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Current Status and Advances in Intraoperative Adjuncts for Glioma Surgery

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Abstract: ***Gliomas, arising from glial cells or their precursors, represent the most prevalent primary tumors of the central nervous system (CNS), accounting for approximately 40% of all CNS neoplasms and up to 80% of malignant brain tumors. These tumors are characterized by high recurrence rates, substantial mortality, and limited curative potential. Maximal safe resection remains the cornerstone of glioma management and a critical determinant of patient survival. However, the diffusely infiltrative nature of gliomas obscures tumor–brain boundaries, rendering complete resection challenging. In response, a range of intraoperative adjunct technologies has rapidly evolved to enhance the extent of resection while preserving neurological function. This review systematically summarizes recent advances in intraoperative imaging, functional mapping, and emerging optical techniques, highlighting their roles in improving surgical precision, minimizing complications, and prolonging survival. The integration of multimodal strategies is expected to further advance precision neurosurgery for glioma.***

Keywords: Glioma, Surgery, Intraoperative adjuncts, Neuro-navigation, Functional mapping**.**

1. Introduction

Gliomas are primary CNS tumors originating from glial cells or progenitor cells, with an annual incidence of 5–8 per 100,000 individuals. Despite advances in multimodal therapy — including surgery, radiotherapy, chemotherapy, and molecularly targeted treatments — clinical outcomes remain poor due to their aggressive and infiltrative behavior [1]. Surgical resection constitutes the primary and indispensable therapeutic modality, with the principle of achieving maximal safe resection.

A substantial body of evidence demonstrates a strong correlation between the extent of resection (EOR) and survival in patients with high-grade gliomas [2,3]. Nevertheless, the indistinct interface between tumor and normal brain tissue makes complete resection rarely achievable using conventional surgical approaches. Consequently, intraoperative adjunct technologies have been developed to optimize tumor removal while minimizing neurological deficits, thereby improving both survival and quality of life.

Intraoperative adjuncts can be broadly categorized into imaging techniques, functional mapping technologies, and emerging optical approaches such as Raman spectroscopy. These modalities provide complementary information that enables surgeons to balance aggressive tumor resection with preservation of critical brain functions.

2. Intraoperative Imaging Technologies

2.1 Multimodal Image Fusion and Three-Dimensional Reconstruction

The central nervous system is structurally and functionally complex, and neurosurgical procedures are inherently high-risk due to limited operative space and the dense distribution of critical neurovascular structures. Accurate preoperative planning therefore relies on comprehensive imaging data.

Single-modality imaging often fails to capture the full spectrum of pathological and anatomical information. Multimodal image fusion integrates data from CT, MRI, PET, and other imaging modalities through advanced registration algorithms, enabling the reconstruction of high-resolution three-dimensional representations of tumors and surrounding structures [4–6]. This approach enhances anatomical delineation, facilitates precise target localization, and improves surgical planning [7,8].

The integration of neuronavigation with multimodal imaging allows individualized surgical strategies, including optimized craniotomy size, cortical entry points, and preservation of functional pathways. Clinical studies have demonstrated improved rates of gross total resection and postoperative functional outcomes using these techniques [9]. However, intraoperative brain shift caused by cerebrospinal fluid loss and tumor resection remains a limitation, reducing spatial accuracy.

Recent advances in artificial intelligence (AI) have further improved multimodal image analysis. Deep learning algorithms, including convolutional neural networks and transformer-based models, enable automated tumor segmentation, enhanced image resolution, and improved detection accuracy [10,11]. AI-driven adaptive learning systems can dynamically refine segmentation strategies, offering promising applications in precision neurosurgery [12].

2.2 Intraoperative Magnetic Resonance Imaging (iMRI)

Since its introduction in the 1990s, intraoperative MRI has become a pivotal tool in neurosurgery. It enables real-time visualization of tumor margins and adjacent critical structures, allowing surgeons to assess residual tumor intraoperatively and extend resection when appropriate [13–15].

High-field iMRI significantly improves the extent of resection by compensating for brain shift and providing updated anatomical information throughout the procedure. Clinical studies have demonstrated substantial increases in gross total resection rates and favorable functional outcomes when iMRI is combined with neuronavigation and functional mapping [16,17].

Despite its advantages, iMRI is associated with high costs, complex workflows, and prolonged operative times, which may increase perioperative risks and limit its widespread adoption.

2.3 Intraoperative Ultrasound (iUS)

Intraoperative ultrasound is a cost-effective, real-time imaging modality that can be seamlessly integrated into surgical workflows. It allows dynamic assessment of tumor location, extent of resection, and vascular characteristics through Doppler and contrast-enhanced techniques [18,19].

Compared with iMRI, iUS offers advantages in accessibility and real-time feedback, particularly in low-grade gliomas [20]. However, its image quality is operator-dependent and historically inferior to MRI. Recent advances in image processing and fusion techniques—such as deformable registration of preoperative MRI with intraoperative ultrasound—have significantly improved its accuracy and clinical utility [21,22].

2.4 Fluorescence-Guided Surgery

Fluorescence-guided techniques enhance intraoperative visualization of tumor margins, improving resection accuracy. Commonly used fluorophores include 5-aminolevulinic acid (5-ALA), sodium fluorescein, and indocyanine green (ICG).

5-ALA induces accumulation of protoporphyrin IX in tumor cells, which emits red fluorescence under blue light excitation, enabling precise visualization of malignant glioma tissue. Although highly effective, its use is limited by potential adverse effects, including photosensitivity and hypotension.

Sodium fluorescein accumulates in regions of blood–brain barrier disruption and emits yellow-green fluorescence under appropriate filters, offering a cost-effective and safe alternative with minimal side effects.

ICG, a near-infrared fluorophore, is primarily used for intraoperative angiography and visualization of tumor-associated vasculature. While useful for assessing residual tumor and vascular anatomy, its short imaging window limits broader applications.

3. Intraoperative Functional Mapping

3.1 Awake Craniotomy and Direct Electrical Stimulation

Awake craniotomy combined with direct electrical stimulation (DES) is the gold standard for functional mapping in eloquent brain regions. This approach allows real-time identification of cortical and subcortical functional areas, enabling maximal tumor resection while preserving neurological function [23,24].

DES can map motor, sensory, and language pathways by eliciting functional responses. During language mapping, tasks such as counting and object naming are used to identify critical regions. This technique significantly reduces the risk of postoperative neurological deficits and improves quality of life.

3.2 Intraoperative Neurophysiological Monitoring (IONM)

IONM provides continuous, real-time assessment of neural pathway integrity during surgery. Techniques such as motor evoked potentials, somatosensory evoked potentials, and subcortical stimulation enable early detection of functional compromise.

IONM enhances surgical safety by guiding resection boundaries and preventing irreversible neurological damage. Clinical studies have shown that its use improves extent of resection, reduces operative time, shortens hospital stay, and enhances long-term neurological outcomes [25–28].

4. Raman Spectroscopy

Raman spectroscopy is an emerging optical technique with high sensitivity and rapid, label-free detection capabilities. It enables molecular-level analysis of tissue composition, distinguishing tumor from normal brain tissue based on differences in nucleic acids, proteins, lipids, and metabolic profiles [29–31].

This technology allows real-time, non-destructive identification of tumor margins and may facilitate intraoperative molecular classification. Despite its promising potential, Raman spectroscopy remains in the experimental stage, with technical challenges limiting its routine clinical application.

5. Conclusions

Intraoperative adjunct technologies have substantially advanced glioma surgery by enabling more precise tumor resection while preserving neurological function. However, no single modality can fully reconcile the trade-off between maximal resection and functional preservation.

Future progress will likely depend on the integration of multiple complementary techniques—such as combining fluorescence guidance with iMRI and neurophysiological monitoring—to achieve optimal surgical outcomes. Continued technological innovation, particularly in AI and optical imaging, is expected to further refine precision neurosurgery and improve prognosis for patients with glioma.

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