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CLINICAL ARTICLE

A series of 309 awake surgeries with transcortical approach for IDH-mutant low-grade glioma involving the insula: long-term onco-functional outcomes in 253 consecutive patients

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OBJECTIVE In low-grade glioma (LGG), awake surgery (AS) with intraoperative functional mapping minimizes morbidity while increasing the extent of resection (EOR). However, the actual role of AS for insular LGG resection through the opercula is still debated. The aim of this study was to investigate the long-term results after AS via a transcortical approach in patients with LGG within the insula, and to compare outcomes between pure insular gliomas and gliomas also invading other lobes.

METHODS Patients who underwent AS with functional-based resection via the opercula performed by the author for an isocitrate dehydrogenase–mutant grade 2 glioma involving the insula were selected (June 2002–January 2024). Functional and oncological outcomes were analyzed by comparing pure insular gliomas (group 1) versus insular-centered gliomas also involving the frontal and/or temporal and/or parietal lobes (group 2).

RESULTS In this consecutive cohort, 309 ASs were achieved in 253 patients (132 men [52.2%], mean age 37.5 ± 9.5 years). Among 214 patients (84.5%) with epilepsy before surgery, 55 had intractable seizures (21.7%). The preoperative mean Karnofsky Performance Scale score was 93.1 ± 7.4, with 206 patients (81.4%) working before surgery. The series included 147 left-sided gliomas (58.1%), with a mean preoperative tumor volume for both sides of 70.1 ± 50.1 cm^3 with 39 total tumors (15.4%) in group 1 and 214 total tumors (84.6%) in group 2. No patients except 2 (99.2%) had a permanent postoperative deficit (mean Karnofsky Performance Scale score 93 ± 6.6), with 199 patients returning to work (96.6%). Only 20 patients (7.9%) continued to suffer from intractable epilepsy. The mean EOR was 89.4% ± 8.4% (mean residual tumor volume: 9.6 ± 13.1 cm^3). There were 166 astrocytomas (65.6%) and 87 oligodendrogliomas (34.4%). Fifty-three patients (20.9%) received immediate postoperative adjuvant therapy and 49 patients (19.3%) underwent subsequent AS. The mean follow-up was 7.1 ± 3.9 years, with an overall survival rate of 80.2% (203 patients were still alive at last evaluation). More patients had an incidental glioma in group 1 ($p = 0.00009$), whereas there was a higher rate of intractable seizures ($p = 0.0019$) and a greater tumor volume before surgery in group 2 ($p < 0.00001$). Nonetheless, the EOR and the rate of postoperative intractable seizures were similar in both groups, with more patients in group 2 resuming work ($p = 0.001$).

CONCLUSIONS This is the largest homogeneous surgical experience of LGGs involving the insula that were resected through the opercula based on awake mapping. The results show a high percentage of functional preservation and return to work, with a high overall survival rate.

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KEYWORDS awake mapping; functional outcomes; insula; low-grade glioma; return to work; survival; tumor; epilepsy; functional neurosurgery

ABBREVIATIONS AS = awake surgery; DES = direct electrostimulation; EOR = extent of resection; IDH = isocitrate dehydrogenase; KPS = Karnofsky Performance Scale; LGG = low-grade glioma; OS = overall survival; RME = read the mind in the eyes; RTW = return to work.

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Low-grade glioma (LGG)—i.e., WHO grade 2 glioma—is a diffuse primary brain cancer that migrates within the CNS and ultimately progresses into a higher grade of malignancy if not treated.[1] Early and active therapeutic strategy, based on surgery as first treatment, led to a prolonged overall survival (OS); approximately 20 years in recent experiences.[2,3] Interestingly, in addition to an increase of the extent of resection (EOR), connectome-based resection performed by means of cortical-subcortical stimulation mapping in awake patients also permitted the preservation of an active quality of life, with a minimization of the risk of severe permanent neurological deficits (< 1%) as well as with a high rate of return to work (RTW)—between 93% and 97%.[3–5]

Remarkably, LGGs are frequently located within the insula,[6,7] an area that still represents a surgical challenge. Indeed, the incidence of new persistent deteriorations, mostly hemiparesis and/or language impairments, is between 2.7% and 17%, even in modern series conducted since 2010.[8–24] In this context, the actual role of awake surgery (AS) for the removal of insular LGG through the opercula is still a matter of debate. This is especially due to the fact that previous studies had the following limitations: 1) mixed asleep and awake craniotomies;[8–10,12,18,24,25] and/or 2) mixed high-grade and low-grade gliomas;[10–24] and/or 3) did not make the distinction between pure insular tumors and insular-centered tumors extended within the frontal and/or temporal and/or parietal structures;[11,12,14–18,21] and/or 4) mixed transsylvian and transopercular approaches;[9,23] and/or 5) did not evaluate the return to an active life, in particular RTW;[8–19,21–24] and/or 6) did not report a lengthy follow-up.[11,17,19,21,23–25]

Here, the first aim was to investigate the long-term oncological and functional results, including RTW, in a homogeneous personal experience based on AS performed in a systematic way via the transcortical approach in isocitrate dehydrogenase (IDH)–mutant LGG involving the insula. The second aim was to compare outcomes between pure insular gliomas and insular-centered gliomas also invading other lobes.

Methods

Study Design, Patient Selection, and Data Collection

From a database of 340 patients operated on by the author for an IDH-mutant WHO grade 2 insular glioma between June 2002 and January 2024, 253 cases with AS were selected. The following groups were excluded: 1) 41 patients who underwent surgery under general anesthesia, because they were operated on during the early experience of the author for a right-sided insular tumor (before the better understanding of the need to map more extensively the so-called nondominant hemisphere[4]); and 2) 46 patients with a wild-type glioma or a not otherwise specified glioma (see flowchart, Fig. 1).

In this retrospective analysis of a consecutive cohort, information regarding the following variables was extracted from medical records: demographics (sex and age); handedness; clinical manifestations (neurological deficit, preoperative seizure including possible intractable epilepsy [defined as failure of adequate trials of 2 tolerated, appropriately chosen and used, antiepileptic drug schedules—whether as monotherapies or in combination—to achieve sustained seizure freedom];[26] tumor characteristics (location and preoperative volume); EOR; postoperative tumor volume; histopathological results; neurological outcome; RTW; and follow-up duration.

This series of patients was split into 2 groups: group 1 included pure insular gliomas (Fig. 2), and group 2 included gliomas that also extended within the frontal and/or temporal and/or parietal lobes (Fig. 3).

Awake Surgery

The same connectome-based awake surgical approach through the opercula was performed in a systematic way, regardless of the side of the tumor, as my colleagues and I previously detailed.[27–30] Intraoperative functional mapping was performed using cortical and axonal direct electrostimulation (DES) in an asleep-awake-asleep protocol. After the opening under general anesthesia, the cortical surface was exposed, and the boundaries of the glioma were detected by intraoperative ultrasound. Once the patient was awake, electrical cortical mapping was performed using a bipolar electrode probe with 5-mm intertip spacing (NIMBUS Stimulator; Newmedic, France), delivering a biphasic electric current (60 Hz, 1-msec pulse width). The amplitude was progressively increased until a positive response from the ventral premotor cortex was obtained in all cases (namely, transitory speech articulatory disturbances regardless of the hemisphere), given that the lateral part of the precentral gyrus had been exposed in a systematic manner in order to select the optimal intensity of electrical stimulation (amplitude between 1.50 and 3 mA to allow identification of critical structures in all patients). These electrical parameters were not modified during the remainder of the intraoperative mapping.

Sensorimotor, visuospatial, language, cognitive, and emotional functions were mapped at the level of the cortex, especially by stimulating the opercula. Patients were asked to achieve real-time multitasking by combining several tests performed simultaneously during the transient presentation of a problem to solve on a computer screen, while enabling the surgeon to stimulate a specific brain structure in this time window. Tests were selected based on the relationships between the glioma and the surrounding pathways, and based on the wishes of the patient à la carte.[31] The possibility of switching from one combination of tests to another was also considered in order to increase the cognitive demand if needed, and depending on the various cortical and subcortical neural networks successively encountered during tumor removal around the surgical cavity.[32] In addition, multitasking was performed with a time constraint (every 4–5 seconds) throughout the resection, without any rest, to monitor sustained attentional processing. Such combinations of tests may include the following: motor tasks with possible evaluation of movement control and complex bimanual coordination by asking the patient to move several limbs simultaneously; a picture naming task; a semantic association task using the pyramids and palm trees test; reading tasks; a mentalizing task based on the recognition of mental states expressed by the eyes of the human face that uses an adapted version of the read the mind in the eyes (RME) test; a visual

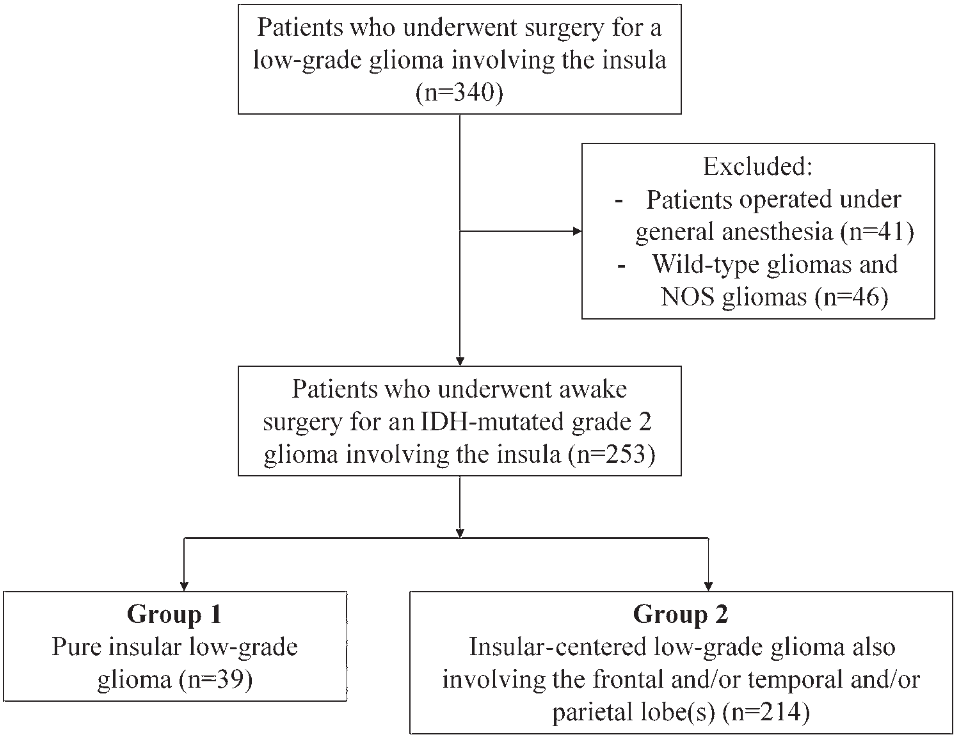

FIG. 1. Data flow diagram. NOS = not otherwise specified.

field monitoring task using a modified picture naming test with 2 pictures placed diagonally on the computer screen; a line bisection task; and a self-evaluation task performed using an index reflecting the level of confidence of the patient in his/her own response (ranging from 1 to 6, with 6 being the most confident) combined with another task (e.g., the RME test).[3,4]

In all cases, following completion of the cortical mapping the glioma removal was achieved using subpial dissection, while the patient benefited from the online neuropsychological monitoring.[32] A transopercular approach was performed (without splitting the sylvian fissure) before removing the insula by using a subpial technique.[27–30] In the depth, axonal DES mapping was achieved to pursue

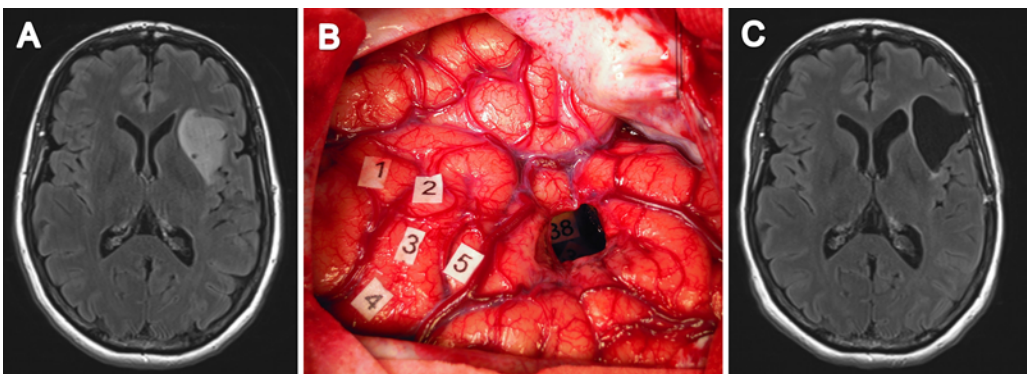

FIG. 2. Awake resection of a left pure insular LGG. **A:** Preoperative axial FLAIR-weighted MR image obtained in a 42-year-old right-handed woman, a nurse's aide, who experienced migraines that allowed the incidental discovery of a left insular LGG. Results of the neurological examination were normal. The tumor volume was 23 cm^3. **B:** Intraoperative view obtained after resection, which was achieved through the frontal operculum (pars triangularis), by preserving the pars opercularis (tag 5); the ventral premotor cortex and the primary motor cortex of the face (tags 1–4) were still critical for the function. Subcortically, the resection was also performed according to functional boundaries identified in the depth. Indeed, white matter stimulation enabled the detection of the left inferior fronto-occipital fasciculus, which elicited semantics paraphasias (tag 38). **C:** Postoperative axial FLAIR-weighted MRI (obtained 3 months after resection) demonstrating a total resection. The patient resumed a normal familial, social, and professional life within 3 months after surgery. A diffuse WHO grade 2 astrocytoma (IDH1-mutated, noncodeleted) was diagnosed, and no adjuvant treatment was administered. The imaging is stable with 8 years of follow-up, and the patient continues to enjoy an active life, working full time, with no symptoms (especially with no seizures, without antiepileptic drugs). Figure is available in color online only.

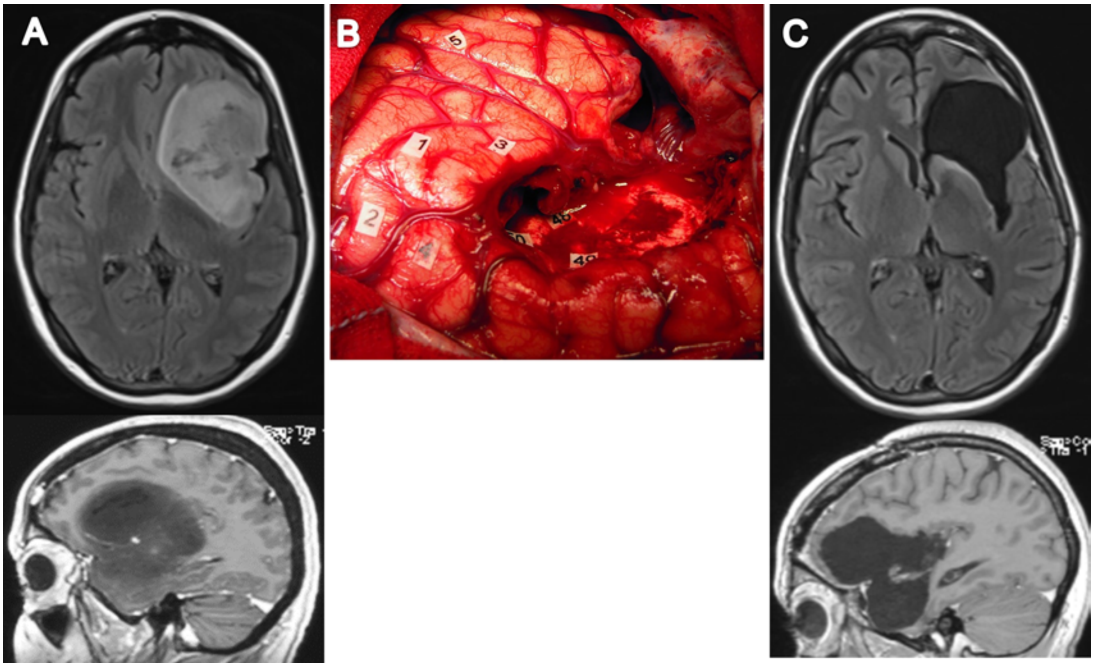

FIG. 3. Awake resection of a left insular-centered LGG also involving the orbitofrontal region and the anterior temporal lobe. **A:** Preoperative axial FLAIR-weighted (*upper*) and sagittal enhanced T1-weighted (*lower*) MRI obtained in a 28-year-old right-handed woman, who had not been able to work (in marketing) for 1.5 years due to intractable seizures (despite 3 antiepileptic drugs), which revealed a left insular-centered LGG also involving the orbitofrontal region and the anterior temporal lobe. The neurological examination revealed mild language deficit (especially with missing words). The tumor volume was 104 cm^3. **B:** Intraoperative view after resection, showing removal of the left inferior frontal gyrus, by preserving the ventral premotor cortex and the primary motor cortex of the face (tags 1–3) as well as the dorsolateral prefrontal cortex (tag 4) still critical for the language function, and with removal of the anterior temporal lobe. Subcortically, the resection was also achieved up to functional boundaries identified in the depth. Indeed, white matter stimulation enabled the detection of the left inferior fronto-occipital fasciculus, which generated semantics paraphasias (tag 48), the superior longitudinal fasciculus, which elicited anomia (tag 50), and the head of the caudate, which induced perseverations (tag 49). **C:** Postoperative axial FLAIR-weighted (*upper*) and sagittal enhanced T1-weighted (*lower*) MRI (obtained 3 months after resection) demonstrating a total resection. Because the patient did not experience seizures anymore, she resumed a normal familial, social, and professional life within 3 months after surgery, with an improvement of the neuropsychological examination results thanks to a postsurgical cognitive rehabilitation. The number of antiepileptic drugs was progressively decreased. A diffuse WHO grade 2 astrocytoma (IDH1-mutated, noncodeleted) was diagnosed, and no early adjuvant treatment was administered. Due to a delayed relapse of the tumor, chemotherapy was administered 5 years later and then radiotherapy was administered 12 years postsurgery. The patient continues to enjoy an active life, including working, with no symptoms. Figure is available in color online only.

glioma removal up to individual white matter tracts and deep gray nuclei critical for brain functions.[33] Photographs of cortical and subcortical responses (marked with sterile tags) were taken before and after resection (Figs. 2 and 3).

Postoperative Course

All patients received motor and/or speech and/or cognitive therapy following surgery. This functional rehabilitation was tailored to the results of the immediate postoperative neurological and neuropsychological assessment.

Clinical examination was performed postoperatively at 3 months and then every 6 months. Postoperative permanent neurological deficit was defined as a persistent deficit 3 months after surgery. The RTW status was also assessed. Postsurgical MRI was obtained within 24 hours after resection, at 3 months, and then every 3–6 months. The EOR and the possible residual glioma volume were calculated on the MRI study performed 3 months after surgery.

Resection subtypes were categorized as follows, in agreement with previously published literature:[3,34] partial resection (postsurgical tumor volume > 10 cm^3); subtotal resection (postsurgical tumor volume > 0 cm^3 and ≤ 10 cm^3); and total resection (no residual signal abnormality visible on FLAIR-weighted MRI).

Standard Protocol Approval and Patient Consent

The study was approved by an independent institutional review board of the ethical comity of research from the French National College of Neurosurgery. Written informed consent was obtained from the patients. Patients were not subjected to interventions outside the routine clinical management.

Statistical Analysis

Descriptive statistics were used to analyze the patient cohort, characteristics of the glioma, treatment details, and oncological and functional outcomes. Continuous variables were expressed as the mean ± SD, and categorical variables were expressed as numbers and percentage. To assess for differences between both groups, categorical variables

TABLE 1. Clinical, radiological, and histopathological characteristics of the total cohort and comparison between both groups

Demographics	Total Cohort No. (%)	Total Cohort Mean (SD)	Group 1 No. (%)	Group 1 Mean (SD)	Group 2 No. (%)	Group 2 Mean (SD)	p Value
Total population	253		39 (15.4)		214 (84.6)		
Sex							
Male	132 (52.2)		18 (46.2)		114 (53.3)		
Female	121 (47.8)		21 (53.8)		100 (46.7)		NS
Age in yrs		37.5 (9.5)		36.7 (10)		37.7 (9.4)	NS
First symptoms							
Epilepsy	214 (84.5)		24 (61.5)		190 (88.8)		
Szs under control	159 (62.8)		21 (53.8)		138 (64.5)		
Intractable Szs	55 (21.7)		3 (7.7)		52 (24.3)		**0.0019**
Intractable Szs & glioma location							**0.003**
FTI					40 (77)		
TI					9 (17.3)		
FI					3 (5.8)		
Incidental glioma	39 (15.4)		15 (38.5)		24 (11.2)		**0.00009**
Preop KPS score		93.1 (7.4)		95.4 (6.4)		92.7 (7.5)	**0.023**
Work before surgery	206 (81.4)		34 (87.2)		172 (80.4)		NS
Tumor side							
Lt	147 (58.1)		22 (56.4)		125 (58.4)		
Rt	106 (41.9)		17 (43.6)		89 (41.6)		NS
Preop tumor vol in cm^3		70.1 (50.1)		35.4 (32.5)		85.1 (49.1)	**<0.00001**

FI = fronto-insular; FTI = fronto-temporo-insular; NS = not significant; Szs = seizures; TI = temporo-insular.
Boldface type indicates statistical significance.

were compared using the Fisher's exact test, whereas continuous variables were compared using the Student t-test. The level of significance was 0.05 for all analyses.

Results

Clinical and pathological characteristics and therapeutic management are summarized in Table 1.

Patient Population

In this consecutive cohort, 309 ASs were achieved in 253 patients (132 men [52.2%] and 121 women [47.8%]), mean age 37.5 ± 9.5 years, including 210 right-handed patients (83%). The glioma was incidentally discovered in 39 cases (15.4%). Among 214 patients (84.5%) who experienced epilepsy before surgery, 55 had intractable seizures (21.7%). The mean preoperative Karnofsky Performance Scale (KPS) score was 93.1 ± 7.4, and there were 206 patients who were working (81.4%).

There were 147 left-sided (58.1%) and 106 right-sided (41.9%) tumors, with 39 pure insular gliomas (15.4%) (group 1) versus 214 insular-centered gliomas (84.6%) also invading other lobes (group 2): 121 fronto-temporo-insular, 46 fronto-insular, 45 temporo-insular, and 2 parieto-insular tumors. The mean preoperative tumor volume was 70.1 ± 50.1 cm^3.

Postoperative Outcomes

Functional, surgical, and oncological results are summarized in Table 2. The surgical approach was performed through 46 frontal, 45 temporal, 121 combined fronto-temporal, and 2 parietal corticectomies.

No patients except 1 (0.39%) had a permanent postoperative deterioration (one language deficit) after the first surgery. Only 20 patients continued to suffer from intractable epilepsy after surgery (7.9% of the full series); note that 11 of these patients had intractable seizures prior to surgery (among 55 patients with preoperative drug-resistant epilepsy—namely 20%). The mean KPS score was 93 ± 6.6 at 3 months after surgery. Within the year following surgery, 199 patients returned to work (96.6%).

The mean EOR was 89.4% ± 8.4%, with 32 total resections (12.7%), 141 subtotal resections (55.7%), and 80 partial resections (31.6%). The mean residual tumor volume was 9.6 ± 13.1 cm^3). Positive subcortical responses during intraoperative mapping were associated with incomplete resection related to a residual tumor within the white matter tracts ($p < 0.001$). No correlation was found between continued intractable seizures and the EOR or the residual tumor volume. There were 166 IDH-mutant astrocytomas (65.6%) and 87 oligodendrogliomas (34.4%). Fifty patients (19.8%) received early postoperative adjuvant chemotherapy in the year following surgery and 10 patients (3.9%) had early postoperative radiation therapy (3 had both treatments). Moreover, 49 patients (19.3%) underwent a second AS and 7 had a third surgery, with 1 patient who experienced a permanent hemiparesis after a third intervention: therefore, in the complete surgi-

TABLE 2. Surgical, histopathological, and functional results, and group comparison

Variable	Cohort		Group 1		Group 2		p Value
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)	
Total population	253		39 (15.4)		214 (84.6)		
Residual vol in cm^3		9.6 (13.1)		3.5 (5.2)		10.7 (13.8)	**<0.0001**
EOR, ratio		89.4 (8.4)		91.6 (9.9)		89 (8.1)	NS
Type of resection, FLAIR							
Partial	80 (31.6)		2 (5.1)		78 (36.4)		
Subtotal	141 (55.7)		25 (64.1)		116 (54.2)		
Total	32 (12.7)		12 (30.8)		20 (9.4)		**<0.0001**
Pathology per WHO 2021							
Astro grade 2, IDHm	166 (65.6)		29 (74.4)		137 (64)		
Oligo grade 2, codel	87 (34.4)		10 (25.6)		77 (36)		NS
Long-lasting neuro def							
S1 + S2	1/302 (0.03)		0/47 (0)		1/255 (0.4)		
S3	1/7 (14.3)		0/2 (0)		1/5 (20)		**0.044**
Chronic epilepsy	20 (7.9)		1 (2.6)		19 (8.9)		NS
Postop KPS score at >3 mos		93 (6.6)		94.6 (6.4)		92.7 (6.7)	NS
RTW	199/206 (96.6)		29/34 (85.3)		170/172 (98.8)		**0.001**
Early postop chemo	50 (19.8)		1 (2.6)		49 (22.9)		**0.001**
Early postop RT	10 (3.9)		1 (2.6)		9 (4.2)		NS
Alive pts; OS rate	203 (80.2)		35 (89.7)		168 (78.5)		NS

Astro = diffuse astrocytoma; chemo = chemotherapy; codel = 1p19q codeletion; IDHm = isocitrate dehydrogenase mutated; neuro def = neurological deficit; Oligo = oligodendroglioma; pts = patients; RT = radiotherapy; S1–S3 = surgery nos. 1–3.
Boldface type indicates statistical significance.

cal series comprising 309 ASs, the neurological morbidity rate was 0.8%. The rate of persistent deficit following the third operation was significantly higher than the rate of persistent deficit following the first and second operations ($p = 0.044$). Pathological examination revealed malignant transformation in 20/49 patients (40.8%) after the second surgery and in 2/7 (28.6%) patients after the third surgery.

The mean follow-up was 7.1 ± 3.9 years, with an OS rate of 80.2% (203 patients were alive at the last evaluation).

Comparison Between Both Groups

By comparing both groups, the proportion of incidental glioma was significantly greater in group 1 ($p = 0.00009$), whereas there was a significantly higher rate of intractable seizures ($p = 0.0019$) correlated to a lower mean KPS score ($p = 0.023$) before surgery in group 2—with a greater percentage of pharmaco-resistant epilepsy for fronto-temporo-insular tumors compared to fronto-insular and temporo-insular tumors ($p = 0.003$). The preoperative tumor volume was greater in group 2 ($p < 0.00001$).

Despite a similar EOR in both groups, the postoperative tumor volume was higher in group 2, with more partial resections ($p < 0.0001$). Although the rate of postoperative intractable seizures did not differ between the 2 groups, the proportion of patients who resumed professional activities after surgery was significantly higher in group 2 ($p = 0.001$) because 12 patients who did not work before surgery were able to work again (due to postoperative control of intractable epilepsy). Finally, the proportion of patients who had early postoperative chemotherapy was greater in group 2 ($p = 0.001$). There were no further significant differences regarding the other clinical, radiological, and pathological variables.

Discussion

Analysis of the Full Cohort

This is the largest ever published consecutive and homogeneous cohort of patients who underwent AS for an IDH-mutant LGG involving the insula via the opercula—moreover, with the comparison of pure insular glioma versus insular-centered glioma extended within the other lobes. Indeed, as mentioned, previous surgical series dedicated to insular glioma were heterogeneous because of mixing various grades of gliomas, asleep and awake patients, transsylvian and transcortical approaches, pure insular glioma, and gliomas also infiltrating peri-insular structures.[8–24]

Here, from a functional perspective, by using mapping-based resection through the opercula, the results show a high percentage of neurological preservation (0.8% of permanent deficits, mean KPS score of 93 ± 6.6 at 3 months after surgery), with an improvement of the quality of life in 35 patients (13.8%) who experienced preoperative intractable seizures and in whom seizures did not occur anymore after surgery. Furthermore, 96.6% of patients were able to return to work. The percentage of persistent deterioration in the present study is lower in comparison with modern series on glioma surgery, which reported between 2.7% and 17% of permanent impairment.[8–24] Nonetheless, it is worth noting that a lower rate of neurological morbidity was already described in experiences in which a transcortical approach was used; namely, < 6%[8,10,12,14,16,18,20,25] (compared to a transsylvian approach, with approximately 6%–17% of long-lasting deficits).[13,15,17,19,23] In addition, the proportion of persistent deficit was also lower in studies in which intraoperative awake mapping was used; namely, 3.5% of permanent deficits versus 15.7% when insular resection was achieved under general anesthesia (see a recent meta-analysis by Di Carlo et al., 2020).[35]

Moreover, in a cohort of patients who underwent asleep resection for a fronto-temporo-insular glioma with the aid of intraoperative MRI, the rate of RTW was only 45%[36] (vs 74%–89% in other experiences based on AS,[20,25] so in agreement with the results of the present series). Therefore, these findings strongly support the use of intrasurgical DES mapping with the transopercular approach, which results in more favorable neurological and professional outcomes for resection of insular LGG. Interestingly, such a surgical access via the opercula, which allows a better exposure of the insula,[37] can be taught in optimal conditions in specimens, to accelerate the learning curve of neurosurgeons.[38] Of note, in case of reoperations in this location, although the risk is not higher for a second surgery,[39,40] it seems that this risk may increase for a third surgery (1 patient among 7 experienced a permanent hemiparesis in the present series). This parameter could be helpful to elaborate the long-term therapeutic strategy, notably by taking into consideration the invasion of the white matter tracts by tumor cells as a limit of resection, given that the subcortical connectivity should be preserved to avoid large-scale neural disconnection.[40,41]

From an oncological perspective, stopping the resection when cortico-subcortical structures critical for brain functions have been reached is not incompatible with favorable long-term outcomes, as supported by a high OS rate of 80.2% with a mean follow-up of 7.1 ± 3.9 years.

Comparison Between Pure Insular LGG Versus Insular-Centered LGG Involving Other Lobes

There was a higher rate of incidentally discovered LGG in group 1, which is consistent with significantly lower tumor volumes for gliomas restricted to the sole insular lobe ($p = 0.00001$)—therefore compatible with a diagnosis at an early stage in the natural history of the disease. Conversely, larger LGGs that extend within the opercula, especially voluminous fronto-temporo-insular tumors, are more prone to elicit seizures, in particular intractable epilepsy (21.7% in this series). Unsurprisingly, pharmaco-resistant seizures were correlated to a lower mean KPS score in group 2 ($p = 0.023$), with a negative impact on professional activities; among 41 patients who did not work before surgery, 23 patients (56%) had chronic epilepsy—as previously described in this tumor location.[42] Remarkably, thanks to a similar EOR in both groups (even though the tumor volume remained higher after surgery in group 2), there was no longer any significant difference between mean KPS scores after resection of pure insular LGG versus insular LGG also involving other lobes. Indeed, the rate of postoperative intractable seizures no longer differed, with only 7.9% of patients who continued to experience chronic epilepsy following surgery; this explains why 12 patients in group 2 who did not to work before surgery were able to resume their professional activities after glioma removal.

Finally, there was a significantly higher rate of earlier chemotherapy in group 2 ($p = 0.001$). This is related to a greater residual tumor volume, due to the complexity of removing more extensive LGGs not restricted to the insula, because these tumors frequently invade the anterior perforating substance. In such cases there is a high risk of inducing stroke by damaging the lenticulostriate arteries[22,43,44] and/or the deep connectivity that is still critical for neural functions as identified by intraoperative axonal stimulation, representing a limit of compensatory mechanisms.[40,45] It is nevertheless important to acknowledge that this is a single-center series, with outcomes that could be difficult to generalize. Additional series are needed as external validation to confirm these results.

Conclusions

This is the largest surgical experience of IDH-mutant grade 2 gliomas involving the insula resected through the opercula based on awake mapping. The results show a high percentage of functional preservation (< 1% of permanent neurological deficit) and a high percentage of RTW (96.6%), with a high OS rate (80.2%, with a mean follow-up of 7.1 ± 3.9 years). AS via a transcortical approach should be considered in a more systematic way in insular-centered LGG.

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Disclosures

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

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