

# Awake craniotomy: A qualitative review and future challenges

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## ABSTRACT

Neurosurgery in awake patients incorporates newer technologies that require the anesthesiologists to update their skills and evolve their methodologies. They need effective communication skills and knowledge of selecting the right anesthetic drugs to ensure adequate analgesia, akinesia, along with patient satisfaction with the anesthetic conduct throughout the procedure. The challenge of providing adequate anesthetic care to an awake patient for intracranial surgery requires more than routine vigilance about anesthetic management.

**Key words:** *Awake craniotomy, neuroanesthesiology*

## INTRODUCTION

It is known that in ancient times, patients were treated for seizures by trepanation of the skull.<sup>[1,2]</sup> Hippocrates, in "On Injuries of the Head," endorsed trepanation for the treatment of head wounds.

Awake craniotomy was introduced for surgical treatment of epilepsy, and has subsequently been used in patients with supratentorial tumors, arterio-venous malformation, deep brain stimulation, and mycotic aneurysms near critical regions of brain.<sup>[3-5]</sup> During awake craniotomies, active participation by the patient is necessary to facilitate cortical mapping as response to stimulation of the cerebral cortex guides the surgeon's intraoperative decisions. Awake craniotomy offers the unique possibility of reducing postoperative morbidity, facilitating early discharge from the hospital.<sup>[6-10]</sup> The primary goal of the

anesthesiologist is to make the operation safe and effective by reducing the psychophysical distress of the patient, who has an open skull with a surgical team manipulating the contents.

Different protocols exist for anesthetic care during awake craniotomy based on monitored anesthesia care (MAC) or general anesthesia (asleep-awake-asleep technique). Nevertheless the administration of anesthetics, expectedly, is not without drawbacks, side effects and risks. A new approach for awake craniotomies emphasizes the need of adequate communication with patients.<sup>[11]</sup>

In this review we compare techniques and new advances in providing anesthetic care for this surgical procedure. We also discuss outcomes of various anesthetic approaches to awake craniotomy and analyze the results of awake craniotomy itself.

## MATERIALS AND METHODS

A thorough PubMed and Medline literature search was conducted for studies investigating the use of key words "awake craniotomy," "scalp block," "asleep-awake-asleep," "awake-awake-awake," in patients for intracranial surgeries. Complete manuscripts were studied and only those that reported on original studies with human subjects or

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preclinical studies and were published between 1990 and 2013 were included.

## HISTORY

The first brain mapping with electrical stimulation in humans was generated by R Bartholow in 1874.<sup>[12]</sup> A decade later, Horsley applied electrical stimulation to human cortex to localize sources of seizure under local anesthesia.<sup>[13]</sup> Davidoff (1934) began to combine local anesthesia and sedation, while Wilder Penfield used sedation following mild electric current to locate the source of the seizure activity and could potentially remove or destroy the specific cerebral tissue.<sup>[14]</sup> He advocated that the patient remain conscious and alert during the procedure so that the surgeon is forewarned about the aura, motor weakness or sensory changes by the patient at the onset of a seizure. His technique of preferred sedation only following electric stimulation testing was often successful, reproducible and was accepted worldwide for epilepsy and brain tumor surgery.<sup>[14]</sup> In 1950s, Pasquet tried general anesthesia after testing with local anesthesia.<sup>[14]</sup>

The first important change in the standard of anesthetic care for awake craniotomy dates back to 1959, when De Castro and P Mundeleer introduced neuro-leptoanesthesia (haloperidol and phenoperidine) administration.<sup>[15]</sup> In 1988, Archer studied 354 awake craniotomies for cortical resection of epilepsy using local anesthesia and intravenous fentanyl with droperidol.<sup>[16]</sup> Welling replaced fentanyl with alfentanil.<sup>[17]</sup> Four years later, DL Silbergeld published his landmark study using propofol sedation in awake craniotomy.<sup>[18]</sup> Silbergeld's work is largely considered to be the second great advance in the field of awake craniotomy. Propofol infusion became popular during awake craniotomies for its rapid onset, titrability, and short recovery time. Subsequent studies have largely focused on propofol sedation in combination with different opioids,<sup>[19,20]</sup> in addition to examining technical aspects of the procedure (laryngeal mask airway [LMA],<sup>[21]</sup> bispectral index [BIS], and target-controlled infusion [TCI]<sup>[22]</sup>).

## ANESTHETIC CONSIDERATIONS

Modern anesthetic approaches may be generally divided as follows: Monitored anesthesia care (MAC)<sup>[23]</sup> and asleep-awake-asleep (AAA) and recently a new approach of awake-awake-awake technique. The success of each different anesthetic technique depends on several factors:

- Appropriate patient selection
- Preoperative psychological preparation
- Rapport building between patient and anesthesiologists

- Comfort in patient positioning
- Appropriate scalp nerve block
- Anesthetic technique selection
- Appropriate intraoperative monitoring
- Continuous team communication

### Appropriate patient selection

Not all patients are fit for awake craniotomy. A team of neurologists/neurosurgeons/anesthesiologists and neurophysiologists together select the right candidate. Through pre-operative assessment of airway and other pre-morbid conditions like sleep apnea, mental impairment, personality disorder, pre-existing paralysis, brain swelling and profound dysphasia is quintessential.

### Preoperative psychological preparations

The anesthesiologist must gain the patient's confidence, as the patient will depend on him during the procedure. Prior to surgery, the patient must be informed about realistic description of the operating room, expected discomforts and level of co-operation expected, potential risks, safety measures and stages of the procedure. The anesthesiologist must not conceal the potential presence of sounds (monitor alarms, cranial drilling, elektroknife, ultrasonic surgical aspirator) or discomforts (unchangeable position, aphasia during cortical mapping) from the patient. The patient must understand that these discomforts are essential for the success of the procedure. A visit to the operating room before surgery in order to familiarize the patient with the sounds and equipment in the rooms is a good idea. The patient should be explained the tasks that will be performed for speech and motor testing. Questions should be encouraged and if possible speaking to a prior patient who has undergone this procedure successfully in the past can be invaluable.

### Comfort in patient positioning

The patients comfort is of utmost importance. The operating room temperature must be appropriate; the surgical table must be covered with soft, thick dressing, and the surgical team must be instructed to speak softly and move only if necessary. It is important to study the position of the instruments in order to minimize unnecessary movements of objects and personnel. The patient's face must be in a position that allows him to look at the anesthesiologist and at pictures during brain mapping, but must also be accessible for adequate access to airway during emergencies. An audio-video recorder system should be used so that the surgeon can see and hear the patient's responses during cortical mapping.<sup>[24]</sup>

### Premedication

Premedication with sedatives and anticholinergic in patients is quite controversial, and decisions should

be made based on the patient's clinical condition and the anesthetic technique. Midazolam and clonidine are among the most efficacious agents. Antiemetic prophylaxis is desirable as a preventive measure. Low dose propofol administration is useful to prevent perioperative nausea and vomiting.<sup>[25]</sup> The majority of antiemetics used were metoclopramide (10 mg)<sup>[26,27]</sup> ondansetron (4-8 mg),<sup>[27-31]</sup> droperidol (0.625-2.5 mg)<sup>[7,30]</sup> and dexamethasone (4-16 mg).<sup>[30,32]</sup>

### Scalp block

Scalp block is quite indispensable for an awake craniotomy. The branches of cranial nerves blocked are supratrochlear, supraorbital, auriculotemporal, greater and lesser occipital, great auricular, zygomatic and infraorbital nerves. Local anesthetic (40-60 mL) with epinephrine assures long duration of block. Large volume of local anesthetic and well-vascularized areas predispose to anesthetic toxicity hence individual nerve blocks are preferred over wide areas of infiltration to decrease probability of LA toxicity. The use of adrenaline (5 µg/mL, 1:200 000 dilution) both minimizes acute rise in plasma concentration and maximizes the duration of the block. Clinical hyper vigilance is particularly indicated within the first 15 min after scalp block.<sup>[33,34]</sup> Bupivacaine is still the most commonly used local anesthetic but ropivacaine and levobupivacaine appear to be safer than bupivacaine.<sup>[35]</sup> In awake-awake-awake technique 28 ml ropivacaine 0.75% with epinephrine 1:200000 and 9 ml of a 1:1 mixture of ropivacaine 0.75% and prilocaine 1.0% at pin sites was used to avoid delay to full effect of the scalp block.

### Monitored anesthesia care

According to the American Society of Anesthesiologists, monitored anesthesia care is a specific anesthetic protocol that includes careful monitoring and support of vital functions. The ASA recommends that the provider of MAC be qualified and prepared to convert to general anesthesia if necessary.<sup>[36]</sup> With regards to awake craniotomy, this type of anesthetic care has developed from the logical evolution of pioneering experiences using neuroleptoanalgesia. The introduction of propofol use has favored this evolution by allowing better patient management.<sup>[13,14]</sup> After Silbergeld's publication,<sup>[13]</sup> Gignac compared droperidol administering combined with fentanyl, alfentanil, or sufentanil in 30 patients and concluded that there was no difference between fentanyl and newer opioids in awake craniotomy.<sup>[19]</sup> Herrick proposed patient-controlled sedation (PCS) with propofol as a valid alternative to neuroleptoanalgesia.<sup>[28]</sup> Neuroleptanalgesia (Droperidol+Fentanyl) was popular but discontinued for prolonged sedation, seizure and QT prolongation predisposing to cardiac dysrhythmias. The

diffusion of new short-acting drugs such as propofol and remifentanyl has simplified sedation and allows for rapid awakening in 5-20 min. Since this study, all awake craniotomy published protocols have included propofol administration except Manninen's study<sup>[10]</sup> and some dexmedetomidine regimens.<sup>[37,38]</sup>

Propofol is widely employed for awake craniotomy because of its easily titratable sedative effect and rapid recovery with clear-headedness.<sup>[39]</sup> Propofol decreases cerebral oxygen consumption, reduces intracranial pressure, and has potent anti-convulsant properties.<sup>[40]</sup> Propofol also has antiemetic properties and may be administered using a target controlled infusion (TCI) technique.<sup>[20,22,29,30]</sup> TCI allows drug titration, allowing the anesthesiologist to predict time for arousal after long-term infusions and avoid oversedation. Normally, propofol infusion for TIVA is set to 100-200 mcg/kg/min; this does not appear to interfere with electrocorticography (ECoG) if infusion is stopped 15 min before recording according to Herrick<sup>[28]</sup> and 20 min in pediatric settings.<sup>[41]</sup> Some employ propofol sedation only in combination with local anesthesia and without opioids infusion and are able to achieve good pain control.<sup>[33,42]</sup>

Propofol (75-150 mcg/kg/min) is usually combined with different opioids alfentanil (0.25-0.75 mcg/Kg/min) or fentanyl (0.5-1 mcg/Kg/hr). Alfentanil can cause epileptiform discharge in hippocampal region so it is used with caution in cases of complex partial seizure. Recently, fentanyl has been replaced by low-dose remifentanyl (0.02-0.05 mcg/kg/min).

Remifentanyl, a clinically versatile opioid is useful for intravenous analgesia and sedation in spontaneously breathing patients. Remifentanyl has favorable pharmacokinetic properties and is minimally altered by extremes of age or renal or hepatic dysfunction. These properties enable easy titration and rapid dissipation of the clinical effects of this agent. In fact, remifentanyl's context-sensitive half-life is very short even after prolonged infusion.<sup>[43]</sup> This short-acting opioid at a low-dose infusion (0.1 µg/kg/min) appears to not interfere with ECoG although additional specific studies on this effect are needed.<sup>[44]</sup>

Commonly, both propofol and opioid infusion are discontinued about 15 min before brain mapping and are resumed at the beginning of closure of the dura. With propofol and remifentanyl combination, infusions are stopped about 9 min before.

In MAC, clinical vigilance concerning respiratory function is necessary throughout the procedure.

During this anesthetic technique, airway management is minimal and non-invasive. In most centers, patients receive supplemental oxygen *via* nasal trumpets or facial mask. Nasopharynx cannula may be a good alternative choice<sup>[26,30]</sup> but is rarely used because of the risk of nasal bleeding, however, once positioned correctly it is well-tolerated and allows ventilation support if a mechanical ventilator is connected and mouth and opposite nostril closed.<sup>[45]</sup> Airway obstruction occurs with variable but not negligible frequency (0-20%), leading to oxygen desaturation and hypoxic episodes (0-20%).

### Asleep-awake-asleep technique

This approach consists of general anesthesia before and after brain mapping. In the 1950s, Penfield,<sup>[46]</sup> Hall<sup>[47]</sup> and Ingvar,<sup>[48]</sup> used nasotracheal intubation to maintain the tracheal tube during craniotomy for intractable epilepsy. Hall administered succinylcholine as continuous infusion to obtain generalized muscle relaxation, and Ingvar administered a local anesthetic in the airways through a fine catheter with small holes (but none of these patients could speak during brain mapping!). In 1993, Weiss placed a tracheal tube in one nostril at 22 cm in order to support ventilation during propofol administration with N<sub>2</sub>O general anesthesia.<sup>[49]</sup>

In 1998, Huncke<sup>[50]</sup> described their experience with 10 patients who, after local anesthesia, underwent awake fiberoptic intubation at the beginning of the procedure and again after cortical mapping (two orotracheal intubations and eight nasotracheal intubations). The tracheal tube was modified by attaching a fine catheter with multiple holes for topical delivery of local anesthetic.

In recent years, LMA has been widely used for awake craniotomy with patients under spontaneous breathing protocols. These patients are supported with mechanical ventilation only if necessary.<sup>[29,51-54]</sup> Shinokuma described a case in which the laryngeal mask was left in place throughout the procedure with clear and comprehensible phonation.<sup>[55]</sup> Finally, others used LMA only during the first part of surgery and finished the craniotomy by providing sedation (this technique was named asleep-awake).<sup>[31,56,57]</sup> Even if LMA cannot ensure the same airway protection as a tracheal tube, it has renewed great interest because it was a recent, accessible, and well-known device. Different techniques of LMA positioning have been widely described<sup>[58]</sup> in awake<sup>[51,59,60]</sup> and in both lateral and semi-sitting positions.<sup>[61,62]</sup>

The AAA technique has been successfully performed using a cuffed oropharyngeal airway (COPA),<sup>[63]</sup> nasal mask with BiPAP®, or proportional-assist ventilation support.<sup>[64]</sup> Schulz suggested placing a nasotracheal tube with the tip

above the rima glottidis throughout the procedure and if necessary the tracheal tube may be advanced into the trachea under fiberoptic guidance.<sup>[32]</sup> Gonzales recently described the use of two nasopharynx cannulas combined with pressure support ventilation in an obese patient.<sup>[65]</sup> Laryngeal mask airway offer significant advantages over tracheal tube approaches, including avoidance of inserting the laryngoscope or the need for head extension, easier placement in difficult patient position, and reduced incidence of coughing and gagging during emergence. ProSeal LMA may be used because it incorporates a second tube permitting blind insertion of a gastric tube, thus reducing risks of gastric insufflation and pulmonary aspiration. As patients are in lateral position, preformed LMA may also be used.

Nowadays, the AAA technique is commonly performed by administering propofol and remifentanyl. Propofol, compared to volatile anesthesia, increases cerebral perfusion pressure, decreases neurophysiologic monitoring interference, appears to ensure neuroprotection, and decreases the incidence of nausea and vomiting.<sup>[39]</sup> The AAA technique offers the advantages of good airway control, adequate deep sedation, and the patient does not have pain/discomfort. Nevertheless, this anesthetic approach is more complex than MAC, particularly when repositioning of an airway device is necessary for closure (while the patient is often in the lateral position with his/her head fixed to the Mayfield head holder).

### Awake-awake-awake technique

Hansen suggested that temporary anesthesia used for awake craniotomy involved substantial risks like hemodynamic instabilities, airway obstruction, hypoventilation, nausea and vomiting, agitation and interference with cortical mapping. They tested the need for sedatives and opioids in patient undergoing awake craniotomy for brain tumor resection in eloquent or motor brain areas when cranial nerve blocks, permanent presence of a contact person and therapeutic communication are provided.

The fundamental idea of awake-awake-awake craniotomy is the effective avoidance of pain due to head fixation and craniotomy by scalp block. They applied selective nerve blocks in contrast to wide circular infiltration. Selective blocking of the sensory branches of trigeminal nerve was less painful and more effective for pain, maintained hemodynamic responses and prevented stress hormone response<sup>[66,67]</sup> compared to scalp block.<sup>[68]</sup> Another advantage of the scalp block is the provision of postoperative analgesia.

An important advantage of the awake-awake-awake technique is the possibility of carefully positioning unseated

patients and finding the best and most comfortable position prior to craniotomy. The efficacy of communication approach is documented by the avoidance of sedative agents and by the reduced need for opioids. The drug sparing effect of communication can only become full operative when following the principle “*as much as necessary but no more than needed.*”

### Dexmedetomidine: A new alternative

Dexmedetomidine is a highly selective  $\alpha_2$ -agonist with dose-dependent sedative, anxiolytic, and analgesic effects without ventilation suppression.<sup>[69]</sup> Compared to clonidine, dexmedetomidine has eight-times greater affinity for  $\alpha_2$ -receptors and a shorter half-life.<sup>[70]</sup> Bekker reported the first application of dexmedetomidine combined with LMA (spontaneous breathing), fentanyl, sevoflurane (0.3-0.7%), nitrous oxide (70%), and BIS monitoring in an awake craniotomy.<sup>[54]</sup> Low-dose infusion of this drug in healthy volunteers provides sedation that can be easily reversed with verbal stimulation.<sup>[71]</sup>

Dexmedetomidine has been used to treat discomfort in patients sedated with a propofol and remifentanyl combination.<sup>[72]</sup> Generally, a dexmedetomidine load of 0.5 to 1  $\mu\text{g}/\text{kg}/\text{h}$  over 20 min is followed by infusion at rates of 0.1 to 0.7  $\mu\text{g}/\text{kg}/\text{h}$  to 20 min prior to testing. During cortical mapping the infusion rate is usually set to 0.1 to 0.2  $\mu\text{g}/\text{kg}/\text{h}$ .

In 2004, Fogarty Mack’s group evaluated dexmedetomidine administration in five patients managed by MAC and five patients under an AAA approach and found the AAA anesthetic approach resulted in more intraoperative discomfort.<sup>[37]</sup> Contrary to the study by Bustillo (2002), they found that neurocognitive testing was successfully completed in all 10 patients.<sup>[73]</sup> The same idea was sustained by Souter.<sup>[38]</sup> A perspective study carried by Ard<sup>[52]</sup> on 17 patients who underwent awake craniotomy (AAA technique) confirmed dexmedetomidine’s validity in reducing the incidence of adverse events, reduction of necessary quantities of other drugs, improved surgical work, and probably decreased cerebral flux.<sup>[74]</sup>

Hassan<sup>[75]</sup> used combination of dexmedetomidine and remifentanyl with scalp block for a case series in patients undergoing awake craniotomy for brain tumors. All patients were comfortable throughout the surgery without any worsening neurological deficits. All tumors were successfully excised while the patients were arousable cooperative and maintained hemodynamic parameters throughout the surgery. Craniotomies with propofol-dexmedetomidine infusion have had less hemodynamic response to pinning and emergence and less overall narcotic use compared to general anesthesia, though

higher incidence of temporary episodes of desaturation and hypoventilation were observed.<sup>[76]</sup>

## INTRAOPERATIVE MONITORING

Intraoperative monitoring typically includes electrocardiogram, invasive and non-invasive blood pressure measurements, pulse oximetry, respiratory rate, capnography, and temperature. If large blood losses are expected, a large bore IV and or a central venous catheter are inserted. Intra-operatively, the respiratory rate and end-tidal carbon dioxide are measured by means of nasal prongs-port with capnometry. Urinary catheter may or may not be inserted.

The monitoring of the level of consciousness during anesthesia or sedation is possible using electroencephalographic analysis by bilateral bispectral index (BIS). This instrument may be useful during the sedation/anesthesia period and also to evaluate the level of responsiveness during awake cortical mapping.<sup>[22,29,53,56]</sup> Most authors use clinical sedation measures such as the Ramsay Sedation Score<sup>[30,37,54,72]</sup> or the Mackenzie and Grant Score.<sup>[28,44]</sup> Tijero have proposed a possible intra-operative use for brain tissue oxygen pressure as a precocious local damage indicator in proximity of the surgical resection area.<sup>[30]</sup>

## MINIMIZING INTRAOPERATIVE COMPLICATIONS

Anesthetic care in awake craniotomy is complex and there is a risk of intraoperative adverse events related to anesthetic procedure and surgical manipulation. These events may be related to anesthesia or surgery [Table 1].

In MAC airway manipulation is minimal so patient is vulnerable to airway obstruction. Cuffed oropharyngeal

**Table 1: Classification of intraoperative complications that may occur during awake craniotomy**

Anesthesia related	Surgical related
Airway obstruction	Focal seizures
Desaturation/hypoxia	Generalized seizures
Conversion to general anesthesia	Aphasia
Hypertension/hypotension	Bleeding
Tachycardia/bradycardia	Brain swelling
Nausea/vomiting	Venous air embolism
Shivering	
Local anesthetic toxicity	
Pain	
Poor cooperation	
Agitation/Restlessness	

airway placement for the AAA technique has caused airway obstruction in 15% of patients.<sup>[63]</sup> Hypoxia and oxygen desaturation occurs more during MAC and are commonly due to over sedation.

The incidence of intraoperative seizures during awake craniotomy is variable. Neuroleptic analgesia has been associated with higher incidence of seizures.<sup>[28]</sup> Use of remifentanyl has been associated with fewer intraoperative seizures than other opioids.<sup>[5,29]</sup> Propofol has protective effect against seizures but the infusion must be discontinued 15 min before cortical stimulation so as not to interfere with EcoG.

Among surgical related complications, Szelényi has observed that the train-of-five stimulation technique has a significantly lower incidence of stimulation-associated seizures than the 60 Hz technique.<sup>[77]</sup> Patients with symptomatic epilepsy are not at a higher risk of intraoperative stimulation-associated seizures than patients without symptomatic epilepsy during awake tumor resection.<sup>[77]</sup>

Seizures may be focal and short, and are usually due to cortical electro stimulation. Myoclonic twitches of one or two extremities typically terminate at the end of each electrical stimulus, and if they continue they may be controlled with iced Ringer's lactate irrigation of the brain<sup>[78]</sup> or administration of benzodiazepines (midazolam 2-5 mg i.v.). Generalized seizures like tonic-clonic seizures are less frequent and must be treated with cold Ringer's lactate irrigation, benzodiazepines infusion (midazolam 2-5 mg, diazepam 5-10 mg), or pentothal sodium administration (25-50 mg). Most seizures, focal or general, self-terminate or are terminated by ice solution irrigation. Propofol, benzodiazepines, or barbiturate administration is not usually a good choice because it changes the cortical excitability and interferes with EcoG. Ventilation must be accurately monitored during the post-ictal period.

Nausea is another frequent complication that may make the patient agitated and un-cooperative and can be prevented by administering antiemetics. These conditions cannot be prevented if they are secondary to dura matter or vessel traction.<sup>[28,32]</sup>

Hemodynamic complications have to be controlled. Labetalol and esmolol are most commonly used for increases in arterial pressure.<sup>[30,79]</sup> Urapidil, a titratable drug, may be used successfully for hypertension during awake craniotomy.<sup>[8]</sup> Hypotension is managed by fluid administration, ephedrine and phenylephrine infusion. Excessive blood losses are uncommon, and cardiovascular homeostasis depends on the site and dimension of the

lesion. During the procedure shivering must be prevented by using warm infusions and blankets. Clonidine, dexmedetomidine, meperidine, tramadol, nefopam, and ondansetron medications are used to prevent shivering.<sup>[80]</sup> Few cases of local anesthetic toxicity have been reported.<sup>[16]</sup> Beta blockers should be used cautiously as they may mask tremors in case of a convulsion at times.

During surgery, pain may arise from poorly-anesthetized areas (often in the temporal area) and from dura mater and brain vessels. In such cases, additional local anesthetic infiltration of the zygomaticotemporal branch is indicated. Since this type of procedure is of prolonged duration, postural related pain may occur and is managed by allowing the patient small movements and by administering drugs such as acetaminophen,<sup>[32]</sup> diclofenac,<sup>[79]</sup> novaminsulfon,<sup>[32]</sup> and fentanyl.<sup>[10]</sup> Poor cooperation and agitation may be related to pain, anxiety, excessive sedation, seizures, and inadequate intraoperative psychological support.

Venous air embolism is a rare adverse complication. The complication of venous air embolism has a high variable incidence (10-80%) in neurosurgical cases performed in sitting position.<sup>[81]</sup> The sitting and semi-sitting positions increases the risk of venous air embolism during awake craniotomy. Furthermore, spontaneous breathing raises the pressure gradient between the surgical site and the right atrium, favoring air suction. However, awake craniotomy is typically performed in the lateral or supine positions, so venous air embolism reports are not so frequent.<sup>[82,83]</sup> Balki reported an incidence of 0.64% and suggested the use of an intraoperative precordial Doppler monitor in the event of air embolism suspicion.<sup>[83]</sup>

## PATIENT PERCEPTION AND ACCEPTANCE OF AWAKE CRANIOTOMY

Many reports have concluded that different anesthetic techniques allow awake craniotomy to be feasible, safe, and well-tolerated<sup>[10,21,28,29,56,84]</sup> even if these considerations are not always supported by objective data.<sup>[21,26,29,56]</sup> Herrick concluded that patient given propofol-based sedation were satisfied with intraoperative comfort and pain control.<sup>[28]</sup> Patients said that they would be prepared to undergo the procedure again if necessary. Danks<sup>[85]</sup> assessed the subjective experience of 21 patients undergoing awake craniotomy with the MAC approach (midazolam premedication). 75% patients recalled none or only short portions of the procedure despite being awake for a substantial portion of the procedure and 50% of the patients did not recall suffering any intraoperative pain, anxiety, or discomfort. Only one patient recalled severe

pain. Complete satisfaction with procedure were expressed by 70% of patients and only two patients (9.5%) had a negative satisfaction score. 81% of patients stated that they would be prepared to undergo awake craniotomy again if indicated. After one-month follow up interview, only one patient showed a worsened mood.

A Scottish study reported analogous results and confirmed the tolerability of awake craniotomy, suggesting the necessity for a multicentric study and adequate multifactorial evaluation of the technique.<sup>[51]</sup> Manninen *et al.* compared the efficacy of remifentanyl to fentanyl in combination with propofol in providing MAC sedation for awake craniotomy.<sup>[10]</sup> Sixty percent of the patients recalled none or short portions of the procedure, 56% reported moderate pain, 22% reported no pain, and over 90% expressed complete satisfaction with anesthetic care.

Wrede *et al.*,<sup>[84]</sup> studied patient acceptance of awake craniotomy under local anesthesia and conscious sedation using a formal questionnaire (PPP33 [Patient evaluation in the Peri-operative Phase consisting of 33 items]). The questionnaire has an overall score and 8 subscales, that represent different aspects of the perioperative phase: Information, autonomy, communication, physical disorders, pain, regeneration, fear and accommodation. The results were compared to a group of patients who had brain surgery under general anesthesia and to the previously published data. The overall mean score for the PPP33 (ranging from 0 to 100) was 84.07 for the awake craniotomy group and 73.88 for the general anesthesia group, suggesting an equal or better overall acceptance for awake craniotomy ( $P = 0.07$ ). The subscale scores for awake craniotomy were also significantly better compared to general anesthesia for the two subscales “postoperative pain” ( $P = 0.02$ ) and “physical disorders” ( $P = 0.01$ ) and equal for the other 6 subscales. The results of the overall mean score and the scores for the subscales of the PPP33 questionnaire verify good patients’ acceptance for awake craniotomy.

In 2011, Wahab *et al.*,<sup>[86]</sup> designed a questionnaire with reference to Royal College of Surgeons (RCS) guidelines and sent out to 60 consecutive patients. Four areas of care were explored, which included the out-patient consultation with the neurosurgeon, anesthetic consultation, operation and the post-operative period. Forty-five responses were received which demonstrated high levels of patient satisfaction and provided surgeons with useful data for consenting patients.

Considering the literature, it could be asserted that awake craniotomy is well-tolerated. The areas for improvement include provision of written information, enhancing post-

discharge support and allowing more time for anesthetic discussion before surgery. It is always necessary to ensure psychophysical support before and throughout the operative procedure. The use and evaluation of a pain score, such as the Verbal Numerical Scale,<sup>[87]</sup> helps to avoid underestimating the patient’s referred pain. It would be helpful for all institutions to evaluate their anesthetic care protocol for awake craniotomy by psychometric and satisfaction score.

## FUTURE PERSPECTIVES OF AWAKE CRANIOTOMY ANESTHETIC CARE

In future, many surgical and anesthetic changes will affect awake craniotomy techniques. Specific studies could demonstrate which anesthetic approach, MAC, AAA or awake-awake-awake, is the safest and best-tolerated [Table 2]. Newer approaches with minimal use of sedatives and opioids have challenged all the previous approaches of anesthetic care in awake craniotomies. New studies could also establish which airway device is most effective in making the procedure easier and safer. Propofol, remifentanyl and dexmedetomidine intravenous infusions should be based on TCI algorithms to achieve safer and more predictable outcomes. Some infusion systems can be implemented with depth of sedation monitoring such as BIS. Gentilini has proposed an arterial pressure-based algorithm for alfentanil infusion.<sup>[88]</sup> Closed-loop control systems for mechanical ventilation can be useful to control EtCO<sub>2</sub> in awake craniotomy and neurosurgery.<sup>[89]</sup>

Levobupivacaine could replace bupivacaine for scalp block with minimal use of sedatives and opioids. Some authors have described this procedure performed without Mayfield’s head holder,<sup>[52,90,91]</sup> this is possible using new electromagnetic navigation systems based on a sensor attached to the mastoid of the patient.<sup>[90]</sup> This avoids head fixation, allowing for minimal movement of the patient, reducing pain incidence, and facilitating anesthesiologist intervention on the patient’s airway if necessary.

Taylor’s study, reported an incidence of postoperative hematoma of 2.2%.<sup>[92]</sup> They observed that clinical signs of postoperative hematoma occur within 6 h following surgery due to active bleeding in the surgical site, and 24 h after the procedure related to intracranial pressure and edema around the hematoma. Based on these findings, Blanshard *et al.*,<sup>[7]</sup> studied early discharge of 241 patients after awake craniotomy and concluded that selected patients, who had no intraoperative complications and received adequate instructions, may be discharged after a 6 h postoperative observation period if they live near a hospital and have satisfactory assistance at home. Manninen *et al.*,<sup>[10]</sup> reported

**Table 2: Intraoperative complication incidence in different studies related to anesthetic management**

Year	Author	Anesthesia	No. of Patients	Airway obstruction	Hypoxia	Hypertension	Hypotension	Tachycardia	Bradycardia	Seizures	Nausea	Poor cooperation	Brain swelling	LA toxicity	conversion to GA
1988	Archer DP <sup>[16]</sup>	MAC	354	—	—	—	—	—	—	16	8	2	1	2	0
1993	Gignac E <sup>[19]</sup>	MAC	30	—	0/20/10	—	—	—	—	10/30/10	50/30/70	20/0/10	—	—	0
1997	Herrick IA <sup>[28]</sup>	MAC	37	5/0	—	—	10/35	—	—	0/41	10/18	—	—	—	5/11
1998	Danks RA <sup>[85]</sup>	MAC	21	0	—	0	—	—	—	0/20	—	—	0	—	—
1998	Huncke K <sup>[59]</sup>	AAA	10	0	—	—	—	—	—	0	0	0	0	—	0
2000	Danks RA <sup>[96]</sup>	MAC	157	—	—	23	—	—	—	7.6	0.6	7	2.5	—	0.6
2001	Blanshard HJ <sup>[7]</sup>	MAC	241	0.4	—	—	0.8	—	—	8	6.6	—	0	—	—
2001	Berkenstadt H <sup>[9]</sup>	MAC	25	4	28	4	0	0	0	8	0	4	0	—	4
2002	Manninen PH <sup>[6]</sup>	MAC	107	—	—	—	—	—	—	—	0	—	—	—	—
2003	Sarang A <sup>[29]</sup>	AAA	99	7/0/0	—	0/11/0	0/6/21	—	—	0/6/0	—	0/3/5	—	0	0
2004	Audu PB <sup>[63]</sup>	AAA	20	15	—	—	—	—	—	—	—	—	—	—	0
2005	Keifer JC <sup>[26]</sup>	MAC	98	—	—	—	0	—	—	3	8	7	—	0	0
2005	Ard JL <sup>[52]</sup>	DEX	17	0	0	24	18	0	0	6	6	12	0	0	0
2006	Picht T <sup>[91]</sup>	MAC	25	0	28	—	—	—	—	32	—	20	8	—	6.2
2006	Manninen PH <sup>[10]</sup>	MAC	50	20/12	4/0	4/0	0/8	—	—	0/16	0	16/8	4/4	—	0
2006	Skucas AP <sup>[42]</sup>	MAC	332	2	2	11	56	14	0.3	3	0.9	1.5	0.6	0	0
2007	Serletis D <sup>[97]</sup>	AAA	610	—	—	—	—	—	—	4.9	—	—	1.1	—	0.4
2010	Andersen JH <sup>[94]</sup>	AAA	44	0	2	2	5	0	10	38	15	—	—	—	6.8
2011	Wrede KH <sup>[84]</sup>	AAA	91	—	—	—	—	—	—	—	—	—	—	—	—
2011	Wahab SS <sup>[86]</sup>	AAA	150	—	—	—	—	—	—	—	—	—	—	—	—
2012	Chung YH <sup>[95]</sup>	AAA	6	—	—	—	—	—	—	—	—	—	—	—	—
2013	Rajan S <sup>[96]</sup>	AAA	178	0	26/1	28/39	53/69	0	0	0	0	0	0	0	0
2013	Hansen E <sup>[13]</sup>	Awake-Awake	50	0	6	44	6	60	6	16	0	0	0	0	2
2013	Hassan WMZ <sup>[75]</sup>	DEX	5	0	0	0	0	0	0	0	0	0	0	0	0

Values expressed in %; MAC: Monitored anesthesia care; AAA: Awake-asleep-awake technique; DEX: Dexmedetomidine; -: not recorded; LA: Local anesthetic; GA: General anesthesia



that 22% of 50 patients who underwent awake craniotomy were discharged the same day of surgery.

A Canadian study<sup>[93]</sup> comprising 200 patients undergoing surgery over a 6-year period showed that with growing experience, the total hospital stay could be reduced from four days to a single day, the number of patients admitted to intensive care postoperatively could be reduced from 80 to 10%, and the mean surgery time could be reduced from 4.25 to 3.25 h. Anderson<sup>[94]</sup> retrospectively studied 44 patients for the success of awake craniotomy for tumor resection and found that three had to be converted to general anesthesia (due to tight brain, leaking LM and tumor hemorrhage).

Dexmedetomidine infusion after skin incision without loading dose slowly decreased the dose of propofol-remifentanyl within the target BIS level (60 without LMA, and 40 with LMA).<sup>[95]</sup> This combination permits rapid onset, and only continuous adjuvant infusion could prevent side effects related with bolus injection. In inevitable cases, the “asleep-awake” technique that uses controlled ventilation with LMA during incision period and deep sedation with adjuvant dexmedetomidine after neurologic exam will be a safe and satisfactory procedure for both the surgeon and patient.

Hansen *et al.*,<sup>[11]</sup> in a perspective study of awake craniotomies tested actual need for sedatives and opioids in patients undergoing awake craniotomy for brain tumor resection in eloquent or motoric brain areas when cranial nerve blocks, permanent presence of a contact person, and therapeutic communication are provided. Therapeutic communication was based on the assumption that patients in such an extreme medical situation enter a natural trance-like state with elevated suggestibility. The anesthesiologist acted as a continuous guide, using a strong rapport, nonverbal communication, hypnotic suggestions, such as dissociation to a “safe place,” and the reframing of disturbing noises, while simultaneously avoiding negative suggestions.

## CONCLUSIONS

Awake craniotomy for tumor resection is a complex technique that requires good patient and equipment engagement where psychological support might be more helpful than the pharmacological approach. The choice of the anesthetic technique, MAC, AAA or awake-awake-awake, must be related to the anesthesiologist's capability and experience. The AAA technique may be preferred for delicate and more complex patients. Dexmedetomidine appears to be the best drug for sedation without interference

with respiratory function. TCI infusion systems allow better drug titration, avoiding over sedation and respiratory depression. Depth of anesthesia monitoring systems, like BIS, are useful in this kind of surgery even if clinical observation of vital signs and specific sedation scores are adequate to manage this type of patients.

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