Advancements in surgical management of glioblastoma: current trends and promising future directions


Abstract. Glioblastoma (GBM) is the most common and malignant adult brain tumor. Despite substantial study and surgical advancements, the prognosis remains poor, demanding ongoing research of the current trends and potential surgical therapy. This abstract summarizes GBM surgical developments and future directions. GBM is treated with maximal safe resection, adjuvant radiation, and chemotherapy. Tumor penetration into eloquent brain areas often complicates surgical excision. Functional brain mapping and intraoperative imaging have increase safe resection. Awake craniotomy and intraoperative fluorescence-guided surgery may help remove more tumor. GBM surgery now incorporates molecular and genetic data. Molecular profiling helps discover mutations and genetic changes for tailored treatment. Immunotherapies and targeted therapies have the potential to enhance treatment outcomes for patients diagnosed with GBM. Precision medicine, which involves tailoring cancer treatments to each patient’s unique characteristics, is expected to play a pivotal role in future research endeavors. Nanotechnology and drug delivery devices offer the opportunity to optimize the delivery of anti-tumor drugs, potentially improving their efficacy. Artificial intelligence and machine learning in preoperative planning and intraoperative decision-making should improve surgical results. Current trends in GBM surgery include maximizing safe resection using advanced mapping and imaging techniques, incorporating molecular information for personalized treatment, and investigating targeted therapies and immunotherapies. The future of GBM surgery lies in the integration of precision medicine, nanotechnology, and artificial intelligence. By adopting these innovations, the surgical management of GBM may experience significant improvements, leading to better patient outcomes and an increase in life quality.

Keywords: glioblastoma; current trends; surgical management

1. Introduction
Glioblastoma (GBM) is an extremely aggressive brain tumor that is responsible for about half of all primary cerebral malignancies. Patients with GBM still have a poor prognosis, despite significant therapy advances. Because of the tumor’s infiltrative nature, GBM surgery is notoriously difficult to successfully perform. The extent of tumor mass removed during surgical excision is positively correlated with higher survival rates in patients diagnosed with GBM, a highly malignant brain tumor characterized by high recurrence rates, and high invasiveness. Neurosurgeons have consistent trouble identifying tumor borders using only their eyes. Hence, intraoperative characterization of tumor and normal brain tissue and stimulation-based functional paradigms have recently been included into surgical methods for GBM excision. This article aims to provide a thorough examination of recent developments in GBM surgery and to speculate on possible future actions in this field.

2. Glioblastoma surgery trends
2.1. Maximal safe resection
GBM surgery is still mostly maximal safe resection that helps removes as much tumor as possible without affecting brain function. GBM survival is strongly correlated
with resection extent. A meta-analysis of 37 trials with approximately 41,000 patients found that gross total resection (GTR) decreased mortality by 21% compared to partial resection (relative risk (RR) = 0.79, 95% confidence interval (CI) 0.75–0.84, p < 0.001) [1].

A retrospective examination of 342 elderly GBM patients found that GTR and adjuvant combination radio- and chemotherapy increase survival. Modern microsurgical dissection procedures and equipment can safely maintain short-term quality of life in GBM patients [2–5]. IDH-wild-type glioblastoma (de novo) constitutes 90% of EGFR/TERT/ MGMT-associated GBMs. ATRX and TP53 mutations increase survival by 10%. Resection improves histology, tumor genotyping, and cytodestruction. Using carmustine polymer wafers in the tumor cavity is possible [6].

Resection of more than 89% of tumor volume increases prognosis. GTR increases 1-year, 2-year, and progression-free survival by 61%, 19%, and 51%, respectively, compared to subtotal resection. GTR should be explored for all newly diagnosed GBM patients. Contrast-enhanced T1 magnetic resonance imaging (MRI) shows tumor cell have spread. T2 MRI or FLAIR abnormality removal increased median survival time from 9.8 to 15.2 months (p < 0.001) [2].

A meta-analysis and comprehensive review found that a combined relative risk (RR) for overall survival (OS) at 12 months is 1.25 with a number needed to treat (NNT) of 6, and at 24 months RR is 1.59 with NNT of 9. Extent of surgical resection slightly but statistically correlates with GBM patients’ overall survival [7]. Butterfly GBM surgery outperforms biopsy at 6 months [8]. Awake craniotomy, intraoperative MRI (iMRI), and fluorescence-guided surgery (FGS) have been shown to optimize tumor visualization during surgical intervention, enabling a more precise delineation and, consequently, an increased tumor size for resection.

2.2. MRI intraoperatively
Surgeons can monitor tissue damage and complete removal with iMRI. iMRI substantially enhanced tissue removal during surgery (odds ratio (OR) = 2.47, 95% CI 1.77–3.45, p = 0.001) [9]. iMRI does not improve GBM survival [10]. Improved intraoperative imaging provides GTR in almost 80% of cohorts with better or stable functional status [11].

2.3. Fluorescence-guided surgery
During surgery, FGS uses 5-aminolevulinic acid (5-ALA) to view the tumor. FGS substantially increased resection (OR = 2.79, 95% CI 2.01–3.88, p < 0.001) in a meta-analysis of 11 investigations including 1,136 patients [12]. The 5-ALA group had more GTR patients (65 vs. 36%, p = 0.001) and improved progression-free survival (RR = 0.63, 95% CI 0.45–0.88, p = 0.007) but not OS [13].

2.4. Awake craniotomy
Awake craniotomy preserves neurosurgical function after tumor removal from eloquent brain areas. A meta-analysis of 17 studies including 727 patients found that awake craniotomy improved resection (OR = 2.70, 95% CI 1.69–4.32, p = 0.001). Awake craniotomy does not improve GBM survival. Awake craniotomy was used for 75% of gross total resections [14].

2.5. Methods
Combining techniques to increase resection has been studied extensively. A prospective investigation found that iMRI and FGS dramatically enhance resection size [15, 16].

2.6. Recurrence
Younger patients with healthy performance status can still undergo GTR for recurrence (DIRECTOR trial subgroup analysis) [6]. Re-operation is recommended for senior recurrent GBM patients with good performance [17].

2.7. Proof
Current GBM resection evidence [18, 19]: level II — 6.6%, III — 65.8%, IV — 10.8%, and V — 16.8%.
Maximal cytoreductive surgery in newly diagnosed supratentorial glioblastoma — level 2.
Based on medical comorbidities, functional level, and tumor location, biopsy, subtotal, or gross total resection is recommended — level 3.
Cytoreductive surgery in butterfly and elderly newly diagnosed glioblastomas — level 3.
Advanced intraoperative guiding in level 3 — cytoreduction.

2.8. Precision medicine
This emerging field of medicine tailors patients’ care to their genetic and molecular makeup. Genomes and proteomics have found many GBM genetic subtypes with varied clinical characteristics and treatment responses. Precision medicine helps surgeons choose surgeries based on a patient’s genetic profile.
Glioblastoma mutations may now be addressed thanks to genomic sequencing. Drugs targeting IDH1 gene alterations, seen in a subpopulation of glioblastomas, are being tested in clinical trials [20].

2.9. Immunotherapy
Immunotherapy uses the body’s defense to treat GBM. GBM immunotherapy includes checkpoint inhibitors, CAR T-cell therapy, and cancer vaccines and is promising. Nivolumab and pembrolizumab early clinical studies showed promising results. CAR T-cell therapy, which genetically engineers immune cells to target tumor cells, is being studied for glioblastoma [21].

2.10. Tumor-treating fields
Tumor-treating fields impair cell division and reduce tumor growth by applying low-intensity electrical fields to the scalp; improve glioblastoma survival rates when used with therapy [22].

2.11. Liquid biopsies
It analyzes tumor DNA in the blood. This approach may disclose the tumor’s genetic makeup and treatment response. Liquid biopsy is being studied for monitoring glioblastoma treatment responses and relapses [23].
2.12. Supportive care
Glioblastoma patients should get palliative care and symptom management. Palliative care helps patients and their families live longer [24]. Individuationed treatment strategies, immunotherapy, tumor-treating fields, and palliative care improve survival rates in glioblastoma.

3. Future glioblastoma surgery
Despite surgical advances, GBM patients have a median survival of 15 months. Hence, novel approaches are needed to improve surgical outcomes and patient survival. These are future GBM surgical concepts.

In a network meta-analysis of recurrent GBM patients, most bevacizumab-based treatments increased progression-free survival. OS was not treatment-related [25]. Active immunotherapy may increase GBM survival [26]. Currently, there are no approved phase III oncolytic viruses for cancer treatment. There have been no reported fatalities due to encephalitis associated with oncolytic virus therapy. Despite three late-stage clinical studies, the Food and Drug Administration has not yet authorized viral gene therapy for medical use. Particular caution is necessary when dealing with suicide-predisposing genes in gene therapy approaches [27].

3.1. Robotic surgery
Robotic surgery solely benefits neurosurgery, it improves precision, vision, and dexterity. Robotic technology may maximize GBM removal while decreasing collateral damage to healthy tissue during GBM surgery. Upcoming projects include targeting genetic heterogeneity with personalized medicine, developing new adjuvant drugs, and improving GBM surgery to better detect tumor margins.

3.2. Targeted therapies
As we learn more about glioblastoma chemical pathways, targeted drugs that selectively disrupt them seem tempting. The tumor microenvironment, immune system, and IDH1 inhibitors are targeted.

3.3. Nanotechnology
It is tiny engineering (1–100 nanometers). Nanoparticles may target particular cells or areas, making them intriguing for drug delivery and imaging. Nanoparticles can help GBM surgeons discover and target tumor cells. Nanotechnology can directly deliver drugs to malignant cells via small particles or devices. This approach reduces adverse effects of chemotherapy and radiation therapy. Nanotechnology-based glioblastoma therapies are under development [29].

3.4. Gene therapy
Vectors like genetically modified viruses deliver therapeutic genes to malignant cells. This approach targets tumor genetic abnormalities and induces an immune response. Glioblastoma gene therapy is being studied [30].

3.5. Artificial intelligence
It uses machine learning algorithms to filter through masses of data to find insights that might help build new medicines and predict their efficacy. Artificial intelligence is being used to identify new therapeutic targets, treatment response predictability, and individuals who may benefit from certain drugs [31].

3.6. Patient-derived models
Patient-derived xenografts and organoids are becoming increasingly important for therapy discovery and assessment. These models better represent the complex biology of the tumor and its environment, allowing for targeted medication testing [20].

4. Conclusions
Glioblastoma surgery is becoming increasingly individualized and multimodal. Imaging, surgical instruments, and intraoperative monitoring have greatly increased tumor excision while reducing brain tissue injury. Functional mapping and awake craniotomy improve tumor targeting and brain function preservation. Fluorescence-guided surgery and intraoperative imaging have enhanced glioblastoma visibility and resection, improving outcomes. Molecular biomarkers including IDH mutation status and MGMT promoter methylation have enabled focused medicines and tailored treatment regimens. Glioblastoma remains aggressive and difficult despite these advances. Surgical treatment of glioblastoma will continue to improve and explore new methods. Precision medicine and molecular profiling may inform surgical decision-making in the future. Surgeons can target particular molecular changes and signaling pathways in some cancers by assessing their genetic and molecular properties. This may improve outcomes. Minimally invasive and non-invasive surgery are promising avenues. Focused ultrasound, laser interstitial thermal therapy, and nanotechnology-based methods can selectively ablate tumor cells while sparing healthy brain tissue. These methods lessen surgical trauma, recuperation time, and quality of life. Immunotherapy using checkpoint inhibitors and tailored cancer vaccines may improve the immune system’s capacity to detect and kill glioblastoma cells. These methods may work synergistically with surgery to improve patient outcomes.

In conclusion, glioblastoma surgery now uses improved imaging, surgical methods, and molecular analysis to tailor treatment. Nevertheless, future glioblastoma surgery will emphasize precision medicine, minimally invasive procedures, and immunotherapy to improve outcomes and our understanding of this deadly illness.

References


Удосконалення хірургічного лікування гліобластоми: поточні тенденції та перспективні напрямки майбутнього

Резюме. Гліобластома (ГБМ) є найпоширенішою та най злоякіснішою пухлиною мозку дорослих. Незважаючи на значні дослідження та прогрес у хірургії, прогноз залишається по- ганім, що вимагає постійних досліджень сучасних тенденцій та потенційної хірургічної терапії. Ця робота підсумовує розробки щодо хірургії ГБМ та майбутні напрямки. Стандартами лікування ГБМ є максимально безпечна резекція, ад'ювантна променева терапія та хіміотерапія. Проникнення пухлини у функціонально важливі ділянки мозку часто перешкоджає хірургічному видаленню. Функціональне картування мозку та інтраопераційна візуалізація сприяють безпечній резекції. Краніотомія у свідомості й інтраопераційна хірургія під контролем флуоресценції можуть допомогти видалити більше пухлини. Хірургія з приводу ГБМ тепер включає молекулярні та генетичні дані. Молекулярне профілювання допомагає виявляти мутації та генетичні зміни для індивідуального лікування. Імунотерапія та цільова терапія мають потенціал щодо покращення результатів лікування пацієнтів із діагнозом ГБМ. Очікується, що персоналізована медицина, яка передбачає адаптацію терапії раку до унікальних характеристик кожного пацієнта, відіграє роль у майбутніх дослідницьких зусиллях. Нанотехнології та пристрій доставити ліки дають можливість оптимізувати доставку протипухлинних препаратів, потенційно підвищуючи їхню ефективність. Штучний інтелект і машинне навчання майбутнє хірургії. Завдяки застосуванню цих інновацій хірургія ГБМ може зазнати значних удосконалень, що сприятиме покращенню результатів лікування пацієнтів і підвищенню якості життя.

Ключові слова: гліобластома; сучасні тенденції; хірургічне лікування