottom of the tumor is dissected. Importantly, the large vessels within the sulci are preserved and the small perforating vessels that enter the gyri/tumor are coagulated and cut, resulting in progressive devascularization of the tumor. The fundamental steps in performing circumferential SGR of LGGs are as follows.

Step 1: Spatial Assessment to Define the Tumor Boundaries

After completing the craniotomy and dural opening (Fig. 1A and B), the surgeon defines the borders of the tumor by identifying the gyri within which the tumor resides

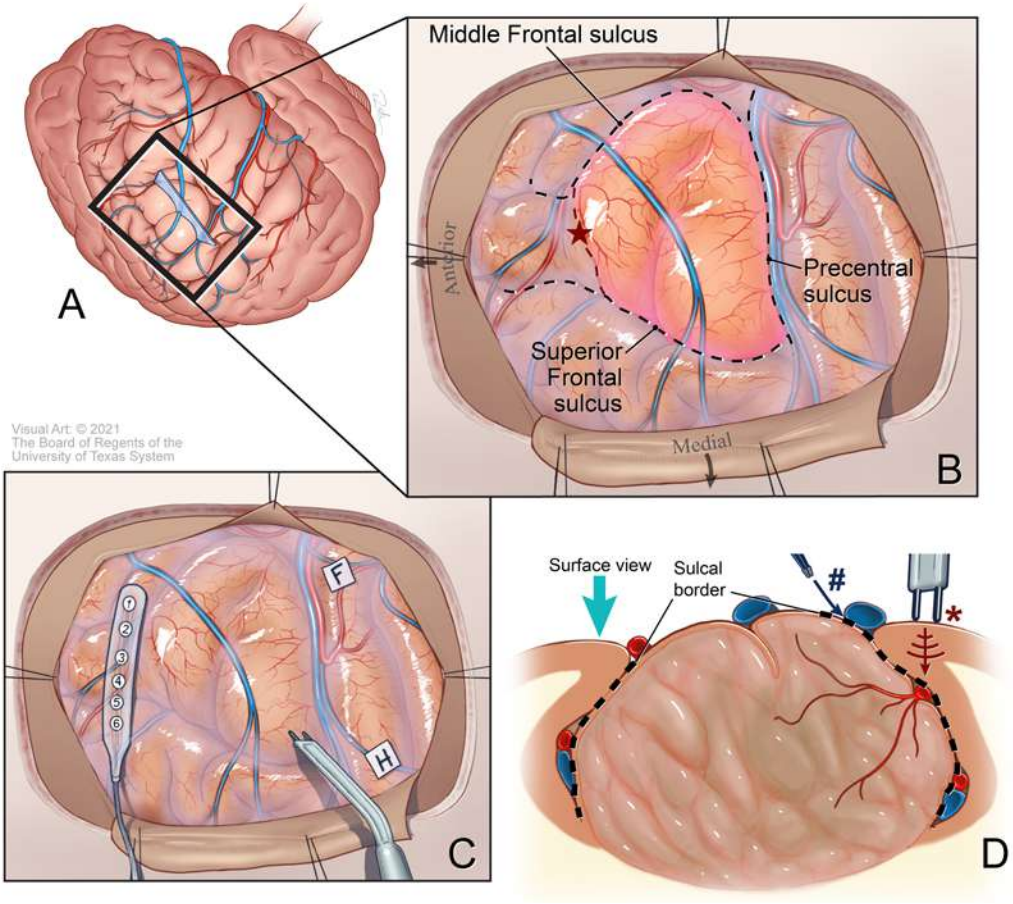

FIG. 1. Artist's depiction of steps 1 and 2 of the SGR technique: spatial and functional assessment. **A:** Overview of the brain showing surgical orientation, with the *black box* defining the orientation of the craniotomy; the tumor is located in the middle frontal gyrus anterior to the precentral (motor) gyrus. **B and C:** Surgical field during step 1 (spatial assessment, B) and step 2 (functional assessment, C). Using MRI-guided computer-assisted navigation, the borders of the tumor are defined based on the surrounding sulci. The *black dashed line* in panel B shows the tumor borders along the precentral sulcus, the superior fontal sulcus, and the middle frontal sulcus. The *red star* and the *dashed line* underneath it show the anterior part of the tumor in the middle frontal gyrus. Panel C depicts an electrode grid placed on the brain to record after-potentials, and the brain is directly stimulated over the tumor, where no positive sites are identified. Stimulation of precentral gyrus results in movement of the hand (tagged with "H") and face (tagged with "F"). **D:** Cross-section depiction of the brain from panel A showing how tumor can expand a gyrus and bulge underneath a neighboring gyrus. Although the neighboring gyrus appears to involve tumor when viewed from the surface, in fact the tumor edge is defined by the sulcus and tumor does not invade into the neighboring sulcus. When this expansion occurs near a positive stimulation site, it may appear that the tumor under the site cannot be resected. Here a stimulation site (marked by an *asterisk*) on the cortex of the precentral gyrus appears to be over the tumor and might be interpreted to mean that the tumor under this site cannot be resected. However, because the sulcus is expanded, dissection along the sulcus [defined by the *arrow* and the *number sign* (#)] defines the border of the tumor and allows for removal of the tumor under the stimulation site without violating the precentral gyrus and thereby not interrupting motor function. A similar dissection along the sulcus is depicted on the opposite side. Artist: David Aten, Senior Medical Illustrator, MD Anderson Cancer Center. Copyright The Board of Regents of the University of Texas System. Published with permission.

and the sulci that surround these gyri (Fig. 1B, Fig. 3). This precise localization is achieved by computer-assisted stereotactic navigation, ultrasound, and visual assessment. In cases in which the tumor appears to be in the center of a gyrus, the surgeon can often identify a nearby sulcus on the surface, and with careful analysis often finds that the sulcus is projecting under the neighboring gyrus, giving the appearance that the neighboring gyrus is involved when it is not (Fig. 1D and Fig. 3E). Once the sulci are defined, the final edges of the tumor in the infiltrated gyrus are defined on the surface of the gyrus, completing the circumferential identification of the tumor. Equally important is identification of any major vessels (arteries or veins) on the cortical surface (Figs. 2B, 3, and 4), which are assessed for their supply to the surrounding brain. Any large arteries and veins overlying the tumor should be preserved.

Step 2: Functional Assessment to Localize Eloquent Brain

The surgeon next defines the functional anatomy of the brain where the tumor resides by using intraoperative mapping paradigms that have been well described in

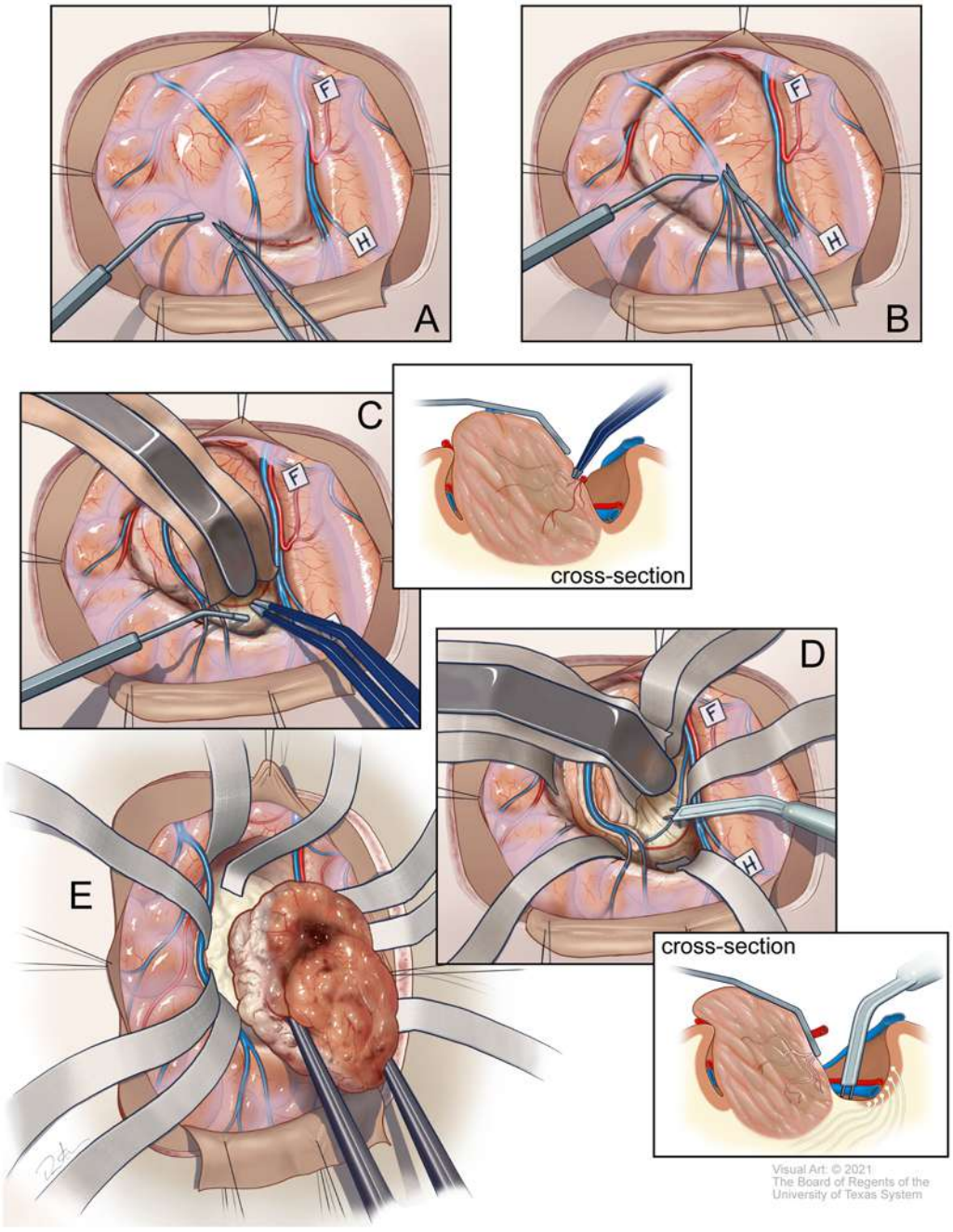

FIG. 2. Artist's depiction of steps 3 and 4 of the SGR technique, sulcus-guided anatomical circumferential resection (panels A–C) and white matter resection (panels C–E). **A–C:** Step 3, sulcus-guided anatomical circumferential dissection begins by opening the arachnoid over the sulci and splitting the surrounding sulci as shown in panel A. This opening is usually done with sharp dissection as shown, or by gentle widening with the bipolar. Overlying veins are preserved if necessary (panel B). The sulci are dissected to their bases as shown in panel C, and larger arteries in the sulci that are supplying surrounding brain are preserved, whereas the small perforators are coagulated and cut (cross-section of panel C). **D:** Once the bases of the sulci are reached, the tumor is dissected along the white matter by using the computer guidance to help define the tumor edge. Direct subcortical stimulation can be used to avoid injury to important descending motor fibers (panel D and its cross-section). **E:** The tumor is ultimately removed as a single en bloc mass. Artist: David Aten, Senior Medical Illustrator, MD Anderson Cancer Center. Copyright The Board of Regents of the University of Texas System. Published with permission.

the literature (Figs. 1C, 3, and 4). SGR is possible even when tumor is surrounded by eloquent brain. In fact, in our experience, many tumors that preoperatively appear to be within eloquent brain are often surrounded by eloquent gyri without evidence of actual function within the tumor-laden gyri (Fig. 1D and Fig. 4). In many cases, stimulation of the cortex identifies a functional site that appears to overlie tumor-infiltrated brain (Fig. 1D and Fig.

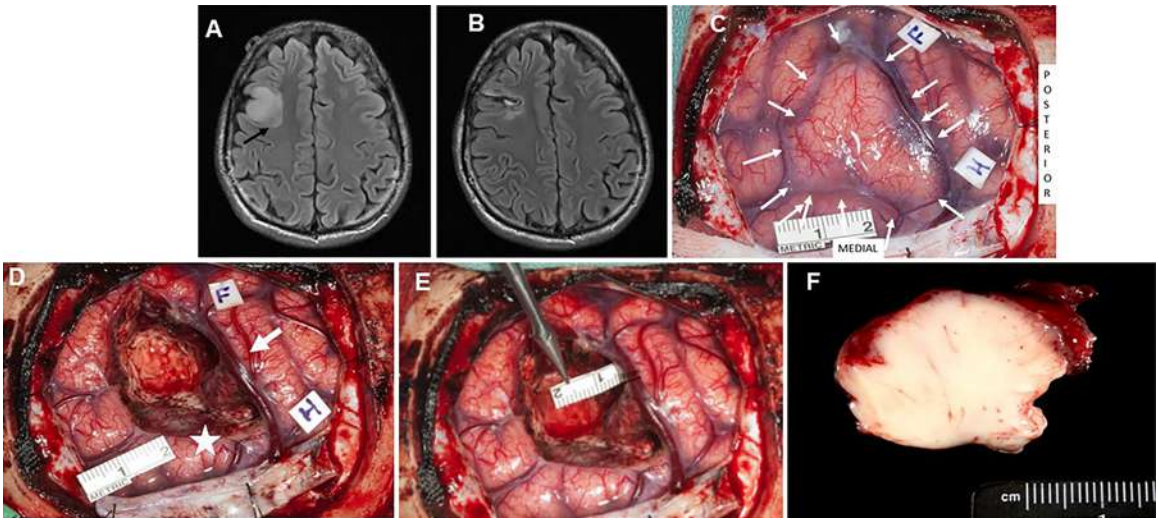

FIG. 3. MRI sequences and intraoperative photographs of right frontal premotor tumor resection using the SGR technique. **A:** Preoperative FLAIR MRI sequence showing nonenhancing tumor located in the middle frontal gyrus anterior to and abutting the motor cortex. The depth of the posterior sulcus often demarcates the depth of the tumor (*arrow*). **B:** Postoperative FLAIR MRI sequence showing complete resection. **C:** Intraoperative photograph of brain after awake mapping and prior to resection. The "F" tag represents facial motor stimulation, and the "H" tag represents hand motor stimulation. Tumor is demarcated by *arrows*, corresponding to the surrounding sulci. **D:** Resection cavity after tumor removal showing intact pia of the wall of the superior frontal gyrus along the superior frontal sulcus (*star*) and preservation of posterior veins in the precentral sulcus (*arrow*). **E:** Resection cavity with ruler showing the distance that the sulcus extended under the precentral gyrus. Imaging suggested that the tumor was within the precentral gyrus, but in fact the tumor was separated from the precentral gyrus by the sulcus. Removal of tumor along the sulcus led to preservation of motor function (the precentral gyrus was never violated) and complete tumor resection. **F:** Formalin-fixed en bloc tumor specimen after SGR.

3E). However, careful analysis of the sulci reveals that the brain beneath the functional cortex is from the neighboring expanded tumor-infiltrated gyrus and that the positive stimulation site is separated from the tumor by a sulcus. The tumor/gyrus under the positive stimulation site can be safely resected right up to the sulcal surface without injury to the stimulation site or to the white matter tracts (Fig. 1D, Figs. 3 and 4).

Step 3: Sulcus-Guided Anatomical Circumferential Resection

Once the surgeon defines the tumor's anatomical boundaries and verifies that eloquent brain regions are not within the tumor mass, the surgeon begins the resection by sharply opening the arachnoid overlying the sulci that define the tumor (Fig. 2A). Veins and arteries on the surface can be preserved if they supply surrounding brain (Fig. 2B and Fig. 4). From here, the dissection is carried down to the base of the sulcus (Fig. 2C and D). In the sulcus, the surgeon will often encounter large vessels that are supplying the tumor via small perforators (Fig. 2C [cross-section] and Fig. 4). The large en passage vessels are identified and preserved, and the small perforators are coagulated and sharply divided (Fig. 2C [cross-section]). Of note, there is often a vein at the base of most sulci that can be coagulated. As an alternative to opening the sulci, the surgeon can perform subpial dissections along the sulci. This approach is particularly effective when the neighboring gyrus is eloquent, because the neighboring gyrus is protected by CSF and pia. The goal of the transsulcal or subpial dissection is to reach the base of each of the sulci surrounding the tumor (Fig. 2D). For the gyri that are partially involved, the edge of the tumor is defined using computer-assisted navigation, the pial surface is coagulated, and the dissection proceeds from one sulcus to the other (see Fig. 1B, red star and dashed line underneath).

Step 4: White Matter Dissection

Once the depths of the sulci are reached, the tumor is demarcated from the underlying white matter. The trajectory of this demarcation is aided by image guidance, ultrasound, and tactile and visual clues (Fig. 2D and E). Often, the depth of the deepest sulcus can be used as a landmark to identify the relative depth of the tumor (Fig. 4A). The intersection between the tumor and white matter is dissected using gentle suctioning and bipolar cautery. This is done in a circumferential manner, with progress marked by patties/cottonoids until all the sides of the tumor meet and the tumor can be removed as a single mass (Fig. 2E, Fig. 3F, and Fig. 5). During this white matter dissection, subcortical stimulation can minimize neurological injury (Fig. 2D).[5,10,11] Stimulation can be performed efficiently with the SGR technique because the operative field is free of blood.

Description of the PMR Technique

With the PMR technique, after performing functional mapping to localize functional brain, a safe entry point into the tumor is identified and the pial surface is opened sharply and, using a combination of suction and ultrasonic

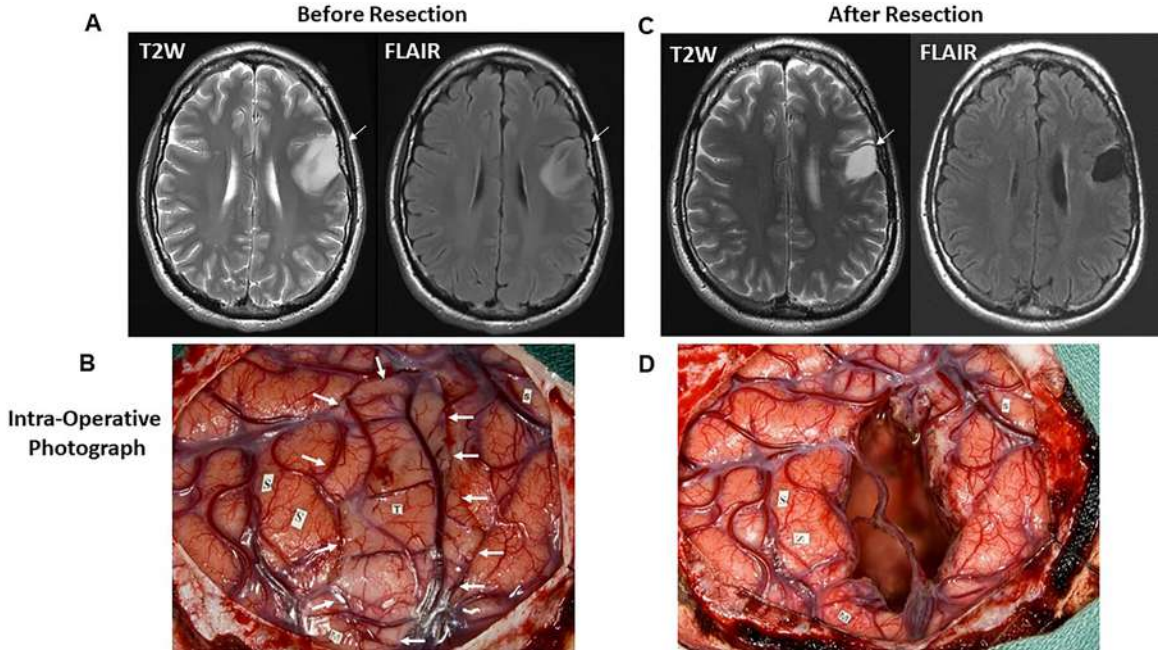

FIG. 4. Left frontal opercular tumor removed using the SGR technique and showing preservation of arteries overlying the tumor and in the sulcus. **A:** Axial FLAIR and T2-weighted MR images showing large nonenhancing tumor in the left frontal operculum, seemingly within the anatomical Broca area. *Arrows* indicate artery on the surface of the tumor. **B:** Intraoperative photograph obtained after awake brain mapping. The "S" tags indicate sites of speech arrest both anterior and posterior to the tumor; the "M" tags indicate positive motor site for face movement; and the "T" tag depicts gyri containing tumor. *Arrows* demarcate tumor edges as defined by sulci surrounding the tumor. Note that there are no functional speech areas within the tumor, despite its location in the frontal operculum where classically the Broca area would be expected to be anatomically located. Note the arteries on the surface of tumor, correlating with MRI. **C:** Postoperative FLAIR and T2-weighted images showing complete resection. *Arrow* indicates position of preserved vessel. **D:** Intraoperative photograph obtained after SGR, illustrating preservation of overlying arteries and arteries within the sulci. The posterior aspect of the tumor was underneath the speech ("S") sites and was removed by following the sulcus, resulting in no interruption of speech function.

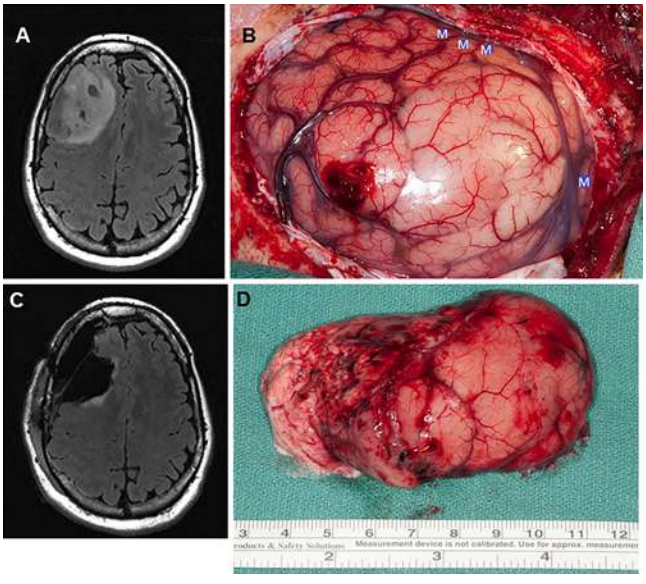

FIG. 5. Right middle frontal gyrus tumor removed using the SGR technique. **A:** Preoperative FLAIR MRI showing larger right frontal tumor. **B:** Intraoperative photograph shows widely expanded middle frontal gyrus. The "M" tags indicate positive motor site for face movement. **C:** Postoperative FLAIR MRI shows near total resection of tumor. **D:** En bloc specimen after removal using the SGR technique.

aspiration, the tumor is removed from this point toward the edges (i.e., from the inside out). Vessels are coagulated as they are encountered from inside the tumor. The resection is completed when the surgeon believes that he/she has reached the edge of the tumor, as determined by image guidance or tumor texture/feel, or when the functional boundaries are reached based on intraoperative mapping.

Results

We identified 519 patients who met the eligibility criteria; 208 (40%) underwent SGR, and 311 (60%) underwent PMR. The baseline characteristics of the resection groups are shown in Table 1. Most patients (64%) presented with seizures. An awake mapping technique was performed in 27% of cases, and there was no significant difference in the proportion of awake mapping between SGR and PMR cases (26% and 29% respectively, $p = 0.5$). The frequency of awake mapping increased over time; it was 19% from 1996 to 2005 versus 36% from 2006 to 2015.

Extent of Resection

The median extent of resection for all patients was 79%, and 111 patients (21%) underwent complete resection of the T2 hyperintense disease. After univariate analysis to evaluate potential predictors of extent of resection, we found that the median extent of resection in the SGR group was

TABLE 1. Preoperative presenting characteristics of 519 patients who underwent resection of a treatment-naïve LGG

Characteristic	Value			p Value
	All	SGR	PMR	
Total	519	208 (40%)	311 (60%)	
Median age in yrs	40.5	41.3	39.3	0.14
Sex				0.9
Male	289 (56%)	115 (55%)	174 (56%)	
Female	230 (44%)	93 (45%)	137 (44%)	
Location				
Frontal	326 (63%)	150 (72%)	176 (57%)	0.0004
Temporal	132 (25%)	44 (21%)	88 (28%)	0.08
Parietal	56 (11%)	12 (6%)	44 (14%)	0.002
Occipital	5 (1%)	2 (1%)	3 (1%)	0.7
Functional location				
Eloquent	187 (36%)	58 (28%)	129 (42%)	0.002
Noneloquent	331 (64%)	150 (72%)	181 (58%)	
Pathological diagnosis				
Astrocytoma	258 (50%)	104 (50%)	154 (50%)	0.9
Oligodendroglioma	246 (47%)	97 (47%)	149 (48%)	0.8
Mixed pathology	15 (3%)	7 (3%)	8 (3%)	0.6
Grade*				
II	188/482 (39%)	73/195 (37%)	115/287 (40%)	0.6
III	294/482 (61%)	122/195 (63%)	172/287 (60%)	0.5
Preop deficits				
Any neurological deficit	224 (43%)	77 (37%)	147 (47%)	0.024
Motor deficits	67 (13%)	25 (12%)	42 (14%)	0.7
Speech deficits	98 (19%)	36 (17%)	62 (20%)	0.5
Sensory deficits	84 (16%)	25 (12%)	59 (19%)	0.04
Visual deficits	67 (13%)	23 (11%)	44 (14%)	0.4
Preop seizures	333 (64%)	128 (62%)	205 (66%)	0.4
Median tumor size (cm^3)	40.5	35.1	40.1	>0.99
Mean tumor size (cm^3)	50.9	50.9	50.9	>0.99
KPS score ≥70	514 (99%)	206 (99%)	308 (99%)	>0.99
Awake mapping	144 (27%)	53 (26%)	89 (29%)	0.5

Results of univariate analyses with p values are reported; $p < 0.05$ was considered significant.
* Analysis of grade excludes 37 patients who were categorized as intermediate; 13 in the SGR group and 24 in the PMR group.

significantly greater than in the PMR group (84% vs 77% respectively, $p = 0.019$). Tumors resected using an SGR technique also had a significantly higher rate of complete resection (i.e., 100% resection) compared with PMR (27% vs 18%, $p = 0.016$) (Table 2 and Fig. 6). Finally, we found that smaller tumor volume was strongly associated with a greater extent of resection ($p < 0.001$) (Fig. 6); that tumors in eloquent brain regions had a lower rate of complete resection ($p = 0.002$); and that Grade II tumors had a higher rate of complete resection ($p = 0.012$) (Table 2). There was no difference in the degree of resection between astrocytomas and oligodendrogliomas.

In subsequent multivariate analyses, SGR and smaller preoperative volumes were found to be independently associated with higher rates of complete resection (OR 1.7, 95% CI 1.1–2.6, $p = 0.03$; and OR 0.97, 95% CI 0.96–0.98, $p < 0.001$, respectively) (Table 2). Of note, tumors resected using an SGR or PMR technique had similar median volumes preoperatively (Table 1).

Neurological/Postoperative Outcomes

Forty-three percent of patients presented with a neurological deficit, most commonly language dysfunction (19% of patients) (Table 1). Postoperatively, 72 patients (14%) developed new or worse short-term neurological complications; these complications persisted at 30 days for 10% of patients (Table 3). There was no statistically significant difference in the rate of these or any of the other postoperative outcomes assessed between the SGR and PMR (all $p > 0.05$) (Table 3).

TABLE 2. Results of univariate and multivariate analyses evaluating correlation with complete resection

	p Value		Multivariate OR (95% CI)
	Univariate	Multivariate	
Sex	0.5		
Age	0.14	0.13	0.9 (0.9–1.004)
SGR	0.016*	0.028†	1.7 (1.1–2.6)
Preop vol	<0.001*	<0.001†	0.97 (0.96–0.98)
Eloquent location	0.002*	0.125	0.6 (0.4–1.1)
Lt-sided tumor	0.16	0.16	0.7 (0.5–1.1)
Grade II tumor	0.012*	0.3	1.3 (0.8–2.1)
Location			
Frontal	0.74		
Temporal	0.4		
Parietal	0.6		
Preop neurological deficits	0.7		
Astrocytoma	0.4		

Multivariate OR with 95% CIs are reported; p < 0.05 was considered significant.
* Statistically significant based on univariate analysis.
† Statistically significant based on multivariate analysis.

Based on univariate analyses, we found that patients with tumors in eloquent locations were more likely to develop postoperative neurological complications compared with tumors in noneloquent cortex (18% vs 11%, p = 0.03). Patients in the SGR group had a lower rate of postoperative neurological complications (11% vs 16%), but this difference did not meet statistical significance (p = 0.09) (Table 3).

TABLE 3. Postoperative characteristics of 519 patients who underwent resection of a treatment-naïve LGG

Characteristic	Value			p Value
	All	SGR	PMR	
New neurological complication, short-term	72 (14%)	22 (11%)	50 (16%)	0.09
Neurological complication, 30 days	52 (10%)	16 (8%)	36 (12%)	0.18
New postop seizure	9 (1.7%)	5 (2.4%)	4 (1.3%)	0.5
Postop infection	6 (1.2%)	4 (1.9%)	2 (0.6%)	0.2
Intraparenchymal hematoma	0	0	0	
Subdural hematoma	2 (0.4%)	2 (1%)	0 (0%)	0.16

Results of univariate analyses with p values are reported; p < 0.05 was considered significant.

Tumors in Eloquent Locations

Overall, 28% of tumors resected using an SGR technique were located in eloquent locations compared with 41.6% of those resected with PMR (p = 0.002). Given the importance of eloquent location with regard to postoperative neurological complications, we performed a subgroup analysis evaluating only tumors in eloquent locations. Importantly, tumors in the SGR group were of similar size compared with tumors in the PMR group (median 41 vs 45 cm^3, respectively, p = 0.6). We found that SGR had a lower rate of postoperative complications compared with PMR (12% vs 21%), but this difference did not reach statistical significance (p = 0.16).

Overall Survival

The median survival was 11.0 years (95% CI 7.7–14.3

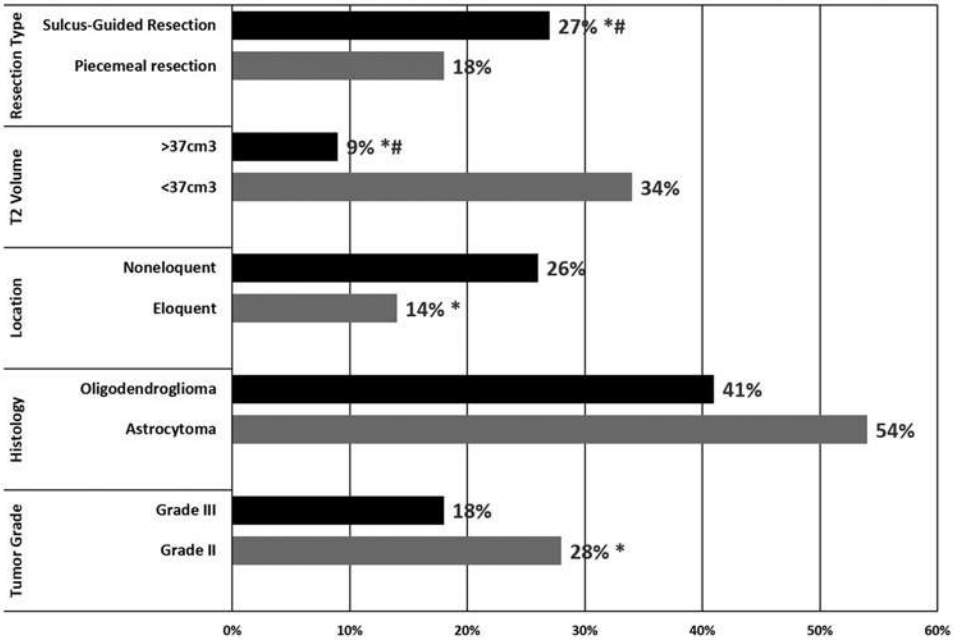

FIG. 6. Graph showing the percentage of complete resection for each variable. Tumor volume is dichotomized based on median initial tumor volume for the purpose of visualization. * Statistically significant based on univariate analysis. # Statistically significant based on multivariate analysis.

years). Based on multivariate Cox regression survival analysis, a resection of > 75% was associated with improved overall survival (HR 0.6, 95% CI 0.4–0.8; p = 0.003). Longer survival was also associated with smaller initial tumor volume based on T2-weighted images (HR 1.004, 95% CI 1.001–1.008; p = 0.015) and a histological diagnosis of oligodendroglioma (HR 0.53, 95% CI 0.4–0.8; p = 0.003). Grade II tumors were not associated with significantly improved survival in this multivariate analysis (p = 0.059), and resection technique (SGR vs PMR) did not affect survival.

Discussion

To our knowledge, this is the first study comparing SGR with PMR for LGGs. We describe the technique of circumferential SGR performed using the surrounding sulci to demarcate the borders of the tumor and demonstrate that SGR is independently associated with a higher rate of complete resection, and that it results in similar or decreased postoperative neurological morbidity compared with PMR. We demonstrate that SGR is safe and feasible, even when tumors are located in eloquent locations.

In systemic malignancies, such as lung cancer and colon cancer, circumferential resection using a no-touch technique is the standard of care.[12–22] Our group has recently shown that, for glioblastoma, circumferential resection of the contrast-enhancing tumor based on T1-weighted images is associated with a higher extent of resection than for PMR.[13]

For diffuse LGGs, the goal of surgery is maximal safe resection of the hyperintense signal on MRI FLAIR/T2-weighted sequences. However, the ideal resection technique has not been clearly defined. Whereas many neurosurgeons resect LGGs from the inside out (i.e., using PMR), we have increasingly advocated for a circumferential SGR technique to resect LGGs. Although circumferential resection has been mentioned in several studies of LGGs,[1,23–25] data are sparse regarding patient outcomes. Therefore, this paper is, to our knowledge, the most comprehensive description of a circumferential resection technique that takes advantage of the tumor sulci to demarcate the borders of the tumor and guide the resection. We show that the SGR technique results in statistically significant improvement in complete resection rates compared with PMR in both univariate and multivariate analyses.

We think that these outcomes are due to the fact that the SGR technique has several advantages over PMR. First, because the boundaries of the tumor are defined by the sulci/gyri and are therefore determined before an incision is made, the surgeon maintains an understanding of the anatomy of the tumor and surrounding brain throughout the resection. Second, because the positions of the sulci do not shift as the tumor is resected, the image guidance system remains accurate throughout most of the resection, and there is minimal or no brain shift because the tumor remains intact until the end of the operation.[23] Third, areas of tumor that appear to be invading eloquent brain and might not be considered resectable are often merely pushing the sulcus under the eloquent brain region. By following the sulcus, the surgeon does not enter the adjacent eloquent gyrus, resulting in complete removal of the tumor without injuring eloquent gyri (Figs. 1–3). Fourth, the base of the sulci can help define the depth of the tumor, given that many tumors do not extend beyond the base of the deepest sulci—when they do, the depth of the sulcus is a point where the tumor interface and the white matter interface can be visually identified, and therefore the depth of the tumor is more easily defined. Fifth, by opening the sulci, en passage vessels can be identified early, preventing injury, and therefore preserving blood supply to the surrounding brain. Last, because LGGs are supplied by small perforators coming off the larger sulcal arteries, these small perforators can be coagulated and cut early, thereby devascularizing the tumor and resulting in a bloodless resection.

A common argument against circumferential resection of LGGs is that this technique increases the potential for neurological dysfunction. In our study, 14% of patients developed short-term neurological complications postoperatively. When comparing SGR with PMR, we found that the rate of neurological complications was lower in the SGR group than in the PMR group (11% vs 16%); however, the difference did not reach statistical significance. Nevertheless, this result indicates that the SGR technique is at least as safe as PMR in this population. The neurological outcome data also provide indirect evidence that SGR does not result in greater postoperative ischemic changes or large strokes than does PMR. In fact, SGR may protect against injury to en passage vessels in the sulci due to early detection of these vessels. To further highlight these findings, a subset analysis was performed to evaluate only tumors in eloquent locations. The tumors were of similar sizes in the two groups. The neurological complication rates were again lower in the SGR group than in the PMR group (12% vs 21%, p = 0.16); although not significant, these findings again indicate that SGR is at least as safe as PMR, even for tumors located in eloquent brain regions. Although it is generally believed that PMR is a safe approach, our data suggest that the SGR technique is also safe, especially considering the potential overlapping anatomical relationships between tumor sulci and positive functional stimulation points, as described in Fig. 1D. Therefore, we suggest that SGR should be considered even for tumors located in eloquent brain, assuming that careful intraoperative functional mapping and monitoring is available to the neurosurgeon.

Despite the increased extent of resection after SGR compared with PMR, we were not able to show a statistically significant improvement in survival after SGR. We suspect that this result was due to the small numbers of tumors in each of the groups and the different survival rates between astrocytomas and oligodendrogliomas. To fully evaluate overall survival, our study would need to assess the molecular profile of each tumor (*IDH* status, *ATRX* status, 1p/19Q status). This information was not known for many of our tumors, precluding this analysis. Nevertheless, we provide strong statistical evidence that SGR results in improved rates of complete resection, and multiple studies support the notion that increased extent of resection is associated with increased survival.[2,4]

An important element of the SGR technique is an emphasis on identification and preservation of the arteries and

veins around the tumor. Discussions of vascular anatomy are often neglected or minimized in operative texts describing the resection of malignant brain tumors. The SGR technique places a premium on the vascular anatomy of the tumor. In general, vessels are encountered early in the dissection, and the SGR technique can help identify the vessels from the outside in rather than from the inside out, which helps differentiate vessels that should be spared. In this manner, sulcal and surface vessels can be protected. Small perforating vessels that are directly entering the tumor can be taken on its margin, helping to devascularize the tumor as it is being dissected. Taken together, this approach results in a bloodless field that aids in identifying tumor borders.

The use of adjuncts to improve extent of resection in LGGs has been discussed in other reports. 5-Aminolevulinic acid has been used for LGGs; however, most LGGs do not fluoresce, and when they do, the fluorescence is confined to regions of malignant transformation.[26–28] Intraoperative MRI is a powerful tool that can improve extent of resection. However, it is not available in most institutions. Given these limitations, because SGR relies primarily on anatomy, it can be universally applied, especially in centers that do not have many advanced technologies.

Our study has several limitations. We recognize that there may be a selection bias when choosing the perilesional technique, and tumors in eloquent brain were less likely to undergo SGR. However, even after multivariate analysis, use of the SGR technique continued to be significantly associated with a more complete resection compared with PMR. Furthermore, we attempted to mitigate this bias by performing a subgroup analysis focusing on eloquent tumors alone. We did note that SGR was used less often when patients presented with neurological symptoms, or when the tumors were in the dominant hemisphere. There was also disparity in different lobes of the brain—we found a higher rate of SGR in frontal tumors and a lower rate in parietal tumors. We suspect that this was a result of a higher prevalence of eloquent sites for tumors of the parietal lobe. However, as mentioned, eloquent location was analyzed separately, and the frontal and parietal location variables had no significant effect on the extent of resection in this subanalysis. In addition, we excluded tumors in deep locations thought to be difficult to resect using an SGR technique, given that inclusion of these tumors may have inflated the complication rate of PMR. Although a randomized trial would definitively address this question, it is unlikely to be successfully conducted.

Conclusions

Because LGGs do not migrate through sulci, the sulci help demarcate the tumor edges, and the SGR technique leverages this normal tumor growth pattern to the advantage of the surgeon. Based on our data, SGR of LGGs is safe and feasible, even in eloquent locations, and SGR is independently associated with a higher rate of complete resection than is PMR. We recommend that neurosurgeons consider applying the SGR technique, when feasible, to maximize the extent of resection of LGGs.

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Disclosures

Drs. Hodges and Freeman are consultants for Medtronic.

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Conception and design: Lang, Al-Holou. Acquisition of data: Al-Holou, Everson, Freeman, Ferguson, McCutcheon, Prabhu, Weinberg, Sawaya. Analysis and interpretation of data: Suki. Drafting the article: Lang, Al-Holou, Suki. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lang. Study supervision: Lang.

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