Volume 4 (2014) // Issue 1 // e-ISSN 2224-3453

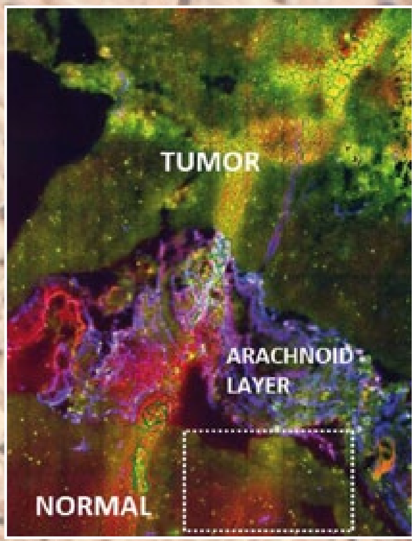
European Association of NeuroOncology Magazine

Neurology · Neurosurgery · Medical Oncology · Radiotherapy · Paediatric Neuro-oncology · Neuropathology · Neuroradiology · Neuroimaging · Nursing · Patient Issues

Awake Craniotomy in Glioma Surgery

Grossman R, Ram Z

European Association of NeuroOncology Magazine 2014; 4 (1) 27-33



THE EUROPEAN ASSOCIATION OF NEUROONCOLOGY

Krause & Pachernegg GmbH · VERLAG für MEDIZIN und WIRTSCHAFT · A-3003 Gablitz, Austria

Awake Craniotomy in Glioma Surgery

Rachel Grossman, Zvi Ram

Abstract: Awake craniotomy for resection of gliomas aims to balance tumour removal with preservation of function. In this article, the authors provide a comprehensive review that summarises the most recent available data regarding various aspects of awake craniotomy including the rationale for using this technique, the potential benefit, and the associated complications in the modern neurosurgical era. **Eur Assoc NeuroOncol Mag 2014; 4 (1): 27–33.**

Key words: awake craniotomy, malignant glioma, tumour resection, cortical mapping

Introduction

Maximal resection of malignant gliomas has been shown to be a favourable prognostic factor for survival. Maximal resection should be achieved, however, with preservation of the patient's neurological functions. Awake craniotomy with intra-operative mapping and monitoring of various neurological functions is a technology used by neurosurgeons to achieve that goal when tumours are located within or adjacent to functional brain regions. In this review, we discuss the rationale for maximal resection as a goal and describe the techniques used during awake craniotomy for intra-operative mapping and monitoring, including the pitfalls and complications associated with the technique.

Benefit of Maximal Tumour Resection

The value of maximal resection of malignant gliomas is controversial. There is consensus regarding the need to obtain pathological diagnosis and to reduce mass effect when present. However, there are no clear data supporting maximal surgical resection and enhanced overall survival, progression-free survival, or improved quality of life. 43 retrospective studies have been reported over the last 2 decades and examined the association between the extent of resection of low- and high-grade gliomas and survival. In 32 studies for high-grade gliomas (HGG), only 5 used volumetric MRI analysis. Three of the studies showed survival benefits of 2–8 months [1–3], and one study showed a trend toward enhanced survival, although it did not reach statistical significance [4]. Eleven studies assessed the correlation between extent of resection in low-grade glioma (LGG) and survival, with only 3 using volumetric MRI analysis [5–15]. All studies showed increased overall survival with maximal resection; in one, increased extent of resection resulted in a reduced incidence of malignant transformation [13].

Potential Benefits from Awake Craniotomy

Awake craniotomy with intra-operative mapping and monitoring has been reported to be associated with better neurological outcome, more extensive tumour resection, and shorter length of stay (LOS) in hospital [16–19]. Patients operated using awake craniotomy are not exposed to possible complications associated with general anaesthesia [20]. In fact, some data even advocate performing awake craniotomy as an outpatient procedure when patients are discharged after 6 hours of observation and a control post-operative CT scan [20]. In a series of 100 patients undergoing resection of supra-tentorial LGG without functional mapping, functional neurological outcome was compared to 122 patients with LGG who underwent tumour resection with intra-operative cortico-sub-cortical direct electrical stimulation [21]. The authors reported that in the non-mapped group 17 % experienced a new permanent neurological deficit compared to 6.5 % in the mapped group ($p < 0.019$). Moreover, postoperative MRI showed that GTR was achieved in only 6 % in the non-mapped group compared to 25.4 % of GTR in the mapped group ($p < 0.001$). Importantly, survival was directly correlated to the extent of resection [21]. In another retrospective analysis of patients with glioma who underwent surgical resection, 20 patients who underwent awake craniotomy were compared to 19 patients who underwent surgery under general anaesthesia. Awake craniotomy was associated with a shorter LOS in hospital [18].

Indications

Traditional indications for awake craniotomy with intra-operative mapping and monitoring include preservation of motor and language functions. Despite advances in functional imaging such as fMRI, diffuse tensor imaging (DTI), as well as intra-operative neuronavigation techniques, our ability to rely on these modalities to identify primary language sites preoperatively is still limited. Thus, awake surgery with intra-operative cortical stimulation-induced language dysfunction to identify functional language centres remains the gold standard for identification of these essential regions.

History of Awake Craniotomy

Awake craniotomy with intra-operative mapping was first used by Penfield [22] in the context of epilepsy surgery. Intraoperative cortical and subcortical mapping of eloquent areas has been used in brain tumour surgery during the last 2 decades. This technique provides the surgeon with real-time localization of functional regions in the brain and allows preservation of these regions by resulting in maximal and safe tumour resection.

Received on April 24, 2013; accepted after revision on June 9, 2013; Pre-Publishing Online on August 12, 2013

From the Department of Neurosurgery, Tel Aviv Sourasky Medical Center, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Israel

Correspondence to: Zvi Ram, MD, Department of Neurosurgery, Tel-Aviv Sourasky Medical Center, 6 Weizmann St., Tel Aviv 64239, Israel; e-mail: zviram@tlvmc.gov.il

Description of the Technique

Preoperative Evaluation

Preoperative evaluation of patients considered candidates for awake-craniotomy with intra-operative mapping and monitoring at our centre includes formal speech evaluation that consists of naming, visual or auditory verb generation, and speech comprehension, which is usually carried out up to 2 days before surgery (baseline) and repeated intra-operatively. A comprehensive neuropsychological evaluation is performed and includes a short interview with the patient and a family member preceded by several cognitive tests such as WAIS III – Similarities and Digit Span, Rey Auditory Verbal Learning Test (RVLT), Rey-Osterrieth Complex Figure Test (RFLT), naming, verbal fluency (semantic and phonetic), WMS III – Special Span, and Stroop Test or MoCA Test [23]. The patient's emotional state and ability to cooperate during awake surgery is usually assessed by questionnaires, such as the Beck Depression Inventory, the State-Trait Anxiety Inventory (for quantifying anxiety), Barratt's Impulsivity Scale (BIS-11), and the Sensitivity to Reward and Punishment Questionnaire (SPSRQ) [24]. Patients also meet with a social worker and a member of the monitoring team for detailed explanation of the hospital course, including preoperative preparation, the nature of the surgical procedure, and the postoperative course. Minimal doses of sedatives and anxiolytic drugs are generally administered on the morning of the operation. Anticonvulsant blood levels are confirmed as being within the desired therapeutic level one day before surgery.

Intraoperative Management

Most patients at our centre receive intravenous midazolam (1–2 mg) and fentanyl (50–100 mcg) upon arrival at the operating room. Each patient receives nerve blocks with local anaesthetics and according to the location of the planned pinning and incision site, ie, supra-orbital, temporal, or occipital. Standard anaesthesia monitoring is accompanied by invasive blood pressure monitoring. Spontaneous ventilation is monitored by capnography. Because urinary catheters are not routinely inserted (found to be particularly disturbing in men), we try to avoid the administration of mannitol or over-hydration. All patients receive oxygen (3 l/min) through a nasal canula during surgery. Light sedation is achieved intra-operatively with continuous administration of remifentanil when needed (Figure 1). In certain situations, such as when sedation with remifentanil does not seem to be adequate, propofol is supplemented under careful supervision. Patients who exhibit a low baseline speech level do not receive propofol or remifentanil at all. All sedatives or analgesics are discontinued briefly after pinning of the skull in order to carry out a second neurocognitive evaluation after the patient's head has been immobilized and before incising the skin. Patients who experience pain from dural manipulation are injected with lidocaine 1 % between the dural leaves. Evaluation of performance in all tasks is assessed by comparing accuracy and speed of response to the preoperative levels. Mild sedation and pain control medication are provided after the resection is completed until the skin incision is closed.

Mapping

Traditionally, mapping is performed with 50-Hz stimulation, however, other strategies are available. At our centre, we use direct cortical 50-Hz bipolar stimulation for cortical mapping of speech and motor functions (Ojemann Cortical Stimulator, Radionics, Burlington, MA) [25]. The cortical surface is stimulated in 2-mA increment intensities, from a baseline of 4 mA to a maximum 10 mA, or until functional response is elicited. Effects of stimulation on behaviour and performance (eg, speech arrest, anomia, hesitation, error in finger tapping, any motor responses) are noted, and the anatomical and radiological locations as well as the intensity applied are recorded.

Monitoring

The tasks used for the purpose of monitoring during surgery vary according to the proximity of the patient's lesion to cortical areas of language functions or according to the patients' specific functional MRI mapping of language functions (as measured by blood oxygen level-dependent activation). Language is checked by free speech after cortical stimulation and throughout the resection itself by sub-cortical stimulation of adjacent tracts (ie, superior longitudinal fascicle, arcuate fasciculus etc). Motor functions are evaluated according to the tumour location by asking the patient to perform various movements (eg, clenching a fist, flexing a foot) as well as by the ability of the patient to plan and initiate movements in cases of lesions in proximity to the supplementary motor area. Motor-evoked potentials and corresponding muscle responses are monitored in most patients.

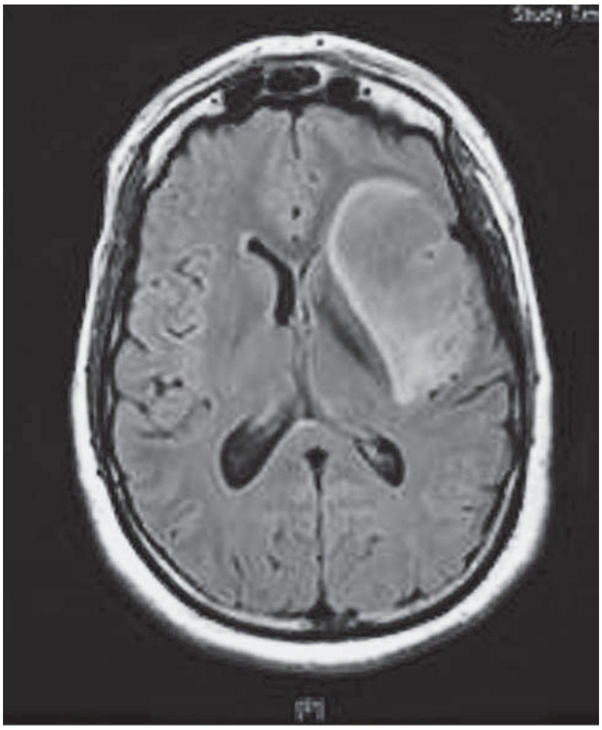
Figure 1. Intra-operative photographs of the surgical team during awake craniotomy.

Neuroanaesthesia in Awake Craniotomy

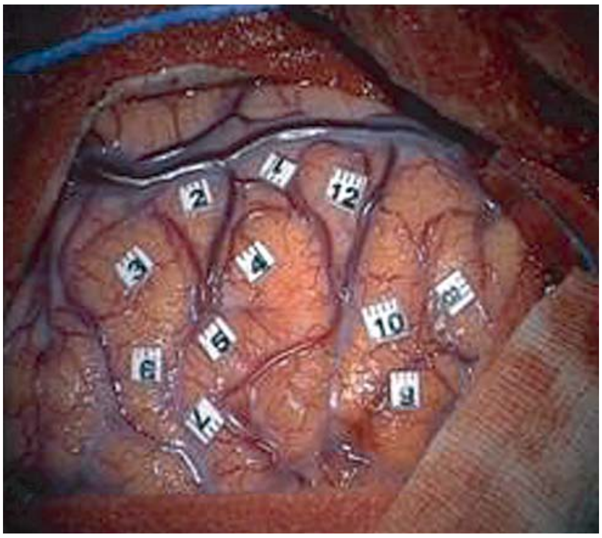
Neuroanaesthesia in awake craniotomy is important for keeping the patient cooperative during the mapping phase as well as for decreasing the physical and psychological stress associated with this procedure. There are several anaesthesia protocols in use. Intermittent general anaesthesia with controlled ventilation for asleep-awake-asleep (AAA) has been described. A laryngeal mask or endotracheal tube is inserted before the beginning of the operation and taken out before mapping is started. At the end of the mapping phase the patient is re-anaesthetized and ventilated through the laryngeal mask or endotracheal tube. In a prospective single-centre study, 140 patients were operated for tumour resection under AAA. They were fully awake for a mean of 98 minutes, discomfort was reported in 17.8 %, with one case of aspiration, and no mortality. AAA has the advantage of sparing the unpleasant phase of craniotomy and hence does not have a time limitation during non-eloquent tumour resection or during the closure phase. However, the main disadvantage is the risk of coughing and aspiration [26]. In our experience, patients are operated under monitored anaesthesia care with no general anaesthesia. Patients are spontaneously breathing throughout the entire procedure. Sedation is achieved with propofol and remifentanil during the insertion of the head holder and craniotomy itself. Once the mapping phase is complete sedation is re-applied. The main complications associated with general anaesthesia are minimized by this approach. Minimal sedation does not usually lead to airway obstruction, hypoxia, or hypercapnea.

Surgical Technique: The Evolution of Craniotomy Size

Intra-operative mapping was first used in the context of epilepsy surgery. In this procedure, large craniotomies with wide cortical exposure are used to identify cortical regions responsible for language and motor function (ie "positive sites"). A different approach has evolved for tumour surgery. Tumour resection is performed through smaller, tailored craniotomies with small cortical exposure of the tumour region. Tumour resection is directed through non-critical cortical regions (absence of stimulation-induced language responses, and sometimes without localization of positive functional sites [27]). This strategy is more time-efficient [28]. However, despite minimizing the risk of causing neurological deficits, these complications may still occur [29].



A



B

Figure 2. (A) Pre-operative axial fluid-attenuated inversion recovery- (FLAIR-) weighted MRI showing a WHO grade-II insular glioma in a 40-year-old woman presenting with episodes of seizures. This patient has no neurological deficit. **(B)** Intra-operative cortical mapping of language during awake surgery.

Intra-Operative Monitoring

Language

Significant inter-individual variability in language site organisation exists. This may be due to an anatomical variation mass effect carried by the tumour or even brain reorganisation due to brain plasticity. Speech arrest may be produced during awake craniotomy far beyond the classical Broca's region. Importantly, it is crucial to differentiate between dysarthria and speech arrest. Speech arrest is recognized by ceasing fluent function (ie, number counting) without simultaneous involuntary motor response in the muscles affecting speech. Since functional brain tissue may be located inside tumours such as malignant gliomas, it is not always safe to presume that the tumour's interior can be resected without functional deterioration. This is the overall rationale for operating lesions located adjacent to presumed speech centres by awake surgery (Figure 2). Brain tumour resection with intra-operative language mapping was performed in 250 patients with gliomas [27]. Tailored craniotomies with limited cortical exposure resulted in only few points of localization of language sites ("positive sites"). Still, 6 months later, only 1.6 % had a persistent language deficit [27]. Interestingly, in a case report of a patient with anaplastic astrocytoma located in Broca's area, only subtotal awake resection was achieved. This patient underwent

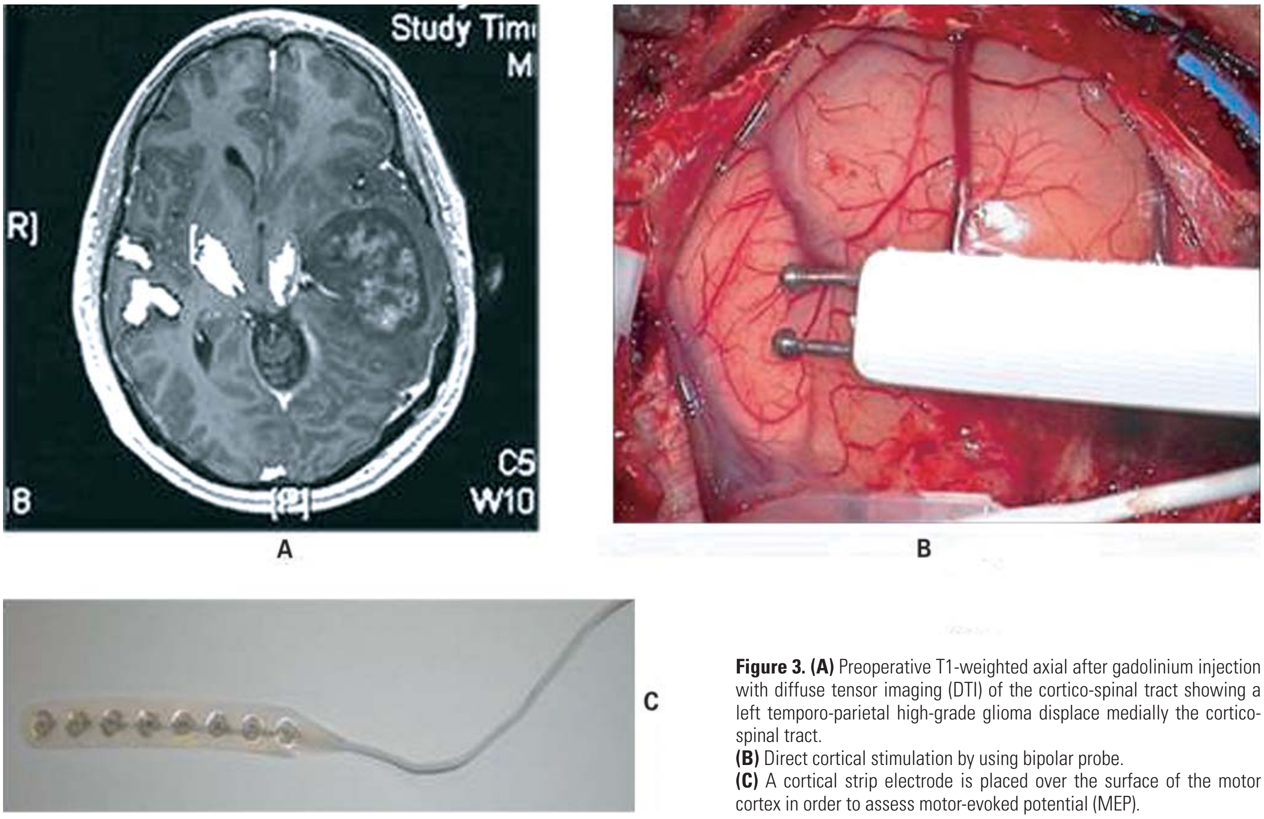


Figure 3. (A) Preoperative T1-weighted axial after gadolinium injection with diffuse tensor imaging (DTI) of the cortico-spinal tract showing a left temporo-parietal high-grade glioma displace medially the cortico-spinal tract.
(B) Direct cortical stimulation by using bipolar probe.
(C) A cortical strip electrode is placed over the surface of the motor cortex in order to assess motor-evoked potential (MEP).

implantation of a subdural grid over his Broca centre within the residual tumour. Continuous high-frequency cortical electrical stimulation (cHFCS) was applied with stimulus intensity that caused mild speech disturbances. After 25 days of stimulation the author reported displacement of speech function and the patient underwent second surgery during which the tumour could be completely removed with no deficit. The authors concluded that this phenomenon was evidence for induction of topographic plasticity by using cHFCS, which allowed more extensive tumour resection [30].

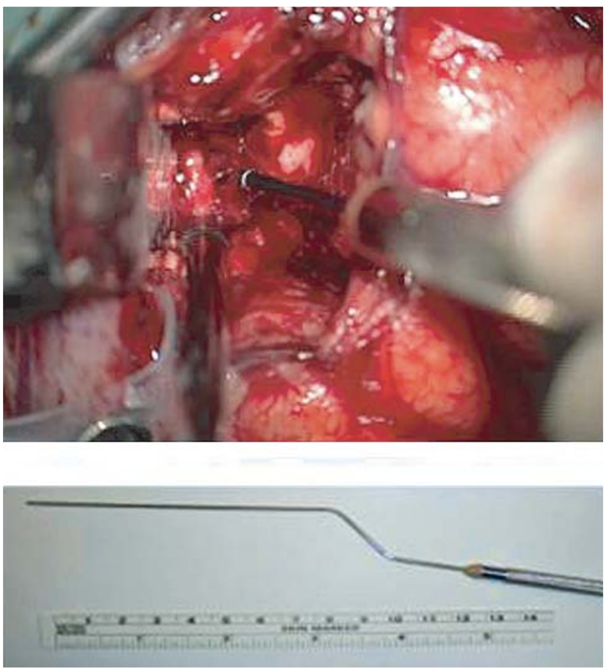


Figure 4. Sub-cortical stimulation of the cortico-spinal tracts by means of a subcortical monopolar electrode.

Motor Function

Motor function is a complex process involving several frontal regions including primary motor cortex, secondary motor areas such as the supplementary motor area (SMA), pre-motor area, and cortico-spinal tracts (CST). Electrical stimulation of the primary motor cortex leads to motor response (ie, movement). Electrical stimulation of certain secondary motor areas such as the pre-motor area and caudal SMA may lead to cessation of voluntary movement. This was first described by Penfield and Jasper [31], and defined later by Lüders et al as “negative motor areas” [32].

Direct cortical stimulation is conducted by bipolar probe with 2 tips at 6–10 mm distance with frequencies of 50–60 Hz. Initial stimulation intensity is usually 2 mA and gradually increased in 2-mA increments up to 10 mA. Somatosensory evoked potential (SSEP) is used for phase reversal and identification of the central sulcus. Electromyography (EMG) is used to record motor response in muscles. In addition to continuously assessing the integrity of the motor pathways, motor-evoked potential (MEP) monitoring is conducted by placing a strip electrode (4–8 contacts) over the surface of the precentral gyrus. MEPs are recorded by needle electrodes inserted into the contra-lateral muscles (same as use for the EMG). During tumour resection sub-cortical stimulation is applied, usually with monopolar probe to identify the proximity to the motor pathways [33] (Figure 3).

In a retrospective analysis in 55 patients with tumours located within or adjacent to the cortico-spinal tract (CST), direct cortical-stimulated motor-evoked potentials and sub-cortical stimulated motor-evoked potentials were assessed and the current intensity used to get motor response was correlated to the distance from CSTs. A linear correlation was found between the distance from CSTs and the threshold of sub-cortical stimulation producing a motor response (0.97 mA for every 1 mm brain tissue distance from CSTs) [33] (Figure 4). Importantly, direct cortical and sub-cortical stimulation can be achieved in awake manner or under general anaesthesia (while avoiding the use of halogenated inhalational and muscle paralysis agents). Our experience shows no significant difference between those methods with regard to immediate post-operative motor status or extent of resection [33].

Outcome of Patients Undergoing Awake Craniotomy

The usefulness of awake surgery with intra-operative cortical and sub-cortical mapping has not been assessed in randomized trials. There is conflicting data based on retrospective studies comparing the outcome of patients with brain tumours located adjacent to the eloquent cortex who were operated under general sedation versus local anaesthesia (awake craniotomy). The most extensive work recently published in the literature is a meta-analysis of 90 reports with 8091 patients who underwent resective surgery for malignant supra-tentorial gliomas with and without intra-operative stimulating mapping. Severe late post-operative neurological deficits were observed in 3.4 % of the patients who underwent intra-operative mapping, and in 8.2 % of patients who were operated without intra-operative mapping [34]. GTR was achieved in 75 % and 58 % of these groups, respectively. The authors have concluded that glioma resection using intra-operative stimulation mapping is associated with less late and severe neurological deficits and more extensive resection and should thus be widely used as a standard of care in glioma surgeries [34].

Patient Satisfaction

Awake craniotomy has been shown to be a safe procedure from a medical point of view. However, several studies investigated patient perception and satisfaction with the procedure [20, 35, 36]. Specifically, their levels of anxiety, expectations, and satisfaction were assessed. It appears that awake craniotomy is well-tolerated by those patients who understand the benefits of the procedure and believe that it may improve their post-operative outcome. Patient recollections of the procedure vary. Some patients have no recollection at all while others vividly remember the sound of the drill or the pressure on the head during the insertion of the Mayfield head holder. Interestingly, most patient recalls are auditory memories (suction, drilling, voices of the surgical team). Half of them do not remember the cortical mapping part despite being fully cooperative during the procedure. They remember talking with the surgical team, being asked to perform tasks such as to move their extremities, and answering questions. Overall, despite experiencing minimal pain and discomfort during certain parts of the operation (placement and removal of cranial fixation, skin incision), it appears that most patients tolerate awake craniotomy well and show an overall high level of satisfaction [20, 37].

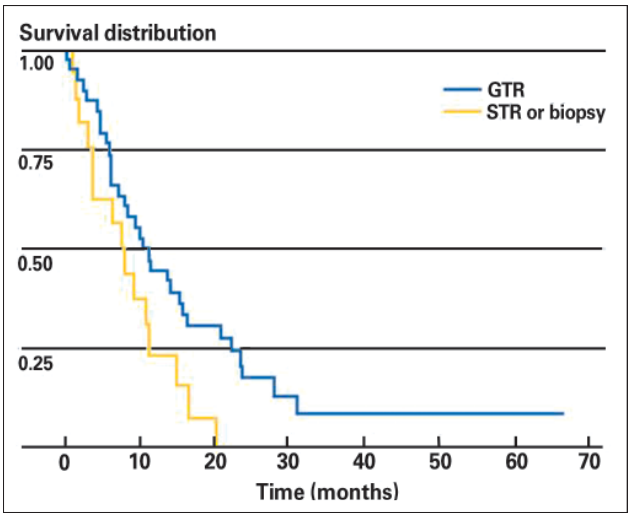


Figure 5. Kaplan-Meier curve of survival for elderly patients (65 years) with high-grade gliomas (HGG) who underwent awake-craniotomy gross tumour resection (GTR) compared to subtotal resection (STR) or biopsy. Median survival was significantly longer for patients with HGG who underwent GTR compared to those who underwent STR or biopsy (10.8 vs 7.8 months, respectively; p = 0.039) [39].

Awake Craniotomy in Special Populations

Awake Craniotomy in the Elderly Population

Despite data linking awake surgical resection of supra-tentorial tumours with maximum extent of resection and overall better outcome, older patients with malignant brain tumours are rarely offered such aggressive treatment. We compared the outcome of 90 elderly patients (> 65 years old) who underwent awake craniotomy to 334 patients < 65 years old. Specifically, the 2 groups were compared for surgical outcome parameters such as postoperative complication, mortality, LOS, and overall survival [38]. There was no higher rate of mortality or post-operative complications in the elderly group of patients, except increased LOS. On average, elderly patients tend to stay 2 days longer in hospital compared to their younger counterparts. Interestingly, a subset of elderly patients with HGG enjoyed a significant survival benefit after awake GTR of their tumours (Figure 5). Taken all of these data together, it appears that awake maximal surgical resection of brain tumours in the elderly population with good pre-operative functional status is feasible, safe, is not associated with increased peri-operative morbidity or mortality, and may increase their survival. Unfortunately, there is no additional data investigating this topic.

Awake Craniotomy in the Paediatric Population

Awake craniotomy has been used in the paediatric population [40–42]. Specific challenges concern cooperation, understanding, and anxiety. Several reports have been published so far including a case of a 9-year-old girl with NF1 who underwent successful awake craniotomy with intra-operative language mapping for resection of a left temporo-parietal GBM [40]. Another report described 2 patients who were 16 years old when diagnosed with intra-axial brain tumours located adjacent to their speech brain regions. They both underwent intra-operative language mapping and resection of their tumours. Overall, it seems that awake craniotomy is feasible and safe also in the paediatric population, but is undoubtedly challenging in younger children, especially the part of brain mapping. Additional neurophysiological strategies are warranted.

Complications

In addition to the complications associated with craniotomy under general anaesthesia such as post-operative infection or post-operative bleeding, there are several complications that are uniquely associated with awake craniotomy.

Awake Craniotomy Failure

Awake craniotomy may need to be converted in certain situations into general anaesthesia surgery. There are several causes that may lead to failure of the procedure and unsuccessful stimulation and mapping. In a review of 424 patients undergoing awake craniotomy, 27 were considered as an awake craniotomy failure [43]. The most common reason was lack of intra-operative communication with the patients (n = 18; 4.2 %), mostly due to pre-operative dysphasia and phenytoin treatment. As one can expect, their outcome compared to those who underwent successful awake surgery was worse in several parameters: their overall complication rate was significantly increased with a higher incidence of postoperative dysphasia, the rate of GTR was significantly lower, and their length of stay was significant longer with an average of an additional 3 days in hospital.

Intra-Operative Seizures during Awake Craniotomy

Seizures are commonly presenting symptoms in patients with brain tumours occurring in 30–50 % prior to their diagnosis. Intra-operative seizures during awake craniotomy may have a negative impact on the surgical course and in certain cases may require conversion into general anaesthesia. The postictal period may negatively affect patient cooperation, especially during electrical cortical and sub-cortical mappings. This may cause reduced tumour resection and a higher rate of post-operative neurological deficits. In a review of 477 patients with brain tumours who underwent awake craniotomy, the incidence of intra-operative seizures was 12.6 % (n = 60). Eleven patients (2.3 %) were considered as a failure while awake craniotomy was converted into general anaesthesia surgery. Interestingly, these failed patients tended to be younger with a history of pre-operative seizures. In general, their outcome was worse with a significantly higher rate of short-term motor deficit, and they tended to stay longer in hospital [39]. In a series of 511 patients who underwent tumour resection with intra-operative brain mapping, 25 (4.9 %) patients experienced intra-operative seizures. Two patients required intubation and induction of general anaesthesia [44]. It is well-known that tumour histology and location may predict seizure occurrence. The incidence of seizures is higher in patients with LGG and is more common when the tumour is located in the frontal and temporal lobes. In a series of 137 patients with gliomas, the occurrence of intra-operative seizures during awake craniotomy was 21.1 %. A significant correlation was found between intra-operative seizures and tumour location. Specifically, patients with tumours located in the supplementary motor area had the highest incidence of intra-operative seizures (73.3 %) regardless of their seizure history.

Intra-Operative Monitoring of Cognition

Intra-operative mapping of non-language or motor function has received less attention. Many patients suffer from post-operative visual and cognitive deficits that negatively affect their quality of life. Thus, there is a need to expand the indications for awake craniotomies for preservation of their functions.

Mapping of SMA

The SMA, part of the frontal lobe, is responsible for the initiation and planning of movements. Unilateral SMA lesion may lead to motor and language deficits. This usually gradually improves within a few weeks (SMA syndrome). Rosenberg et al [45] investigated SMA activity in 26 patients with tumours located in this region. All patients underwent awake tumour resection with motor and language monitoring. The motor paradigm consisted of finger tapping that was validated before by fMRI studies to activate the SMA [46]. In this task, the patient had to plan sequences of finger movements. Language was assessed by verb generation tests and free speech. Task dysfunction during direct cortical stimulation was associated with critical involvement of the SMA in this task. Stronger activation of the lesioned SMA was seen in patients without direct cortical stimulation-induced dysfunction. The authors suggested that this phenomenon was the result of higher functional sites that were able to compensate for the disruption caused by electrical stimulation.

Mapping of Optic Radiation

Post-operative visual deficits have received little attention in the past and have been considered an acceptable postoperative neurological deficit although they may have negative consequences on daily activity. Epilepsy surgeons traditionally used anatomical criteria to preserve optic pathways during mesiotemporal surgeries. However, it appears that there is much inter-individual variability in the optic pathways, especially the part located posterior to the lateral geniculate body [47, 48]. A series of 14 patients with grade-I, -II, and -III gliomas who underwent awake tumour resection with intra-operative mapping of the optic radiation using sub-cortical electrical stimulation has been recently reported. These patients had tumours involving the optic radiation with none of them having had a pre-operative visual field deficit. During surgical tumour resection, direct sub-cortical electrical stimulation was repeatedly performed until the optic radiation was identified by transient visual disturbances. All patients experienced visual disturbances during mapping and tumour resection was stopped at this point. Only one patient experienced permanent post-operative hemianopsia [49].

Future Directions

Individually Tailored Mapping

Mapping of non-language, non-motor, essential functions such as spatial perception and memory has received less attention and is considered highly experimental. Individually tailored mapping is desired not only in the sense of portraying functional organisation at the individual patient level, but also in terms of selecting the functions to be mapped. Ideally, the selection process should rely not only on tumour location and clinical symptoms but also on each patient's particular occupational needs and habits (eg, perception of tempo and pitch for musicians, sense of space for pilots or civil engineers) to improve surgical outcome for this particular patient. Indeed, several clinical reports have recently published the use of awake mapping for various tasks with good clinical outcome. There is one case report describing intra-operative mapping of calculation in a school teacher operated for resection of a left parietal tumour involving the angular gyrus [50]. She was neurologically intact before surgery and during mapping performed some mild serial arithmetical subtraction errors. She underwent GTR of the tumour and left with a mild post-operative deficit for arithmetical subtraction. In another report, 4 amateur singers, pre-operatively intact, with brain tumours who underwent awake surgery using a singing task during direct cortical stimulation, demonstrated clear distinction between speech and singing in the Broca region [51]. We have recently related pre-operative fMRI activation in the supplementary motor area and the functional deficit aroused during intra-operative direct cortical stimulation [45].

Conflict of Interest

None.

References:

1. Keles GE, Anderson B, Berger MS. The effect of extent of resection on time to tumor progression and survival in patients with glioblastoma multiforme of the cerebral hemisphere. Surg Neurol 1999; 52: 371–9.

2. Lacroix M, Abi-Said D, Fourney DR, et al. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg 2001; 95: 190–8.

3. Sanai N, Polley MY, McDermott MW, et al. An extent of resection threshold for newly diagnosed glioblastomas. J Neurosurg 2011; 115: 3–8.

4. Keles GE, Chang EF, Lamborn KR, et al. Volumetric extent of resection and residual contrast enhancement on initial surgery as predictors of outcome in adult patients with hemispheric anaplastic astrocytoma. J Neurosurg 2006; 105: 34–40.

5. Claus EB, Horlacher A, Hsu L, et al. Survival rates in patients with low-grade glioma after intraoperative magnetic resonance image guidance. Cancer 2005; 103: 1227–33.

6. Johannesen TB, Langmark F, Lote K. Progress in long-term survival in adult patients with supratentorial low-grade gliomas: a population-based study of 993 patients in whom tumors were diagnosed between 1970 and 1993. J Neurosurg 2003; 99: 854–62.

7. Leighton C, Fisher B, Bauman G, et al. Supratentorial low-grade glioma in adults: an analysis of prognostic factors and timing of radiation. J Clin Oncol 1997; 15: 1294–301.

8. McGirt MJ, Chaichana KL, Gathinji M, et al. Independent association of extent of resection with survival in patients with malignant brain astrocytoma. J Neurosurg 2009; 110: 156–62.

9. Nakamura M, Konishi N, Tsunoda S, et al. Analysis of prognostic and survival factors related to treatment of low-grade astrocytomas in adults. Oncology 2000; 58: 108–16.

10. Philippon JH, Clemenceau SH, Fauchon FH, et al. Supratentorial low-grade astrocytomas in adults. Neurosurgery 1993; 32: 554–9.

11. Rajan B, Pickuth D, Ashley S, et al. The management of histologically unverified presumed cerebral gliomas with radiotherapy. Int J Radiat Oncol Biol Phys 1994; 28: 405–13.

12. Shaw E, Arusell R, Scheithauer B, et al. Prospective randomized trial of low- versus high-dose radiation therapy in adults with supratentorial low-grade glioma: initial report of a North Central Cancer Treatment Group/Radiation Therapy Oncology Group/Eastern Cooperative Oncology Group study. J Clin Oncol 2002; 20: 2267–76.

13. Smith JS, Chang EF, Lamborn KR, et al. Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. J Clin Oncol 2008; 26: 1338–45.

14. van Veelen ML, Avezaat CJ, Kros JM, et al. Supratentorial low grade astrocytoma: prognostic factors, dedifferentiation, and the issue of early versus late surgery. J Neurol Neurosurg Psychiatry 1998; 64: 581–7.

15. Yeh SA, Ho JT, Lui CC, et al. Treatment outcomes and prognostic factors in patients with supratentorial low-grade gliomas. Br J Radiol 2005; 78: 230–5.

16. Gupta DK, Chandra PS, Ojha BK, et al. Awake craniotomy versus surgery under general anesthesia for resection of intrinsic lesions of eloquent cortex – a prospective randomised study. Clin Neurol Neurosurg 2007; 109: 335–43.

17. Manninen PH, Balki M, Lukitto K, et al. Patient satisfaction with awake craniotomy for tumor surgery: a comparison of remifentanil and fentanyl in conjunction with propofol. Anesth Analg 2006; 102: 237–42.

18. Peruzzi P, Bergese SD, Viloria A, et al. A retrospective cohort-matched comparison of conscious sedation versus general anesthesia for supratentorial glioma resection. Clinical article. J Neurosurg 2011; 114: 633–9.

19. Sacko O, Lauwers-Cances V, Brauge D, et al. Awake craniotomy vs surgery under general anesthesia for resection of supratentorial lesions. Neurosurgery 2011; 68: 1192–9.

20. Khu KJ, Doglietto F, Radovanovic I, et al. Patients' perceptions of awake and outpatient craniotomy for brain tumor: a qualitative study. J Neurosurg 2010; 112: 1056–60.

21. Duffau H, Lopes M, Arthuis F, et al. Contribution of intraoperative electrical stimulations in surgery of low grade gliomas: a comparative study between two series without (1985–96) and with (1996–2003) functional mapping in the same institution. J Neurol Neurosurg Psychiatry 2005; 76: 845–51.

22. Rasmussen T, Penfield W. The human sensorimotor cortex as studied by electrical stimulation. Fed Proc 1947; 6: 184.

23. Kave G. Standardization and norms for a Hebrew naming test. Brain Lang 2005; 92: 204–11.

24. Iwamoto FM, Reiner AS, Nayak L, et al. Prognosis and patterns of care in elderly patients with glioma. Cancer 2009; 115: 5534–40.

25. Berger MS, Ojemann GA. Intraoperative brain mapping techniques in neuro-oncology. Stereotact Funct Neurosurg 1992; 58: 153–61.

26. Deras P, Moulinié G, Maldonado IL, et al. Intermittent general anesthesia with controlled ventilation for asleep-awake-asleep brain surgery: a prospective series of 140 gliomas in eloquent areas. Neurosurgery 2012; 71: 764–71.

27. Sanai N, Mirzadeh Z, Berger MS. Functional outcome after language mapping for glioma resection. N Engl J Med 2008; 358: 18–27.

28. Sanai N, Berger MS. Operative techniques for gliomas and the value of extent of resection. Neurotherapeutics 2009; 6: 478–86.

29. Taylor MD, Bernstein M. Awake craniotomy with brain mapping as the routine surgical approach to treating patients with supratentorial intraaxial tumors: a prospective trial of 200 cases. J Neurosurg 1999; 90: 35–41.

30. Barcia JA, Sanz A, Balugo P, et al. High-frequency cortical subdural stimulation enhanced plasticity in surgery of a tumor in Broca's area. Neuroreport 2012; 23: 304–9.

31. Penfield W. Mechanisms of voluntary movement. Brain 1954; 77: 1–17.

32. Lüders HO, Lesser RP, Dinner DS, et al. A negative motor response elicited by electrical stimulation of the human frontal cortex. Adv Neurol 1992; 57: 149–57.

33. Nossek E, Korn A, Shahar T, et al. Intraoperative mapping and monitoring of the corticospinal tracts with neurophysiological assessment and 3-dimensional ultrasonography-based navigation. Clinical article. J Neurosurg 2011; 114: 738–46.

34. De Witt Hamer PC, Robles SG, Zwinderman AH, et al. Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. J Clin Oncol 2012; 30: 2559–65.

35. Manchella S, Khurana VG, Duke D, et al. The experience of patients undergoing awake craniotomy for intracranial masses: expectations, recall, satisfaction and functional outcome. Br J Neurosurg 2011; 25: 391–400.

36. Wahab SS, Grundy PL, Weidmann C. Patient experience and satisfaction with awake craniotomy for brain tumours. Br J Neurosurg 2011; 25: 606–13.

37. Grossman R, Ram Z, Perel A, et al. Control of postoperative pain after awake craniotomy with local intradermal analgesia and metamizol. Isr Med Assoc J 2007; 9: 380–2.

38. Grossman R, Nossek E, Sitt R, et al. Outcome of elderly patients undergoing awake-craniotomy for tumor resection. Ann Surg Oncol 2013; 20: 1722–8.

39. Nossek E, Tal Shahar IM, Barzilai O, et al. Intraoperative seizures during awake craniotomy: incidence and consequences – analysis of 477 patients. Neurosurgery 2013; 73: 135–40.

40. Klimek M, Verbrugge SJ, Roubos S, et al. Awake craniotomy for glioblastoma in a 9-year-old child. Anaesthesia 2004; 59: 607–9.

41. Ojemann G, Ojemann J, Lettich E, et al. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. 1989. J Neurosurg 2008; 108: 411–21.

42. Everett LL, van Rooyen IF, Warner MH, et al. Use of dexmedetomidine in awake craniotomy in adolescents: report of two cases. Paediatr Anaesth 2006; 16: 338–42.

43. Nossek E, Matot I, Shahar T, et al. Failed awake craniotomy: a retrospective analysis in 424 patients undergoing craniotomy for brain tumor. J Neurosurg 2013; 118: 243–9.

44. Serletis D, Bernstein M. Prospective study of awake craniotomy used routinely and nonselectively for supratentorial tumors. J Neurosurg 2007; 107: 1–6.

45. Rosenberg K, Nossek E, Liebling R, et al. Prediction of neurological deficits and recovery after surgery in the supplementary motor area: a prospective study in 26 patients. J Neurosurg 2010; 113: 1152–63.

46. Roland PE, Larsen B, Lassen NA, et al. Supplementary motor area and other cortical areas in organization of voluntary movements in man. J Neurophysiol 1980; 43: 118–36.

47. Ebeling U, Reulen HJ. Neurosurgical topography of the optic radiation in the temporal lobe. Acta Neurochir (Wien) 1988; 92: 29–36.

48. Jeelani NU, Jindahra P, Tamber MS, et al. Hemispherical asymmetry in the Meyer's Loop: a prospective study of visual-field deficits in 105 cases undergoing anterior temporal lobe resection for epilepsy. J Neurol Neurosurg Psychiatry 2010; 81: 985–91.

49. Gras-Combe G, Moritz-Gasser S, Herbet G, et al. Intraoperative subcortical electrical mapping of optic radiations in awake surgery for glioma involving visual pathways. J Neurosurg 2012; 117: 466–73.

50. Duffau H, Denvil D, Lopes M, et al. Intraoperative mapping of the cortical areas involved in multiplication and subtraction: an electrostimulation study in a patient with a left parietal glioma. J Neurol Neurosurg Psychiatry 2002; 73: 733–8.

51. Roux FE, Borsa S, Demonet JF. "The mute who can sing": a cortical stimulation study on singing. J Neurosurg 2009; 110: 282–8.