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# Application of a Standardized Treatment Paradigm as a Strategy to Achieve Optimal Onco-Functional Balance in Glioma Surgery

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**Background** Gliomas, characterized by their invasive persistence and tendency to affect critical brain regions, pose a challenge in surgical resection due to the risk of neurological deficits. This study focuses on a personalized approach to achieving an optimal onco-functional balance in glioma resections, emphasizing maximal tumor removal while preserving the quality of life.

**Methods** A retrospective analysis of 57 awake surgical resections of gliomas at the National University Hospital, Singapore, was conducted. The inclusion criteria were based on diagnosis, functional boundaries determined by direct electrical stimulation, preoperative Karnofsky Performance Status score, and absence of multifocal disease on MRI. The treatment approach included comprehensive neuropsychological evaluation, determination of suitability for awake surgery, and standard asleep-awake-asleep anesthesia protocol. Tumor resection techniques and postoperative care were systematically followed.

**Results** The study included 53 patients (55.5% male, average age 39 years), predominantly right-handed. Over half reported seizures as their chief complaint. Tumors were mostly low-grade gliomas. Positive mapping of the primary motor cortex was conducted in all cases, with awake surgery completed in 77.2% of cases. New neurological deficits were observed in 26.3% of patients at 1 month after operation; most showed significant improvement at 6 months.

**Conclusion** The standardized treatment paradigm effectively achieved an optimal onco-functional balance in glioma patients. While some patients experienced neurological deficits postoperatively, the majority recovered to their preoperative baseline within 3 months. The approach prioritizes patient empowerment and customized utilization of functional mapping techniques, considering the challenge of preserving diverse languages in a multilingual patient population.

**Keywords** Glioma; Craniotomy; Surgical procedures, operative; Neuropsychological tests; Brain mapping.

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## INTRODUCTION

Over the past decade, our comprehension of glioma biology has advanced significantly. Gliomas are now understood as an invasive, persistent condition that progressively spreads along white matter pathways, evolving into more aggressive tumors over time, leading to associated health issues and eventual death [1]. The discovery of molecular markers has enhanced our understanding and management of this disease [2]. Surgery has emerged as the primary treatment for gliomas of all grades [3]. High and low-grade gliomas benefit from extensive tumor removal, which is linked to improved survival rates [3]. Recent research indicates that gliomas are often heterogeneous

[4], with some “low-grade” tumors containing high-grade elements, and current imaging techniques frequently underestimate the extent of tumor growth [5]. Moreover, evidence suggests that removing more than the visible tumor (supra-total resection) further enhances survival [6]. Beyond extending life expectancy, reducing tumor burden through surgery improves seizure management, alleviates symptoms caused by mass effect, enhances neurocognitive function, and increases the effectiveness of adjuvant therapies like chemotherapy and radiotherapy [7]. In recurrent cases, more extensive tumor removal is associated with better outcomes [8].

However, the main challenge in maximizing glioma resection is the risk of causing neurological deficits due to their diffuse infiltration and tendency to affect critical brain regions, often referred to as “eloquent areas” [9]. Recent studies using intraoperative techniques like direct electrical stimulation (DES) and functional MRI have challenged traditional notions of eloquent areas and identified additional brain regions crucial for neurocognitive functions [10]. While many gliomas were previously deemed inoperable, recent studies have shown that extensive tumor removal can be safely achieved without causing significant long-term neurological damage, using various methods to identify and avoid functional areas during resection [11]. Functional brain mapping, particularly with DES, is a cornerstone technique in our institution for glioma surgery. DES’s effectiveness and safety depend on its application’s precision and consistency [12]. Additionally, the closer surgical boundaries come to functional areas, the higher the risk of postoperative neurological deficits [13]. Therefore, the success of safe maximal resection relies heavily on two factors: the reliability of functional brain mapping techniques and the utilization of the brain’s neuroplasticity to its fullest potential [14].

In our institution, we adopt a personalized approach to enhance the onco-functional balance in glioma resections, ensuring patients achieve a satisfactory quality of life (QoL) and maximal tumor removal. This paper aims to outline our methods for achieving this optimal balance and evaluate the resulting clinical outcomes. Our approach involves implementing a standardized treatment protocol, wherein each patient’s onco-functional objectives of glioma resection are tailored according to various feedback components within this treatment framework.

## MATERIALS AND METHODS

We conducted a retrospective analysis of 57 instances of awake surgical resection of gliomas at our institution, which occurred between 2015 and 2023 at the National University Hospital in Singapore. These cases involved 53 patients, including 4 cases of recurrence. The surgeries were all carried out by the same surgeon, Kejia Teo, the senior author of this study. Approval to conduct the study was obtained from the appropriate institutional ethics review committee (IRB number 2019/00068). Informed consent was waived by committee.

The inclusion criteria encompassed patients who met the following conditions: 1) were diagnosed with any form of glioma and underwent treatment at our institution according to our specified treatment protocol; 2) underwent glioma resection guided by functional boundaries determined through intra-operative brain mapping using DES; 3) had a preoperative Karnofsky Performance Status score of 70 or higher; and 4) no evidence of multifocal disease was observed on preoperative MRI scans.

We comprehensively reviewed operative logbooks, clinical charts, and imaging records. Follow-up information was collected based on clinical notes over 90 days. All patients underwent a comprehensive MRI study, which included fluid-attenuated inversion recovery (FLAIR) and T2-weighted sequences, contrast-enhanced sequences, MR perfusion, and spectroscopy. These imaging modalities were utilized to guide preoperative planning. However, advanced techniques such as functional MRI and diffusion tractography imaging were not routinely employed for preoperative assessment. Additionally, stereotactic images were obtained for utilization with the intraoperative navigation system.

Regarding the extent of resection, total excision was defined as the absence of residual FLAIR signal in low-grade gliomas (LGGs) and the lack of residual contrast enhancement in high-grade gliomas (HGGs) by the Response Assessment in Neuro-Oncology (RANO) criteria. Subtotal resection was characterized by residual tumor volume of less than 10 $cm^3$, while partial resection was defined by residual tumor volume exceeding 10 $cm^3$. Consistent data entry and follow-up procedures were ensured because all surgeries were conducted under the supervision of the senior author of this study.

### Standardized treatment paradigm

The comprehensive treatment protocol followed by all patients is outlined in Fig. 1.

### Evaluation of patient expectations

All patients diagnosed with gliomas and deemed suitable for surgery undergo a thorough consultation with a specialized multidisciplinary team. During this consultation, the team evaluates the patients’ expectations in detail. Specifically, patients are questioned about their readiness to tolerate temporary neurological impairments post-surgery, including the specific deficits and their potential impact on their daily lives. Furthermore, the patients’ willingness to undergo intensive postoperative rehabilitation and their support system during

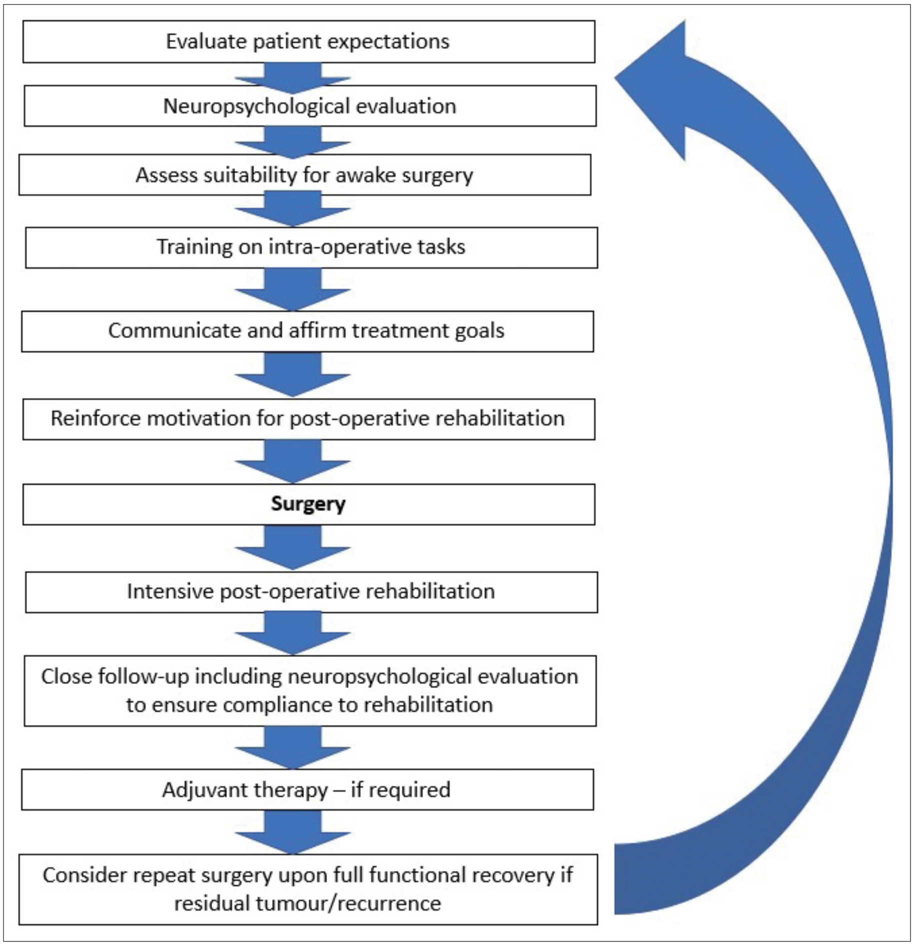


**Fig. 1.** Standardized treatment protocol for patients considered suitable for awake surgery.

recovery are carefully assessed.

Multiple sessions as needed educate patients on the concept of onco-functional balance in glioma surgery. Additionally, for bilingual/multilingual patients, discussions focus on preserving language function, language usage, and dominance. After the evaluation process, the treatment team and the patient align on the onco-functional treatment goal, and the importance and motivation for postoperative rehabilitation are emphasized.

As part of the routine assessment, a comprehensive medical history is obtained, which includes information about handedness, occupation, coexisting medical conditions, seizure history, and social and educational background.

**Neuropsychological evaluation**

Baseline preoperative neurological and neuro-cognitive functions are meticulously documented. A comprehensive neuropsychological evaluation is deemed essential due to the high prevalence of cognitive disturbances among patients preoperatively, even if they appear asymptomatic during their initial assessment upon presentation [15]. Our cognitive testing battery includes the Montreal Cognitive Assessment, which is utilized for screening gross cognitive deficits.

Specific testing is conducted across various cognitive domains, encompassing: 1) auditory, visuospatial, and sustained attention; 2) visuomotor and information processing speed; 3) visuospatial and visuoconstructional skills; 4) verbal and visual immediate and delayed memory; 5) confrontation naming and receptive language tests; 6) basic planning and organization; 7) auditory and visuospatial working memory; 8) mental set-shifting; 9) executive functioning; 10) praxis; and 11) emotional functioning.

This comprehensive battery of tests thoroughly assesses preoperative cognitive function across various domains.

**Assessment of suitability for awake surgery and preoperative training**

Patients undergo an assessment to determine if they are suitable for glioma resection under awake conditions. Patients considered suitable for awake mapping undergo a detailed neuropsychological assessment and training for preselected intraoperative tasks tailored to the lesion's location (e.g., counting, picture naming, semantic association, dual-tasking with a motor task). Tasks are translated into appropriate languages for bilingual patients who can tolerate a more extended surgery, with patients informed about the additional time and effort required for tasks in different languages. Training is performed closer to the day of surgery to avoid big fluctuations. For glioblastoma patients, the intraoperative tasks/training might be repeated just before surgery or a day before obtaining the latest baseline. Any task items deemed unreliable preoperatively excluded upon evaluation by the neuropsychologist. Those deemed likely to encounter potential anesthetic complications or exhibit challenges in cooperating with awake tasks (e.g., depressed consciousness, significant cognitive impairments, severe obstructive sleep apnea, obesity), as well as those with substantial preoperative neurological deficits, are not offered mapping under awake conditions.

The treating team (neuroanesthetist, neurosurgeon, neuropsychologist) provides patients with a detailed briefing on the intraoperative plan and sequence of events. Significant emphasis is placed on mentally preparing the patient, emphasizing the necessity of an awake procedure for optimal clinical outcomes, and addressing potential sources of patient anxiety, such as discomfort from positioning and perioperative pain management.

For patients unsuitable for awake surgery or unable to tolerate awake conditions intraoperatively, the option of performing surgery under asleep motor mapping conditions is offered. This approach may involve a more limited resection to minimize the risk of postoperative neurological deficits.

## Surgery

### Anesthesia

The awake craniotomy procedure is conducted following an asleep-awake-asleep approach. A dedicated team, including a neuro-anesthetist and a neuropsychologist, collaborates closely with the neurosurgeons throughout the operation. Initially, patients are placed under general anesthesia. Total intravenous anesthesia (TIVA) is administered using propofol target-controlled infusion (TCI) based on the Schneider pharmacokinetic model and remifentanil TCI based on the Minto pharmacokinetic model. The depth of anesthesia is monitored using the Bispectral Index (Medtronic, Minneapolis, MN, USA). A scalp ring block is then performed using bupivacaine 0.5% with a maximum dose of 2 mg/kg.

For patients undergoing awake brain mapping, once sufficiently anesthetized, a laryngeal mask airway (LMA) is inserted, and positive pressure ventilation is maintained. TIVA is discontinued during the awake phase, and the LMA is removed to enable speech and motor mapping. Depending on the lesion's location, patients are positioned in a full lateral position, with the head secured using a Mayfield-Kees clamp to ensure stability. Typically, a sizeable front-parietal-temporal craniotomy is performed to provide adequate exposure for positive mapping.

TIVA is resumed, and the LMA is reinserted once speech and motor mapping is completed, facilitating wound closure. For patients undergoing motor mapping under asleep conditions, standard general anesthesia using TIVA and endotracheal intubation is maintained throughout the procedure.

### Motor mapping

To locate M1, anodal high-frequency monopolar stimulation was initially employed, utilizing a train-of-five monophasic pulse with a pulse duration of 0.5 ms, an interstimulus interval of 3 ms, and a repetition rate of 1 Hz. If M1 cannot be located using this method, adjustments to stimulation parameters may be made, as described by Bertani et al. [16].

Following M1 localization, a subdural strip is positioned over M1 for motor evoked potential (MEP) monitoring of the corticospinal tract (CST) and electrocorticography to monitor for after-discharges and electrographic seizures. The motor threshold utilized for monitoring is the lowest intensity that elicits a reproducible MEP in the upper limb, which varies for each patient. During tumor resection, cathodal stimulation is employed for subcortical mapping of the CST.

### Mapping of language and other tasks

During awake brain mapping, low-frequency bipolar stimulation was utilized, employing parameters of 60 Hz, biphasic pulses with a total duration of 1 ms, and a probe featuring 1 mm tips spaced 5 mm apart. The current intensity began at 1.5 mA.

Stimulation initially targeted the ventral pre-motor cortex to achieve speech arrest. The working current employed was the minimal intensity necessary to induce anarthria without triggering epileptiform activity. This same intensity was used for subsequent language assessment during the operation. A site was deemed eloquent when an error was reproduced from at least 2 out of 3 stimulations at that site, with consecutive stimulations of the same site avoided to prevent inducing language errors.

Intraoperative tasks, such as language assessments including naming and semantics, praxis, visual field evaluations, and mentalizing tasks, were selected based on identified functional boundaries for lesion resection, contingent on the lesion's location and extent.

### Tumor resection

A subpial dissection technique is employed to remove intra-axial lesions, utilizing noneloquent cortical windows mapped as nonfunctional using DES. This approach allows access to subcortical structures, with excision boundaries determined by functional structures as delineated by DES.

During the asleep phase, mapping of the CST is conducted using monopolar probes with anodal polarity for cortical areas and cathodal polarity for subcortical structures, with parameters similar to those utilized for identifying M1 as previously described. Ice-cold saline is consistently available for irrigation in the surgical field during intraoperative seizures or after-discharge detection on electrocorticography.

**Postoperative care**

Patients underwent intensive speech, cognitive, and physical therapy delivered by a dedicated multidisciplinary rehabilitation team for at least 3 months. Emphasis was placed on reinforcing compliance with the rehabilitation process, with neuropsychological support to optimize motivation for participation. Approximately 3 months after surgery, patients will undergo a postoperative neuropsychological evaluation, which assists in determining their readiness to resume work or school activities.

Adjuvant therapy, if deemed necessary, was administered after a satisfactory postoperative recovery, following discussion at a multidisciplinary tumor board. Postoperative MRI, consistent with preoperative sequences, was conducted for all patients at 3 months.

For patients experiencing recurrence or those with less than subtotal resections, repeated resection would be offered once the patient had completed recovery from sustained neurological deficits.

## RESULTS

We examined 57 cases of awake surgical resection for gliomas involving 53 patients, including 4 cases of recurrence (all male patients). The average age of the patients at the time of surgery was 39 years, ranging from 15 to 62 years. Sex distribution showed that 30 patients were male (55.5%) and 23 were female (44.5%). The majority of patients were right-handed (91.2%), with a smaller proportion being left-handed (5.3%) or ambidextrous (3.5%) (Table 1).

Over half of the patients (52.6%) reported seizures as their chief presenting complaint. Other complaints included motor weakness (14%), headache (5.3%), and altered mental status (1.8%). Preoperatively, most patients had reasonable seizure control (54.4%), while some had poor control (12.3%), and others did not experience seizures (33.3%).

Tumor distribution was almost evenly split between the right and left sides of the brain (43.9% and 56.1%, respectively). The frontal lobe was the most commonly affected brain area by

**Table 1.** Patient demographics

| Demographic/disease characteristic | Cases (n=57) |
|---|---|
| Age (yr), mean (range) | 39 (15–62) |
| Sex | |
| Male | 30 (55.5) |
| Female | 23 (44.5) |
| Handedness | |
| Right | 52 (91.2) |
| Left | 3 (5.3) |
| Ambidextrous | 2 (3.5) |
| Chief presenting complaint | |
| Seizures | 30 (52.6) |
| Altered mental status | 1 (1.8) |
| Headache | 3 (5.3) |
| Motor weakness | 8 (14.0) |
| Unsteady gait | 1 (1.8) |
| Asymptomatic (incidental) | 1 (1.8) |
| Multiple symptoms | 13 (22.8) |
| Preoperative seizure control | |
| Good | 31 (54.4) |
| Poor | 7 (12.3) |
| Not applicable | 19 (33.3) |
| Side of tumor | |
| Right | 25 (43.9) |
| Left | 32 (56.1) |
| Predominant brain areas involved in tumor | |
| Frontal | 21 (47.4) |
| Temporal | 7 (12.3) |
| Insula | 12 (21.0) |
| Parietal | 5 (14.0) |
| Cingulum | 2 (3.5) |
| Basal ganglia | 1 (1.8) |
| Multiple lobes | 9 (15.8) |
| Tumor type | |
| HGG | 14 (24.6) |
| IDH mutant | 4 (28.6) |
| IDH wild type | 10 (71.4) |
| LGG | 43 (75.4) |
| IDH mutant | 38 (88.4) |
| IDH wild type | 4 (9.3) |
| Undifferentiated | 1 (2.3) |
| Tumor histology | |
| Astrocytoma | 32 (56.1) |
| Oligodendroglioma | 12 (21.0) |
| Glioblastoma | 11 (19.3) |
| PLNTY | 1 (1.8) |
| LGG (undifferentiated) | 1 (1.8) |

Values are presented as n (%) unless otherwise noticed. HGG, high-grade glioma; IDH, isocitrate dehydrogenase; LGG, low-grade glioma; PLNTY, polymorphous low-grade neuroepithelial tumor of the young the tumor (47.4%), followed by the insula (21.0%) and temporal lobe (12.3%). Regarding tumor type, the majority were LGGs (75.4%), with a smaller proportion being HGGs (24.6%). Astrocytoma was the most common tumor histology (56.1%), followed by oligodendroglioma (21.0%) and glioblastoma (19.3%) (Table 1).

In all 57 cases, positive mapping of the primary motor cortex (M1) was conducted during awake surgical resection of gliomas, with an average current of 11.9 mA utilized, ranging from 2 mA to 30 mA (Table 2). Continuous monitoring of MEP was carried out in 56 cases, alongside positive subcortical mapping of the CST in 52 cases, using an average current of 11.4 mA, varying from 4 mA to 20 mA. Awake surgery was performed in all instances; however, it failed in 13 cases, constituting 22.8% of the total, due to various reasons such as patient fatigue, emotional distress, and difficulty in following instructions or sustaining cooperation. Speech arrest was induced in 43 cases (89.5%), with an average current of 2.7 mA, ranging from 1.5 mA to 5 mA. Language mapping demonstrated that a single language was mapped in half of the cases, while two languages were mapped in the remaining half. Additionally, mapping of other cognitive functions included visual field mapping in 5 instances, praxis mapping in 16 cases, semantics mapping in 33 cases, and mentalization mapping in 3 cases (Table 2).

At 1 month postoperative, 15 cases (26.3%) exhibited new neurological deficits, with a mean Eastern Cooperative Oncology Group (ECOG) score of 2.64, ranging from 2 to 4. Among these cases, 8 (53.3%) showed residual deficits at 3 months postoperative, with an average ECOG score of 2.45, ranging from 1 to 4. By 6 months postoperative, 5 cases (33.3%) still had residual neurological deficits, with a mean ECOG score of 3.5, ranging from 2 to 5 (Table 3).

Regarding the extent of resection, 4 cases (7%) achieved supratotal resection, while 24 cases (42.1%) achieved gross total resection. Subtotal resection was performed in 28 cases (49.1%), and partial resection was conducted in 1 case (1.8%) (Table 3).

**Table 2.** Mapping of motor, language, and other tasks

| Characteristic | Value (n=57) |
|---|---|
| Motor mapping | |
| Positive mapping of M1 | 56 (98.2) |
| Current used (mA) | 11.9 (2–30) |
| Continuous MEP monitoring | 56 (98.2) |
| Positive subcortical mapping of CST | 52 (91.2) |
| Current used (mA) | 11.4 (4–20) |
| Awake surgery | |
| Completed | 44 (77.2) |
| Failed | 13 (22.8) |
| Language mapping | |
| Number of patients performed | 48 (84.2) |
| Speech arrest induced | 43 (89.5) |
| Current used (mA) | 2.7 (1.5–5) |
| Single language mapped | 24 (50) |
| Two languages mapped | 24 (50) |
| Mapping of other cognitive functions | |
| Visual field | 5 |
| Praxis | 16 |
| Semantics | 33 |
| Mentalisation | 3 |

Values are presented as n (%) or mean (range). MEP, motor evoked potentials; CST, corticospinal tract

## DISCUSSION

The benefits of maximizing surgical resection in glioma patients, irrespective of grade, are widely recognized [17]. However, the diffuse infiltration of this disease into critical white matter tracts and its heterogeneous nature in both anatomical and functional aspects present significant challenges in achieving complete or near-complete resection [18]. Any treatment approach must prioritize preserving the patient's QoL, particularly from the patient's perspective, to achieve an optimal onco-functional balance. This balance aims to prolong survival while ensuring an acceptable QoL.

It is crucial to acknowledge that even when achieving gross or near-total tumor resection is not feasible from an oncological perspective, cytoreductive glioma resections offer significant functional benefits. These benefits encompass seizure management, improvement in neurological deficits such as cognition, and relief from symptoms associated with tumor mass effects [19]. Further complicating these considerations

**Table 3.** Extent of resection and new neurological deficits postoperatively

| Characteristic | Value (n=57) |
|---|---|
| Neurological deficit | |
| New neurological deficit (1 month postop) | 15 (26.3) |
| ECOG (1 month postop) | 2.64 (2–4) |
| Residual of new neurological deficit (3 months postop) | 8/15 (53.3) |
| ECOG (3 months postop) | 2.45 (1–4) |
| Residual of new neurological deficit (6 months postop) | 5/15 (33.3) |
| ECOG (6 months postop) | 3.5 (2–5) |
| Extent of resection | |
| Supratotal resection | 4 (7) |
| Gross total resection | 24 (42.1) |
| Subtotal resection | 28 (49.1) |
| Partial resection | 1 (1.8) |

Values are presented as n (%) or mean (range). ECOG, Eastern Cooperative Oncology Group score is the ongoing debate regarding the acceptability of inducing neurological deficits during glioma resection. This debate arises from the potential to harness the patient's capacity for neuroplasticity, allowing for greater oncological clearance [20]. However, the timing and extent of neurological recovery following such deficits significantly influence patient expectations, QoL, and suitability for adjuvant therapy, especially in cases of HGGs.

While numerous studies have investigated glioma patient cohorts focusing on resection extent and neurological outcomes, few have provided a systematic approach to achieving an optimal onco-functional balance for each patient, integrating the abovementioned factors. This study seeks to bridge this gap by demonstrating our approach to achieving such a balance.

Using our standardized treatment paradigm, we achieved a supratotal or gross resection in 49.1% of patients, comparable to, if not better, many published series with similar patient demographics [21]. Regarding functional outcomes, although most patients experienced new or worsened neurological deficits immediately after surgery (26.3%), many recovered neurologically to their preoperative baseline within 30 days, with the majority recovering within 3 months post-surgery. We observed an increased incidence of transient neurological deficits only in cases where resection margins were pushed close to functional boundaries identified based on electrophysiological parameters. Such resections were performed only if the patient deemed such deficits acceptable, with functions known to have good neuroplastic potential for recovery.

These results suggest that our standardized treatment paradigm has the potential to achieve an optimal onco-functional balance in glioma patients undergoing surgical resection. This case series demonstrates our institution's standard treatment paradigm, which relies on two key pillars: empowering the patient through thorough evaluation of functional status, expectations, communication, and alignment of treatment goals, as well as mandatory motivation for rehabilitation after surgery and the individualized application of functional mapping techniques, which requires a deep understanding of functional brain connectomes and anatomical correlates, rational and reproducible use of DES and relevant parameters, and strict limitation of resection based on functional boundaries.

A significant challenge in managing our patients' expectations revolved around preserving language abilities, particularly within our institution's effectively bilingual population. Preserving language abilities is crucial for maintaining QoL, especially in Asia, where bilingualism is a fundamental aspect of the nation's language policy. In our context, where most of the population is effectively bilingual, languages such as English, Mandarin, Malay, and Tamil are commonly spoken and written, with varying permutations of fluency, age of language acquisition, and first language [22].

Preserving more than one language is often mandatory for many patients, as these languages are integral to their psychosocial identity and livelihood. However, we could only map more than one language in 50% of patients in our series due to various limitations. Previous studies have indicated that while there are patterns of common cerebral organization for both languages in bilinguals [23], there appear to be functionally independent neural populations within common sites and topographically separate cortical areas of activation for each language [24]. These patterns are influenced by language proficiency and age of acquisition for each specific language [25].

Incorporating the routine preservation of multiple languages into our intraoperative language tasks adds complexity and challenge to glioma resection surgery. This complexity stems from the need for additional time to map relevant languages, understand functional language organization at the cortical and subcortical levels for various languages, and develop a validated and standardized set of intraoperative language tasks to map relevant language pathways accurately. Further research is needed in this area, as this challenge becomes increasingly relevant to glioma surgeons worldwide in an increasingly globalized and interconnected world.

### Limitation

This study, while providing insightful findings, is subject to certain limitations that should be considered when interpreting the results.

As this study involved a limited number of patients, a more extensive study with longer follow-up is necessary to establish the efficacy of this treatment paradigm in achieving an optimal onco-functional balance, particularly for patients with LGGs who undergo partial resections and may eventually require repeat resections. Furthermore, additional efforts are needed to identify glioma patients who may not benefit from this treatment paradigm, such as those unable to tolerate awake conditions, cooperate during surgery, or engage in rehabilitation.

A key constraint is the study's dependence on data from a single cohort, which limits its scope. This reliance restricts our capacity to compare and validate the findings against other groups. However, we draw reference from other studies employing comparable treatment methods, which have demonstrated positive outcomes in their respective patient groups.

In a recent 2024 publication, Moniz-Garcia et al. [26] documented the standardized awake craniotomy approaches in their neurosurgical department, involving 164 patients. Their approach similarly utilizes a standardized treatment method but with a greater emphasis on economic analysis rather than treatment outcomes. They demonstrated a notable decrease in hospital stay duration, ICU time, and direct healthcare expenses following the introduction of an optimized protocol. This was accomplished without affecting patient results, maintaining comparable levels of surgical resection and complication frequencies, and even achieving lower rates of patient readmissions. Additionally, they outlined an enhanced post-surgery recovery program that could be beneficial for our institution to consider.

In 2020, Leon-Rojas et al. [27] presented their approach to awake craniotomies, centering on patient consciousness, surgical methods, and expertise. This was based on a series of 50 consecutive cases. They achieved gross total resection in 68% of the patients and subtotal resection in 20%. Notably, severe early and late deficits were observed in 12% and 2% of cases, respectively. Postoperative surveys indicated a high level of patient satisfaction.

In 2017, Groshev et al. [28] outlined their method for awake craniotomies, applied to 76 patients undergoing surgeries for primary and metastatic brain tumors. They also incorporated diffusion tensor imaging and functional MRI to precisely trace motor and speech pathways. Their findings indicate that awake surgeries can yield favorable oncological and functional results.

These studies collectively highlight that while awake craniotomy centers may vary in their specific treatment methods tailored to local demographics, adopting a standardized treatment protocol is critical to achieving the best possible balance between oncological effectiveness and functional preservation in glioma surgery. Besides maintaining function, as highlighted in the aforementioned studies, emphasizing speech and language has also been an integral part of our treatment approach. Although our patient group may be smaller, our outcomes are on par with those of larger-scale centers. Furthermore, the consistent collaboration of our team, comprising a neurosurgeon, neuroanesthetist, and neuropsychologist, has also contributed to our favorable outcomes.

Although most patients in this study achieved the desired onco-functional outcome, there is a lack of objective measures detailing the impact of the resection on the patient's QoL. Therefore, a follow-up study involving a formal survey to assess the surgery's effects on various aspects of patient expectations [29] and QoL was performed in other studies [30].

## Conclusion

Establishing the optimal onco-functional equilibrium represents a fitting treatment objective for patients undergoing glioma resection surgery. Our research demonstrates that such equilibrium can be achieved systematically in this complex disease, utilizing a standardized treatment framework tailored to individualized outcomes. Key to this framework is empowering patients in their treatment journey and customizing the utilization of functional mapping techniques. However, a notable challenge is preserving diverse languages within a multilingual patient population to uphold their overall QoL.

### Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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