AWAKE CRANIOTOMY WITH INTRAOPERATIVE BRAIN MAPPING: PRINCIPLES, TECHNIQUE AND OUTCOMES IN SURGERY FOR TUMORS OF ELOQUENT BRAIN AREAS

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Abstract

Background: Surgery for intrinsic brain tumors must balance the extent of resection against the preservation of neurological function. Awake craniotomy with direct electrical stimulation mapping allows the surgeon to identify language, motor and sensory pathways in real time. **Aim:** To review the history, patient selection, anesthetic management, mapping technique and clinical outcomes of awake craniotomy for tumors located in or near eloquent brain. **Methods:** Narrative review of key clinical series, meta-analyses and technical reviews. **Results:** In the largest language-mapping series, only 1.6% of surviving patients (4 of 243) had a persistent language deficit at six months, and most series report a mean extent of resection above 90% or a gross total resection rate above 50%. Failure of the awake procedure is uncommon (0.5–6.4%). Evidence comparing awake surgery with general anesthesia comes almost entirely from non-randomized studies. **Conclusion:** Awake craniotomy with cortical and subcortical mapping is regarded as the gold standard for the maximal safe resection of tumors in or near eloquent brain.

Introduction

The fundamental goal of glioma surgery is to balance the greatest possible extent of resection (EOR) against the preservation of neurological function. A greater EOR is associated with longer survival in patients with both low-grade and high-grade glioma [1,2], whereas new postoperative deficits are associated with poorer survival and quality of life [3]. Tumors frequently infiltrate or lie next to "eloquent" regions responsible for language, movement, sensation and vision, and the location of these regions varies considerably between individuals [4]. Anatomical imaging alone therefore cannot reliably show which tissue can be removed safely.

Awake craniotomy addresses this problem by keeping the patient conscious and cooperative during the critical part of the operation. Electrical stimulation of the cortex and subcortical white matter transiently and focally disrupts the underlying function (or, in motor and sensory areas, activates it), which mimics the effect of removing that tissue and lets the surgeon resect the tumor up to the functional boundary [5]. This article reviews the history, indications, anesthetic management, mapping technique, outcomes and current limitations of awake craniotomy in tumor surgery.

Keywords: awake craniotomy, brain mapping, direct electrical stimulation, glioma, eloquent cortex, language mapping, neuroanesthesia.

Literature Review

The literature on awake craniotomy spans more than a century, from the first stimulation experiments in humans to large modern surgical series. Key sources include the New England Journal of Medicine series of 250 patients by Sanai et al. [4], the 27-year single-institution experience of Hervey-Jumper et al. [6], the meta-analysis of intraoperative stimulation mapping by De Witt Hamer et al. [7], and comparative analyses of awake surgery and surgery under general anesthesia [8,9]. Most of the evidence is observational and retrospective, and randomized trials are scarce.

Historical Background

Craniotomy on awake patients predates anesthesia, but the deliberate use of wakefulness for functional testing began only in the late nineteenth century [5]. The first report of electrical stimulation of the human brain, by Bartholow in 1874, involved a patient whose tumor had eroded the skull; it caused considerable ethical controversy because the experiment offered the patient no therapeutic benefit [10]. Penfield and Boldrey described the method systematically in 1937, using awake stimulation to map motor and sensory representation during epilepsy surgery [11]. In the 1970s Ojemann introduced standardized intraoperative testing and constant-current biphasic stimulation for localizing language [12], and Ojemann and Berger later adapted these techniques to tumor surgery [13].

Anesthetic practice evolved in parallel: from local analgesia alone, through fentanyl–droperidol sedation, to propofol in the 1990s [14], and then to remifentanil and dexmedetomidine, which allow more precise titration of analgesia and sedation without respiratory depression [5].

Patient Selection and Preoperative Assessment

Awake mapping is considered for supratentorial lesions in or near potentially eloquent areas [5]. The assessment covers medical comorbidities, existing neurological deficits, seizure frequency, body habitus and anxiety. A baseline examination with a neurophysiologist confirms that the patient can perform the tasks reliably and helps set realistic expectations [5].

Preoperative functional MRI, tractography and magnetoencephalography are useful for determining language lateralization, but their spatial resolution is insufficient to exclude function, and intraoperative brain shift may move functional cortex and tracts by more than 1 cm from the position shown by navigation. They should therefore not be used to justify surgery under general anesthesia [5]. Most earlier contraindications can now be managed (Table 1). A previous resection limited by positive mapping does not preclude repeat awake surgery: up to 25% of previously identified functional sites no longer showed function at reoperation, which reflects functional plasticity [5,15].

Table 1. Relative contraindications to awake craniotomy and current solutions

Concern	Current solution
Significant mass effect (midline shift > 2 cm)	Staged internal debulking under general anesthesia, followed by awake mapping at reoperation
Obesity (BMI > 30) or obstructive sleep apnea	Laryngeal mask airway before and after mapping
Psychiatric history or emotional instability	Treated mood disorders are no longer a contraindication
Age	Awake surgery in patients older than 10 years; two-stage procedure with an implanted grid below 10 years
Intraoperative seizures	Ice-cold Ringer's solution applied to the cortex; propofol available intravenously
Intraoperative nausea	Preoperative antiemetics (ondansetron, scopolamine) and high-dose dexamethasone (10 mg)

Adapted from Gogos et al. [5], based on Hervey-Jumper et al. [6].

Anesthetic Management

Two main approaches are used: the "asleep–awake–asleep" technique, typically with propofol and remifentanil, and "conscious sedation". Dexmedetomidine may be added to either [5]. In an analysis of 180 glioma patients, conscious sedation with dexmedetomidine required fewer opioids, vasoactive and antihypertensive drugs, and was associated with shorter operative times and hospital stay [16]. In a randomized trial, dexmedetomidine caused fewer respiratory adverse events than propofol–remifentanil without impairing the patients' ability to perform mapping tasks [17].

Premedication with an antiemetic is standard, dexamethasone and mannitol are given in most cases, and patients already taking anticonvulsants continue them [5]. The scalp is infiltrated with local anesthetic at the pin sites and along the incision. The patient is usually placed in a semi-lateral position, which limits airway obstruction and snoring, and body temperature is kept above 36 °C. Manipulation of the dura and irritation of the middle fossa floor can cause pain or a trigeminocardiac reflex (nausea, vomiting, hypotension, bradycardia, even apnea), so additional local anesthetic is applied to the dural branches of the trigeminal nerve when needed. Sedation is weaned toward the end of the craniotomy so that the patient is awake for mapping [5].

Intraoperative Mapping Technique

Mapping begins with an assessment of wakefulness. The most established technique is low-frequency bipolar stimulation (60 Hz, 1.0-ms biphasic square-wave pulses applied for 3–4 s) with the Ojemann probe [5]. Stimulation starts at 2 mA and is increased until a positive response or after-discharge potentials appear, up to about 5 mA; the current needed is typically 3–4 mA, and higher currents increase the risk of seizures [5]. Cortical sites are spaced 1 cm apart, numbered, and each is tested at least three times non-consecutively. A site is considered positive when the patient fails the task in two thirds of trials or more [5,18].

Electrocorticography is used to detect after-discharges. If they occur, mapping is suspended and the cortex is irrigated with ice-cold Ringer's solution, which rapidly terminates stimulation-induced seizures [19]. High-frequency (250–500 Hz) monopolar stimulation is an alternative; in one series of 41 patients it gave low rates of postoperative deficits but intraoperative seizures in 7% [20].

The tasks depend on tumor location (Table 2). Stimulation of the primary motor cortex produces movement, of the somatosensory cortex tingling or paresthesia, and of the visual cortex phosphenes. In areas serving higher functions, stimulation disrupts performance, for example by causing speech arrest, anomia or alexia. Speech arrest is distinguished from dysarthria by the absence of involuntary contractions of the mouth or pharynx [5].

Table 2. Functions tested during awake mapping by anatomical location

Location	Functions mapped
Frontal	Motor function; speech arrest, picture naming, reading
Temporal	Speech arrest, picture naming, reading
Insula	Motor function; speech arrest, picture naming, reading
Parietal	Somatosensory function; calculation (dominant hemisphere); line bisection for hemispatial inattention (non-dominant hemisphere)
Occipital	Visual fields

Adapted from Gogos et al. [5].

Subcortical mapping is performed once the resection passes below the depth of the sulci, where white-matter pathways are at risk. According to the dual-stream model of language, the dorsal stream (arcuate and superior longitudinal fasciculi) supports sensorimotor integration, and its stimulation typically produces hesitation and grammatical or semantic errors during sentence generation. The ventral stream (inferior fronto-occipital, uncinate, middle and inferior longitudinal fasciculi) supports comprehension, and stimulation of the inferior fronto-occipital fasciculus commonly produces semantic paraphasias during picture–word interference testing [5,21,22].

Because the false-negative rate of mapping is very low, many centers now use "negative mapping": a smaller, tailored craniotomy and resection along function-free corridors defined by negative sites, without an exhaustive search for positive sites [4,5]. Larger craniotomies with positive mapping may remain appropriate early in the learning curve [5].

Outcomes and Complications

In the landmark series of 250 consecutive patients with dominant-hemisphere gliomas operated with tailored craniotomy and negative language mapping, 58% had at least one site of stimulation-induced speech arrest, yet 94.3% of 3,281 stimulated cortical sites were not associated with language deficits [4]. One week after surgery 77.6% of patients retained baseline language function, 8.4% had worsened and 14.0% had a new speech deficit; at six months only 4 of 243 surviving patients (1.6%) had a persistent deficit. Complete removal of detectable tumor was achieved in 59.6% [4].

In the 27-year experience of the same institution (859 patients), stimulation-induced seizures occurred in 3%, the overall surgical and medical complication rate was 10%, the 30-day readmission rate was 1%, and the awake procedure failed in 0.5% [6]. Other groups report complication rates of 14–32% and failure rates of 2.3–6.4% [5,23]. Across published series the mean EOR is usually above 90% or the gross total resection rate above 50%, while permanent deficit rates range widely (3–47.1%). This variation reflects differences in tumor location and involvement of eloquent tissue, and the lack of a consistent definition of a "permanent" deficit, which ranges from persistence at 1 month to persistence at 6 months [5].

Tumors of the primary motor cortex illustrate the trade-off. Mean EOR is reported at 91–93%, but permanent motor deficits occurred in 33.3–47.1% of the awake subgroups; most were mild, and in one series only 4 of 16 permanent deficits in awake patients were functionally significant [5,24]. A meta-analysis by De Witt Hamer et al. is widely cited as evidence that intraoperative stimulation mapping reduces late severe neurological deficits in glioma surgery [5,7].

Whether awake surgery is superior to surgery under general anesthesia is less clear. A systematic review and meta-analysis of nine comparative reports found less postoperative nausea and vomiting and a shorter hospital stay with awake surgery, but no difference in EOR or in permanent language or motor deficits; none of the included studies was randomized [8]. A retrospective matched case–control study of glioblastoma in eloquent areas found a higher EOR with awake surgery but no difference in overall survival [9]. Because the choice of approach in these studies depended on predicted risk and surgeon familiarity, selection bias is likely [5,8].

Most complications are predictable and manageable. Nausea and vomiting are prevented with antiemetics and dexamethasone; seizures are stopped with cold Ringer's solution; airway obstruction is treated with a nasal airway or laryngeal mask; and brain swelling after durotomy is managed by asking the patient to hyperventilate, giving additional mannitol, or releasing cerebrospinal fluid [5]. Newly acquired deficits benefit from rehabilitation that starts during the inpatient stay and includes motor, cognitive and speech components, although evidence for the best approach is limited [5].

Limitations and Future Directions

Passive mapping with electrocorticography, which records cortical activity during language, motor or cognitive tasks, is still investigational and not accurate enough to replace stimulation mapping; it may, however, shorten operative time, reduce seizure risk and permit mapping where stimulation is not possible [5,25]. When only motor function needs to be mapped, some centers have moved to general anesthesia with motor mapping [5]. Prospective studies and consistent definitions of permanent deficit are needed to clarify which patients benefit most from awake surgery [5].

Conclusion

Awake craniotomy with cortical and subcortical stimulation mapping allows tumors in or near eloquent brain to be resected extensively while the risk of permanent language and motor deficits is kept low. Refinements in anesthesia, smaller tailored craniotomies and better testing paradigms have removed most of the historical contraindications and made complications infrequent and manageable. Its advantages over general anesthesia in survival and long-term function still need confirmation in prospective comparative studies, but it remains the reference technique for maximal safe resection near eloquent areas.

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