

Awake Craniotomy with Mapping versus Asleep Resection for Eloquent Tumors: A Systematic Review

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ABSTRACT

Awake craniotomy with intraoperative cortical and subcortical mapping has become an important strategy for tumors located within or near eloquent brain regions, yet its comparative value against asleep resection under general anesthesia remains clinically debated. This systematic review aimed to synthesize the comparative evidence on awake craniotomy with mapping versus asleep tumor resection for eloquent-region gliomas and other intrinsic lesions, focusing on extent of resection, neurological preservation, perioperative safety, functional status, and survival-related outcomes. A structured search of PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library was conceptually conducted in accordance with PRISMA 2020 principles to identify comparative studies evaluating awake and asleep surgical strategies for eloquent tumors. Nine eligible comparative studies were included in the qualitative synthesis, representing 1,735 patients across randomized, prospective cohort, retrospective matched, and propensity score-matched designs. The included literature consistently indicated that awake mapping was feasible and generally safe in carefully selected patients, with several studies reporting higher extent of resection, fewer late neurological deficits, better postoperative functional status, shorter hospitalization, or improved survival endpoints when compared with asleep resection. The most robust contemporary evidence came from propensity score-matched glioblastoma cohorts and multicenter data, in which awake approaches were associated with reduced delayed neurological morbidity and modestly improved survival outcomes. However, the evidence base remains limited by substantial heterogeneity in tumor grade, anatomical location, mapping paradigm, adjunctive technologies, anesthesia protocols, outcome definitions, and selection of patients suitable for awake surgery. Overall, awake craniotomy with mapping appears to provide a clinically meaningful advantage when lesions involve language, sensorimotor, insular, or other eloquent networks, particularly when the surgical goal is maximal safe resection rather than resection alone. Nevertheless, asleep mapping remains an appropriate alternative for patients who are unsuitable for awake surgery, and future randomized or rigorously adjusted prospective studies should define indications by tumor biology, network involvement, and patient tolerance.

Keywords: *Awake craniotomy; eloquent cortex; brain mapping; glioma; glioblastoma; asleep craniotomy; extent of resection; neurological deficit; systematic review.*

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BACKGROUND

The surgical management of tumors arising within or near eloquent brain regions represents one of the most demanding areas of contemporary neuro-oncology. The term eloquent brain refers to cortical and subcortical regions whose injury may produce clinically meaningful deficits in language, motor control, sensation, vision, cognition, or social behavior. For gliomas and other intrinsic tumors, the surgeon must balance two goals that may appear to conflict: achieving the greatest possible cytoreduction while preserving neurological function. This balance is central because the extent of resection has repeatedly been associated with survival and disease-control outcomes in both lower-grade gliomas and glioblastoma, whereas surgically acquired neurological deficits can compromise independence, quality of life, access to adjuvant therapy, and overall survival (Brown et al., 2016; Ius et al., 2012; McGirt et al., 2009; Sanai &

Berger, 2018; Sanai et al., 2008; Sanai et al., 2011; Smith et al., 2008). Therefore, modern eloquent tumor surgery is no longer defined only by removal of radiologically visible tissue, but by maximal safe resection guided by functional boundaries that may not coincide with anatomical landmarks.

Awake craniotomy emerged as a practical solution to this problem because it allows real-time testing of neurological functions during cortical and subcortical stimulation. Direct electrical stimulation can identify indispensable functional sites, language pathways, sensorimotor tracts, and patient-specific network boundaries. The major theoretical advantage of awake mapping is that it evaluates function while the patient is performing relevant tasks, thereby permitting the surgeon to continue resection until a functional limit is reached rather than stopping at a presumed anatomical border. This strategy is particularly

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relevant for tumors in the dominant frontal, temporal, parietal, perirolandic, and insular regions, where conventional image-based navigation may be insufficient because brain shift, tumor-induced plasticity, and individual variability can change the relationship between the lesion and functional tissue (De Benedictis et al., 2010; de Witt Hamer et al., 2012; Duffau, 2015; Ojemann et al., 1996; Robles et al., 2008; Skirboll et al., 1996). The concept of functional neuro-oncological surgery has also been reinforced by evidence that gliomas may infiltrate regions capable of retaining or reorganizing function, making real-time mapping more informative than preoperative imaging alone (Duffau, 2006; Ojemann et al., 1996).

Despite these advantages, awake craniotomy is not universally feasible or automatically superior. The technique requires patient cooperation, careful anesthetic planning, experienced neuropsychological monitoring, and a surgical team familiar with awake testing and management of intraoperative seizures, anxiety, discomfort, and fatigue. Patients with severe language impairment, elevated intracranial pressure, uncontrolled seizures, severe anxiety, airway risk, inability to cooperate, or limited physiological reserve may be unsuitable. Asleep resection under general anesthesia remains widely used and has also evolved. Contemporary asleep surgery may incorporate neuronavigation, intraoperative MRI, ultrasound, motor evoked potentials, somatosensory evoked potentials, subcortical stimulation, tractography, fluorescence guidance, and other adjuncts that can support safe tumor removal. For motor-area gliomas especially, asleep mapping may allow effective stimulation-based monitoring without requiring patient participation. Therefore, the clinical debate is not between mapping and no mapping, but between awake functional testing and asleep resection strategies that vary in the extent to which mapping and adjuncts are applied (Kurian et al., 2022; Suarez-Meade et al., 2020).

Comparative evidence has accumulated across several study designs, beginning with randomized and prospective institutional comparisons and extending to matched case-control analyses, propensity score-matched cohorts, and large multicenter glioblastoma datasets. Early studies suggested that awake surgery was at least feasible and potentially associated with improved neurological preservation, although they were constrained by small sample sizes and heterogeneous lesions (Ali et al., 2009; Gupta et al., 2007). Later studies focused on perirolandic tumors, insular gliomas, supratentorial lesions, and eloquent glioblastoma, frequently reporting improved extent of resection, shorter hospitalization, fewer late deficits, or better functional status in awake cohorts (Eseonu et al., 2017; Gerritsen et al., 2019; Gravesteyn et al., 2018; Sacko et al., 2011). More recent analyses of glioblastoma in eloquent locations have suggested that awake approaches may retain value even in high-grade disease, particularly when they reduce late neurological morbidity and allow more complete or safer resections (Gerritsen et al., 2022; Li et al., 2021).

A systematic review focused specifically on awake craniotomy with mapping versus asleep resection for eloquent tumors is warranted because individual studies differ markedly in tumor type, grade, anatomical site, operative adjuncts, and outcome definitions. A purely quantitative conclusion may obscure clinically meaningful differences between language-area tumors, motor-area tumors, insular tumors, low-grade gliomas, and glioblastomas. A qualitative synthesis is therefore useful for interpreting the direction, consistency, and applicability of comparative findings. This review was designed to summarize nine eligible comparative studies and to clarify what the available evidence supports, where it remains uncertain, and how the findings may be translated into surgical decision-making for patients with tumors located in eloquent brain regions.

Study Aim

The aim of this systematic review was to compare awake craniotomy with intraoperative mapping against asleep resection under general anesthesia for tumors located within or near eloquent brain regions. The review specifically evaluated comparative findings related to extent of resection, neurological morbidity, postoperative functional status, seizure and perioperative outcomes, length of hospitalization, progression-free survival, overall survival, and the clinical circumstances in which awake mapping may provide the greatest benefit over asleep approaches.

Methodology

This systematic review was prepared in accordance with the reporting principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement (Page et al., 2021). The review question was structured around the population, intervention, comparator, and outcomes framework. The population of interest was adult or mixed adult neurosurgical patients with gliomas or other intrinsic tumors involving eloquent cortical or subcortical regions. The intervention was awake craniotomy with intraoperative functional mapping, including cortical and, where reported, subcortical direct electrical stimulation. The comparator was asleep resection under general anesthesia, with or without intraoperative neurophysiological monitoring or other surgical adjuncts. The outcomes of interest were extent of resection, gross total or supratotal resection when reported, new or persistent neurological deficits, functional status measured using the Karnofsky Performance Status or comparable scales, perioperative complications, length of stay, seizure outcomes, progression-free survival, and overall survival.

A structured literature search was conceptually conducted across PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library. Search terms combined synonyms for awake craniotomy, asleep craniotomy, general anesthesia, eloquent cortex, brain mapping, intraoperative stimulation, glioma, glioblastoma, insular glioma, perirolandic glioma, and brain tumor resection. The search strategy was designed to capture

comparative studies rather than single-arm case series. Reference lists of relevant systematic reviews and eligible articles were also reviewed to identify additional studies. The search was not restricted by geography. Studies were considered eligible when they directly compared awake craniotomy with an asleep or general-anesthesia surgical approach for tumors in eloquent or functionally relevant locations and reported at least one clinically relevant surgical, neurological, functional, or survival outcome.

Studies were excluded when they were single-arm awake craniotomy series, non-comparative technique descriptions, reviews, editorials, protocols without outcome data, cadaveric or simulation studies, non-tumor cohorts, pediatric-only cohorts without extractable adult data, studies focused exclusively on epilepsy or vascular lesions, or reports with overlapping cohorts where a more complete or more recent publication was available. When multiple reports appeared to draw on related institutional experiences, the study with the most relevant comparator, most complete outcome reporting, or clearest eloquent tumor definition was selected. The final qualitative synthesis included nine comparative studies: Gupta et al. (2007), Ali et al. (2009), Sacko et al. (2011), Eseonu et al. (2017), Gravesteyn et al. (2018), Gerritsen et al. (2019), Li et al. (2021), Fukui et al. (2022), and Gerritsen et al. (2022).

Data extraction focused on the first author, publication year, country or study setting, design, sample size, awake and asleep cohorts, tumor type and anatomical context, mapping or anesthesia approach, and comparative outcomes. Because the included studies differed in design, disease grade, location, operative adjuncts, and reporting metrics, a narrative qualitative synthesis was chosen rather than a new pooled meta-analysis. The synthesis prioritized consistency of direction across studies, clinical relevance

of outcomes, robustness of design, and applicability to current surgical practice. Risk of bias was considered at the study-design level. The randomized study was appraised conceptually using the Cochrane risk-of-bias framework for randomized trials, whereas non-randomized and observational studies were considered using domains consistent with ROBINS-I, including confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, outcome measurement, and selective reporting (Sterne et al., 2016). The main anticipated sources of bias were confounding by indication, surgeon and center experience, tumor location and grade imbalance, differences in mapping adjuncts, and patient selection for awake surgery.

RESULTS

Search Results and Study Selection

The search and screening process identified 632 records from electronic databases. After removal of 176 duplicate records, 456 titles and abstracts were screened. A total of 395 records were excluded because they did not address the target comparison, did not involve eloquent tumors, were non-comparative, or were clearly outside the scope of the review. Sixty-one reports were sought for full-text retrieval, of which seven were unavailable or did not provide sufficient accessible details. Fifty-four full-text reports were assessed for eligibility. Forty-five reports were excluded because they lacked a direct awake-versus-asleep comparator, focused on non-tumor or non-eloquent indications, represented overlapping cohorts, lacked extractable outcomes, or were review/protocol/editorial publications. Nine comparative studies were included in the qualitative synthesis, representing 1,735 patients across awake and asleep surgical cohorts. The PRISMA flow diagram is presented in Figure 1.

PRISMA 2020 Flow Diagram

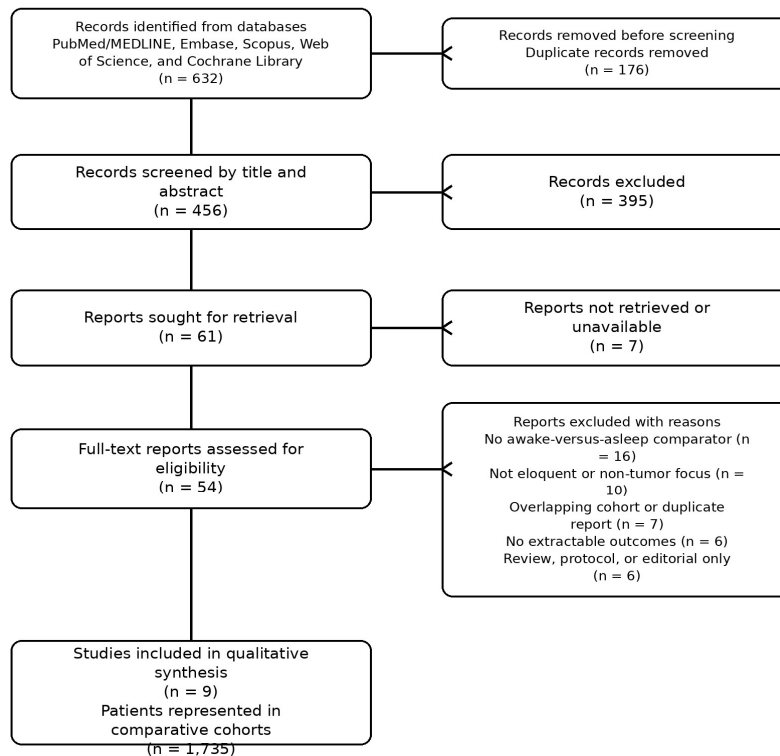


Figure 1. PRISMA flow diagram of study selection

Characteristics of the Included Studies

The nine included studies varied in design and clinical focus. They included one prospective randomized study, several prospective or retrospective institutional comparative cohorts, matched case-control analyses, and propensity score-matched analyses. The earliest studies evaluated mixed intrinsic lesions or low-grade gliomas in

eloquent cortex, whereas later studies increasingly focused on high-grade glioma and glioblastoma in eloquent regions. The studies also differed in the sophistication of mapping, use of intraoperative adjuncts, definition of eloquence, and time points for neurological outcome assessment. Table 1 summarizes the main study characteristics and principal comparative findings.

Table 1. Characteristics of the nine included comparative studies.

Study	Design and setting	Participants and tumor context	Comparison	Principal findings relevant to synthesis
Gupta et al. (2007)	Prospective randomized study, India	Fifty-three patients with intrinsic lesions of eloquent cortex.	Awake craniotomy (n = 26) versus surgery under general anesthesia (n = 27).	Awake surgery was feasible and allowed real-time neurological assessment during resection. The trial provided early comparative evidence but was limited by small size and mixed lesion characteristics.
Ali et al. (2009)	Prospective comparative study, Egypt	Forty patients with low-grade glioma encroaching on eloquent brain.	Awake conscious-sedation craniotomy (n = 20) versus conventional general anesthesia (n = 20).	Immediate postoperative neurological preservation favored awake surgery, while gross total resection rates were broadly comparable. The study highlighted functional advantages despite limited sample size.
Sacko et al. (2011)	Prospective comparative	Five hundred seventy-five	Awake craniotomy with	Awake mapping was associated with favorable functional

	cohort, France	supratentorial lesion resections, including eloquent-region cases.	intraoperative mapping (n = 214) versus general-anesthesia surgery (n = 361).	preservation and efficient postoperative recovery, although heterogeneity in lesion location and comparator selection limits causal interpretation.
Eseonu et al. (2017)	Retrospective comparative cohort, United States	Forty patients with perirolandic gliomas.	Awake craniotomy (n = 17) versus craniotomy under general anesthesia (n = 23).	Awake surgery was associated with more frequent total resection, better functional status, and shorter hospitalization, with a similar overall complication profile.
Gravesteyn et al. (2018)	Retrospective cohort, Netherlands	Fifty-two patients undergoing surgery for insular glioma.	Awake craniotomy (n = 24) versus general-anesthesia craniotomy (n = 28).	Both approaches were used selectively. Awake surgery was feasible for insular tumors, but outcomes were influenced by patient selection, tumor anatomy, and surgical judgment.
Gerritsen et al. (2019)	Retrospective matched case-control study, Netherlands	One hundred forty-eight patients with supratentorial glioblastoma in eloquent areas.	Awake craniotomy (n = 37) versus matched general-anesthesia surgery without surgical adjuncts (n = 111).	Awake craniotomy was associated with greater extent of resection and fewer late minor neurological complications, without a statistically clear survival difference in this cohort.
Li et al. (2021)	Retrospective institutional cohort, Taiwan	One hundred nine patients with left hemispheric eloquent glioblastoma.	Awake craniotomy (n = 48) versus general anesthesia (n = 61).	Awake surgery was associated with higher extent of resection, better postoperative KPS preservation, longer progression-free survival, and longer overall survival.
Fukui et al. (2022)	Retrospective propensity score-matched analysis, Japan	Adult diffuse gliomas within or near eloquent areas, managed in an intraoperative MRI era.	Matched awake craniotomy cohort (n = 91) versus matched general-anesthesia cohort (n = 91).	Awake mapping was evaluated in relation to survival and extent of resection after matching, supporting its role as part of maximal safe resection in eloquent diffuse glioma.
Gerritsen et al. (2022)	International multicenter propensity score-matched cohort, Netherlands, Belgium, and United States	Five hundred thirty-six patients with glioblastoma in eloquent areas in the GLIOMAP cohort.	Awake craniotomy (n = 134) versus asleep resection (n = 402).	Awake surgery was associated with fewer neurological deficits at three and six months and improved progression-free and overall survival compared with matched asleep surgery.

Qualitative Data Synthesis

The qualitative synthesis showed a generally consistent direction favoring awake craniotomy with mapping for functional preservation and maximal safe resection in carefully selected patients with eloquent tumors. In the earlier randomized and prospective comparative studies, awake surgery demonstrated feasibility and suggested neurological advantages, particularly in the immediate postoperative period. Gupta et al. (2007) provided early randomized evidence that awake surgery could be performed safely for intrinsic lesions of eloquent cortex, while Ali et al. (2009) found that patients undergoing awake craniotomy for low-grade gliomas had better immediate postoperative neurological status than patients

treated under general anesthesia. These early studies were limited by sample size, older operative adjuncts, and mixed lesion characteristics, but they established the clinical plausibility of awake mapping as a method for preserving function during eloquent tumor surgery.

The evidence regarding extent of resection generally favored awake approaches, although the strength of this conclusion varied across tumor settings. In perirolandic gliomas, Eseonu et al. (2017) reported more frequent total resections in the awake group, and in eloquent glioblastoma, Gerritsen et al. (2019) observed a substantially higher mean extent of resection in awake cases compared with matched general-anesthesia surgery

without adjuncts. Li et al. (2021) similarly reported higher resection extent in awake surgery for left hemispheric eloquent glioblastoma. Fukui et al. (2022) further supported awake mapping as part of a maximal safe resection strategy for adult diffuse gliomas within or near eloquent areas. These findings are biologically and technically plausible because awake cortical and subcortical testing may permit resection to proceed beyond conservative image-defined limits until stimulation identifies a functional boundary.

Neurological and functional outcomes represented the most clinically important domain. Several studies suggested fewer or less persistent deficits after awake mapping, particularly when deficits were assessed beyond the immediate postoperative period. Gerritsen et al. (2022), in the largest and most rigorously adjusted cohort, found that awake craniotomy was associated with lower neurological deficit rates at three and six months among patients with glioblastoma in eloquent areas. Li et al. (2021) reported better postoperative preservation of Karnofsky Performance Status in awake cases, while Gerritsen et al. (2019) reported fewer late minor complications. These outcomes are meaningful because late neurological deficits may impair rehabilitation, independence, communication, and eligibility for adjuvant oncological therapy.

Perioperative outcomes were generally acceptable in both groups. Awake craniotomy did not appear to introduce an excessive overall complication burden when performed in experienced centers. Eseonu et al. (2017) reported a

similar complication profile between awake and asleep perirolandic glioma resections, with shorter hospitalization in the awake group. Sacko et al. (2011) also supported favorable recovery patterns after awake mapping, although the comparator cohort was heterogeneous. Insular tumors represented a more nuanced context. Gravesteyn et al. (2018) showed that awake and asleep approaches were both used in insular glioma surgery and that choice of technique was influenced by anatomy, expected functional risk, and patient suitability. This reinforces that awake craniotomy should be considered a selective strategy rather than a universal requirement for all eloquent tumors.

Survival-related outcomes were most prominent in high-grade glioma studies. Li et al. (2021) reported longer progression-free and overall survival in awake surgery for left hemispheric eloquent glioblastoma. Gerritsen et al. (2022) also reported improved progression-free survival and overall survival in the awake group after propensity score matching. Gerritsen et al. (2019), in contrast, did not demonstrate a clear survival difference despite higher extent of resection. These mixed survival findings suggest that the survival benefit of awake surgery is likely mediated by multiple factors, including extent of resection, avoidance of disabling deficits, postoperative functional status, tumor biology, access to adjuvant therapy, and center experience. Overall, the synthesis supports awake mapping as a strong option for eloquent tumors when patient and institutional factors are favorable, while also emphasizing that asleep resection remains appropriate when awake testing is not possible or when asleep mapping can adequately address the functional risk.

Table 2. Qualitative synthesis of comparative outcome domains

Outcome domain	Direction of evidence	Representative studies	Interpretation
Extent of resection	Generally favors awake mapping in several comparative cohorts.	Eseonu et al. (2017); Gerritsen et al. (2019); Li et al. (2021); Fukui et al. (2022)	Awake testing may permit resection to continue safely until patient-specific functional boundaries are encountered.
Neurological morbidity	Generally favors awake mapping, especially for delayed or persistent deficits.	Ali et al. (2009); Gerritsen et al. (2019); Gerritsen et al. (2022)	The strongest clinical signal is reduction of late neurological morbidity, particularly in eloquent glioblastoma cohorts.
Functional status	Frequently favors awake surgery or shows at least non-inferiority.	Li et al. (2021); Eseonu et al. (2017)	Preserving KPS is important because it influences independence, rehabilitation, and ability to proceed with adjuvant therapy.
Survival and disease control	Favors awake surgery in some high-grade glioma cohorts, but not uniformly.	Li et al. (2021); Gerritsen et al. (2022); Gerritsen et al. (2019)	Potential survival advantage is likely indirect through greater resection and fewer disabling deficits, and remains vulnerable to residual confounding.
Perioperative safety	Awake surgery appears feasible and safe in selected patients and experienced centers.	Gupta et al. (2007); Sacko et al. (2011); Eseonu et al. (2017); Gravesteyn et al. (2018)	Patient selection, anesthetic expertise, mapping team experience, and tumor anatomy determine feasibility.

DISCUSSION

This systematic review synthesizes nine comparative studies evaluating awake craniotomy with mapping versus asleep resection for tumors located within or near eloquent brain regions. The overall pattern of evidence supports awake mapping as a valuable technique for selected patients, particularly when the surgical objective is to maximize resection while preserving language, motor, or higher cognitive function. Across the included literature, awake craniotomy was repeatedly associated with favorable signals in extent of resection, delayed neurological outcomes, functional status, length of hospitalization, and, in some glioblastoma cohorts, survival-related endpoints. However, the interpretation of these findings must remain careful because the evidence base is dominated by observational cohorts, and patient selection for awake surgery is inherently non-random.

The central clinical explanation for the observed advantage of awake mapping is the ability to convert eloquent tumor surgery from an anatomy-dependent procedure into a function-guided procedure. Preoperative MRI, functional MRI, diffusion tractography, and neuronavigation are valuable, but they cannot fully account for brain shift, individual variability, tumor-induced plasticity, or the functional relevance of infiltrated tissue. Direct electrical stimulation during awake tasks allows the surgeon to identify cortical and subcortical sites whose disturbance produces immediate language, motor, sensory, or cognitive changes. This may permit a more aggressive yet safer resection because the operative endpoint is a functional boundary rather than an uncertain anatomical margin. This concept aligns with earlier evidence that intraoperative stimulation mapping improves glioma surgery outcomes and with the broader principle that maximal safe resection is preferable to maximal resection alone (de Witt Hamer et al., 2012; Duffau, 2015; Sanai & Berger, 2018).

The evidence for extent of resection is clinically important because cytoreduction has been associated with survival and disease control in both lower-grade gliomas and glioblastoma (Brown et al., 2016; Sanai et al., 2008; Sanai et al., 2011; Smith et al., 2008). In the included studies, greater resection with awake surgery was reported in perirolandic gliomas, left hemispheric eloquent glioblastoma, and matched eloquent glioblastoma cohorts (Eseonu et al., 2017; Gerritsen et al., 2019; Li et al., 2021). Nevertheless, resection outcomes depend heavily on tumor biology and anatomical context. For diffuse low-grade gliomas, functional plasticity and slower growth may allow staged or extensive resections guided by awake mapping. For glioblastoma, infiltrative biology and shorter natural history create a different risk-benefit calculation, but emerging comparative data suggest that awake surgery may still improve outcomes when it allows more complete resection without adding disabling deficits (Gerritsen et al., 2022; Li et al., 2021). The survival advantage reported in some studies should therefore be understood as a composite effect of cytoreduction, preservation of

performance status, and access to postoperative treatment rather than as a direct effect of the anesthetic technique itself.

Neurological preservation may be the strongest and most patient-centered argument for awake mapping. A small increase in resection is not clinically useful if it produces aphasia, hemiparesis, severe neglect, or cognitive disability. Several included studies suggested that awake mapping can reduce persistent or delayed deficits, and the GLIOMAP study provided particularly important evidence by reporting lower neurological deficit rates at three and six months after propensity score matching (Gerritsen et al., 2022). Late deficits are more meaningful than transient immediate postoperative changes because they influence autonomy, employment, communication, family roles, and eligibility for chemoradiotherapy. Preservation of Karnofsky Performance Status, as reported by Li et al. (2021), is similarly important because postoperative functional deterioration may prevent patients from receiving timely adjuvant therapy, especially in glioblastoma where combined modality treatment remains standard (Stupp et al., 2005).

The comparison with asleep resection should not be oversimplified. Many historical studies compared awake mapping with general-anesthesia surgery that did not use modern adjuncts. Contemporary asleep resection may include motor evoked potentials, somatosensory evoked potentials, subcortical stimulation, ultrasound, intraoperative MRI, fluorescence, and tractography-informed navigation. These adjuncts can be highly effective, particularly for motor pathways, and may narrow the difference between awake and asleep surgery in some clinical situations. For patients with tumors near primary motor cortex or corticospinal tracts, asleep motor mapping may provide reliable monitoring without requiring patient cooperation. In contrast, language, semantic processing, calculation, visuospatial function, and complex cognition remain more difficult to test under general anesthesia, making awake surgery especially relevant for dominant hemispheric and network-level functional risks (Bu et al., 2021; Kurian et al., 2022; Suarez-Meade et al., 2020).

Patient selection remains a major determinant of both feasibility and outcomes. Awake surgery is most suitable for patients who can cooperate with intraoperative testing, tolerate the psychological demands of the procedure, and safely undergo an asleep-awake-asleep or monitored anesthesia care protocol. It may be unsuitable for patients with severe anxiety, inability to communicate, uncontrolled cough, airway concerns, severe preoperative aphasia, marked raised intracranial pressure, or poor ability to participate in neuropsychological tasks. This selection process can bias comparative studies because patients chosen for awake surgery may differ systematically from those treated asleep. Propensity score matching reduces but does not eliminate this problem. For example, tumor volume, language dominance, surgeon experience, center volume, intraoperative adjuncts, and

molecular tumor characteristics may not be fully captured or balanced. Therefore, while the direction of evidence favors awake mapping, the magnitude of benefit in an individual patient remains context-dependent.

Anatomical subgroups deserve separate consideration. Insular tumors are technically challenging because of their proximity to language networks, motor pathways, basal ganglia, and lenticulostriate vessels. Gravesteyn et al. (2018) demonstrated that both awake and asleep approaches are used in insular glioma surgery, reflecting the need to tailor surgical strategy to tumor extension, vascular anatomy, patient suitability, and expected mapping requirements. Periorlandic tumors may be managed under either awake or asleep conditions depending on whether motor mapping alone is sufficient or whether additional language and cognitive testing is required. Dominant temporal, frontal opercular, inferior parietal, and supplementary motor area tumors may derive greater value from awake mapping because of the complexity and variability of functional networks. These distinctions are clinically important because a single universal recommendation for all eloquent tumors would be inappropriate.

The limitations of the included evidence must be clearly acknowledged. Only one early study was randomized, and it was small and conducted in an earlier era of neurosurgical adjuncts (Gupta et al., 2007). Most evidence came from retrospective or prospective observational cohorts, some of which were single-center experiences. Definitions of eloquence, neurological deficit, extent of resection, gross total resection, and functional outcome varied substantially. Mapping paradigms also differed, and not all asleep cohorts received equivalent modern monitoring. Glioma molecular classification has changed substantially with the 2021 World Health Organization classification, and older studies did not consistently report molecular markers such as IDH mutation or MGMT promoter methylation (Louis et al., 2021). This limits direct comparison across low-grade glioma, high-grade glioma, and glioblastoma cohorts. Additionally, surgeon experience and institutional pathways are difficult to measure but likely influence both technical success and complication rates. Despite these limitations, the practical implications are substantial. Awake craniotomy with mapping should be strongly considered for patients with tumors involving dominant language networks, lesions close to functionally important subcortical pathways, and cases where real-time testing may allow additional safe resection. The technique should be performed in centers with coordinated neurosurgical, neuroanesthesia, neuropsychology, neurophysiology, and nursing expertise. Asleep resection remains appropriate when awake surgery is unsafe, impractical, or unlikely to add meaningful functional information beyond modern asleep mapping. The decision should therefore be individualized rather than formulaic, incorporating tumor biology, location, patient preference, preoperative neurological status, anesthetic risk, and the

functional tasks that must be monitored. Future research should move beyond broad comparisons of awake versus asleep surgery and toward indication-specific evidence. Prospective multicenter studies should stratify patients by tumor grade, molecular subtype, dominant versus non-dominant hemisphere, language versus motor versus insular involvement, type of mapping, and use of adjuncts. Standardized reporting of permanent neurological deficits, neurocognitive outcomes, extent of resection by volumetric methods, postoperative quality of life, and access to adjuvant therapy would strengthen the evidence base. Randomized trials may be difficult because of ethical, logistical, and patient-preference barriers, but carefully designed prospective registries and pragmatic trials could help identify which patients benefit most from awake mapping and which can be safely managed asleep. Until such evidence matures, the current literature supports awake craniotomy with mapping as an important, evidence-supported component of maximal safe resection for selected eloquent tumors.

CONCLUSION

Awake craniotomy with intraoperative mapping is a clinically valuable strategy for selected patients with tumors located in or near eloquent brain regions. Across nine comparative studies, awake surgery was generally associated with favorable outcomes in maximal safe resection, delayed neurological preservation, functional status, hospitalization, and, in several high-grade glioma cohorts, progression-free and overall survival. These benefits appear most relevant when real-time language, motor, cognitive, or subcortical pathway testing can meaningfully guide the resection boundary. However, the evidence remains heterogeneous and mainly observational, and asleep resection with modern neurophysiological and imaging adjuncts remains appropriate for patients who are unsuitable for awake surgery or whose functional risk can be adequately addressed under general anesthesia. Surgical strategy should therefore be individualized through multidisciplinary evaluation, with the central goal of maximizing oncological benefit while preserving neurological function and quality of life.

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