Surgical assessment of the insula. Part 2: validation of the Berger-Sanai zone classification system for predicting extent of glioma resection

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OBJECTIVE Though challenging, maximal safe resection of insular gliomas enhances overall and progression-free survival and deters malignant transformation. Previously published reports have shown that surgery can be performed with low morbidity. The authors previously described a Berger-Sanai zone classification system for insular gliomas. Using a subsequent dataset, they undertook this study to validate this zone classification system for predictability of extent of resection (EOR) in patients with insular gliomas.

METHODS The study population included adults who had undergone resection of WHO Grade II, III, or IV insular gliomas. In accordance with our prior published report, tumor location was classified according to the Berger-Sanai quadrant-style classification system into Zones I through IV. Interobserver variability was analyzed using a cohort of newly diagnosed insular gliomas and independent classification scores given by 3 neurosurgeons at various career stages. Glioma volumes were analyzed using FLAIR and T1-weighted contrast-enhanced MR images.

RESULTS One hundred twenty-nine procedures involving 114 consecutive patients were identified. The study population from the authors' previously published experience included 115 procedures involving 104 patients. Thus, the total experience included 244 procedures involving 218 patients with insular gliomas treated at the authors' institution. The most common presenting symptoms were seizure (68.2%) and asymptomatic recurrence (17.8%). WHO Grade II glioma histology was the most common (54.3%), followed by Grades III (34.1%) and IV (11.6%). The median tumor volume was 48.5 cm³. The majority of insular gliomas were located in the anterior portion of the insula with 31.0% in Zone I, 10.9% in Zone IV, and 16.3% in Zones I+IV. The Berger-Sanai zone classification system was highly reliable, with a kappa coefficient of 0.857. The median EOR for all zones was 85%. Comparison of EOR between the current and prior series showed no change and Zone I gliomas continue to have the highest median EOR. Short- and long-term neurological complications remain low, and zone classification correlated with short-term complications, which were highest in Zone I and in Giant insular gliomas.

CONCLUSIONS The previously proposed Berger-Sanai classification system is highly reliable and predictive of insular glioma EOR and morbidity.

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KEY WORDS anaplastic astrocytoma; glioma; glioblastoma; low-grade glioma; insular glioma; oncology

INSULAR gliomas remain a challenge to manage. Given the complexity of the insular lobe, its proximity to functionally significant areas, and its intimate relationship with middle cerebral and lenticulostriate artery branches, these tumors were often deemed too dangerous for surgical treatment. However, improvements in neuroanesthesia, microsurgical technique, and functional mapping have allowed greater access to these tumors with a low complication rate. Prior published reports suggest that aggressive resection of both low- and high-grade insular

gliomas may be accomplished with an acceptable morbidity profile.^{2,3,7–10,13,14,17} Maximal extent of resection (EOR) predicts superior overall and progression-free survival as well as improved seizure control.^{6,11,13} The majority of insular gliomas not only involve the insular lobe but can also infiltrate into portions of the frontal operculum and temporal lobe. Given their proximity to functional language and motor networks, the surgical approach may vary depending on the predominant component of the tumor within the insula. Recent publications have focused on the role of

ABBREVIATIONS EOR = extent of resection; FLAIR = fluid-attenuated inversion recovery; IDH = isocitrate dehydrogenase; WHO = World Health Organization.

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surgery to improve survival for patients with insular gliomas.^{6,8,13–15} In our prior retrospective series, we analyzed perioperative outcomes after surgery for 115 consecutive insular gliomas focusing on morbidity and the effect of EOR on patient outcome and proposed an anatomical classification system for insular gliomas to help preoperatively predict the likely extent of tumor resection.¹³ In this current study, we assign the previously described “Berger-Sanai” classification system to a new cohort of insular gliomas to determine the interobserver reliability among clinicians at different levels of clinical experience and expertise in order to validate our previous EOR predictions.

Methods

Patient Selection

Using a prospectively collected database of insular gliomas assigned to one of 4 previously described zones,¹³ we studied 114 consecutive patients undergoing a total 129 resections between September 2007 and April 2014. All procedures were performed by the study’s senior author (M.S.B.). Patients were all adults older than 18 years of age who had undergone surgery at the University of California, San Francisco. Perioperative patient parameters including zone classification based on preoperative fluid-attenuated inversion recovery (FLAIR) and T1-weighted postcontrast MR images, clinical presentation, handedness, age at diagnosis, immediate postoperative MRI (within 48 hours of surgery), and histopathology review (in accordance with World Health Organization [WHO] guidelines) were prospectively collected. Given substantial differences in their natural history, patients with WHO Grade I histology, those with multifocal glioma, and gliomatosis cerebri were excluded from analysis. All aspects of microsurgical tumor removal, including a description of the functional mapping, have been previously described in our prior publication on insular gliomas.¹³ Approval for this study was granted by the University of California, San Francisco Committee on Human Research.

Interobserver Reliability of Berger-Sanai Insular Glioma Classification System

According to our prior published protocol, the insula was divided into 4 zones (Fig. 1). Along the horizontal plane in a sagittal view, the insula was seen to straddle the overlying sylvian fissure. This plane was intersected by a perpendicular line at the foramen of Monro. Tumor location was assigned to one or more of these zones.¹³ For tumors occupying more than 1 zone, this condition was denoted as such (e.g., Zones I+II). For cases in which the tumor occupied all 4 zones, these insular gliomas were defined as “Giant.” Using this method, a total of 9 possible options existed for classification: Zones I, II, III, IV, I+II, I+IV, II+III, and III+IV and Giant.

To test agreement of insular zone assignment between clinicians, a subset of 80 cases of newly diagnosed insular glioma were independently scored by 3 examiners. With the goal of testing clinicians across a varied distribution of clinical experiences, 1 junior level neurosurgery resident (J.O.), 1 junior level neurosurgery faculty member (S.H.J.), and 1 senior neurosurgeon (M.S.B.) were chosen to participate. Participants were blinded to each other’s score.

The kappa coefficient was used to determine the significance of this agreement. Interpretation of the kappa coefficient was performed in accordance to prior published reports in which 0 indicated agreement equivalent to chance, 0.01–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, 0.81–0.99 almost perfect agreement, and a kappa coefficient of 1 indicated perfect agreement.⁵

Patient Outcome Measurements

Patients underwent sequential neurological examinations performed by 4 clinicians during the perioperative period: the senior attending neurosurgeon, a neurosurgical resident, a speech and language neurophysiologist, and the attending neuro-oncologist. Clinical examinations were performed preoperatively, every day during the postoperative period, and at each follow-up appointment by at least 1 of the above-mentioned clinicians (4–6 weeks and 3–6 months following surgery). Short-term neurological morbidity was defined as new-onset language or sensorimotor deficits within the first 3–5 postoperative days. Long-term neurological morbidity was defined as persistent dysfunction 90 days after surgical intervention. Our protocol for language function testing has been previously described.¹² Differences between findings of the 4 examiners were adjudicated by accepting the results showing the greatest impairment if more than 1 examiner was involved at a given time point. MRI results were reviewed to confirm that the patient’s symptoms were not a function of tumor progression at each time point. Malignant progression was defined as a change in histopathology of WHO Grade II or III tumors to higher-grade lesions on a subsequent procedure.

Volumetric Analyses

One author (J.L.) conducted volumetric measurement of pre- and postoperative imaging. Each measurement and calculation was examined for accuracy by another author (S.H.J.) and the primary surgeon (M.S.B.). Low- and high-grade tumors were volumetrically analyzed by measuring hyperintense regions on axial T2-weighted FLAIR MR images (low-grade gliomas) and T1-weighted contrast-enhanced MR images (high-grade gliomas). For each case, the tumor was segmented manually across all slices with region-of-interest analysis to compute pre- and postoperative volumes in cubic centimeters. The EOR was calculated as follows: $[100 - (\text{postoperative tumor volume} / \text{preoperative tumor volume}) * 100]$, with 100% indicating gross total resection and < 100% representing subtotal resection. Determination of tumor volume and EOR was made without consideration of the clinical outcome.

Statistical Analyses

Descriptive statistics were calculated for all variables and stated as median (unless otherwise specified) for continuous variables and frequency of distribution for categorical variables. Cross-tabulations were generated, and the Wilcoxon signed-rank test (for continuous variables) and chi-square (for categorical variables) tests were used to compare distributions. The Fisher exact test was used if more than 80% of values were less than 5. The kappa coefficient was used to determine strength of agreement be-

FIG. 1. Illustration showing insular surface with Berger-Sanai insular glioma classification system. **A:** The insula is covered by the frontoparietal and temporal opercula. **B:** Zones I to IV are divided along the Sylvian fissure and a perpendicular plane crossing the foramen of Monro. **C:** Insular tumor location is determined by the position of the majority of the tumor mass. **D:** Axial illustration of Zones I and II located anterior to the foramen of Monro and Zones II and III located behind the foramen of Monro. Copyright Kenneth X. Probst. Published with permission.

tween clinicians. All *p* values were obtained from 2-sided tests, with statistical significance defined as *p* < 0.05. A biostatistician (A.M.) assisted with statistical analyses in this study, using JMP statistical software, version 10.0.2 (SAS Institute, Inc.).

Results

Patient Demographics

The study population included 114 consecutive patients for a total of 129 procedures representing 74 men and 55 women with a median age of 41 years (range 18–72 years) (Table 1). The study population from our previously published experience included 115 procedures involving 104 patients. As such, our total experience included 244 procedures involving 218 patients with insular glioma treated at our institution. Eighty (62.0%) of the 129 procedures in the current experience represented primary craniotomies, whereas 49 (38.0%) of the operations involved patients who had undergone at least 1 prior surgical procedure for the treatment of insular glioma. Sixty-eight (52.7%) of the procedures were for the treatment of left-sided tumors, and there were 58 awake craniotomy procedures (45.0%). Pa-

tients most commonly presented with new-onset seizures (88 cases, 68.2%), or asymptomatic tumor progression (23 cases, 17.8%); other presentations included headaches (9 cases, 7.0%), cognitive decline (3 cases, 2.3%), motor deficits (3 cases, 2.3%), and language deficits (1 case, 0.8%). Insular gliomas were rarely discovered incidentally, representing 1.6% of cases (2 patients). In the 129 operations, the most common histological grade was WHO Grade II (70 tumors, 54.3%), followed by WHO Grade III (44 tumors, 34.1%), and WHO Grade IV (15 tumors, 11.6%). The median tumor volume was 48.5 cm³ (range 0.11–245.7 cm³). Fifteen percent of insular tumors (19) were confined entirely within the insula, while 85% of tumors were primarily based in the insula (i.e., > 75%) with tumor extending beyond the insula to involve portions of the frontal, temporal, or parietal lobes. The median duration of clinical follow-up was 3.5 years (range 0.26–25.8 years) and, as part of planned adjuvant therapy, 107 patients (82.9%) were treated with chemotherapy and 82 (63.6%) underwent radiation therapy after surgery (decisions about use of adjuvant chemo-radiation were made on a case-by-case basis dependent on tumor recurrence, WHO grade, and histol-

TABLE 1. Demographic and clinical characteristics of study patients who underwent surgery for treatment of insular glioma (129 procedures)*

Parameter	Value
Age at diagnosis (yrs)	
Median	41
Range	18–72
Sex	
Male	74 (57.4%)
Female	55 (42.6%)
Side of tumor	
Left	68 (52.7%)
Right	61 (47.3%)
WHO tumor grade	
II	70 (54.3%)
III	44 (34.1%)
IV	15 (11.6%)
Tumor volume (cm ³)	
Median	48.5
Range	0.11–245.7
Insular glioma location by zone	
I	40 (31.0%)
II	2 (1.6%)
III	17 (13.2%)
IV	14 (10.9%)
I+II	4 (3.1%)
I+IV	21 (16.3%)
II+III	7 (5.4%)
III+IV	12 (9.3%)
Giant	12 (9.3%)
Median insular glioma volume by zone (cm ³)	
I	49.1
II	11.4
III	22
IV	20.1
I+II	72
I+IV	52.3
II+III	63.8
III+IV	41.4
Giant	91.2
Handedness	
Right	126 (97.7%)
Left	3 (2.3%)
Symptoms at presentation	
Seizure	88 (68.2%)
Cognitive decline	3 (2.3%)
Headache	9 (7.0%)
Incidental	2 (1.6%)
Language deficit	1 (0.8%)
Motor deficit	3 (2.3%)
Asymptomatic recurrence	23 (17.8%)

(continued)

TABLE 1. Demographic and clinical characteristics of study patients who underwent surgery for treatment of insular glioma (129 procedures)* (continued)

Parameter	Value
Type of surgery	
Motor mapping	122 (94.6%)
Language mapping	58 (45.0%)
Awake surgery	58 (45.0%)
New	80 (62.0%)
Reoperation	49 (38.0%)
Adjuvant oncologic treatment	
Patients with postoperative chemotherapy	107 (82.9%)
Patients with postoperative radiation	82 (63.6%)
Malignant transformation	49 (38.0%)
Clinical follow-up (yrs)	
Median	3.5
Range	0.26–25.8
EOR	
0–40%	1 (0.8%)
41–69%	19 (14.7%)
70–89%	58 (45.0%)
>90%	51 (39.5%)
Median	85%
Range	40–100%

* Values indicate numbers of cases (by procedure) unless otherwise indicated.

ogy). Histologically confirmed malignant transformation from WHO Grade II to WHO Grade III or from WHO Grade III to WHO Grade IV occurred in 49 cases (38.0%). Tumor laterality was evenly distributed (Table 1).

Distribution of Insular Glioma Location

Based on our prior published report,¹³ insular gliomas were assigned to 1 of 4 zones (Table 1). The majority of insular gliomas were located in the anterior portion of the insula (anterior to the foramen of Monro), with 31.0% (40 cases) within the anterior-superior quadrant (Zone I), 10.9% (14 cases) within the anterior inferior quadrant (Zone IV), and 16.3% (21 cases) within Zones I+IV (total of 58.2% of cases within the anterior insula). Twelve insular gliomas (9.3%) were classified as Giant, occupying all 4 zones.

Interobserver Reliability of Berger-Sanai Insular Glioma Classification System

Interobserver reliability was tested using preoperative FLAIR or T1-weighted gadolinium-enhanced MR images obtained in 80 patients with new WHO Grade II, III, or IV insular gliomas. Three neurosurgeons with varying amounts of clinical experience scored each tumor's location according to our previously published zone classification criteria.¹³ Interobserver agreement was 89.1% (41 of 46 cases) for WHO Grade II gliomas, 84.0% (21 of 25 cases) for WHO Grade III anaplastic gliomas, and 100% (9 of 9 cases) for WHO Grade IV gliomas. Overall observer agreement was 89%. Interobserver reliability testing showed strong agreement with a kappa coefficient of

0.857 (95% CI 0.77–0.94; $p < 0.001$). There was no correlation between observer agreement and WHO grade ($p = 0.42$).

Extent of Resection

EOR was determined as follows: in 1 case (0.8%), the EOR was less than or equal to 40%; in 19 (14.7%), it was between 41% and 69%; in 58 (45.0%), it was between 70% and 89%; and in 51 (39.5%), it was greater than 90%. The median EOR was 85% (range 40%–100%) across all zones (Table 1). Among cases of WHO Grade II glioma (70 cases), the median EOR was 81%; in 55 cases (78.6%), the EOR was greater than or equal to 70% (this included 32 cases [45.7%] with 70%–89% resection and 23 [32.9%] with > 90% resection). A total of 44 operations were for treatment of anaplastic astrocytoma (WHO Grade III), with a median EOR of 88%. In 41 cases (93.2%), the EOR was 70% or greater (this included 23 cases [52.3%] with a 70%–89% resection and 18 [40.9%] with a > 90% resection). Among cases of WHO Grade IV glioma (15 cases), the median EOR was 97%, and 13 cases (86.7%) had an EOR greater than or equal to 70% (this included 3 cases [20.0%] with 70%–89% resection and 10 [66.7%] with > 90% resection). Zone II insular gliomas were the smallest, with a median tumor volume of 11.4 cm³, while Giant insular gliomas had a median volume of 91.2 cm³ (Table 1). The greatest EOR was accomplished in tumors located in Zones I (median EOR 90.1%) and IV (median EOR 89.5%), compared with Zones I+IV (median EOR 75%) and Giant tumors (median EOR 80%) ($p = 0.008$) (Table 2). In our initial series, the smallest EOR was associated with Zone II tumors; however, with a greater willingness to maximize resections using either a transcortical surgical corridor through silent portions of the face motor cortex or splitting the posterior sylvian fissure, the median EOR increased to 83.5%. There were no significant differences in median EOR between tumors across all zones in our 2 insular glioma series (Table 2).

In addition to zones predictive of EOR, there was also a positive correlation between tumor size and EOR. The median glioma volume was highest in Giant (91.2 cm³), Zone I+II (72.0 cm³), and Zone II+III (63.8 cm³) tumors. The smallest median tumor volumes were observed in

Zone II (11.4 cm³), Zone III (22.0 cm³), and Zone IV (20.1 cm³) tumors (median volumes for Zone I, Zone I+IV, and Zone III+IV tumors were 49.1 cm³, 52.3 cm³, and 41.4 cm³, respectively) ($p = 0.002$). In cases with EOR < 40%, the median tumor volume was 38 cm³ (mean 38 cm³); in those with EOR of 41%–69%, the median tumor volume was 46 cm³ (mean 61 cm³); in those with EOR of 70%–89%, the median volume was 62 cm³ (mean 62 cm³); and in those with an EOR > 90%, the median glioma volume was 25 cm³ (mean 46 cm³) ($p = 0.0183$). This suggests a more complete resection for smaller insular tumors.

Insular Glioma Molecular Characteristics and Impact on EOR

There is inconsistency in the literature regarding the rate of 1p and 19q chromosomal co-deletions in insular gliomas.^{4,16} In 60 (46.5%) of the cases in our new series, the tumors were either WHO Grade II oligodendroglioma ($n = 24$), WHO Grade II oligoastrocytoma ($n = 24$), or WHO Grade III anaplastic oligodendroglioma or oligoastrocytoma ($n = 12$). Forty-three percent ($n = 23$) of WHO Grade II and III insular oligodendroglioma and oligoastrocytomas had 1p19q co-deletions ($p = 0.04$). Other previously published reports have suggested that isocitrate dehydrogenase (IDH) status confers a higher degree of resectability on WHO Grade III and IV gliomas.¹ We therefore analyzed EOR focusing on insular gliomas that were positive for the IDH mutation (IDH+). There was no significant difference in the volume of IDH+ and nonmutated (IDH–) insular gliomas (IDH+ gliomas had a median tumor volume of 47.1 cm³, while IDH– insular gliomas had a median tumor volume of 28.9 cm³; $p = 0.18$). Furthermore, IDH+ insular gliomas were evenly distributed across zones, with no statistically significant differences noted (Zone I, 36%; Zone II, 2%; Zone III, 13%; Zone IV, 2%; Zones I+II, 4%; Zones I+IV, 19%; Zones II+III, 6%; Zones III+IV, 9%; Giant, 4%; $p = 0.13$). Among WHO Grade II insular gliomas, IDH+ tumors had a median EOR of 81%, while IDH– WHO Grade II insular gliomas had a median EOR of 86% ($p = 0.62$). WHO Grade III IDH+ insular gliomas had a median EOR of 79%, while IDH– WHO Grade III insular gliomas had a median EOR of 88% ($p = 0.06$). The median EOR for WHO Grade IV

TABLE 2. Summary of resected insular gliomas by zone ($n = 244$)

Zone	WHO Grade II	WHO Grade III	WHO Grade IV	Median EOR, % (new series, $n = 129$)	Median EOR, % (combined series, $n = 244$)*	p Value†
I ($n = 80$)	50 (62.5)	21 (26.3)	9 (11.3)	90.1	92	0.47
II ($n = 8$)	4 (50.0)	3 (37.5)	1 (12.5)	83.5	75.5	0.41
III ($n = 23$)	11 (47.8)	8 (34.8)	4 (17.4)	88	89	0.75
IV ($n = 20$)	9 (45.0)	8 (40.0)	3 (15.0)	89.5	89.2	0.79
I+II ($n = 8$)	5 (62.5)	2 (25.0)	1 (12.5)	86.5	78.9	0.35
I+IV ($n = 47$)	25 (53.2)	20 (42.6)	2 (4.3)	75	78	0.06
II+III ($n = 16$)	13 (81.3)	2 (12.5)	1 (6.3)	85	84	0.77
III+IV ($n = 16$)	8 (50.0)	6 (37.5)	2 (12.5)	82	83	0.61
Giant ($n = 26$)	15 (57.7)	9 (34.6)	2 (7.7)	80	76.4	0.60
Totals	140 (57.4)	79 (32.4)	25 (10.2)			

* Bold type is used to highlight the values for the combined series.

† For comparison of EOR between Sanai et al.¹³ and the current series.

IDH+ insular gliomas was 83%, while IDH- WHO Grade IV insular gliomas had a median EOR of 95% ($p = 0.31$).

Morbidity Profile

There were no deaths related to surgery in this series. The overall short-term complication rate was 26.4% (34 complications in 129 procedures) (Table 3). Short-term (within 3–5 days after surgery) neurological complications occurred most frequently after procedures involving Zone I and Giant insular gliomas. New motor neurological deficits excluding face motor weakness (within 3–5 days after surgery) occurred after 7.8% of the procedures (10 of 129). New face motor deficits occurred after 9.3% (12 of 129). Early postoperative language deficits occurred after 16.3% (21 of 129). At the 3-month follow-up visit, 99.2% of face motor deficits resolved. The overall long-term (90-day) neurological deficit rate was 3.2%. All but 1 language deficit resolved (0.8%), while the long-term rate of motor disability also remained low at 1.6% ($n = 2$). These rates compared favorably with results from our prior retrospective series.

Discussion

The insula's proximity to middle cerebral artery vessels, primary motor and sensory areas, and the perisylvian language network makes accessing and resecting gliomas in this area challenging. Prior studies demonstrated that maximal resection of insular gliomas enhances overall and progression-free survival and improves seizure outcome.^{6,11,13} Furthermore, surgery can be accomplished with a median EOR of 80%–82% and minimal morbidity of long-term language (0.8%) and motor function (1.6%).^{2,3,8,13,14} The significance of volumetric EOR on overall survival for patients with both low- and high-grade insular gliomas has been demonstrated in multiple previously published reports.^{6,13,14} Sanai et al. analyzed 115 procedures involving 104 patients with insular glioma and demonstrated a 5-year overall survival of 100% when the EOR was 90% and 84% for an EOR less than 90% in cases of low-grade glioma. In cases of high-grade glioma, the 2-year overall survival was 91% with an EOR of 90% and 75% when the EOR was less than 90%.¹³ This observation was later confirmed by Skrap et al., who found an overall survival of 92% for patients with an EOR greater than 90% and overall survival of 57% for those with an EOR less than 70%.¹⁴ With respect to WHO Grade III gliomas, greater than 90% EOR has been shown to be associated with a 2-year overall survival of 78%, in contrast with less than 90% EOR, which was associated with a 2-year overall survival of 19.6%.¹⁴ Recently it has been further demonstrated that EOR greater than 90% for insular gliomas is predictive of a favorable postoperative seizure outcome.⁶

In our previously published retrospective series of patients with insular gliomas, we assessed postoperative morbidity and patient survival while describing an anatomical characterization system to help predict extent of tumor resection. In this study, we use the previously described classification scheme to 1) determine if it is robust when used by other surgeons and 2) determine if it continues to be predictive of extent of tumor resection. We found this system to be highly reliable with minimal variability

TABLE 3. Postoperative morbidity and complication rates in 129 procedures

Variable	Short Term*	Long Term†	Prior Series Long-Term Disability	p Value‡
Morbidity				
Language deficit	21 (16.3%)	1 (0.8%)	1 (1.0%)	
Motor deficit	10 (7.8%)	2 (1.6%)	2 (1.7%)	
Face motor deficit	12 (9.3%)	1 (0.8%)	2 (1.7%)	
Complication rates				0.03
Zone I	9 (26%)			
Zone II	0 (0%)			
Zone III	3 (8.8%)			
Zone IV	1 (3%)			
Zones I+II	2 (5.9%)			
Zones I+IV	4 (12%)			
Zones II+III	5 (15%)			
Zones III+IV	4 (12%)			
Giant	6 (18%)			

* Occurring postoperative Days 3–5.

† Remaining at 90-day-postoperative examination.

‡ Boldface indicates statistical significance.

between clinicians and highly predictive of the expected EOR across all zones.

Few insula-based gliomas are confined entirely within the insula (15% in this series). Furthermore, depending on where within the insula a glioma is based, the surgical approach and anatomical considerations vary. For this reason, a common terminology is helpful when discussing individual lesions. Yaşargil et al. proposed a classification system based on whether the lesion is restricted to the insula (Type 3), part of the insula (Type 3A), or included in the adjacent operculum (Type 3B).^{18,19} In that classification system, insular lesions involving one or both of the paralimbic orbitofrontal and temporopolar areas are classified, respectively, as Type 5A or Type 5B.^{18,19} We found that this classification system failed to address many of the anatomical features relevant to surgery for insular gliomas, such as proximity to potentially functional areas. Additionally, it is difficult to use this classification to preoperatively predict EOR. We therefore proposed a classification system based on an anatomical split of the insula along the sylvian fissure and foramen of Monro, thereby dividing it into 4 parts (Zones I–IV) using preoperative high-resolution MR images.¹³ This approach allowed us to consider and describe each insular tumor in relation to 1) the perisylvian language network (above and below the sylvian fissure in the dominant hemisphere), 2) primary sensory and motor areas (commonly for Zone I or II gliomas), 3) Heschl's gyrus (Zone III gliomas), and 4) middle cerebral artery branches (particularly lateral lenticulostriate branches found within the suprasylvian region of Zone I). It is critically important that a classification system have little variability between examiners. We tested this by asking 3 clinicians at varying stages in their careers to rate a cohort of insular gliomas, and found a strong correlation among examiners (kappa coefficient 0.857).

We set out to determine if the zone classification was predictive of EOR based on the previously described EOR in our original series. We found no differences in EOR for any zone between these 2 series. In this current patient series, we therefore reconfirmed our prior observation that zone classification was predictive of EOR, with the highest EOR seen in Zone I and Zone IV tumors. We also showed that the zone classification appears to be predictive of short-term postoperative morbidity, with a modestly higher early complication rate seen in Giant and Zone I tumors, and lowest complication rates seen in Zone II and Zone IV tumors ($p = 0.03$). In this current series of patients, we identified a slightly higher rate of short-term face motor deficits, which likely corresponds to using a transcortical window of entry through silent portions of the face motor area for purposes of enhancing exposure. The rate of long-term morbidity continued to be minimal at 3.5% and virtually unchanged from our initial series (3.8%).¹³

To our knowledge, the combined experience of this and our previously published report represents the largest series of insular glioma resections. The Berger-Sanai classification system is robust with little interobserver variability, and appears to validate our original description using this classification to predict EOR. Even so, there are study limitations that must be considered. Although there was little interobserver variability between clinicians with varying degrees of clinical experience and expertise, the investigation remained a single-institution study. The adoption of this classification system with external clinical validation is a topic of future study.

Conclusions

Maximal safe resection of insular gliomas continues to be associated with improved patient outcome and acceptable morbidity. Our previously proposed classification system is highly reliable and predictive of insular glioma EOR and perioperative morbidity.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Hervey-Jumper, Li, Berger. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Hervey-Jumper. Critically revising the article: Hervey-Jumper, Berger. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Hervey-Jumper. Study supervision: Berger.

Supplemental Information

Companion Paper

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