Surgical resection of intrinsic insular tumors: complication avoidance

FREDERICK F. LANG, M.D., NANCY E. OLANSEN, P.A.C., FRANCO DEMONTE, M.D., ZIYA L. GOKASLAN, M.D., ERIC C. HOLLAND, M.D., PH.D., CHRISTOPHER KALHORN, M.D., AND RAYMOND SAWAYA, M.D.

Department of Neurosurgery, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Object. Surgical resection of tumors located in the insular region is challenging for neurosurgeons, and few have published their surgical results. The authors report their experience with intrinsic tumors of the insula, with an emphasis on an objective determination of the extent of resection and neurological complications and on an analysis of the anatomical characteristics that can lead to suboptimal outcomes.

Methods. Twenty-two patients who underwent surgical resection of intrinsic insular tumors were retrospectively identified. Eight tumors (36%) were purely insular, eight (36%) extended into the temporal pole, and six (27%) extended into the frontal operculum. A transsylvian surgical approach, combined with a frontal opercular resection or temporal lobectomy when necessary, was used in all cases. Five of 13 patients with tumors located in the dominant hemisphere underwent craniotomies while awake. The extent of tumor resection was determined using volumetric analyses. In 10 patients, more than 90% of the tumor was resected; in six patients, 75 to 90% was resected; and in six patients, less than 75% was resected. No patient died within 30 days after surgery. During the immediate postoperative period, the neurological conditions of 14 patients (64%) either improved or were unchanged, and in eight patients (36%) they worsened. Deficits included either motor or speech dysfunction. At the 3-month follow-up examination, only two patients (9%) displayed permanent deficits. Speech and motor dysfunction appeared to result most often from excessive resection, retraction and manipulation of the middle cerebral artery (MCA), interruption of the lateral lenticulostriate arteries (LLAs), interruption of the long perforating vessels of the second segment of the MCA (M2), or violation of the corona radiata at the superior aspect of the tumor. Specific methods used to avoid complications included widely splitting the sylvian fissure and identifying the bases of the perinsular sulci to define the superior and inferior resection planes, identifying early the most lateral LLA to define the medial resection plane, dissecting the MCA before tumor resection, removing the tumor subpially with preservation of all large perforating arteries arising from posterior M2 branches, and performing craniotomy with brain stimulation while the patient was awake.

Conclusions. A good understanding of the surgical anatomy and an awareness of potential pitfalls can help reduce neurological complications and maximize surgical resection of insular tumors.

Key Words • insula • brain neoplasm • resection • complication

Resection of intrinsic tumors of the insula remains a challenge for neurosurgeons because the insula is surrounded by critical vascular and neural structures.1, 4, 6, 9, 13, 20, 21, 23, 24 The insula lies deep with respect to the sylvian fissure and is covered by the frontoparietal and temporal opercula, which subserve important language, sensorimotor, and cognitive functions, particularly in the dominant hemisphere.9, 12 Located deep in relation to the insula are the basal ganglia, internal capsule, and thalamus.1, 6, 20, 23 Moreover, the insula is covered by and receives its blood supply from the MCA and has important relationships with the perforating LLAs.21, 23 Because of this complex anatomy, intrinsic tumors of the insular region, particularly those in the dominant hemisphere, are often considered to be resectable.3, 36 Instances of significant surgical morbidity, including hemiplegia, aphasia, and stroke, may result from dissecting the sylvian fissure, circumnavigating the MCA and its branches, violating the internal capsule, or injuring the LLAs.

Yaşargil25, 26 deserves credit for his pioneering work, which drew the neurosurgical community’s attention to resection of tumors in the insular region. He revitalized the idea, initially proposed in the mid-1900s, that most low-grade tumors of the insula spread within the confines of the anatomical limbic system and spared the deep mesial and neocortical structures. He demonstrated that insular tumors could be resected safely via the transsylvian approach.

Since Yaşargil’s seminal publications, interest in the resectability of these tumors has grown, and several recently published descriptions of the normal topography and vasculature of the insula have greatly added to our knowledge of the surgical anatomy.20, 21, 23, 25 Nevertheless, literature on the resection of insular tumors remains sparse, and only a few surgeons have reported their experiences.2, 3, 5–7, 15, 22, 26, 27 Although these works have provided valuable insight into complications and resection techniques, a systematic evaluation of the anatomical bases of postoper-
Resection of insular tumors

The purpose of this report is to review our experience with 22 patients with primary tumors intrinsic to the insular region and, during the past 4 years, have taken a particularly aggressive approach to these tumors. As our surgical experience evolved, we added cadaveric dissections and a careful review of the anatomical and clinical literature to maximize the extent of resection and avoid complications. The purpose of this report is to review our experience with intrinsic tumors of the insula with an emphasis on neurological dysfunction and potential avenues of avoidance has not been published.

During the past 10 years, we have surgically treated 22 patients with primary tumors intrinsic to the insular region and, during the past 4 years, have taken a particularly aggressive approach to these tumors. As our surgical experience evolved, we added cadaveric dissections and a careful review of the anatomical and clinical literature to maximize the extent of resection and avoid complications. The purpose of this report is to review our experience with intrinsic tumors of the insula with an emphasis on neurological complications. We determined the anatomical substrate underlying complications and defined potential methods of complication avoidance.

### Clinical Material and Methods

Thirty-three patients who underwent treatment of intrinsic insular tumors at The University of Texas M. D. Anderson Cancer Center between June 1, 1992 and June 30, 2000 were identified from the database of the Department of Neurosurgery. Of these 33 patients, two underwent stereotactic biopsies and nine underwent frontal or temporal resections without removal of the insular tumor component. The remaining 22 patients, all of whom underwent operations specifically directed at removing the insular component of the tumor, form the basis of this analysis.

Table 1 lists the clinical, histological, and radiographic features of the 22 cases. There were seven male and 15 female patients with a median age of 36 years (range 2–78 years). The most common presenting symptoms were seizures (64%), mild-to-moderate weakness/hemiparesis (32%), and dysphasia/dynomia (18%).

Clinical and pathological information had been prospectively entered into the Department of Neurosurgery database and were later retrospectively reviewed. Radiographic studies were reviewed for tumor features and tumor location. Tumors were classified as insular, temporal polar–insular, and frontal opercular–insular. The extent of tumor resection was determined in all cases by a comparison of tumor volume on postoperative MR images with tumor volume on preoperative MR images, which was performed using a computerized volumetric analysis technique, as previously described by Shi, et al.17 For nonenhancing or minimally enhancing tumors, the zone of increased signal on T1-weighted images was considered to represent the volume of the tumor. For enhancing tumors, the enhanced volume on T1-weighted images was used.

The surgical approach was prospectively recorded. In most cases, the surgeon’s impression of intraoperative events that may have influenced surgical outcome was also prospectively recorded. Operative reports were retrospectively analyzed for these features. The postoperative neurological outcomes of patients were prospectively recorded and confirmed by a retrospective review of all hospital records and physician notes. Immediate postoperative neurological function was determined during the first 7 days following surgery, and long-term function was determined between 3 and 6 months after surgery. Postoperative deficits were graded as mild (minimal deficit that is noticeable, but does not interfere with activity), moder-
Patients' long-term outcomes were determined at their 3- to 6-month follow-up clinical examinations.

Results

Clinical Features

Almost all tumors were gliomas; the one exception was a primitive neuroectodermal tumor (Table 1). There were 11 high-grade and 11 lower-grade tumors. All patients with GBMs presented with neurological symptoms, whereas all but one patient with an oligodendrogloma had seizures.

Tumors were located on the dominant hemisphere in 13 cases (59%). The insular lobe was the epicenter of the tumor in all cases. Eight tumors (36%) were purely insular, eight (36%) extended into the temporal pole, and six of 2 (27%) extended into the frontal operculum (Table 1).

Eleven tumors, all of which were GBMs or had anaplastic features (Table 1), enhanced heterogeneously on $T_1$-weighted MR images after administration of gadolinium. The border of the tumor, defined by the edge of the increased signal on $T_1$-weighted images, was sharp in 12 cases and diffuse in 10 cases (Fig. 1). In two cases (one patient with an anaplastic astrocytoma and another with an anaplastic oligoastrocytoma), the tumor violated the basal ganglia medially. In all other cases, the medial border was clearly defined. Magnetic resonance imaging revealed flow voids consistent with vessels on the medial aspects of many tumors; these were interpreted to be LLAs juxtaposed to the tumor edge (Figs. 1 and 2). The MCA on the tumor surface was often encased in tumor (Fig. 2).

Surgical Approach

In all cases, surgery was performed for oncological tumor removal. A transsylvian approach was used in all eight cases of purely insular tumors (Table 1). In the eight tumors with temporal extension, an anterior temporal lobectomy was first performed followed by a transsylvian resection of the insular component. In the six cases in which there was frontal extension, the frontal opercular portion of the tumor was resected first (transopercular approach). The insular tumor was then resected, usually after further dissection of the sylvian fissure.

Adjunctive Procedures to Surgery

In all cases, surgical navigation was aided by frameless computer-assisted stereotaxy in conjunction with intraoperative ultrasonography. Although computer-guided neuronavigation was advantageous for planning the craniotomy and for initially defining the tumor, its use was limited because brain shift occurred once the sylvian fissure was opened and tumor resection began. Although intraoperative ultrasonography was more helpful as resection continued, when deep and more critical regions were approached its reliability was also limited by interface signals.

In the 13 patients with tumors located in the dominant (left) hemisphere, an anesthetic technique and intraoperative language mapping were performed while the patients were awake in five cases (38%). In all five cases, speech arrest in the region of the Broca area occurred in response to cortical stimulation (typical parameters 60 Hz, 1-msec duration, 3–8 mAmp); however, in no case did stimulation of the insula result in speech arrest. In four of these five cases, intraoperative speech dysfunction arose during resection. In two of these cases, the speech alterations did not resolve, and the procedure was terminated before complete resection was achieved (see Extent of Resection). In the other two cases, an adjustment in retraction of the frontal operculum resolved the problem and allowed the resection to continue.

Cortical mapping of the motor strip was performed in 10 of the 22 cases. In our first cases, phase reversal was used while the patient was in a state of general anesthesia to identify the motor strip prior to tumor resection, which allowed us to locate and avoid disruption of the rolandic artery during tumor resection and limit the retraction of the motor strip. In our later experience, patients in a state general anesthesia were monitored continuously by using phase reversal; however, the value of this technique is unclear because no intraoperative or immediate post-op course could be over-come, or severe (deficit that significantly disables function). The patients' long-term outcomes were determined at their 3- to 6-month follow-up clinical examinations.
operative changes occurred in the few cases in which the method was used. Direct electrical stimulation of the deep white matter was used only intermittently. In one case, stimulation of the deep white matter at the superior pole of the tumor produced arm movement and resulted in termination of the resection (see Extent of Resection). When the patient was awake during craniotomy, the motor cortex was identified by electrical stimulation. Subcortical stimulation was used infrequently during tumor resection and patients were monitored primarily by observing their limb movements. In one awake patient, mild arm weakness developed during the operation and the procedure was terminated (see the following subsection).

Extent of Resection

Table 1 outlines the extent of resection in each case, as determined by quantitative volumetric analysis. In 10 patients, more than 90% of the tumor was resected (Figs. 1 and 3); in six patients, 75 to 90% was resected (Figs. 2 and 4); and in six patients, less than 75% was resected.

Enhancement on MR images was demonstrated in only two of the six patients in whom less than a 75% resection was achieved. When we reviewed the reasons for these incomplete resections (Table 2), we discovered two main categories. First were cases in which neurological dysfunction (with awake craniotomy) or stimulus-evoked changes (with general anesthesia) occurred during tumor dissection, prompting the surgeon to stop the operation to prevent significant functional deterioration. In these cases, the surgeon recognized intraoperatively that a less-than-complete resection had been accomplished because of the potential for neurological impairment. Second were cases in which resection was stopped because portions of the tumor displayed a more fibrous texture (typically in the superior or medial regions of the tumor), and the surgeon reported experiencing difficulty identifying the top of the tumor and/or its relationship to the corona radiata or perforating vessels (see Discussion). In these cases there was a discrepancy between intraoperative localization using frameless stereotaxy and ultrasonography, and the surgeon’s perception of the percentage of tumor resected.

Neurological Morbidity

No patient died within 30 days after surgery. Compared with their preoperative levels of neurological function, 14 patients (64%) experienced improvement or no change, and eight patients (36%) experienced increased deficits during the immediate postoperative period (Table 3). All patients who improved following surgery had displayed moderate to severe preoperative neurological dysfunction. Of the nine patients whose neurological functions was unchanged, seven had been neurologically intact before surgery and two had displayed mild preoperative deficits. In one of these nine patients, a postoperative hematoma developed that required evacuation, but did not change her neurological status. Of the eight patients (36%) who experienced postoperative focal neurological deficits, six had intact function before surgery and two had exhibited preoperative neurological dysfunction. All improved by their 3-month follow-up examination. Nevertheless, two...
patients (Cases 2 and 4) were considered to have permanent deficits that interfered with their daily activities. Therefore, for all 22 patients, the rate of permanent neurological dysfunction was 9%.

The focal postoperative neurological deficits were either motor or speech dysfunctions. Weakness occurred in four patients: two with hemiplegia, one with moderate hemiparesis, and one with hand/arm weakness. Both patients with hemiplegia displayed persistent, but moderate deficits at their most recent follow-up examination, whereas in the other two patients the deficits resolved. In one patient (Case 2) who had hemiplegia, coagulation of the LLA at the depth of the surgical cavity was thought to be the most likely cause of the postoperative problem because the surgeon reported persistent bleeding in the depth (medial portion) of the tumor cavity, which was controlled by coagulation of a clearly defined vessel and because an infarction in the internal capsule was noted on postoperative MR images. In the other case of hemiplegia the patient harbored a small tumor in the posterior insula (Case 4). The surgeon initially concluded that coagulation of the distal portion of an LLA was the cause of the deficit, but considering the location of the tumor, interruption of a long perforating vessel arising from the M1 portion of the MCA, which supplied the corona radiata, may have been responsible. In the other cases, edema within the motor fibers at the superior end of the basal ganglia was thought to be the cause because these deficits worsened initially and then resolved over several weeks. In the patient with arm and hand weakness, manipulation of the MCA was thought to be the cause because the leg was spared; however, in this patient the deficit began during dissection of the posterior aspect of the tumor (during awake craniotomy) and may have been related to the long perforating vessels that arose from the M1 segment.

Transient speech dysfunction occurred in six of the 13 patients with dominant-hemisphere tumors. All six patients displayed essentially normal speech at their 3-month follow-up examination. Craniotomy had been performed while five of these 13 patients were awake. Although direct electrical stimulation of the insula did not result in speech arrest in any of these patients, intraoperative speech dysfunction was observed in four of these five patients during tumor resection. In these cases, speech dysfunction appeared to be related to retraction of the operculum, particularly of the frontal operculum. For example, in Case 15, placement of a frontal retractor resulted in dysnomia, which resolved once the retractor was removed. This patient experienced postoperative word-finding difficulties 24 hours after surgery, probably as a result of edema or de-
layed ischemia. It was of interest that speech dysfunction commonly occurred while the neurosurgeon operated on the posterior aspect of the insula. Possible explanations for this observation are as follows: 1) the posterior insula was resected toward the end of the operation, after much of the MCA had been skeletonized and, therefore, was more susceptible to spasm; 2) retraction of the posterior temporal operculum could have caused dysfunction of the Wernicke area; or 3) the posterior insula may subserve speech function. Ojemann and Whitaker\textsuperscript{11} have reported that stimulation of the dominant posterior insula resulted in dysnomia. In contrast, Duffau and colleagues\textsuperscript{2} recently reported that speech arrest was induced by stimulation of the anterior insula during tumor surgery.

Discussion

Surgical resection of insular tumors remains a challenge. In a recently published pilot study, Ebeling and Kolthbauer\textsuperscript{4} concluded that the risk associated with operating on insular tumors outweighed the potential for radical resection and suggested that these tumors are best treated using biopsy and nonsurgical therapy. Although there is much debate about the role of radical resection in the treatment of gliomas, authors of several studies have suggested that aggressive surgery is important for their management,\textsuperscript{8,10,19} therefore, improving the extent of resection and reducing neurological complications are important goals in the treatment of insular tumors. To this end, we objectively analyzed the extent of resection by using volumetric analyses and determined the anatomical factors underlying surgically related neurological decline in a series of 22 patients with insular tumors.

Review of the Literature on the Extent of Resection and Postoperative Complications

Although early descriptions of operations on the insula, primarily those performed to treat epilepsy, can be found,\textsuperscript{12,13,15,18} Yaşargil et al.\textsuperscript{25,26} were the first to report on surgical resection of tumors located in the insular region. Their large experience, which included 57 insular and insular–opercular tumors and 23 frontal insular–temporal tumors, will not soon be matched. These authors emphasized that many of these tumors had been incorrectly diagnosed as frontal–temporal tumors and that surgical problems arose because implications of the tumors’ anatomical locations within the insular lobe were often unrecognized. Most of their patients had harbored benign tumors, presented with seizures, and were neurologically intact. Although 53% of the tumors were located in the left hemisphere and 67% were larger than 5 cm in diameter, radical resection presumably was achieved in all cases. The extent of resection, however, was not reported for each case. Eight (14%) of 57 patients with purely insular or insular–opercular tumors and one (4%) of 23 patients with insular and frontal–temporal pole tumors achieved a “moderate” outcome, which was defined as requiring assistance because of hemiparesis. Postoperative speech dysfunction was not reported.

Since the publications of Yaşargil and colleagues\textsuperscript{25,26} several case reports and smaller series have been published.\textsuperscript{2,5,7,15,22,27} Vanaclocha et al.\textsuperscript{23} described their experience with 23 insular region tumors treated in 28 operations. Nearly 75% were low-grade gliomas and 16 (70%) were located in the left hemisphere. Complete resection

### Table 2

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Resection (%)</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>65</td>
<td>stimulation of deep medial region caused movement of arm; operation was stopped</td>
</tr>
<tr>
<td>9</td>
<td>40</td>
<td>texture of tumor was firm in posterosuperior area; location of the Broca area was unclear &amp; the patient was in a state of general anesthesia</td>
</tr>
<tr>
<td>16</td>
<td>22</td>
<td>headache &amp; vomiting due to MCA manipulation, followed by speech dysfunction during awake resection; operation was stopped</td>
</tr>
<tr>
<td>19</td>
<td>50</td>
<td>tumor texture was firm and difficult to distinguish from white matter</td>
</tr>
<tr>
<td>21</td>
<td>55</td>
<td>speech dysfunction was apparent during awake resection; operation was stopped</td>
</tr>
<tr>
<td>22</td>
<td>56</td>
<td>texture of tumor became firm as its superior limit was approached; position of corona radiata was not clear</td>
</tr>
</tbody>
</table>

Fig. 4. Case 18. Preoperative (upper) and postoperative (lower) T\textsubscript{2}-weighted MR images. Resection was stopped because the patient exhibited speech dysfunction as the posterior aspect of the tumor was approached. Nevertheless, 75% of the tumor was resected.
was achieved in 20 (87%) of the 23 cases, based on estimates of tumor resection from MR images. Postoperative deficits included hemiparesis and dysphasia and occurred after six (21%) of the 28 operations. In the long term, all patients except one were living independently.

Zentner, et al., 27 reported a detailed analysis of 30 patients with insular tumors, including five purely insular cases, nine insular–opercular cases, and 16 insular–paralimbic cases. Overall, 100% resection was achieved in five cases (17%), more than 80% resection in 21 cases (70%), and less than 80% in four cases (13%), based on estimates from comparisons of preoperative and postoperative MR images. There were no deaths, but 19 patients (63%) experienced a complicated postoperative course. Hemiparesis occurred in four cases (13%). Aphasia occurred in three (21%) of the 14 cases in which tumors were located in the left hemisphere. Twelve patients exhibited a generalized decline in performance without focal deficits. In the long term, however, only three cases of focal deficit persisted. Zentner, et al., concluded that resection of insular tumors was feasible but that the risks of insular tumor resection were not insignificant.

Most recently, Duffau and associates 2 described their series of 12 resected insular tumors. All patients had harbored low-grade gliomas. Only one tumor (8%) was purely insular and only two (17%) were located in the dominant hemisphere. Four patients (33%) underwent complete resection of their tumor, six patients (50%) underwent subtotal resection (< 10 cm³ of tumor remaining), and two patients (17%) underwent partial resection (> 10 cm³ of residual tumor). Although analyses of postoperative MR images were performed by two neurosurgeons, the methods used to quantify the residual tumor were not described. There were no operative deaths, but seven patients (58%) displayed an immediate postoperative deficit. One of the two patients with dominant-hemisphere tumors experienced transient dysphasia, and six (60%) of the 10 patients with nondominant-hemisphere tumors exhibited motor deficits; however, only one patient (8%) displayed permanent weakness at the 3-month follow-up examination. These authors emphasize the role of direct brain stimulation to identify the internal capsule and avoid postoperative motor deficits.

Our experience with a series of 22 patients is comparable with the results of these other studies. Most of our patients presented with seizures, and 50% harbored low-grade tumors. A 75% or greater resection was achieved in five cases (17%), more than 80% resection in 21 cases (70%), and less than 80% in four cases (13%), based on estimates from comparisons of preoperative and postoperative MR images. There were no deaths, but 19 patients (86%) experienced a complicated postoperative course. Hemiparesis occurred in four cases (13%). Aphasia occurred in three (21%) of the 14 cases in which tumors were located in the left hemisphere. Twelve patients exhibited a generalized decline in performance without focal deficits. In the long term, however, only three cases of focal deficit persisted. Zentner, et al., concluded that resection of insular tumors was feasible but that the risks of insular tumor resection were not insignificant.

Most recently, Duffau and associates 2 described their series of 12 resected insular tumors. All patients had harbored low-grade gliomas. Only one tumor (8%) was purely insular and only two (17%) were located in the dominant hemisphere. Four patients (33%) underwent complete resection of their tumor, six patients (50%) underwent subtotal resection (< 10 cm³ of tumor remaining), and two patients (17%) underwent partial resection (> 10 cm³ of residual tumor). Although analyses of postoperative MR images were performed by two neurosurgeons, the methods used to quantify the residual tumor were not described. There were no operative deaths, but seven patients (58%) displayed an immediate postoperative deficit. One of the two patients with dominant-hemisphere tumors experienced transient dysphasia, and six (60%) of the 10 patients with nondominant-hemisphere tumors exhibited motor deficits; however, only one patient (8%) displayed permanent weakness at the 3-month follow-up examination. These authors emphasize the role of direct brain stimulation to identify the internal capsule and avoid postoperative motor deficits.

Our experience with a series of 22 patients is comparable with the results of these other studies. Most of our patients presented with seizures, and 50% harbored low-grade tumors. A 75% or greater resection was achieved in five cases (17%), more than 80% resection in 21 cases (70%), and less than 80% in four cases (13%), based on estimates from comparisons of preoperative and postoperative MR images. There were no deaths, but 19 patients (86%) experienced a complicated postoperative course. Hemiparesis occurred in four cases (13%). Aphasia occurred in three (21%) of the 14 cases in which tumors were located in the left hemisphere. Twelve patients exhibited a generalized decline in performance without focal deficits. In the long term, however, only three cases of focal deficit persisted. Zentner, et al., concluded that resection of insular tumors was feasible but that the risks of insular tumor resection were not insignificant.

Most recently, Duffau and associates 2 described their series of 12 resected insular tumors. All patients had harbored low-grade gliomas. Only one tumor (8%) was purely insular and only two (17%) were located in the dominant hemisphere. Four patients (33%) underwent complete resection of their tumor, six patients (50%) underwent subtotal resection (< 10 cm³ of tumor remaining), and two patients (17%) underwent partial resection (> 10 cm³ of residual tumor). Although analyses of postoperative MR images were performed by two neurosurgeons, the methods used to quantify the residual tumor were not described. There were no operative deaths, but seven patients (58%) displayed an immediate postoperative deficit. One of the two patients with dominant-hemisphere tumors experienced transient dysphasia, and six (60%) of the 10 patients with nondominant-hemisphere tumors exhibited motor deficits; however, only one patient (8%) displayed permanent weakness at the 3-month follow-up examination. These authors emphasize the role of direct brain stimulation to identify the internal capsule and avoid postoperative motor deficits.

TABLE 3

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Immediate Outcome</th>
<th>Cause of Dysfunction</th>
<th>Status at 3-Mo Follow Up</th>
<th>Status of Survival (mos postop)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>improved</td>
<td>—</td>
<td>stable</td>
<td>D (5)</td>
</tr>
<tr>
<td>2</td>
<td>hemiplegia</td>
<td>interrupted blood flow in perforating LLA</td>
<td>walks w/cane</td>
<td>A (48)</td>
</tr>
<tr>
<td>3</td>
<td>mild speech dysfunction</td>
<td>MCA manipulation</td>
<td>normal speech</td>
<td>D (5)</td>
</tr>
<tr>
<td>4</td>
<td>hemiplegia</td>
<td>interrupted blood flow in perforating LLA, &amp; perhaps in long perforating branch of M₂</td>
<td>walks w/cane</td>
<td>A (46)</td>
</tr>
<tr>
<td>5</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>D (28)</td>
</tr>
<tr>
<td>6</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>A (8)</td>
</tr>
<tr>
<td>7</td>
<td>NC, lethargy (48 hrs)</td>
<td>postop hematoma†</td>
<td>normal</td>
<td>A (36)</td>
</tr>
<tr>
<td>8</td>
<td>dysphasia, hemiparesis</td>
<td>frontal opercular retraction, corona radiata edema</td>
<td>normal speech; minimal hand weakness, but useful</td>
<td>A (37)</td>
</tr>
<tr>
<td>9</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>A (32)</td>
</tr>
<tr>
<td>10</td>
<td>improved</td>
<td>—</td>
<td>NC</td>
<td>D (5)</td>
</tr>
<tr>
<td>11</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>D (7)</td>
</tr>
<tr>
<td>12</td>
<td>improved</td>
<td>—</td>
<td>NC</td>
<td>A (25)</td>
</tr>
<tr>
<td>13</td>
<td>improved</td>
<td>—</td>
<td>NC</td>
<td>D (2)</td>
</tr>
<tr>
<td>14</td>
<td>improved</td>
<td>—</td>
<td>NC</td>
<td>A (24)</td>
</tr>
<tr>
<td>15</td>
<td>moderate dysphasia</td>
<td>frontal opercular retraction, MCA manipulation</td>
<td>normal speech</td>
<td>A (19)</td>
</tr>
<tr>
<td>16</td>
<td>mild dysphasia</td>
<td>frontal opercular retraction</td>
<td>normal speech</td>
<td>A (19)</td>
</tr>
<tr>
<td>17</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>A (14)</td>
</tr>
<tr>
<td>18</td>
<td>moderate dysphasia</td>
<td>frontal opercular retraction, dissection at back end of tumor, &amp; possible temporal retraction M₂ perforating vessel</td>
<td>normal speech &amp; movement</td>
<td>A (12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>minimal face/arm weakness</td>
<td>MCA manipulation, interrupted blood flow in M₂ perforating vessel</td>
<td>normal</td>
</tr>
<tr>
<td>19</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>A (12)</td>
</tr>
<tr>
<td>20</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>A (8)</td>
</tr>
<tr>
<td>21</td>
<td>mild dysphasia</td>
<td>frontal or temporal opercular retraction, MCA manipulation</td>
<td>normal speech</td>
<td>A (7)</td>
</tr>
<tr>
<td>22</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>A (3)</td>
</tr>
</tbody>
</table>

* A = alive; D = dead; NC = no change; — = not applicable.
† A second operation was performed, and the patient’s status returned to normal baseline.

F. F. Lang, et al.
Resection of insular tumors

Anatomical Characteristics Leading to Complications and Methods of Avoidance

Despite these promising results, it is clear that suboptimal resections are not uncommon and that the risk of neurological deficits, typically hemiparesis and dysphasia, is not insignificant. The primary goal of this analysis was to define more clearly the causes of incomplete resections and the reasons for postoperative hemiparesis and dysphasia so that techniques can be developed to maximize resection and minimize the risk of these deficits. As shown in Tables 2 and 3, it is not surprising that incomplete resections and postoperative speech and motor dysfunction were always attributable to interactions between the intrinsic features of the tumor growth pattern and the regional anatomy of the insula. In this context, as our experience evolved we continually compared our intraoperative findings with details of normal anatomy described in several recent cadaver studies and observed in our own cadaver dissections (Fig. 5). When combined with observations of other surgeons, our analysis confirmed that theTABLE 2. Variations of Insular Sulci, MCA, and LLA

<table>
<thead>
<tr>
<th>Insular Sulcus</th>
<th>MCA</th>
<th>LLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior</td>
<td>31</td>
<td>6.5</td>
</tr>
<tr>
<td>Inferior</td>
<td>23</td>
<td>6.5</td>
</tr>
<tr>
<td>Anterior</td>
<td>38</td>
<td>6.5</td>
</tr>
<tr>
<td>Posterior</td>
<td>23</td>
<td>6.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Insular Sulcus</th>
<th>MCA</th>
<th>LLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior</td>
<td>31</td>
<td>6.5</td>
</tr>
<tr>
<td>Inferior</td>
<td>23</td>
<td>6.5</td>
</tr>
<tr>
<td>Anterior</td>
<td>38</td>
<td>6.5</td>
</tr>
<tr>
<td>Posterior</td>
<td>23</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Incomplete Resections. One of the main problems with surgery on tumors in the insula is the frequency of inadequate resections. We were disappointed with the extent of resection in six of our patients, half of whom had low-grade tumors in which radical resection may have the most impact on increasing the patient’s long-term survival and preventing tumor transformation to a higher grade. Similarly, Zentner, et al., achieved complete resection with “absolutely no residual tumor” in only one of their cases of benign tumors.

In our study, the inability to identify the margin of the tumor was one of the main causes of incomplete resection (Table 2). Although neuronavigation with computer-assisted frameless stereotaxy and intraoperative ultrasonography were important adjunctive procedures in our cases, neither ensured complete resection because brain shift limited the former and dissection artifacts limited the latter. Although difficulties with defining the tumor margin may always be a limitation of resecting lesions with infiltrative edges, many insular tumors have sharp borders (at least on imaging studies) and, as pointed out by Yaşargil, et al., often expand within the confines of the insula. Therefore, based on our evolving experience, we currently use the intrinsic anatomy of the insula to help identify the tumor borders (Fig. 6). Specifically, as suggested by Yaşargil, splitting the sylvian fissure along its entire length is critical to achieving adequate exposure and helping to identify the insular apex, which is almost always the first part of the tumor encountered. This maneuver is necessary for locating the lobes of the insula (Fig. 6A); however, similar to Yaşargil, et al., we have found that the borders of the tumor can be further defined if the dissection of the sylvian fissure is carried over the insula into the superior and inferior perinsular sulci (Fig. 6B). The goal of this dissection is to reach the bases of these sulci. This helps define the superior and inferior planes of the tumor-infiltrated, expanded insular cortex. Because only the most aggressive tumors violate the pia-arachnoid of these peri-insular sulci, this dissection defines the superior and inferior borders of the tumor early in the operation. This method is most applicable for purely insular tumors, but even those tumors that infiltrate the opercula typically grow around the base of the sulci and do not cross the pia-arachnoid. Although the tumor may extend slightly more superiorly or inferiorly than the horizontal plane defined by the perinsular sulci, at least, these sulci are good landmarks for maintaining spatial orientation (Fig. 6D). Moreover, the bases of these perinsular sulci can be used to help define the parasagittal surgical plane that demarcates the depth of the resection. To delimit this parasagittal plane further, one can also rely on the position of the LLA, as suggested by Yaşargil and colleagues. This may be accomplished by identifying early in the operation the most lateral LLA that arises from the MCA, by dissecting the horizontal portion of the sylvian fissure until the first perforating vessel arising from the back of the MCA is identified (Fig. 6C). The plane defined by the bases of the perinsular sulci and the first perforating LLA delineates the deepest part of the dissection and allows the surgeon to orient the depth of the field (Fig. 6D). Once these planes are demarcated, a subpial dissection along the superior and the inferior perinsular sulci can be performed down to the base, and the tumor located within the confines of these planes can be removed (Fig. 6D).

Postoperative Neurological Deficits. It has been suggested that the insula exerts an influence over a variety of neurological functions. Although neuropsychological dysfunction has been reported to be associated with resection of tumors in the insula, the most devastating insults involve motor and speech dysfunction. Whereas Duffau and associates were able to cause speech arrest by stimulating the anterior insula, in our experience direct stimulation of the tumor-infiltrated insula did not elicit motor movement or speech arrest. Thus, although resecting insular tumors may result in deficits because specific functions reside within the insula, it is certainly arguable that avoidable complications are more related to disruption of the surrounding structures and their vascular supply (Fig. 5).

Opercular Retraction. The anatomical relationship of the frontal operculum to the insula affects the surgeon’s ability to reach the superior end of many tumors and may be an important cause of postoperative deficits. In their examination of 25 formalin-fixed brains, Ture, et al., found that the mean distance from the insular apex to the superior perinsular sulcus was 19.1 mm, with a range of 17 to 23 mm. The expansive nature of tumors further increases this distance. In our eight cases of purely insular tumors, the distance from the sylvian fissure to the top of the tumor, as measured on coronal MR image, ranged from 31 to 38 mm. Moreover, in our cadaver dissections, which were performed to simulate a transsylvian approach to the insula, the bases of the inferior and anterior perinsular sulci were more easily reached than the base of the superior perinsular sulci. In particular, to reach the point where the superior sulcus met the anterior sulcus (the anterior insular point) required significant angulation of the microscope or retraction of the frontal operculum between 2 and 2.5 cm (Fig. 5A). Thus, reaching the superior perinsular sulci via a transsylvian approach may require a fair amount of retraction of the frontal operculum. This retrac-
Fig. 5. Topography of an insular tumor and the anatomical basis for neurological dysfunction. The artist’s depiction of an insular tumor and the surrounding structures is supplemented by six photographs of the normal topography and vasculature of the insular region, as viewed during a transsylvian approach in six latex-injected cadaveric hemispheres (obtained from the Department of Anatomy, Saint Louis University, St. Louis, MO). A: Splitting the sylvian fissure reveals the insular apex (asterisk) and anterior and posterior insular gyri.
Resection of insular tumors

...tion may result in motor dysfunction or speech dysfunction if the tumor is in the dominant-hemisphere insula, because the Broca area is located near the anterior insula point. In addition, retraction may compress the M, branches of the MCA and result in frontal lobe ischemia. In at least two of our cases, repositioning the frontal retractors in patients who were awake during craniotomy restored normal speech function. Similarly, retraction of the posterior temporal lobe could also result in speech problems.

Neurological deficits caused by compression of surrounding structures, even if transient, may result in premature termination of the procedure before a complete resection is achieved (Table 2). To avoid this problem, Yaşargil, et al.,26 recommended abandoning retractors entirely and preferred using “dynamic” retraction and cotton balls to keep the fissure open. Another approach is to open the ascending sulcus of the sylvian fissure, but this did not help reach the more posterior aspect of the superior sulcus. An alternative, particularly for treatment of large non-dominant-hemisphere insular tumors with significant superior extension, is to modify the transsylvian approach to include resection of the frontal operculum. Obviously, this approach can be used for all tumors with frontal or temporal opercular extension; elective resection of the frontal operculum to gain access to purely insular tumors has been recommended and is a reasonable approach.2 In our opinion, performing craniotomy in an awake patient is most beneficial for avoiding complications related to manipulation of the structures around the insula. Using this technique the surgeon has warning of a potential problem.

From this vantage point, the normal insula looks like an asymmetrical pyramid with a long axis directed posteriorly. In a tumor-filled insula, these gyri are typically distorted and expanded. Even in the normal anatomy, significant retraction is required to reach the perinsular sulci (note retractor blade). B: The large (2–3 mm) M, branches pass over the insula on their way to becoming M, branches and supplying the cortex (arrowhead). The branching pattern of these vessels was unique in each of our cadavers, although an anterior group of vessels typically passed over the insular apex to supply the anterior insula, and an inferior segment supplied the posterior insula. These vessels are often encased in tumor. Also shown are medium-sized vessels that branched from the parent M, vessels and appeared to be end arteries (arrow). C: Multiple small (<1 mm) vessels, which arise from the undersurface of the M, branches (short M, perforating arteries), are exposed by the spatula and are the primary blood supply to insular tumors. These vessels are best approached subpially. D: The LLAs can be identified by dissecting along the anterior aspect of the insula, starting from the limen of the insula and following the M, branch. The first LLA usually appeared 1 cm from the insular surface in the cadaver (revealed by the spatula), but can be distorted in the presence of a tumor. E: Dissection of the LLAs along their course showed that they typically have multiple small branches arising from them and that they travel in a plane perpendicular to the M, segment deep in relation to the insula. F: Dissection deep with respect to the superior perinsular sulcus leads to the corona radiata (top arrow). Laying deep in relation to the midportion of the insula is the basal ganglia (middle arrow). The inferior perinsular sulcus leads to the uncinate fasciculus (bottom arrow); thus, the corona radiata is at risk during dissection of the superior margin of an insular tumor. G: Also shown in the artist’s drawing are the long perforating arteries arising from the M, segment. Disruption of this vessel can lead to hemiparesis because it supplies the corona radiata.

Middle Cerebral Artery Dissection. The MCA is particularly vulnerable during removal of an insular tumor because of several anatomical features. First, although the MCA is easily visualized on the surface of the insula during cadaver dissection (Figs. 5B and C; see also the study by Vanaclocha and colleagues22), insular tumors typically envelop the MCA and obscure it from view. This description of gross tumor pathology was noted by Yaşargil, et al.,26 and confirmed by Vanaclocha, et al.22 Moreover, in our cadaveric specimens the normal central insular sulcus was 0.5 to 10 mm deep, and thus it is easy to understand how tumors can bury a vessel within such a deep sulcus. This observation is also evident on MR images in which M, vessels are surrounded by tumor. This circumferential growth pattern places the MCA branches at considerable risk for inadvertent damage during tumor dissection (Figs. 2 and 4).

Second, there are multiple small perforating vessels that arise from the undersurface of the M, portion of the MCA and they provide the primary blood supply to insular tumors.20,26 These vessels can be torn from the parent vessel during tumor resection, placing the parent M, vessel at risk (Fig. 5C). Yaşargil, et al.,26 emphasized that each of these insular vessels must be individually coagulated to devascularize the tumor. Thus, even if the parent vessel is preserved, the manipulation required during the process of removing these small perforating vessels increases the potential for postoperative deficits due to MCA vasospasm. The occurrence of immediate postoperative vasospasm was suspected in several of our cases.

One way to avoid injury to the MCA branches during tumor dissection is to identify the MCA (the M, segment) medial to the limen of insula prior to its bifurcation and to follow all the branches (of the M, segment) over the surface of the insula and then to the frontal and temporal operculum. This often requires uncovering branches engulfed by tumor. Revealing the MCA branches before beginning tumor dissection makes the vessels less likely to be inadvertently disrupted. To minimize MCA manipulation and avoid tearing the many small insular vessels arising from the undersurface of the M, branches that supply the insula and tumor, subpial dissection is recommended. Subpial dissection allows one to coagulate and cut away the vessels from the parent vessel, which lies on the surface of the pia (Fig. 6D). Subpial dissection permits minimal manipulation of the parent vessel while affording maximum control of the small vessels.

Interruption of Perforating Vessels. All reports in the literature emphasize that the LLAs are an important source of complications because they supply the internal capsule. Although these vessels do not supply the insular cortex and do not communicate with the M, branches,20,22 Ture and associates26 have suggested that the external capsule is supplied by both the LLAs and the insular arteries (that is, the so-called short insular perforating vessels). In addition, radiographic studies often reveal flow voids on the medial side of insular tumors, which we interpret to be LLAs (Figs. 1 and 2), and our cadaveric specimens demonstrated multiple branches arising from the LLAs (Figs. 5D and E). Thus, it is probable that many insular tumors...
FIG. 6. An artist’s depiction of the method of surgical resection. A: Initial splitting of the sylvian fissure allows identification of the apex of the insula and the posterior extent of the tumor. The MCA vessels are often seen but may be encased by tumor. B: The superior and inferior perinsular sulci are dissected to their bases to define the superior and inferior aspects of the tumor. C: The MCA is dissected proximally until the first LLA is identified. This defines the deep plane of the tumor and protects the LLA from injury. The MCA is dissected in a proximal to distal direction. D: Once the three planes of the tumor are defined, the tumor is resected in a subpial fashion with preservation of M1 vessels and coagulation of small M2 branches.
Resection of insular tumors

parasitize the LLAs. Consequently, as Yaşargil, et al.,26 have clearly stated, the medial aspect of insular tumors may envelop these LLAs. Coagulation of LLAs has been reported to be a major cause of postoperative hemiplegia in all other surgical series2,21,25 and accounted for paralysis in at least one of our patients (Case 2). In our opinion, avoiding injury to the LLAs that supply the internal capsule is one of the most challenging aspects of insular surgery. Nevertheless, the LLAs may be preserved by identifying the most lateral LLA early in the operation by using the method described earlier (Fig. 6C). This perforating artery helps define the parasagittal plane through which these vessels will course and, in conjunction with the bases of the periinsular sulci, marks the depth of the resection, allowing the surgeon to avoid injury to these perforating vessels.24,26

Although it is emphasized less often in the literature, another source of vascular injury to motor fibers is the so-called long perforating arteries arising from M2 vessels. Ture and associates20 have shown that these long perforating arteries provide critical blood supply to the corona radiata. Yaşargil, et al.,26 have emphasized that these vessels most commonly arise from the posterior M1 branches. Because of their anatomical origin, coagulation of these long perforating arteries from the M1 segment may result in hemiparesis (Fig. 5G). In one of our cases, hemiparesis was thought to have resulted from interruption of blood flow through one of these perforating vessels. Unfortunately, in our transsylvian cadaver dissections, it was difficult to distinguish long M1 perforating arteries (supplying the coronal radiata) from short M1 perforating arteries (supplying the insula and tumor). In our surgical experience, identifying long M1 perforating arteries in the pathological situation was quite challenging. As pointed out by Ture and associates21 and Yaşargil, et al.,26 to avoid injury to these long perforating vessels, it is generally recommended that any large perforating branches, particularly vessels that do not taper and that arise from M1 branches overlying the posterior insula, should be preserved.

Internal Capsule. Several authors2,6,22 have noted the vulnerability of the internal capsule at the superior aspect of an insular tumor where the motor fibers pass over the basal ganglia. Because we could not determine the location of deep structures via the surgical view, we attempted to gain some orientation during our cadaver dissections by placing probes along different surgical axes and then cutting coronal sections through the probes (Fig. 5F). Whereas probing deep with respect to the inferior periinsular sulcus led to the uncinate fasciculus and probing into the middle of the insula led to the basal ganglia, probing deep with respect to the superior periinsular sulcus led into white matter fibers that pass over the top of the basal ganglia. Thus, the corticospinal tract is susceptible to direct injury just deep in relation to the superior periinsular sulcus, where it is not protected by the basal ganglia, and dissection along the superior margin of many insular tumors can result in hemiparesis.30

To avoid injury to this region, the superior periinsular sulcus can be an important surgical landmark because it often defines the upper limit of many tumors, as described earlier (Fig. 6B). If dissections are limited to the base of this sulcus, interruption of the corticospinal tract can be avoided. Difficulties arise, however, when the tumor extends beyond the base. For these cases, intraoperative subcortical electrical stimulation is probably the best adjunctive procedure to avoid complications. In one of our cases, direct stimulation of the subcortical white matter in this region led to movement of the patient’s arm and resulted in termination of the procedure. Daffau, et al.,2 have described their experience with electrical stimulation in 12 cases of insular tumors. They were able to identify the corona radiata or the internal capsule in all cases. Nevertheless, this is not a failsafe technique because patients still displayed neurological dysfunction postoperatively. In our experience, direct cortical and subcortical stimulation, as well as continuous phase-reversal monitoring, often do not provide adequate warning of ensuing neurological compromise, but merely report the loss of neurological function. For example, interruption of motor fibers could occur between direct brain stimulation trials. Moreover, even awake craniotomy may not be adequate, as a deficit may occur during an irreversible maneuver. Thus, although electrical stimulation and awake methods of surgery are valuable adjuncts for limiting motor deficits, a topographic and anatomical approach remains a necessary component of surgery on tumors of the insula.

Patient Selection

An important aspect of complication avoidance is patient selection. In this regard, Zentner, et al.,27 suggested that resection of insular GBMs in elderly patients was of little benefit, whereas resection of low-grade gliomas was potentially beneficial.

In our series, four (80%) of the five patients with GBMs were dead as of the last follow-up examination (Tables 1 and 3). Three of these four were older than 65 years old, and in only one case was the resection greater than 98% (Case 14). The one living patient, who has survived for 2 years, is young and underwent a 99% resection. These findings are consistent with a large retrospective study of 416 patients with GBMs who have undergone surgery at our institution during the past 5 years.8 This study demonstrated that increased survival was associated with resection, young patient age, a Karnofsky performance score of 70 or greater, and a nonnecrotic tumor. Most important, there was a progressive increase in survival following each incremental increase in the extent of resection, with the most significant survival benefits occurring in patients in whom resection was more than 95 to 98%. Thus, considering the significant risks associated with operating in this region, we agree with Zentner, et al.,27 that beyond a reduction in mass effect, surgery may provide little benefit for elderly patients with GBMs. We would suggest that for younger patients, aggressive surgery may be beneficial, assuming that neurological deficits can be avoided.

For patients with lower-grade gliomas, including low-grade astrocytomas (World Health Organization Grade II), oligodendrogliomas, and mixed gliomas, the role of radical resection is also controversial.10,11 Because no consensus exists for the best treatment of easily resected low-grade gliomas, it is not surprising that the dilemma is even greater for cases of complex insular gliomas, in which induction of neurological dysfunction is possible and achieving a complete resection is difficult. Obviously,
it was not the purpose of this study to resolve the question of whether resection of low-grade gliomas improves patient survival. Despite the fact that only one patient with a low-grade glioma died in our series and none of the other patients’ tumors progressed to a higher grade, the short period of follow up makes it difficult to draw meaningful conclusions from these observations. However, it is our general philosophy that the potential long-term survival in patients with low-grade tumors warrants this radical surgical approach, assuming that neurological function can be preserved. As described earlier, the results of our study of 416 patients with GBMs indicate that improvement in survival occurs with incremental increases in resection. Although application of these results to lower-grade tumors may not be justified, it can be argued that more extensive tumor resection will increase patient survival.

Nevertheless, any residual low-grade tumor is a nidus for growth and progression to a higher-grade lesion. In this context, we believe that for cases of nonenhancing low-grade gliomas, the entire area that is represented as an increased signal on T2-weighted MR images should be resected. In our series, 67% of the cases in which resection was less than 75% had tumor margins that appeared diffuse on T2-weighted MR images. Thus, in our opinion the optimal surgical candidates are patients in whom T2-weighted MR images display sharp tumor margins. For patients with diffuse low-grade gliomas on T2-weighted MR images, our bias is against surgery because it is unlikely that complete resection of the entire region that appears hyperintense on T2-weighted images can be achieved.

Conclusions

As was the case in earlier studies, our analysis focused on outcomes that are easily measured by the neurosurgeon, including the extent of resection and motor and language functions. Assessments of changes in neurocognitive and neuropsychological functions are certainly required to obtain a more comprehensive understanding of the impact of resection of intrinsic insular tumors. These types of analyses, as well as long-term follow-up studies in which the influence of surgical interventions on patient survival and tumor recurrence are assessed, should be the focus of future investigations. Nevertheless, the results of our study demonstrate that resection of intrinsic insular tumors is feasible. Although the risks are not insignificant, with a good understanding of the surgical anatomy and an awareness of potential pitfalls, neurological complications can be reduced and the extent of resection can be maximized.

References


Address reprint requests to: Frederick F. Lang, M.D., Department of Neurosurgery, The University of Texas M. D. Anderson Cancer Center, Box 442, 1515 Holcombe Boulevard, Houston, Texas. email: flang@mdanderson.org.