The classic transopercular and transsylvian approaches are used to resect insular tumors laterally from the top to the bottom of the pyramidal insular lobe; we refer to both approaches as the transinsular cortex approach. Surgery proceeds through the insular cortex before entering the insula, and the tumor is then removed.1–4 The posterior insula, especially in patients with Berger-Sanai zone II tumors, is difficult to reach with either classic approach.5,6

Is there a new way for glioma surgery? Over many years of insular glioma surgery, we have found a new transfrontal isthmus approach for insular glioma surgery. The cerebral isthmus is a discrete strip of white matter between the peri-insular sulcus and the lateral ventricle. The cerebral isthmus seems to play a key role in the dissemination of insular gliomas from (and to) the insula and insula-related structures.7,8 Insular gliomas always extend into the frontal lobe via the anterior and/or superior isthmus (i.e., the spaces between the lateral surface of the ventricle, basal ganglia, and anterior and/or superior limiting sulcus). So, with the new approach, we first resect the frontal tumor and then enter the insular lobe through the enlarged isth-
mus. We resect the insular glioma by using an anterior-posterior rather than lateral-medial working angle. This approach is most suitable for treating giant insular gliomas with extensive frontal involvement. The extent of resection (EOR) for insular tumors and preservation of function are satisfactory, and the shortcomings of the classic lateral approaches are avoided.

Methods

We retrospectively included 59 adults with primary insular gliomas with at least Berger-Sanai zone I involvement who were treated at our hospital from 2011 to 2021. All patients underwent resection via a transfrontal isthmus approach. The frontal tumor was removed first. We then entered the insular lobe via the isthmus to remove the insular tumor, and we finally removed the temporal lobe tumor (if present). Pathological review was based on WHO guidelines. We excluded those patients with recurrent insular glioma, as well as those without Berger-Sanai zone I involvement. Our hospital ethics committee approved this study, and all patients (or their family members) gave written informed consent. All patients consented to the publication of their images.

Surgical Procedure

Patient Positioning

The patient is placed supine with the head tilted to the opposite side by about 15°–30° and slightly backward to render the superior limiting sulcus perpendicular to the ground. The goal is to resect the insular tumor from an anteroposterior or nearly anteroposterior direction (Fig. 1).

Localization of Functional Structures

All patients underwent preoperative functional MRI to localize the language and motor function networks. During the operation, intraoperative MRI and functional neuro-navigation were used to locate lesions and eloquent areas, and intraoperative motor-evoked potential monitoring was employed for motor function preservation. For patients with a tumor in the dominant hemisphere, we performed awake craniotomy (if needed) to localize the functional language networks. These details were reported previously.\(^9,10\)

Defining the Frontal Window for Entering the Insular Lobe

The anterior/superior insular window in the frontal lobe should allow full access to the insular lobe, especially the posterior insular point. Location of the window can be determined by using the junctions of the lines extending from the anterior and superior limiting sulci to the frontal cortex as the anterior and posterior borders of the frontal window (Fig. 2A). The lateral borders are lines medial to the superior frontal sulcus and lateral to the lateral fissure (excluding Broca’s area). In this manner, the frontal window normally fully exposes the insular tumor (Fig. 2B).

Identification of the Frontal Isthmus and Entry into the Insular Lobe

The cerebral isthmus is a strip of white matter between the peri-insular sulcus and lateral ventricle that connects the brain’s central core and its hemispheres. The cerebral isthmus can be divided into 3 segments: anterior, superior, and inferior. The frontal isthmus contains the upper part of the anterior isthmus and the anterior part of the superior isthmus (Fig. 3A), which is located between the frontal horn of the lateral ventricle and the anterior/superior limiting sulcus (Fig. 3B).

The frontal isthmus is a bottleneck connecting the frontal and insular lobes, and it is often widened by gliomas (Fig. 4). After the frontal tumor (lobe) has been resected, the insular glioma is resected through the widened isthmus. The anatomical marker for identifying the frontal isthmus during surgery is the frontal horn of the lateral ventricle. The head of the caudate nucleus is also identified along the outer wall of the lateral ventricle, as its lateral side is the frontal isthmus. The space between the lateral ventricle and the anterior-superior limiting sulcus is the frontal isthmus as well as the route to enter the insula.

Key Anatomical Markers and the Safe Frame for Insular Tumor Resection

The insular tumor is resected mainly from anterior to...
posterior. Surgery is performed in a safe space defined by several key markers. The first markers identified include the frontal horn of the lateral ventricle and the head of the caudate nucleus, which help surgeons to recognize the frontal isthmus and thereby enter the insular lobe. Then, after tumor resection, the lateral surface of the putamen is exposed laterally along with the head of the caudate nucleus. Tumor resection continues downward until the sylvian fissure can be used to identify the M1 segment of the middle cerebral artery (MCA). By tracing the MCA from distal to proximal, the surgeon can identify the lenticulostriate arteries (LLAs). The LLAs and the lateral surface of the putamen define the medial safe border for surgery (Fig. 5A). After resection of the anterior part of the insular tumor, the lateral border formed by vascular grid of the M2 segments is revealed. The inferior trunk of M2 is a good landmark for guiding resection of the inferior part of the tumor to the posterior insular point. The superior limiting sulcus is used as a reference marker for resection of the superior part of the tumor (Fig. 5B). For better preservation of the patient’s motor function, tumors near the posterior insular point are resected under electrophysiological monitoring.

A safe frame is composed of the peri-insular sulcus,
medial border, and lateral border (Fig. 5C). All surgical operations are performed under the safe frame formed by these anatomical markers in order to achieve anatomical resection of the tumor in the insular lobe.

EOR and Neurological Preservation

T2-weighted FLAIR imaging was used to classify the EOR of low-grade gliomas (LGGs), and T1-weighted enhancement was employed to evaluate resection of high-grade gliomas (HGGs). The EOR was evident on the last intraoperative MRI scan. Near-total tumor resection refers to ≥ 95% EOR for LGGs and 100% EOR for HGGs. Tumor volume was calculated with iPlan 3.0 software (Brainlab).

The follow-up evaluations for motor and language function were performed 2 weeks and 3 months after surgery.

Statistical Analysis

All statistical analyses were performed with SPSS software version 22.0 (IBM Corp.). The Spearman test was performed to analyze whether there was a correlation between EOR of the insular tumors and the angle between the lateral plane of the putamen and the sagittal line or width of the isthmus near the anterior insular point. A p value < 0.05 was considered significant.

Results

Patient Demographic Characteristics

We treated 35 men and 24 women with a mean (range) age of 44.3 (19–75) years. Twenty patients (33.9%) had HGGs and 39 (66.1%) had LGGs. Twenty-nine tumors were on the left side and 30 were on the right. The Berger-
Sanai classification indicated that the most common tumor type was giant glioma (67.8%), followed by involvement of zones I and IV (18.6%). Twenty-two cases were Yaşargil type 3A/B and 37 were type 5A/B. The average angle between the lateral plane of the putamen and the sagittal line was 33.53°, and the average width of the isthmus near the anterior insular point was 33.33 mm. Intraoperative diffusion-weighted imaging showed no cases of MCA- or LLA-related stroke among all patients. The patient characteristics are listed in Table 1.

### TABLE 1. Characteristics of the patients with insular gliomas

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (range) age, yrs</td>
<td>44.3 (19–75)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>35 (59.3)</td>
</tr>
<tr>
<td>Female</td>
<td>24 (40.7)</td>
</tr>
<tr>
<td>Side of tumor</td>
<td></td>
</tr>
<tr>
<td>Lt</td>
<td>29 (49.2)</td>
</tr>
<tr>
<td>Rt</td>
<td>30 (50.8)</td>
</tr>
<tr>
<td>WHO tumor grade</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>39 (66.1)</td>
</tr>
<tr>
<td>III+IV</td>
<td>20 (33.9)</td>
</tr>
<tr>
<td>Median (IQR) tumor volume, cm³</td>
<td>67.82 (57.64–92.19)</td>
</tr>
<tr>
<td>Median (range) EOR, %</td>
<td>100 (73.7–100)</td>
</tr>
<tr>
<td>Total resection</td>
<td></td>
</tr>
<tr>
<td>LGG</td>
<td>26/39 (66.7)</td>
</tr>
<tr>
<td>HGG</td>
<td>19/20 (95.0)</td>
</tr>
<tr>
<td>Berger-Sanai zone</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (5.1)</td>
</tr>
<tr>
<td>I+II</td>
<td>5 (8.5)</td>
</tr>
<tr>
<td>I+IV</td>
<td>11 (18.6)</td>
</tr>
<tr>
<td>Giant</td>
<td>40 (67.8)</td>
</tr>
<tr>
<td>Yaşargil type</td>
<td></td>
</tr>
<tr>
<td>3A/B</td>
<td>22 (37.3)</td>
</tr>
<tr>
<td>5A/B</td>
<td>37 (62.7)</td>
</tr>
</tbody>
</table>

Values are shown as number (%) unless indicated otherwise.

### Discussion

#### Individualization of the Frontal Insular Windows

The extent and position of the anterior-superior insular window of the frontal lobe are localized for the purpose of exposing the posterior insular point. The resection range can be designed by using the junction of the extention lines of the anterior limiting sulcus and the superior limiting sulcus at the frontal cortex as the anterior and posterior borders of the frontal window, as well as the medial-to-superior frontal sulcus and the lateral-to-lateral fissure (excluding Broca’s area), to ensure that the frontal window can be used to expose the insular tumor. The frontal tumor can be resected first in cases with frontal involvement, and most cases meet the criteria for insular tumor exposure. If exposure cannot be performed, part of the nonfunctional frontal area can excised to achieve satisfactory exposure. If the tumor is larger than this range, the tumor could be resected directly according to the tumor range.

#### Why Should We Enter the Insular Lobe via the Frontal Isthmus?

The cerebral isthmus is the white matter area located between the peri-insular sulcus and the lateral ventricle. For insular gliomas, the cerebral isthmus is one of the main white matter diffusion pathways through which tu-
Tumors spread to insula-related structures. When an insular tumor invades its related structures through the cerebral isthmus, the space between the limiting sulcus and the ventricle/basal ganglia increases; this means that the isthmus dilates. So, the enlarged cerebral isthmus may naturally provide a new frontal-route surgical corridor for the resection of insular glioma.

Over many years of experience with insular glioma surgery, we have found that resection of an insular glioma with large frontal invasion can continue along the surgical cavity of the frontal lobe, thereby entering the insula in a nearly anteroposterior direction. After entering the insula, we remove the insular tumor by referencing the appropriate anatomical safe frame markers. At this time, the functional opercular cortical structure lies outside the area of surgical manipulation. Thus, frequent/long-term awake craniotomy is not required to locate the functional opercular cortical structure. The pia mater of the insular lobe is not directly contacted; thus, damage to the functional opercular cortex is avoided. The tumor is not removed via the M2 grid, and the risk of vascular damage is low. Greater isthmus expansion means a wider path from the frontal to the insular lobes, thus aiding resection of insular lobe tumors in the anteroposterior direction. At this time, the tumor is removed along the long axis of the insular lobe, which can be fully exposed easily. Our new approach resolves the dilemma posed by posterior insular tumor exposure with the classic approach. Simon et al. also reported that resection of insular glioma through a frontal route tends to provide better results.11

FIG. 6. A: Preoperative axial, sagittal, and coronal contrast-enhanced T1-weighted MR images showing a left-sided insular tumor. B: Preoperative T2-weighted images showing the tumor in different sections. C: Postoperative T2-weighted images of the same section showing that the tumor was completely resected.

The Berger-Sanai classification indicates that almost all tumors with zone I involvement exhibit frontal invasion and dilation of the prefrontal isthmus. As reported in the literature, 75% of all insular gliomas were at least zone I tumors. Therefore, our approach is appropriate for at least 75% of patients with insular gliomas.12–14 If the
prefrontal isthmus is not enlarged enough, we could use the additional adjacent limiting sulcus to enter the insular lobe.

Classic Transinsular Cortex Approach Versus Transfrontal Isthmus Approach

Classic Transinsular Cortex Approach

The transopercular or transsylvian approaches (transinsular cortex approach) are proven classic approaches for maximal safe removal of an insular glioma. These two classic approaches remove insular gliomas laterally, i.e., from the top to the bottom of the pyramidal insular lobe via the insular cortex of the M2 vascular grid. The inferior central gyrus cannot be sacrificed during the transopercular approach, which compromises zone II exposure. In addition, Broca’s area cannot be sacrificed when the tumor is in the dominant hemisphere, which reduces satisfaction with exposure of the insular lobe. A tumor in the anterior part of the insula is easily exposed with the transsylvian approach, but the ends of the sylvian fissure are difficult to separate. Sometimes, the veins at the end of the sylvian fissure must be sacrificed, and the frontal and temporal cortices are pressed with a brain spatula. Frequent manipulation of the M2 vessels may trigger vasospasm and in turn ischemia and neurological dysfunction. When using the classic transinsular cortex approach to treat insular gliomas with extensive frontal lobe involvement, generally the surgeon must turn the patient’s head more contralaterally to facilitate access to both the deep frontal lobe and insular tumor. However, it is difficult to achieve an appropriate balance.

FIG. 7. Intraoperative pictures of landmarks during tumor resection. A: The frontal window is marked with a dotted circle on the cortex of the left frontal lobe. B: After resection of the tumor in the frontal lobe, the frontal horn of the lateral ventricle (LV) was exposed and the tumor in the frontal isthmus was resected, too. C: The anterior-inferior portion of the insular tumor was resected to reveal the MCA. The frontal horn of the LV was covered with a cotton patty. D: The LLAs (dotted circles) were carefully protected. E: The lateral surface of the putamen was revealed. F and G: After the tumor was debulked, the lateral border of the tumor was dissected according to the M2 segments of the MCA. H: The superior part of the insular tumor was resected along the superior limiting sulcus. I: The posterior part of the insular tumor was resected along the inferior and superior limiting sulci. The cortex of Heschl’s gyrus came into view behind the tumor around the posterior insular point. ACA = anterior cerebral artery; CN = caudate nucleus; ICA = internal carotid artery. Figure is available in color online only.
Positioning the transcortical approach, the transfrontal approach removes the tumor anteroposteriorly and enters the insula from the enlarged isthmus rather than through the insular cortex. After we enter the insular lobe, insular tumor resection can be performed on the basis of the anatomical safe frame structures.

The transfrontal approach for removal of insular tumors requires less electrophysiological monitoring than the transopercular approach because there is no need to locate the relatively non-functional part of the opercular cortex when approaching an insular tumor from the lateral side.3,5,21

Also, the new approach does not need difficult dissection of the sylvian fissure ends, which is necessary for zone II tumor resection with the transsylvian approach. Another main concern with tumors in zone II is damage to the deep located pyramidal tract.20 Because the inner border of the tumor is anteroposteriorly removed along the lateral boundary of putamen, the superior border should not proceed beyond the superior limiting sulcus. Thus, the risk of pyramidal tract damage is low. Zone II resection should be performed under electrophysiological monitoring, and bipolar coagulation should be avoided to minimize thermal damage to the pyramidal tract.3,5,21

The most lateral extrapial lenticulostriate perforator can be easily identified with the transfrontal isthmus approach. After the frontal tumor has been removed and the frontal lobe decompressed, the sylvian fissure is easy to separate. The sylvian fissure can then be entered, and the lateral LLA can be easily identified from the subarachnoid space. This is much safer than visualization of the lenticulostriate perforator through the tumor.22,23 The artery marks the medial resection limit because the LLA itself is a landmark for resection, and protecting the LLA is the key to avoiding stroke. There were no LLA-related or MCA-related strokes in this group, and the stroke rate in this group was lower than those of the transsylvian/cortical approaches reported in the literature.24

Important Landmarks When Entering the Insula via the Frontal Isthmus

It has been reported that the average width of the isthmus at the anterior insula point is about 10.8 mm.7 When a tumor invades the isthmus, the lesion is often tangential to the lateral wall of the frontal horn. The frontal horn of the lateral ventricle is easier to identify than the other neighboring structures. The frontal horn is a reliable landmark even in the presence of intraoperative brain shift. Therefore, the first step to resection of a frontal lobe tumor is often to go straight to the frontal horn in order to find a clear deep landmark. After opening the frontal horn of the ventricle, the surgeon must look for the head of the caudate nucleus along the anterolateral side of the frontal horn and continue outward to find the front border of the putamen. The frontal horn of the lateral ventricle, the head of the caudate nucleus, and the putamen are the medial landmark systems that enter the insula. The anterior limiting sulcus, the anterior insular point, the anterior part of the superior limiting sulcus, and the pia on the surface of the insula are the anterolateral markers that enter the insula.

Anatomical Landmarks During Insular Resection

After the insula has been entered via the isthmus in an anterosuperior-to-posteroinferior direction, the medial boundary of resection should be the lateral surface of the putamen or lateral LLA. The “nutmeg” appearance of the putamen aids boundary identification. Resection should not proceed beyond the lateral LLA when the tumor involves the putamen; excessive resection may cause severe and irreversible neurological dysfunction. The lateral boundary of resection is the insular pia; subpial tumor resection reduces the likelihood of blood vessel injury and vasospasm. Anatomical resection of the insula is achieved with subpial resection of the tumor to the entire peri-limiting sulcus.

Factors Associated With EOR and Functional Preservation

If an insular glioma is present (especially when the tumor has invaded into its relative frontal lobe), the isthmus widens and thus provides a generous window for entry and tumor resection via the frontal surgical cavity. If the anterior and superior isthmuses are widened, then the basal ganglia is displaced medially and the angle between the lateral surface of the putamen and the midsagittal plane increases, thereby providing a wide surgical space. We found that EOR of insular tumors and short-term functional preservation also increased as the angle increased. On T2-weighted imaging, the black basal ganglia against a white background (the ventricle and tumor) constitutes the “basal ganglia island sign.” An insular glioma with this sign is easy to resect with functional preservation. The sign tends to indicate a lack of involvement with the putamen.

Indications for and Limitations of the Frontal Isthmus Approach

All patients with primary insular glioma and at least Berger-Sanai zone I tumor involvement can undergo resection with this approach. The most suitable case is an insular glioma with a high degree of frontal lobe involvement and a larger working channel that naturally forms after resection of the frontal tumor. Giant insular gliomas are also suitable because large insular tumors are often at high risk for expansion of the isthmus, and such tumors are difficult to completely resect with the classic lateral approach.25 Our approach avoids the need to separate the ends of the sylvian fissure and/or to create a subcentral fistula to access zone II tumors. Some patients are reluctant to undergo awake craniotomy, and some are contraindicated because of preoperative cognitive dysfunction. For patients without dilation of the frontal isthmus, such as those with only Berger-Sanai zone II involvement, this approach is also achievable but may require resection of more normal frontal brain tissue.

Conclusions

The transfrontal isthmus approach changes the working angle from lateral to longitudinal and allows for safe removal of insular gliomas.
Acknowledgments

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References


Disclosures

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: Sun. Acquisition of data: Shu, Ma, Liu. Analysis and interpretation of data: Sun, Ma, Cheng. Drafting the article: Sun, Shu. Critically revising the article: Sun, Shu, Chen. Reviewed submitted version of manuscript: Cheng. Statistical analysis: Zheng. Administrative/technical/material support: Zhang, Zheng, Liu, Chen. Study supervision: Zhang.

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