

# Initial Experience with Brain Mapping under Awake Craniotomy for Resection of Insular Gliomas of the Dominant Hemisphere

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## Abstract

**Background & Importance:** Insular lobe is located at the depth of sylvian fissure and is hidden by frontal, temporal and parietal lobes in close vicinity of internal capsule and basal ganglia and adjacent to the speech centers in the dominant hemisphere. Thus, radical resection of insular gliomas can be even more difficult. Brain mapping techniques can be used to maximize the extent of tumor removal and minimize postoperative morbidities.

**Case Presentation:** Patients with newly diagnosed gliomas of dominant insula were enrolled. The exclusion criteria were severe cognitive and/or psychological disturbances, those with difficulty in communication, older than 65 years, severely obese patients, those with difficult airways for intubation and severe cardiovascular or respiratory diseases. All patients were evaluated by contrast enhanced brain MRI, functional brain MRI and diffusion tensor tractography of language and motor systems preoperatively. All were operated under awake craniotomy with the same anesthesiology protocol. Intraoperative monitoring included continuous motor evoked potential, electromyography, electrocorticography, direct electrical stimulation of cortex and subcortical tracts. They were followed with serial neurological examination and imaging.

**Conclusion:** Seven patients were enrolled including 3 man and 4 women with mean age of 44.4 years. 5 patients suffered from low grade and 2 from high grade glioma. The most common clinical presentation was seizure followed by speech disturbance, hemiparesis and memory loss. Extent of tumor resection ranged from 73 to 100%. No mortality or major postoperative neurological deficit was encountered. Seizure control improved in 3/4 of patients with medical refractory epilepsy. One patient suffered from permanent deterioration of speech after surgery.

Brain mapping under awake craniotomy may be considered a safe method to maximize the extent of tumor resection, while preserving neurological function in patients with gliomas of the dominant insular lobe.

**Keywords:** Insular Glioma; Awake Craniotomy; Brain Mapping; Cortical Stimulation

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## Background and Importance

Gliomas are the most common primary tumors of brain (1,2). Currently, the optimal management of gliomas is based on maximal safe resection for patients suffering from high or low grade gliomas (3-5). Because of the infiltrative nature of gliomas, it is not always possible to achieve gross total resection (GTR) and preserving the function of the eloquent structures. GTR with a low risk of morbidity i.e. onco-functional balance is considered as the goal of surgery for all these patients (6).

Insular lobe is located at the depth of sylvian fissure and is hidden by frontal, temporal and parietal lobes in close vicinity of internal capsule and basal ganglia and adjacent to the speech centers in the dominant hemisphere (7). Radical resection of insular gliomas can be even more difficult.

Brain mapping techniques can be used to detect the eloquent areas of the brain intraoperatively; so that the

extent of tumor removal is maximized and postoperative morbidities are minimized (8-12).

In this article, we presented our preliminary experience with application of intraoperative functional mapping of motor and speech functions for surgical resection of cerebral gliomas.

## Case Presentation

### Patient Population

We have prospectively enrolled patients with gliomas of the dominant insular lobe without previous surgery and/or chemoradiation. Complete neurological, psychological and neuroradiological evaluations were done preoperatively.

Patients with severe cognitive and/or psychological disturbances, those with difficulty in communication, older than 65 years, severely obese patients, those with difficult airways for intubation and severe cardiovascular or respiratory diseases were excluded from this study.

### **Imaging and Neurophysiologic Tests**

The topography of the tumor was assessed on a preoperative MRI (T1-weighted images before and after Gd-enhancement, T2-weighted and FLAIR images in 3 orthogonal planes and volumetric sequences). MR spectroscopy was done for all patients to obtain a multipixel MR spectroscopic map of the tumor. We performed functional MRI (fMRI) for motor and language tasks for all patients, and interpreted fMRI images for hemispheric dominance and surgical planning. DTI tractography of the white matter fiber tracts involved in motor (corticospinal tract) and language functions (Arcuate fasciculus, inferior and superior longitudinal fasciculus, Uncinate fasciculus and inferior fronto-occipital fasciculus) was done for all of the patients.

Intraoperatively, direct electrical stimulation (DES) along with electromyography (EMG) and electrocorticography (ECoG) and motor evoked potential (MEP) were performed for neurophysiological monitoring.

We recorded ECoG continuously during the entire duration of surgery using subdural strip electrodes with 4–8 contacts from the cortex near the mapping area to monitor occurrence of electrical seizures and after-discharges during resection. We used EMG electrodes for face and limb muscle groups to detect motor activities. Continuous MEP recording was used in alternation with DES especially with regard to cerebral ischemia while working in the depth of sylvian fissure and around the perforator branches of middle cerebral artery.

Mapping with DES was done using a constant current generator delivering biphasic square wave pulses across 5mm spaced bipolar electrodes. Each point was stimulated 2-4 seconds (2 for motor and 4 for language areas) and at least 3 times. No point was stimulated two successive times to avoid occurrence of seizure. The intensity of stimulation ranged from 1.5 to 8 mA. We defined speech arrest when number counting was blocked and none of the below findings were present: 1- Subclinical seizure activity, 2- Simultaneous motor activity in the mouth and/or oropharynx, 3- Visible or perceived muscle contraction affecting speech.

Tumor resection was done alternately with subcortical stimulation. We stopped resection when no gross tumor was visible under microscopic observation, or a functional cortical area or fiber tract was encountered.

The extent of tumor resection was estimated by comparing the early postoperative FLAIR images with the preoperative images and was coined by percentile (Table 1).

### **Findings**

Seven consequent patients diagnosed to have cerebral glioma for the first time were enrolled including 3 men and 4 women with age range of 28-70 years (mean age=44.4). There were 2 cases of high grade and 5 cases of low grade glioma. The most common clinical presentation was seizure (5 patients) which was medically refractory in 4 patients. Other symptoms included mild speech disturbance (each in 3 patients), hemiparesis and memory disturbance (1 patient) (Table 1).

Extent of resection ranged from 73-100% (mean:86.2%). There was neither a mortality nor any major new morbidity (neurological deficit) in this series. Two patients experienced intraoperative seizure (one clinically evident and one recorded electrically) successfully managed by irrigation with cold saline. All the patients were presented in the neuro-oncology tumor board of our department to reach a consensus about adjuvant therapies. They were followed regularly with serial clinical examination and

neuroimaging. The follow-up period in this study ranged from 8 to 11 months (median 9.5 months). Only one patient with pre-existing speech problem, had worsening of speech that improved after 3 months postoperatively. Among 4 patients with medically refractory epilepsy, 3 had favorable seizure control during follow-up; one of them experienced no seizure during the 7 months postoperative period of follow up. Speech disorder remained unchanged in 1, worsened in 1 and became normal in one patient.

### **Illustrative Case**

A 30-year-old woman presented with temporal lobe epilepsy since 4 months ago that was controlled. She developed mild receptive dysphasia since one week before admission. A contrast enhanced brain MRI (Figure 1) was compatible with a suspected low grade glioma of the left insula. FMRI and DTI fiber tractography (motor and language) were done (Figure 2). During surgery, stimulation of the posteroinferior part of the tumor induced severe conductive aphasia. The tumor was grossly visible in this area under the microscope, but it was left behind due to positive response in multiple attempts of stimulation. Postoperative MRI confirmed gross removal of the tumor except for the postero-inferior part of it (Figure 3).

Postoperatively, the patient had significant deterioration of speech (receptive), but it started to resolve rapidly during the hospital stay. At 3 months of follow-up, her speech comprehension was similar to the preoperative status.

### **Discussion**

Brain mapping is used with the aim of localization and preservation of functional cortical and subcortical areas during resection of the maximum possible tumor mass. We would like to discuss our results and compare them with the related literature. We will also have a brief review on 1) how mapping helps to achieve better neurological outcome and 2) how much does it affect the extent of tumor excision.

#### **1-Improvement of Neurological Outcome**

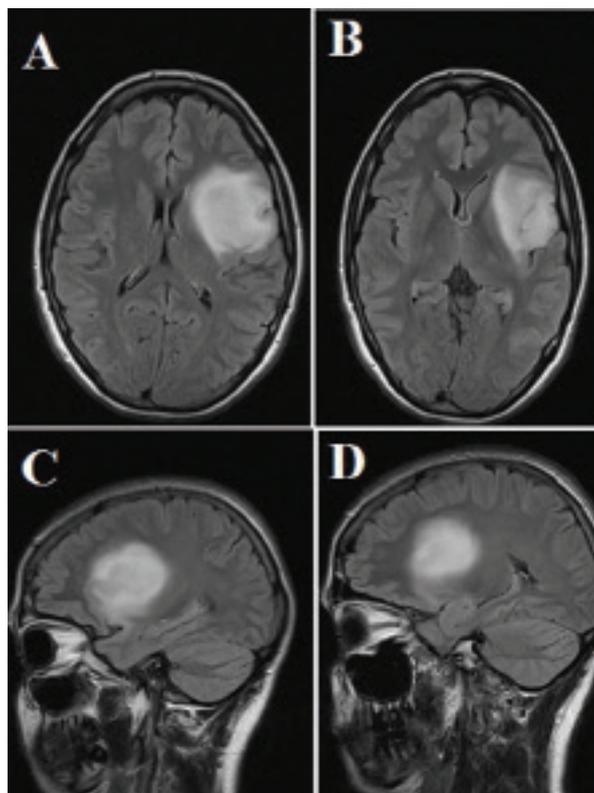
Our results show that no new neurological deficit occurred postoperatively and only one patient (10%) experienced deterioration of previously disturbed language function. This can convey a 90% precision of technique in this small series of cases in our hands.

Bertani G. et al. reported that permanent motor or speech deficits occurred in 2.3% of their cases. However, this figure increased to 7% among patients who had some degree of preoperative neurological impairments (8). They reported a neurological complication rate of 23% before administration of intraoperative mapping in their institute. Their study included heterogeneous cases with tumors at different locations of the brain, and from both dominant and non-dominant hemispheres. Some of their patients were operated under awake craniotomy and some under general anesthesia only.

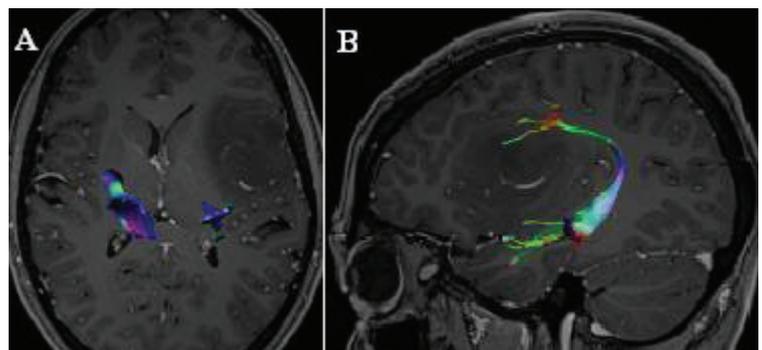
Duffau et al. reported the largest homogenous group of insular low grade gliomas of the dominant hemisphere (24 patients) which were all operated under awake craniotomy (6). 3 month after surgery, none of their patients suffered from new speech problem, and 6 of 7 patients with preoperative speech disturbance, improved significantly. Seizure control was also satisfactory in 83% of their cases after operation. The major difference between their study and ours is that our series included both low grade and high grade gliomas. It is known that low grade gliomas usually cause neurological deficit via

**Table 1. Comparing the Early Postoperative FLAIR Images with the Preoperative Images**

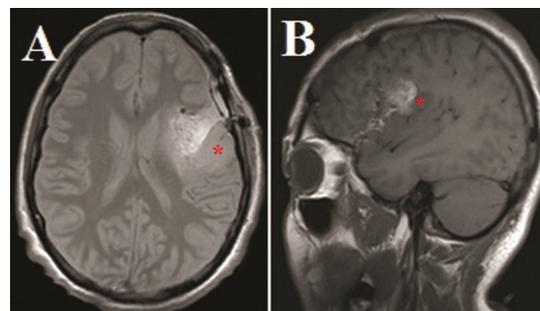
No.	Age	Sex	Clinical Presentation	Histopathology	Extent of Resection	Early Postoperative Neurological Deficit	Neurological Outcome (3 Months)
1	47	Male	Seizure (Medical Refractory)	LGG	100%	3 Episodes of Seizure	Significant Improvement of Seizure Control
2	58	Male	Hemiparesis, Speech Disturbance (Mostly Expressive)	HGG	92%	None	Deteriorated Expressive Aphasia, Hemiparesis Unchanged
3	30	Female	Seizure, Speech Disturbance, (Mostly Wernicke)	LGG	86%	Deteriorated Wernicke Aphasia	Speech Returned to Preoperative Status
4	70	Female	Seizure (Medical Refractory)	HGG	90%	Transient Global Aphasia	No Improvement in Seizure Control
5	43	Male	Seizure (Medical Refractory), Memory Disturbance	LGG	93%	Mild Dysphasia	No Seizure Occurred during Follow-up
6	28	Female	Speech Disturbance (Conductive)	LGG	88%	None	Nearly Normal Speech
7	35	Female	Seizure (Medical Refractory)	LGG	73%	None	Improvement in Seizure Control



**Figure 1. Axial (A&B) and Sagittal (C&D) Sections of Preoperative MRI; Showing a Left Insular Tumor with Involvement of the Left Opercular Cortex. Gd-enhanced MRI Revealed no Contrast Enhancement by the Tumor.**



**Figure 2. A: Axial DTI-fiber Tractography; Showing a Stretched Corticospinal Tract at the Postero-medial Border of the Tumor. B: Sagittal DTI-fiber Tractography Images Showing Close Proximity of the Postero-inferior Tumor Margin to the Temporal Speech Centre and the Arcuate Fasciculus.**



**Figure 3. Postoperative Axial Proton Density (A) and Sagittal FLAIR Images; Showing Tumor Residue at the Postero-inferior Border (Red Star).**

compression of the surrounding structures, while the high grade lesion tends to infiltrate the neighboring brain regions. Furthermore, progressive tumor growth and application of radiotherapy to the tumor bed may also reduce the chance of recovery of neurological function of the surrounding eloquent areas.

Like the above series, most of the postoperative neurological deficits were temporary in our series, and an interval of 3 months could be considered before judgment about permanency of the deficits.

As long as a 5 mm margin is preserved between the resection cavity and eloquent regions, permanent neurological deficits seem to be less likely (8,13).

It is said that temporary neurological deficits occur when tumor resection is carried close to subcortical white matter tracts, as a result of fiber tract edema or retraction injury (6,8). Ischemic insult to the corticospinal tract can be best avoided using continuous MEP monitoring which is very sensitive to vascular injuries. This is very crucial when dealing with insular tumors infiltrating between small perforating branches of MCA.

Most of the permanent complications after surgery of insular gliomas reported in the literature are due to vascular insult and stroke (6,14-20). According to Duffau et al. the main language pathways in the dominant hemisphere, run medial to insula but just lateral to the anterior perforated substance which embeds lenticulostriate perforator vessels. Thus, localization of these pathways acts also as a functional barrier to prevent damage to perforating arteries. This may explain lack of vascular injury in our series and the others who have used intraoperative mapping for resection of insular gliomas (6,8,21).

## 2- Extent of Tumor Removal

Since first description of insula by Johann C. Reil, it has been considered as a "no man's land" for many years (22). Due to close proximity of insula to motor, language and memory pathways (especially in the dominant hemisphere), insular gliomas were subjected to conservative policies such as "wait and see" or "biopsy and adjuvant therapy" until they grow very large or caused significant neurological morbidity for the patients (7). However, this strategy is suboptimal for treatment of gliomas, especially the LGGs in which the bulk of evidence show that extent of resection plays an important role in lengthening of progression free survival (7,21,23,24).

After advent of intraoperative brain mapping, surgical resection became feasible for insular gliomas even in those patients who do not have significant preoperative neurological deficits (43). Several studies have proven the positive impact of brain mapping on maximizing the extent of resection in gliomas (9, 24-29).

One proposed mechanism for enhancing extent of resection of dominant insular gliomas by intraoperative mapping is brain plasticity and functional reorganization of brain areas involved in important tasks (6,30). This has been previously demonstrated in gliomas of extra-insular locations (31). Based on such reorganization, lack of functional response during subcortical mapping implies that a permanent postoperative deficit is much less likely to occur (8), and makes it possible to continue tumor resection even in anatomically eloquent regions.

To our knowledge, there are few focused reports on the outcome of intraoperative mapping under awake craniotomy in patients with glioma of the dominant insula. Except one study (6), the others have generally reported the safety and efficacy of intraoperative brain mapping disregarding tumor histopathology and location. The major shortcoming of our study was, however,

inclusion of LGG and HGG in the same series, despite remarkable difference in the biological behavior of the two groups. This could be overcome in larger studies with stratification of patients according to the biologic features of their tumors.

## Conclusion

Gliomas of the dominant insula represent a challenging subgroup of cerebral gliomas. Their intricate location and proximity to a complex meshwork of functional cortical and subcortical pathways makes their resection challenging.

Based on the results of our series, application of intraoperative brain mapping is an appropriate method in preserving the neurological functions and maximizing tumor resection at the same time. This technique is well tolerated by most, but not all, patients and has no direct long-term complication. Optimal patients for this technique are young patients with LGGs of dominant insula who do not have intense preoperative neurological impairment.

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## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contribution

All authors of the present study helped in the whole processes from designation to collecting the data and preparing the manuscript.

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