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AANHS Journal

Journal homepage: http://aanhsj.usu.ac.id

AANHS Asian Australasian Neuro & Health Science Journal Universitas Sumatera Utara - Indonesia

Functional Surgical Resection in Glioma Patients: A Literature Review on Techniques and Outcomes

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ARTICLE INFO

Article history:
Received : Apr, 25th 2025
Revised : Apr, 26th 2025
Accepted : Apr, 27th 2025
Available :Apr, 30th 2025

E-ISSN: 2686-0848

How to cite:
Sihombing EJN, Karima AP. The Role of Neurosurgery in Reducing Parkinson's Symptoms: A Case Study on the Use of DBS Technology. Asian Australasian Neuro and Health Science Journal (AANHS J) Vol. 07, No. 01 (2025)
14 - 20

DOI: 10.32734/aanhsj.v7i01.20622

ABSTRACT

Background: Gliomas frequently invade eloquent cortical and subcortical regions, necessitating surgical strategies that optimize oncological resection while preserving neurological integrity. Functional surgical resection integrates advanced modalities to achieve maximal safe resection.

Method: A structured qualitative literature review was performed, synthesizing current evidence from high-impact databases on intraoperative techniques—including awake craniotomy, cortical and subcortical mapping, fluorescence-guided resection, and intraoperative imaging—and their impact on surgical outcomes in glioma patients.

Discussion: Functional mapping and imaging adjuncts significantly improve the extent of resection and mitigate postoperative deficits, particularly in IDH-mutant low-grade gliomas and eloquent high-grade lesions. However, limitations in fluorescence efficacy, imaging resolution, and resource availability persist across institutions.

Conclusion: Functional resection techniques enhance survival and quality of life by enabling individualized, anatomically precise glioma surgery. Future directions include integration of molecular diagnostics, intraoperative tools, and global standardization to reduce outcome disparities.

Keyword: Glioma, Functional Surgical Resection, Awake Craniotomy, Cortical Mapping, Neuronavigation, Electrophysiological Monitoring

1. Introduction

Gliomas, a heterogeneous group of primary brain tumors originating from glial cells, account for approximately 30% of central nervous system tumors and 80% of malignant brain neoplasms, presenting significant challenges in neuro-oncology due to their infiltrative nature and diverse biological behavior [1]. The 2021 World Health Organization (WHO) classification categorizes gliomas into grades I–IV, with low-grade gliomas (LGGs, grades I–II) characterized by slower progression and high-grade gliomas (HGGs, grades III–IV), such as glioblastoma (GBM), marked by aggressive behavior and poor prognosis [2]. Molecular markers, including isocitrate dehydrogenase (IDH) mutations, have redefined glioma classification, with IDH-mutant LGGs demonstrating a median survival of 10–15 years and greater amenability to surgical resection compared to IDH-wildtype HGGs, which typically have a median survival of 1–2 years, as reported in Cancers [3]. The extent of resection (EOR) is a critical prognostic factor, with gross total resection (GTR) in HGGs extending median overall survival (OS) to 18–24 months, as demonstrated in a JAMA Oncology meta-analysis [4].

The infiltrative growth of gliomas, which enables tumor cells to invade eloquent brain regions responsible for motor, sensory, language, and cognitive functions, complicates surgical resection and increases the risk of neurological deficits [5]. In LGGs, GTR is associated with improved survival and reduced malignant

transformation, particularly in IDH-mutant cases, as noted in Neuro-Oncology Advances [6]. Functional surgical resection, aimed at maximizing tumor removal while preserving neurological function, is a cornerstone of glioma management, particularly for tumors in eloquent areas like the insula, where awake craniotomy reduces perioperative complications, as reported in Frontiers in Oncology [7]. Neuroplasticity in LGGs facilitates functional reorganization, enabling safer resection but requiring dynamic intraoperative mapping, as highlighted in Frontiers in Neurology [8].

Advanced intraoperative techniques, such as awake craniotomy, fluorescence-guided surgery with 5-aminolevulinic acid (5-ALA) or fluorescein, intraoperative neuromonitoring (IONM), intraoperative MRI (iMRI), and diffusion tensor imaging (DTI)-based tractography, have enhanced resection precision and safety [9]. Awake craniotomy reduces permanent deficits to below 10% in high-volume centers, as shown in a Brain Sciences survey [10]. The tumor microenvironment, characterized by hypoxia and immune evasion in HGGs, contributes to therapeutic resistance, necessitating advanced visualization techniques like fluorescence-guided surgery, as discussed in Frontiers in Oncology [11]. Fluorescein-guided surgery achieves GTR in 70% of LGG cases, offering a cost-effective alternative to 5-ALA, per Journal of Neuro-Oncology [12]. In LGGs, residual tumor volume and molecular features predict survival, with supratotal resection further improving progression-free survival (PFS), as reported in Neuro-Oncology Advances [13,14]. However, challenges such as 5-ALA's limited fluorescence in LGGs, DTI's sensitivity to edema, and iMRI's high cost exacerbate global disparities in access to advanced care [15].

2. Method

This study employs a qualitative approach using a literature review method. This method is widely utilized in medical and health sciences research to gain a deeper understanding of techniques and outcomes associated with various clinical procedures, including functional surgical resection in glioma patients. The qualitative approach in this study emphasizes the collection of descriptive and interpretative data from various relevant sources.

In this study, the literature review is used to establish a strong theoretical foundation regarding functional surgical resection techniques, including the use of intraoperative technologies such as functional MRI (fMRI), neuronavigation, awake craniotomy, and intraoperative cortical mapping. Additionally, this study evaluates clinical outcomes such as the extent of tumor resection, neurological function recovery, and improvements in patients' postoperative quality of life. The literature sources include scientific journals, medical textbooks, clinical research reports, and neurosurgical practice guidelines obtained from databases such as PubMed, Google Scholar, and ScienceDirect. Keywords used in the literature search include "functional neurosurgery," "glioma resection," "awake craniotomy," and "neurosurgical outcomes."

Data analysis in this study is conducted using a qualitative approach, involving an in-depth examination of the content from various academic sources related to functional surgical resection procedures. The primary focus of this analysis is to compare different surgical approaches, intraoperative technologies, and clinical outcomes reported in previous studies. Through this approach, the study aims to identify the advantages and challenges associated with the implementation of this technique.

3. Discussion

Glioma and Its Characteristics

Gliomas, a diverse group of primary brain tumors originating from glial cells, constitute approximately 30% of all central nervous system tumors and 80% of malignant brain tumors, presenting a formidable challenge in neuro-oncology due to their histopathological, molecular, and clinical heterogeneity [1]. The World Health Organization (WHO) classifies gliomas into grades I–IV based on histological features, with low-grade gliomas (LGGs, grades I–II) exhibiting slower growth and high-grade gliomas (HGGs, grades III–IV), such as glioblastoma (GBM), characterized by aggressive behavior and poor prognosis [2]. The 2021 WHO classification integrates molecular markers, including isocitrate dehydrogenase (IDH) mutations, 1p/19q codeletion, and O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation, which

have revolutionized glioma diagnosis and prognostication [3]. A study in Cancers reported that IDH-mutant LGGs are associated with a median survival of 10–15 years, compared to 1–2 years for IDH-wildtype HGGs, highlighting the prognostic significance of molecular profiling [4].

The infiltrative nature of gliomas complicates surgical resection, as tumor cells often extend beyond radiographically visible margins, invading eloquent brain regions responsible for motor, sensory, language, and cognitive functions [5]. This infiltration is driven by glioma cells' ability to migrate along white matter tracts, blood vessels, and perineuronal spaces, as detailed in a Frontiers in Oncology review [6]. Peritumoral edema, a hallmark of HGGs, further distorts normal anatomy, challenging intraoperative navigation and increasing the risk of neurological deficits [7]. Neuroplasticity, particularly in LGGs, allows functional reorganization of eloquent areas, enabling safer resection in some cases but requiring dynamic intraoperative mapping to account for patient-specific variability [8]. A Brain Sciences study emphasized that LGGs in the dominant hemisphere may induce compensatory cortical reorganization, which complicates preoperative planning but enhances functional preservation post-resection [9]. Glioma heterogeneity extends to their microenvironment, with HGGs exhibiting hypoxia, angiogenesis, and immune evasion, driven by vascular endothelial growth factor (VEGF) and programmed death-ligand 1 (PD-L1) expression [10]. In contrast, LGGs often display a less immunosuppressive microenvironment, contributing to their slower progression [11]. Molecular subtypes, such as 1p/19q-codeleted oligodendrogliomas, show distinct chemosensitivity and longer progression-free survival (PFS) compared to IDH-mutant astrocytomas, as reported in Neuro-Oncology Advances [12]. Additionally, tumor location influences clinical presentation and surgical feasibility, with insular gliomas posing unique challenges due to their proximity to critical vascular and functional structures [13]. The interplay of these characteristics necessitates individualized surgical strategies, integrating molecular, radiographic, and functional data to optimize outcomes [14]. Emerging research in Journal of Personalized Medicine suggests that single-cell RNA sequencing could further elucidate intratumoral heterogeneity, potentially guiding targeted resection strategies [15].

Functional Surgical Resection Techniques in Glioma Patients

Functional surgical resection seeks to maximize tumor removal while preserving neurological function, employing a suite of advanced intraoperative techniques tailored to the infiltrative and heterogeneous nature of gliomas. Awake craniotomy with direct cortical and subcortical stimulation mapping is a cornerstone for tumors in eloquent areas, enabling real-time identification of motor, language, and cognitive functions. This technique minimizes postoperative deficits by allowing surgeons to delineate functional boundaries with high precision, achieving gross total resection (GTR) in up to 78% of perirolandic gliomas, as reported in a Brain Sciences study [9]. The procedure's success hinges on patient cooperation and specialized neuroanesthesia, which can be challenging in pediatric, elderly, or anxious patients, and requires extensive preoperative counseling to optimize outcomes [14]. Recent advancements, such as high-frequency monopolar stimulation, have improved mapping accuracy, reducing permanent deficits by 60% compared to traditional methods, though intraoperative seizures remain a risk in 5–10% of cases [6].

Fluorescence-guided surgery has transformed HGG resection by enhancing tumor visualization, with 5-aminolevulinic acid (5-ALA) being the most widely adopted agent. A Cancers meta-analysis demonstrated that 5-ALA increased GTR rates to 65% in GBM compared to 36% with conventional white-light microscopy, significantly extending PFS [4]. The agent's fluorescence relies on protoporphyrin IX accumulation, which is robust in HGGs but weaker in LGGs, limiting its utility in lower-grade tumors. To address this, fluorescein has emerged as a cost-effective alternative, achieving GTR in 70% of LGG cases, as reported in a Journal of Neuro-Oncology study [1]. Fluorescein's affordability and compatibility with standard operating microscopes make it particularly valuable in resource-limited settings, though its non-specific uptake in edematous tissue can reduce specificity [12]. Emerging fluorescence agents, such as indocyanine green and targeted molecular probes, are under investigation to improve margin delineation across glioma grades, with early trials showing promise in Frontiers in Oncology [10].

Intraoperative neuromonitoring (IONM), encompassing motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs), and direct electrical stimulation, enhances safety during resection near critical structures like the corticospinal tract or internal capsule. A Frontiers in Oncology review highlighted that continuous MEP monitoring reduced postoperative motor deficits by 55% in insular gliomas, though false-positive alerts, often triggered by brain shift or anesthesia, can interrupt surgery and prolong operative time [6]. Combining IONM with subcortical mapping improves specificity, allowing surgeons to maintain a 5–10 mm safety margin from functional tracts, as emphasized in Neuro-Oncology Advances [12]. However, the technique's efficacy depends on operator experience and standardized protocols, which vary across centers.

Intraoperative MRI (iMRI) has revolutionized resection accuracy by providing real-time imaging to assess residual tumor, achieving GTR in 82% of cases compared to 60% with standard neuronavigation, according to a Neuro-Oncology Advances analysis [12]. iMRI is particularly valuable in LGGs, where indistinct tumor margins challenge conventional visualization, but its high cost, prolonged operative time, and need for specialized operating suites limit its adoption, particularly in low-resource settings [7]. Hybrid approaches, integrating iMRI with 5-ALA, have shown synergistic benefits, with a Cancers study reporting GTR rates of 90% in HGGs when both modalities are combined [4].

Diffusion tensor imaging (DTI)-based tractography, used preoperatively to visualize white matter tracts like the arcuate fasciculus and corticospinal tract, facilitates tailored surgical corridors, reducing language and motor deficits by 40% in left-sided gliomas, as noted in Neuro-Oncology Advances [13]. However, DTI's accuracy is compromised by peritumoral edema and tumor distortion, necessitating intraoperative validation with stimulation mapping [8]. Advanced tractography algorithms, such as constrained spherical deconvolution, are improving resolution, with early data suggesting a 20% increase in tract identification accuracy [15].

Emerging technologies, such as stimulated Raman histology and intraoperative mass spectrometry, offer real-time molecular profiling, enabling surgeons to distinguish tumor from normal tissue at a cellular level. A Journal of Personalized Medicine review highlighted that these techniques could increase EOR by 15% by identifying infiltrative margins missed by conventional imaging [15]. Artificial intelligence (AI)-driven intraoperative decision support, including automated tumor segmentation and predictive modeling, is also gaining traction, with potential to reduce operative time and enhance precision, as discussed in Frontiers in Neurology (7). These innovations, while promising, require validation in large-scale trials to establish their clinical and cost-effectiveness.

Outcomes of Functional Surgical Resection in Glioma Patients

The outcomes of functional surgical resection in glioma patients are shaped by a complex interplay of extent of resection (EOR), tumor grade, molecular profile, surgical technique, and institutional factors, with significant implications for survival, functional preservation, and quality of life (QoL) [2]. For HGGs, achieving GTR is a critical prognostic factor, with a Cancers meta-analysis demonstrating a median overall survival (OS) of 18–24 months for GTR compared to 12–15 months for subtotal resection (STR) [4]. Each 10% increase in EOR beyond 90% adds approximately 1–2 months to survival, as reported in Neuro-Oncology Advances, underscoring the importance of maximal safe resection [12]. However, resections in eloquent areas carry a 25–30% risk of transient neurological deficits, with permanent deficits occurring in 5–10% of cases, particularly in insular or perirolandic gliomas, as noted in Surgical Neurology International [14]. The use of awake craniotomy and IONM has mitigated these risks, reducing permanent motor and language deficits to <10% in high-volume centers, according to a Brain Sciences study [9].

In LGGs, EOR is a key determinant of long-term outcomes, including seizure control, malignant transformation, and survival. A Neuro-Oncology Advances study found that GTR in IDH-mutant LGGs resulted in a 10-year OS of 85%, compared to 62% with STR, with seizure freedom achieved in 90% of GTR cases [12]. Supratotal resection, extending beyond radiographic margins, has shown additional benefits, with a Neuro-Oncology Advances meta-analysis reporting a 50% reduction in malignant transformation rates in

LGGs [13]. Molecular markers further stratify outcomes: 1p/19q-codeleted oligodendrogliomas exhibit superior survival and chemosensitivity post-resection, with a median PFS of 8–10 years, compared to 5–7 years for IDH-mutant astrocytomas, as highlighted in Cancers [5]. However, achieving GTR in eloquent areas often requires staged or partial resections to minimize deficits, delaying maximal resection and increasing recurrence risk, as noted in Frontiers in Oncology [6].

Functional preservation is a central goal, particularly for tumors in eloquent cortex or subcortical networks. Techniques like 5-ALA-guided resection improve QoL by minimizing postoperative complications, with a Frontiers in Oncology study reporting a 20% improvement in QoL scores in HGG patients [6]. Awake craniotomy enhances language and cognitive preservation, with a Brain Sciences survey indicating that 85% of patients resume normal activities within 3 months post-surgery [9]. Conversely, iMRI, while improving EOR, is associated with a 15% rate of intraoperative complications, such as hemorrhage or brain shift, which can offset functional benefits, as reported in Cancers [4]. Longitudinal QoL data remain limited, with most studies focusing on short-term outcomes, highlighting the need for standardized metrics like the EORTC QLQ-C30 questionnaire to capture patient-reported outcomes [11].

Socioeconomic and institutional factors significantly influence outcomes, with high-volume centers achieving 20% higher GTR rates and 50% fewer complications due to specialized expertise and access to advanced technologies, as emphasized in Frontiers in Neurology [7]. Patients in low-resource settings face higher complication rates and lower EOR due to limited access to iMRI, 5-ALA, or trained neuroanesthesiologists, as noted in Journal of Personalized Medicine [15]. Surgeon experience also plays a critical role, with a Surgical Neurology International analysis reporting that surgeons performing >50 glioma resections annually achieve 15% higher GTR rates [14].

Challenges in outcome assessment include variability in defining GTR (e.g., volumetric vs. qualitative criteria), inconsistent reporting of neurological deficits, and underreporting of cognitive outcomes, which are particularly relevant in LGG patients [8]. The integration of molecular data into outcome analyses is also inconsistent, despite its prognostic significance [10]. Future research should prioritize multicenter registries to standardize outcome measures, incorporate advanced imaging for precise EOR quantification, and explore AI-driven predictive models to optimize surgical planning, as suggested in Journal of Personalized Medicine [15]. Additionally, addressing disparities in access to advanced techniques is essential to ensure equitable outcomes globally [11].

4. Conclusion

Functional surgical resection is a cornerstone of glioma management, leveraging advanced techniques like awake craniotomy, fluorescence-guided surgery (5-ALA, fluorescein), intraoperative neuromonitoring (IONM), intraoperative MRI (iMRI), and DTI-based tractography to maximize tumor resection while preserving neurological function. These methods have significantly improved outcomes, particularly for IDH-mutant low-grade gliomas (LGGs) and high-grade gliomas (HGGs), with gross total resection (GTR) extending median overall survival (OS) to 18–24 months for HGGs and achieving a 10-year OS of 85% for LGGs, alongside enhanced seizure control and reduced malignant transformation. Awake craniotomy and IONM reduce permanent deficits to <10% in high-volume centers, improving quality of life (QoL). Molecular profiling (e.g., IDH, 1p/19q codeletion) refines surgical planning and outcome prediction.

However, challenges include 5-ALA's limited efficacy in LGGs, fluorescein's non-specificity, DTI's sensitivity to edema, and iMRI's high cost, which exacerbate global access disparities. Glioma heterogeneity and microenvironmental factors (e.g., hypoxia, immune evasion) complicate standardized approaches, while socioeconomic barriers increase complications in low-resource settings. Inconsistent outcome metrics hinder evidence-based guidelines.

Future advancements include stimulated Raman histology, intraoperative mass spectrometry, and AI-driven tools, which could enhance precision and EOR by 15%. Novel fluorescence agents and single-cell RNA sequencing may improve margin delineation and target aggressive tumor subpopulations. Cost-effective solutions and standardized IONM protocols are needed to address disparities, alongside multicenter registries

for unified outcome metrics. Continued innovation and global collaboration are essential to optimize glioma outcomes equitably.

Acknowledgements

None.

Conflict of Interest

The authors declare no conflicts of interest in preparing this article.

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