

Patients selection for awake neurosurgery

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ABSTRACT

Background: Based upon the surgical location and indication, including redundant regions, eloquent areas, deep brain stimulation, and epilepsy foci, some patients will benefit from an awake craniotomy, which allows completion of neurocognitive testing during the intra-operative period. This paper suggests patient selection criteria through a new decision algorithm.

Methods: We completed a retrospective chart review at Tampa General Hospital after IRB approval; data were obtained concerning total number of craniotomies, indications, and problems experienced for selection of awake vs. general anesthetic techniques.

Results: A total of 397 craniotomies were performed during the two years 2005 and 2006: among those 79 patients received an awake craniotomy (20%). We have utilized a sedation sequence which includes dexmedetomidine, propofol and LMA placement. A skull block is then performed to anesthetize pin placement, and desflurane and remifentanyl are used for maintenance until the dural incision. At this time the inhalation agent is stopped and the LMA is removed while breathing spontaneously: the patient remains sedated on dexmedetomidine and remifentanyl for the duration of the operation and can communicate effectively if closely coached. Analysis of all patient data led us to a decision tree to guide the surgeon and anesthesiologist in selecting the awake patients.

Discussion: We describe the sequence of steps and anesthetic agents which has proved successful for our group. Finally, the use of the proposed decision algorithm simplifies preoperative anesthetic selection and prevents erroneous assignment of inappropriate patients to an awake technique.

Keywords: awake craniotomy, anesthesia for neurosurgery, patient selection.

INTRODUCTION

There is a paucity or absence of studies reporting data on patient outcome, following awake or asleep craniotomies. The ideal anesthetic for neurosurgical procedures should provide optimal surgical conditions, stable hemodynamics, appropriate cerebral oxygen supply and demand, a secure airway,

control of ventilatory level, and rapid emergence for rapid neurological evaluation. Current practices vary, and include the use of general anesthesia involving volatile or intravenous anesthetics, or a combination of both, as well as awake techniques (1), each of which has benefits and drawbacks. The awake anesthetic technique for elective craniotomy is usually selected based on surgical indications, such as supratentorial cortical tumors, thalamic and brainstem tumors or removal of epileptic foci.

The precise location of different tumors causes significant consequences in regards to the anesthetic choice. Amongst all patients, approximately 65-70% of tumors

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are located in the redundant cortex, 10-15% in eloquent regions such as the motor/sensory strip and speech/language centers and a final 10-15% in the thalamic region (2, 3). Because of tumor location, the first group of interventions can be usually completed with general anesthesia, while the remaining 30% would most likely require an awake craniotomy, in order to map eloquent regions and permit evaluating responses to deep brain stimulation and/or recognize onset of seizures. Patients undergoing resection of seizure foci might also require awake craniotomy, as these regions are often located in proximity of speech and language centers. Piccioni and Fanzio have recently described a variety of techniques in the current literature (4). Advances in neurosurgical technique have utilized automated stereo-tactic navigation equipment to aid in the complete removal of supratentorial pathology. Crucial to this system, however, is the maintenance of proper alignment between the patient and the navigation system, which is challenging for the awake participant. Regardless of the technique used, an established method of firmly stabilizing the head is necessary when performing intracranial microsurgical procedures. Utilization of regional anesthesia (skull blocks) with a combination of short and long-acting local anesthetic offers benefits for both general and awake craniotomy, allowing for intra- and post-operative pain control as well as decreased needs for sedation during pin placement, skin incision and craniectomy (5).

There has been no consensus on indications, inclusion and exclusion criteria in the literature: in order to determine the best fit between a patient and the indication for awake supratentorial craniotomy the database of all craniotomies performed at our institution during 2005 and 2006 were retrospectively reviewed, in order to identify selection criteria to aid the clinician to

choose the anesthetic technique based on surgical indication and few additional criteria. In this paper we describe an awake craniotomy technique that is commonly used in our practice.

METHODS

We completed a retrospective chart review of all craniotomies performed at our Institution in 2005 and 2006. Tampa General Hospital is a large, tertiary-referral center in Tampa, along the western coast of Florida. After obtaining approval for the retrospective review from the University of South Florida IRB, charts were abridged and data obtained concerning description of the type of craniotomies, indications, and anesthetic technique. During the two years study period (2005 and 2006), 397 craniotomies [64% were male (N = 254) and 36% female (N = 143)] were completed at Tampa General Hospital by the faculty from the department of Neurosurgery at the University of South Florida. Amongst these patients, 79 (20%) received an awake anesthetic technique: 64 of the awake patients (81%) received awake craniotomy for epileptic foci while 15 patients (19%) received awake craniotomy for eloquent regions. A further breakdown revealed that craniotomies were performed for supratentorial and brain stem tumors, epileptic foci resection, or resection for vascular abnormalities (*Table 1*). Amongst the 110 supratentorial tumors

Table 1 - Indications for craniotomy performed at Tampa General Hospital in 2005 and 2006.

Surgical Indication	Number of Patients	Percentage
Supratentorial Tumor	110	27%
Brain Stem Tumor	26	6%
Vascular Abnormality	186	46%
Epileptic Foci	75	21%

resected, 77 (70%) were in redundant regions, 17 (15%) in eloquent regions, and 16 (15%) in the thalamus.

This review also revealed that the patients selected for the “awake” technique needed to provide enthusiastic cooperation. This section required excellent communication between the surgeon and the anesthesiologist, as well as accepting of a prolongation of the surgical time required for the need of awake testing and for the additional requirement at an early stage to initiate skull blocks for the insertion of pins.

Common Sequence for “Awake” Craniotomy

The common sequence of steps executed at our institution when providing anesthesia for awake craniotomy comprise first, a loading dose of dexmedetomidine 0.5 mcg/kg over 20 minutes in the pre-operative holding area, followed by an intra-operative infusion rate of 0.4 to 1.0 mcg/kg/h. Induction of anesthesia is accomplished with propofol (3 mg/kg), followed by laryngeal mask airway (LMA) placement. Finally,

a skull block is performed with 30 ml of 0.5% bupivacaine and the placement of an arterial line.

Skull Block Technique

Appropriate doses of different local anesthetic agents used are listed in *Table 2*, while an anatomical drawing of injection sites is illustrated in *Figure 1*. Injected volumes may need adjustment to ensure that less than toxic levels of local anesthetic are used, although the volumes of these injections are kept relatively small (6-8). The first nerve block starts with the supraorbital and supratrochlear nerve and then progresses to involve the auriculotemporal, postauricular, greater, lesser and third occipital nerves.

Table 2 - Anesthetic technique; awake versus general in supratentorial craniotomy subgroups.

Local Anesthetic	Volume
0.5% Bupivacaine	30 ml
0.75% Ropivacaine	20 ml
0.5% Bupivacaine + 1% Lidocaine	15 ml + 15 ml

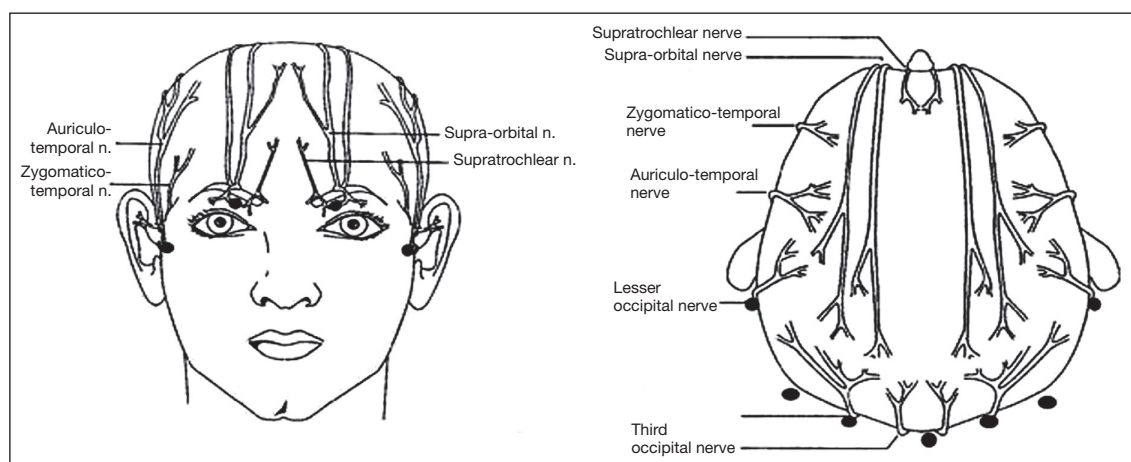


Figure 1
Skull block diagram for cranial vault analgesia. Full circles are indicating major insertion points for needle placement, • = injection sites. Adapted from Pinosky PL, Fishman RL, Reeves ST, Harvey SC, Patel S, Palesch Y, Dorman H. *The Effect of Bupivacaine Skull Block on the Hemodynamic Response to Craniotomy. Anesth Analg*, 1996; 83: 1256-61.

The supraorbital and supratrochlear nerves are blocked with 2 mL of solution injected just superior to the supraorbital foramen at the supraorbital ridge. The auriculotemporal nerves, branches of the trigeminal (V3) are blocked next with 5 mL of solution injected 1.5 cm anterior to the tragus of the ear. Care should be taken while infiltrating these nerves, as there is potential to block the facial nerve as well at this location. Therefore, the injection is performed just deep to the subcutaneous tissues. Next, the postauricular branches of the greater auricular nerves are injected with 2 mL of solution 1.5 cm posterior to the antitragus. The greater, lesser, and third occipital nerves are injected last with 5 mL of solution. This is accomplished by inserting a 22 gauge spinal needle at the mastoid process and injecting along the nuchal ridge until the midline is reached (6). The concentrations of local anesthetic can be manipulated based on the anesthetic goals of intra-operative or post-operative pain control.

Scalp incision, craniectomy, and dural resection proceed, while the patient is spontaneously breathing 0.5 MAC of desflurane. At this time a remifentanyl infusion (0.1-0.2 mcg/kg/min) is usually started, the desflurane is discontinued and the LMA can be removed. Patients are then able to converse with the surgical team and neurocognitive testing is accomplished, followed by tumor or epileptic foci resection. At the conclusion of the procedure the dural closure and craniectomy closure proceed while the patient is still awake, although at times patients need to be anesthetized at this stage for the completion of the procedure.

General Anesthetic Technique

Induction is with fentanyl 2-4 mcg/kg, propofol 3 mg/kg, lidocaine 1-2 mg/kg, and rocuronium 0.6 mg/kg, followed by endotracheal intubation.

A skull block as previously described is then also performed. Maintenance of anesthesia includes remifentanyl 0.05-0.1 mcg/kg, isoflurane up to 0.5 MAC, and intermittent boluses of rocuronium to maintain 1 of 4 Train-of-Four twitch.

RESULTS

Distribution of anesthetic techniques can be found in *Table 3*. This table illustrates that most of the patients having neurosurgeries for eloquent regions and epileptic foci were predominantly selected for an awake craniotomy technique, denoting the preference of our surgery/anesthesia team for this technique in both these groups. Of the patients with a lesion in the eloquent region, two were unable to undergo awake anesthesia.

The first patient was 14 years old, unable to cooperate, while the second patient spoke only Korean and an appropriate interpreter was not available. In the epileptic foci group, 11 patients were unable to receive awake anesthesia. Four patients refused, 6 were less than 10 years old and unable to cooperate, and 1 had altered mental status. The criteria for the selection of patients for awake craniotomy group was based on two major principles, the first being patients who needed surgery within an eloquent areas or patients with epileptic foci and sec-

Table 3 - Three common local anesthetic concentrations and total volumes necessary for skull block.

Procedure	Awake Anesthetic (Number of Patients/Percent)	General Anesthetic (Number of Patients/Percent)
Eloquent Regions	15/88 %	2/12 %
Epilepsy Surgery	64/85 %	11/15 %

only, the patients' willingness to participate in awake craniotomies.

Results drawn from our retrospective study illustrated that patients selected for the awake craniotomy did not experience any major complications from airway obstruction, local anesthetic toxicity, and did not require re-intubations during the procedure or post-operatively, nor complained of severe pain from rigid head pin fixation. However, these patients experienced extended surgery duration, compared to patients in the general anesthesia group.

In conclusion, our surgeons demonstrated a preference for the awake craniotomy technique for patients with supratentorial tumors, epileptic foci, and other lesions in the eloquent areas, with the aim to minimize complications, maximally resect the lesions as well as sparing motor, sensory and language areas.

Based on these data we can propose the use

of a *decision-tree algorithm* to assist the team in choosing appropriate patients (*Figure 2*). This algorithm fits all individual cases observed in these two years and would have excluded all patients who were not appropriate candidates. Presently this algorithm continues to be used for forward selection of patients who will require an “awake” craniotomy.

DISCUSSION

Utility of the “awake” technique

Patients undergoing craniotomy for resection of tumors and epileptic foci in many circumstances benefit from techniques involving at least some wakeful period with opportunity for intraoperative communications. Patients can be selected for awake craniotomy when the planned procedure involves eloquent areas of the brain, and

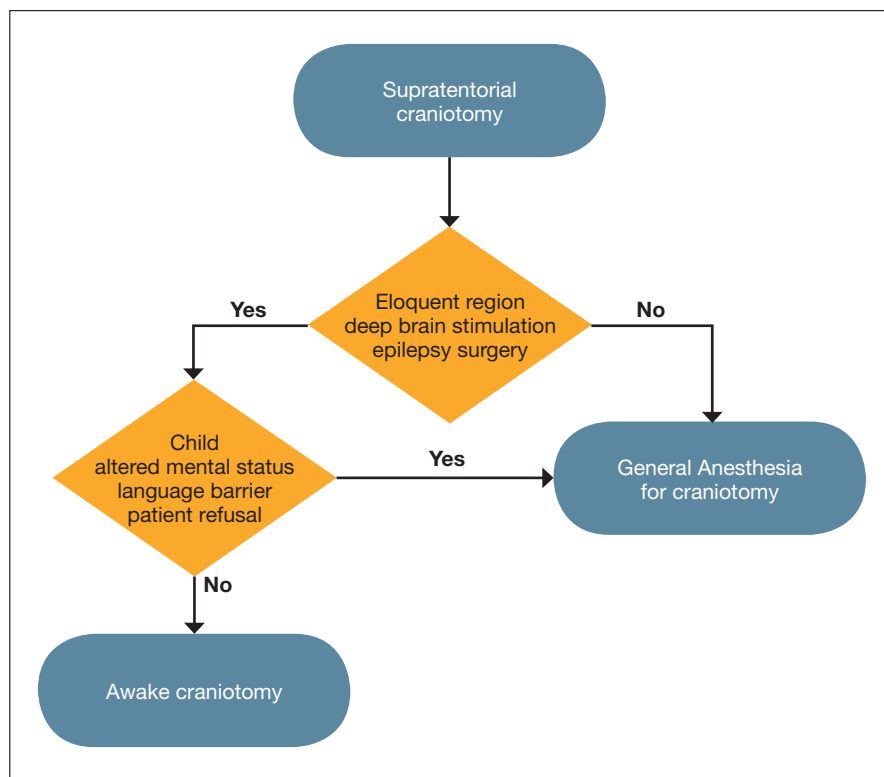


Figure 2
Decision tree.

an awake cooperative patient is capable to undergo neurocognitive and sensory-motor testing in order to minimize postoperative neurological dysfunction. The patient must be comfortable during the procedure, which can be very lengthy, yet still be alert enough to cooperate and participate in complex neurological and cognitive testing.

Localization of the motor and sensory cortex is important to minimize the risk of contralateral motor and sensory deficits resulting from surgical procedures in its vicinity. The location of primary motor cortex varies to a high degree. Direct cortical stimulation of the brain surface is one technique of localization that allows patients to respond when motor regions are stimulated.

The opportunity to perform intraoperative neurocognitive and language testing decreases the chance of permanent disability (3) leads to decreased incidence of postoperative seizure (3, 9) reduces hospital stay (3, 9) and necessitates fewer invasive monitors (9).

However when awake methods are contraindicated or impossible to continue, evoked potentials may be used even in the anesthetized, paralyzed patient (10) and provide the anesthesiologist and surgeon some information in regards to the motor and sensory cortex.

When recording somatosensory evoked potentials (SSEP), the primary sensory cortex and motor cortex generate potentials that are mirror images of each other. This "phase reversal" across the central sulcus is a highly reproducible characteristic that can aid in the localization of the primary motor and sensory cortex (11).

Common Pitfalls of "awake" techniques

Neuroleptic anesthesia, propofol with or without opioid infusions, and asleep-awake-asleep (AAA) techniques with laryngeal mask airways have been used, but in all combinations, except solitary dexmedetomidine infusion, respiratory depression has been shown to cause complications. Awake and asleep-awake-asleep sequences can be accomplished utilizing several total intravenous anesthetic (TIVA) techniques. Drugs such as propofol, remifentanyl and dexmedetomidine have been described as combinations in the literature.

As an example, one of such techniques in the literature (12) utilizes both intravenous and regional anesthesia: In this case, general anesthesia was induced at the onset of the procedure with a combination of IV infusions of propofol 75 mcg/kg/min and remifentanyl 0.1 mcg/kg/min along with intermittent boluses of propofol (10-20 mg) as needed, until loss of lid reflex. Spontaneous ventilation was maintained throughout the procedure. The Mayfield pin head holder was applied after anesthetizing the pin sites with a local anesthetic consisting of equal volumes of 1% lidocaine with epinephrine 1:100000 and 0.25% bupivacaine with epinephrine 1:200000.

A six-point scalp block was placed using the same local anesthetic. A total of 20 mL of local anesthetic mixture was used for both procedures. Incision, bone flap removal, and dural opening proceeded without incident in all cases. Neurocognitive testing was completed over an average of forty-five minutes.

All patients in this series tolerated the procedure well and reported high satisfaction postoperatively in regards to incidence of post-op nausea and vomiting (PONV) and recall (12). However respiratory depression was noted in over 33% of the subjects. Keifer et al. (13) reports similar results in regards to respiratory depression (i.e., PaCO₂ 50 mm Hg, range: 36-69 mm Hg, minimum respiratory rate 0, range 0-3 breaths/min, lowest SaO₂ 95%, range: 92-98%) during awake craniotomy and reaffirms that "some" patients required laryngeal mask airway or endotracheal tube placement dur-

ing the operation; however, this was usually easily accomplished when necessary.

Novel agents such as dexmedetomidine have been recently proposed as sparing respiratory depression, but this has not been extensively documented. In this regard, Mack et al. describe a series of 10 patients that received a dexmedetomidine load of 0.5 to 1.0 mcg/kg over 20 minutes followed by an infusion at rates of 0.1 to 1.0 mcg/kg/h. The dexmedetomidine infusion was continued throughout initial evaluation; all patients underwent motor or neurocognitive testing, based on the particular areas or regions of cortical or subcortical resection. Infusion continued throughout the procedure and stopped once the dressings were in place (14).

Multiple reports describe general anesthetics, including volatile only and volatile-intravenous combinations. All the volatile anesthetics cause dose-dependent cerebral vasodilation. The net effect on cerebral blood flow of introducing a volatile anesthetic will depend on the interaction of several other factors: concentration of the anesthetic, the extent of previous cerebral metabolic rate depression, simultaneous blood pressure changes acting in conjunction with previous or anesthetic-induced autoregulation abnormalities, and simultaneous changes in PaCO₂ acting in conjunction with any disease-related impairment in CO₂ responsiveness. Inhalational agents cause vasodilation, leading to increases in cerebral blood flow and increases in intracranial pressure in the closed cranium. However, according to Holmstrom, increases in cerebral blood flow are agent-dependent, with Desflurane inducing changes larger than Isoflurane, and respectively larger than Sevoflurane at 1.0 Mac; but at values less than 0.5 Mac and at low doses the difference between agents becomes negligible. It also appears that for the most part, autoregulation and CO₂ responsiveness are

preserved during the administration of all intravenous drugs (15).

Similarly, Petersen et al. (16) compared two general anesthetic techniques: all patients received 0.9% NaCl at a rate of 2 to 3 mL/kg before induction. After obtaining baseline values, anesthesia was induced with propofol (1.5-2 mg/kg) in both groups. After the induction of anesthesia, patients were randomized to a desflurane-remifentanyl group (n = 30; 50% nitrous oxide in oxygen, 1.5% -2% desflurane, and 0.25 mg/kg/min remifentanyl continuous infusion) or a desflurane (n = 30; 50% nitrous oxide in oxygen and up to 6% desflurane-fentanyl group). Before intubation, fentanyl (2 mcg/kg) was administered in the desflurane-fentanyl group and remifentanyl (0.5 mcg/kg) was administered in the desflurane-remifentanyl group. Muscle paralysis was induced with administration of intravenous vecuronium bromide (0.1 mg/kg). For the desflurane-fentanyl group, after endotracheal intubation, the concentration of desflurane was reduced to 2% to 3%. Before application of the head holder and performance of the skin incision and craniotomy, fentanyl was repeated at the same dose. All patients received appropriate steroid therapy and mannitol infusion (0.2 g/kg). No significant differences in outcome were found between the two groups and are therefore equally acceptable (17).

It has been postulated that emergence time may be decreased following an awake craniotomy procedure and will facilitate early evaluation of the patient's neurological status. However, techniques including propofol/remifentanyl, remifentanyl/isoflurane, sevoflurane/remifentanyl, and desflurane/remifentanyl all show similar emergence times and vary between 3 and 10 minutes (1,4, 17). All these times are quite reasonable in regards to evaluation of neurological function postoperatively. Awake craniotomy does not require an "emergence,"

however as the emergence time for general anesthesia is significantly small, no real difference exists.

Proposed advantages of Awake Craniotomy

In a recent study published by Pirjo H et al. (18), the authors explored the clinical impression that patients who undergo awake craniotomy have less PONV (Nausea and Vomiting) and require fewer analgesic drugs for pain control than patients who have a general anesthetic. They found in fact that the volatile general anesthetic was a risk factor for PONV: nausea occurred less often in the awake craniotomy group, but this difference was short-lived. Patients who had an awake craniotomy for tumor surgery had less PONV and received fewer antiemetics when compared with patients having a general anesthetic, but only in the first 4 postoperative hours. Another recent study by Bilotta and Rosa (19), supported local anesthesia for awake craniotomy stating that adequate local anesthesia, aimed to block the sensory branches of the trigeminal nerve, is sufficient to provide 'anesthesia' for awake neurosurgery. Scalp block with local anesthetic provides reversible regional loss of sensation, reduces pain perception and global energy expenditure.

Not only was the anesthesia management better tolerated by the patients but also the inflammatory response was less in patients with awake craniotomy, as this is considered a stressful procedure because being awake while a neurosurgeon removes pathological brain tissue appears connected to a more intense emotional response than undergoing the same procedure under general anesthesia. However, perhaps good psychological support and active coping mechanisms may actually make awake craniotomy less stressful for the patient. A recent study by Klimek et al. (20), demonstrated that there was a significant plasma IL-6 increase in time for both groups (General anesthesia

and awake craniotomy). IL-8 levels did not significantly change with time, nor did for IL-10 values.

These results showed that patients undergoing awake function-controlled craniotomy experience less postoperative pain for the first 12 hours than their general anesthesia counterparts, having a decrease also in the immunologic and stress and pain responses.

CONCLUSIONS

The anesthetic management of patients for craniotomy and intraoperative neurocognitive testing present the challenges of providing analgesia, sedation, patient comfort, avoiding airway obstruction, hypoventilation, and hypoxemia. The assortment of techniques, general, neuroleptic anesthesia, propofol infusion with or without remifentanyl, and asleep-awake-asleep maneuvers with dexmedetomidine all have benefits and disadvantages.

Based on the review of the cases completed in two years at our Institution we generated a decision tree algorithm that will assist the anesthesia provider in choosing the appropriate patient for awake supratentorial craniotomy.

A careful approach to the patient will provide optimal surgical conditions, appropriate cerebral oxygen supply and demand, stable hemodynamics, a secure airway, control of ventilatory parameters, rapid emergence and minimization of complications with both awake and/or general techniques.

Careful attention to tumor location, physiological parameters, anesthetic concentrations and the operative field allow the anesthesiologist to administer a safe anesthetic.

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REFERENCES

1. Pasternak JJ, Lanier WL. Neuroanesthesiology Review-2005. *J Neurosurg Anesthesiol* 2006; 18: 93-105.
2. Bekker A, Kaufman B, Samir H, Doyle W. The use of dexmedetomidine infusion for awake craniotomy. *Anesth Analg* 2001; 92: 1251-1253.
3. Sahjapaul R. Awake craniotomy: controversies, indications and techniques in the surgical treatment of temporal lobe epilepsy. *Can J Neurol Sci* 2000; 27: S55-S63.
4. Piccioni F, Fanzio M. Management of anesthesia in awake craniotomy. *Minerva Anestesiologica* 2008; 74: 393-408.
5. Biswas BK, Bithal PK. Preincision 0.25% bupivacaine scalp infiltration and postcraniotomy pain: a randomized double-blind, placebo-controlled study. *J Neurosurg Anesthesiol* 2003; 15: 234-239.
6. Pinosky PL, Fishman RL, Reeves ST, et al. The Effect of Bupivacaine Skull Block on the Hemodynamic Response to Craniotomy. *Anesth Anal* 1996; 83: 1256-1261.
7. Costello TG, Cormack JR, Hoy C, et al. Plasma ropivacaine levels following scalp block for awake craniotomy. *J Neurosurg Anesthesiol* 2004; 16: 17-50.
8. Costello TG, Cormack JR, Mather LE, et al. Plasma levobupivacaine concentrations following skull block in patients undergoing awake craniotomy. *Br J Anaesth* 2005; 94: 848-51.
9. Kanazawa O, Blume WT, Girvin JP. Significance of spikes at temporal lobe electrocorticography. *Epilepsia* 1996; 37: 50-55.
10. Bloom MJ. Monitoring the brain and spinal cord. Proceedings of the american society of anesthesiologists annual meeting; Refresher Course; 2006 Oct 14-18; Chicago, Illinois.
11. Sloan TB. Anesthetic effects on electrophysiologic recordings. *J Clin Neurophysiol* 1998; 15: 217-226.
12. Moore TA, Markert JM, Knowlton RC. Dexmedetomidine as rescue drug during awake craniotomy for cortical motor mapping and tumor resection. *Anesth Analg* 2006; 102: 1556-1558.
13. Keifer JC, Dentchev D, Little K, et al. A retrospective analysis of a remifentanyl/propofol general anesthetic for craniotomy before awake functional brain mapping. *Anesth Analg* 2005; 101: 502-508.
14. Mack PF, Perrine K, Kobylarz E, et al. Dexmedetomidine and neurocognitive testing in awake craniotomy. *J Neurosurg Anesthesiol* 2004; 16: 20-25.
15. Holmström A, Akeson J. Cerebral blood flow at 0.5 and 1.0 minimal alveolar concentrations of desflurane or sevoflurane compared with isoflurane in normoventilated pigs. *J Neurosurg Anesthesiol* 2003; 15: 90-97.
16. Petersen KD, Landsfeldt L, Cold GE. Intracranial pressure and cerebral hemodynamics in patients with cerebral tumors: A randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. *Anesthesiology* 2003; 98: 329-336.
17. Talke P, Caldwell JE, Brown R, et al. A comparison of three anesthetic techniques in patients undergoing craniotomy for supratentorial intracranial surgery. *Anesth Analg* 2002; 95: 430-435.
18. Manninen PH, Tan TK. Postoperative nausea and vomiting after craniotomy for tumor surgery: a comparison between awake craniotomy and general anesthesia. *Journal of Clinical Anesthesia* 2002; 14: 279-283.
19. Bilotta F, Rosa G. Anesthesia for awake neurosurgery. *Anesthesiology* 2009; 22: 560-565.
20. Klimek M, Hol JW, Wens S, et al. Inflammatory profile of awake function-controlled craniotomy and craniotomy under general anesthesia. Hindawi Publishing Corporation: Mediators of Inflammation, Volume 2009, Article ID 670480, 8 pages doi:10.1155/2009/670480.