Awake craniotomy for glioma resection: Technical aspects and initial results in a single institution

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Original Article

Abstract

Introduction. Although variations in the technique of awake craniotomy (AC) have been widely reported, a key member of this interdisciplinary procedure is the healthcare professional performing assessments of neurological function during resection. The expertise of the latter will depend on the neurological function to be tested and on available resources of the institution. This report details our initial experience of an AC service utilizing the expertise of a speech and language therapist (SLT) and an experienced neuro-physiotherapist (NP) to monitor patient function during glioma resection. Methods. Forty-five patients underwent 50 AC procedures for eloquently located gliomas over a 3-year period. Patients with a glioma involving speech or sensorimotor areas were assessed preoperatively by the SLT/NP respectively. The same therapist monitored the patient's neurological function intraoperatively and executed a rehabilitation program tailored to the needs of the patient in the postoperative period. Results. Three patients underwent biopsy only, due to intraoperative seizures precluding intraoperative mapping (2 cases) or speech arrest on stimulation of a small recurrent tumor. The remaining 47 cases were suitable for repetitive neurological assessment “awake” during tumor debulking. One patient with a large sensorimotor tumor developed intraoperative hemiparesis due to outward brain herniation (which recovered postoperatively). Ten patients developed a new or worsened neurological deficit in the initial postoperative period (6 were detected intraoperatively), of which 5 eventually had resolution and returned to baseline function within 2 weeks. Conclusions. In our initial experience based anecdotally on a previous similar “non-awake” caseload, we have found AC with the input of the SLT/NP to be a key component in ensuring optimal functional outcomes for patients with gliomas in eloquently located areas.

Keywords: awake craniotomy; neurophysiotherapist; speech and language therapist

Introduction

Awake craniotomy (AC) is becoming a standard procedure for improving the extent of resection of gliomas involving language and sensorimotor regions.1,2 The procedure is associated with improved neurological preservation rates compared with similar cases performed under general anesthesia.3 Although diffusely infiltrative gliomas will inevitably relapse close to the margins of tumor resection, maximal safe resection has been shown to extend survival in both low- and high-grade tumors.4,5 Indeed, the concept of “supra-complete” resection of low-grade gliomas involving “non-eloquent areas” is gaining vogue in an attempt to delay onset of progression to higher-grade tumors.6

The technique of AC has evolved from a large craniotomy to expose “positive” stimulation-induced language and motor responses to smaller tailored craniotomies, which may not expose any positive sites. This “negative mapping” strategy allows for minimal cortical exposure, less extensive intraoperative mapping, and a more time-efficient neurosurgical procedure.1

Direct electrical stimulation of cortical and subcortical areas within the vicinity of gliomas helps identify functionally important areas that need to be preserved. While the surgeon is stimulating these areas, there is a reliance on the skill of the assessor to detect any subtle changes in function.
Furthermore, having an effective “early warning system” will help ensure that no new neurological deficits develop during resection. While the operative conditions depend heavily on the experience of the surgeon and anesthetist, the personnel responsible for clinical assessment of the patient are key to ensuring optimal functional outcome of the patient.

Although prevention of neurological deficit is paramount, the concept of “brain plasticity”, which may facilitate improvement in neurological function (particularly in low-grade gliomas), is gaining credence. This “reactional plasticity” of the nervous system following surgery may be due to an induction in compensatory mechanisms that recruit latent neural networks. This functional reorganization may also provide the basis for a significant response to a tailored rehabilitation program early in the postoperative period.

This paper, based on our preliminary experience of a new AC service, highlights the key contributions an experienced SLT and NP make to ensure good functional outcomes for glioma patients.

**Methods**

**Case selection and assessment**

Since February 2012, our institution has performed “asleep-aware-asleep” craniotomy for gliomas involving eloquent areas (language and/or sensorimotor areas). Case selection was based on mode of presentation and correlation with the patient imaging to predict those likely to benefit from AC. Patients were initially seen in the pre-assessment clinic (following MDT approval) where the patient was counseled by nursing and medical staff (surgeon and anesthetist) as to the need for an AC and what the procedure entails.

Pre-assessment also affords the patient an opportunity to visit the operating theater, and undergo detailed SLT/NP assessment which reassures the patient and allays any anxieties they might have regarding the procedure. Anesthetic involvement is key early in the process of case selection to ensure that there are no anesthetic contraindications to the procedure (e.g., difficult airway, morbid obesity). The standard volumetric magnetic resonance imaging datasets (T1 contrast, volumetric DTI for tractography planning, and FLAIR for low-grade tumors) for surgical planning are also performed during this visit, and patients get an opportunity to review their imaging with their surgeon.

Adjustment of patient’s dexamethasone (for high-grade gliomas) and anti-seizure medication is also undertaken at pre-assessment to reduce the chance of brain swelling and seizure activity intraoperatively. Low-grade glioma patients tend not to be on dexamethasone preoperatively. Following this initial preparation, the patient then undergoes a detailed baseline clinical evaluation by the SLT/NP.

**Speech and language therapy preoperative assessment**

The patient’s speech and language is assessed using formal tests covering the full spectrum of receptive and expressive language tasks (Table 1). The SLT and patient also plan a range of speech and language tasks to be used intraoperatively, for example, describing an aspect of their occupation, details of a hobby, or daily routine. These tasks are based on the patient’s known premorbid ability. Any preoperative “baseline” language deficit is documented for careful monitoring during the operation, to aid with identification of new errors during stimulation. The preoperative assessment also facilitates a rapport to be established with the patient, which lends itself to “free-flowing” speech with which language function can be closely monitored during tumor resection.

**Preoperative physiotherapy assessment**

For sensorimotor tumors, the patient undergoes an assessment by an experienced NP to record muscle power throughout all limbs using the Oxford grading scale, and an assessment of muscle tone using the Ashworth scale. Sensation is tested for light touch, "pin-prick," joint position sense, finger–nose–heel–shin coordination, and stereognosis to establish any baseline deficits. The therapist assesses the ability to perform a variety of simple functional tasks that can be replicated in theater to test dexterity and strength, for example, grip strength, the ability to direct a plastic needle through a button hole, dab a swab to the mouth, or use a key to open a padlock.

**Awake craniotomy for tumor resection**

The “asleep-aware-asleep” craniotomy performed is broadly similar to that described by Sarang, Dinsmore, and Murphy et al. Briefly, patients are positioned in a head clamp and woken up following bone flap removal prior to dural opening. The therapist ensures that the patient responds readily to voice with normal tone and normal speech and facial expression, is orientated, and clearly demonstrates receptive and expressive language function, before allowing the surgeon to proceed.

The boundaries of the tumor are verified using surgical navigation (BrainLAB) and intraoperative ultrasound (Flex Focus 800, BK Medical Systems) guidance systems. Cortical stimulation with an Osiris Neurostimulator (Inomed) bipolar electrode is performed to identify a corridor of safety into the tumor and adjacent eloquent sites that need to be avoided while tumor removal is performed using the

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**Table 1. Language tests used to test speech perioperatively.**

| Test Description                        | Test Details                                                                 |
|-----------------------------------------|------------------------------------------------------------------------------|
| Comprehensive Aphasia Test (CAT)        | Single-word naming, Comprehension of spoken sentences, Spoken picture description |
| Mount Wilga high-level language test     | Absurdities, Idioms, Sequencing                                              |
| Mount Wilga                            |                                                                              |
| Mount Wilga                            |                                                                              |

*Graded for: Reverse roles round the verb, passive sentences, and relative clauses; Looking at connected speech with regard to: accuracy, appropriacy, speed, fluency and syntactic accuracy; Explanation of underlying meaning, verbal reasoning; Verbal planning, verbal explanation, and delineated steps of verbal explanation*
cavitating ultrasonic aspirator. The stimulation settings (for cortical and subcortical mapping) used for speech mapping are: a frequency of 50 Hz (continuous mode), “Burst” of 5, and a current of 3–15 mAmp, while sensorimotor stimulation settings are: a frequency of 1 Hz (continuous mode), “Burst” of 5, and a current of 3–25 mAmp. Early in our experience, our current setting was typically 7 mAmp, but we have since reduced it to 3–5 mAmp, to reduce seizure risk.

Each approximately 1 × 1 cm area of cortex exposed directly over the tumor is stimulated in a methodical fashion three times, taking care not to retest the same area in succession. An area of positive stimulation is regarded as exhibiting a response (either movement or speech arrest) to confirm eloquence. Low settings are generally used to minimize risk of inducing seizures. In the event of a seizure, which was usually detected at an early stage by the therapist, the operative field was copiously irrigated with ice-cold saline, allowing resection to continue.

Speech and language assessment intraoperatively
The SLT’s aim is to elicit continuous language function using as many language elements as possible (e.g., monologue, automatic speech, language sequencing tasks, explanation of idioms, and word association; see Table I), while avoiding gaps and hesitation that could be mistaken as errors. As the neurosurgeon stimulates and/or resects, the SLT alerts him to ‘new’ speech errors, highlighting his proximity to the eloquent speech area to be avoided. This process continues until the neurosurgeon has completed resection, incurred a deficit, or until patient discomfort becomes problematic.

Intraoperative neuro-physiotherapy assessment
Intraoperatively, there is continual assessment of upper and lower limb movements of all joints, sensory testing, and assessment of functional performance by the NP. In some cases, combined SLT/NP intraoperative monitoring is used in particular for patients with preoperative speech and sensorimotor symptoms, and tumors involving the dominant posterior frontal (pre-motor/supplementary motor) areas.

Postoperative general management
Management of these patients followed standard practice including gradual weaning of dexamethasone in the postoperative period. Typically, patients with high-grade gliomas are weaned to 2 mg of dexamethasone daily (or taken off dexamethasone completely) by the time of oncology review 2–3 weeks postoperatively. Usually, low-grade glioma patients are not commenced on dexamethasone postoperatively unless they have a neurological deficit, and weaning takes place after a week on a reasonable dose (e.g., 4 mg twice daily). An early postoperative MRI (with standard sequences, for example, T1, T1 + contrast, T2, FLAIR, DWI) is usually performed within 72 h to document the extent of tumor removal and identify surgery-induced hemorrhage, edema, or infarction.

The extent of tumor resection (EOR) was graded as follows: gross total resection (GTR) indicated complete resection of the enhancing mass in high-grade gliomas, or high-signal lesion in T2/FLAIR in low-grade gliomas; subtotal resection (STR) indicated anything from 90% resection and above, while anything less than 90% was regarded as partial resection (PR).

Postoperative therapy
The same SLT/NP involved in preoperative and intraoperative assessment also assesses the patient in the postoperative period to avoid any inter-observer variation in functional assessments. Follow-up and review is planned regardless of whether the patient has a deficit or not.

Our team has devised a postoperative patient questionnaire suitable even for patients with a high-level language deficit (Supplementary file to be found online at http://informahealthcare.com/doi/abs/10.3109/02688697.2015.1054354). It captures the patient’s experience including pain, discomfort, positioning, information given pre-/intraand postoperatively, and relates to all neurosurgical, anesthetic, speech and language, and physiotherapy aspects of the patient’s journey.

Results
In-patient stay
Over a 3-year period, 50 consecutive AC procedures were performed on 45 patients: 3 patients underwent repeat debulking for recurrence of a high-grade glioma at 9, 11, and 15 months after initial surgery, while low-grade glioma patients underwent repeat debulking 32 and 33 months after initial surgery (Table II). The patients were aged between 15 and 68 years (mean of 45 years), comprising 28 male and 17 female. Twenty-nine procedures were performed with the SLT, 18 with the NP, and 3 cases (both low-grade tumors involving the dominant premotor area) with combined SLT/NP input. The duration of the awake phase of the operation ranged from 1–2.5 h (median 1.5 h). The median length of in-patient stay was 6 days (range: 4–42 days), with all except 3 patients being discharged home within 2 weeks.

| Table II. Demographics of the study population (n = 50 cases). |
|---------------------|---------------------|
| **Age** | Mean: 45 years, Range: 15–68 years |
| **Gender** | Male: 28, Female: 17 (one underwent second AC) |
| **Tumour location** | Speech area: 29, Sensorimotor: 18, Combined: 3 |
| **Histopathology** | Glioblastoma: 27, WHO Grade III glioma: 8, WHO Grade II glioma: 15 |
| **Postoperative imaging performed** | MRI: 39, CT: 8, None: 3 |
| **New/worsened deficit postoperatively** | Yes: 10 (6 resolved within 6 weeks), No: 40 |
Tumor location and pathology
Thirty-one patients initially presented with seizures, 5 presented with dysphasia, 6 with sensorimotor symptoms, 2 with headaches, and another with depressed conscious level. The most common tumor locations were the left temporal and frontal lobes (18 and 15 cases respectively), most of which underwent speech monitoring. An additional left-handed patient underwent speech monitoring for a right temporal tumor (having presented with speech disturbance). Eight cases were “redo” AC cases, three of which had their original AC elsewhere — one of whom has undergone a subsequent repeat resection “awake” in Belfast (3 in total). The pathological diagnosis was glioblastoma in 27 cases (2 of which were GBM recurrences), 9 were cases of WHO grade III gliomas (4 cases of anaplastic astrocytoma, 3 of anaplastic oligodendroglioma, 2 of anaplastic oligoastrocytoma), and 14 cases that were WHO grade II gliomas (4 cases of astrocytoma, 7 of oligodendroglioma, and 3 of oligoastrocytoma).

Initial phase (wakening and initial stimulation)
One patient had a tonic-clonic seizure while emerging from anesthesia, while a second had multiple seizures in quick succession after initial cortical stimulation resulting in a prolonged postictal recovery time, which precluded further mapping and tumor resection (both cases were anaplastic astrocytoma). A third case had consistent speech arrest following stimulation overlying a small nodular recurrence of a GBM. Selective needle sampling of tumor using image-guidance in these 3 cases was performed to obtain a histopathological diagnosis. All 3 patients’ neurological function returned to baseline within 24 h postoperatively.

Tumor resection
The remaining 47 cases had a good baseline functional status intraoperatively and underwent debulking, with the exception of 1 patient with a large sensorimotor tumor who developed progressive intraoperative contralateral limb weakness due to outward brain herniation. The resultant cortical compression and venous congestion at the bone edge of a small craniotomy likely contributed to the transient hemiparesis which resolved postoperatively—an observation similar to that reported by Khu and Ng.11

Using the electrical stimulation parameters outlined above, consistently positive cortical/subcortical sites were mapped in 13 cases that were subsequently avoided during resection. Although there were no positively mapped sites identified in the remaining 34 cases, tumor resection was halted in areas associated with a significant decline in neurological function, leading to a cessation of resection in 6 cases. These patients experienced new-onset facial weakness (2 cases), proprioceptive loss (2 patients), hand clumsiness, and dysphasia.

Resection of infiltrative zones of sensorimotor tumors extending into the internal capsular territory was also avoided to minimize postoperative neurological deficit (5 cases).

Seven patients had a clinically obvious stimulation-evoked focal seizure, which was quickly arrested with ice-cold saline irrigation, allowing tumor resection to continue following return to baseline neurological function (typically within 5–10 min of seizure).

Postoperative neurological function
Of the 6 patients with a new intraoperative deficit, 5 returned to baseline function within 2 weeks while 1 patient had persistent proprioceptive loss requiring prolonged in-patient rehabilitation.

Four patients developed a new neurological deficit (not noticed intraoperatively in the initial week post-surgery—3 experienced worsening of their preoperative sensorimotor deficit while another developed new-onset expressive dysphasia following debulking of a dominant pre-motor tumor. One of the cases with worsened hemiparesis also developed new-onset expressive dysphasia (Fig. 1a–d). All 4 patients had a persistent albeit improved deficit at 6-week review. In all cases, a rehabilitation program tailored to the needs of each patient was executed by the responsible therapist in the postoperative period.

Early postoperative imaging
Of the 50 cases, 39 underwent early postoperative MR imaging while 8 underwent CT imaging and 3 did not undergo any early postoperative imaging, as only a biopsy was performed (2 patients), and 1 patient was discharged before postoperative imaging could be performed. GTR was achieved in 11 cases (all HGGs), and STR in 13 cases.
(8 HGG, 5 LGG), while PR was achieved in 15 cases (10 HGG, 5 LGG).

Five cases had evidence of diffusion restriction near the resection cavity, in keeping with ischemia, one of which had clinically significant neurological deterioration likely due to involvement of deep white-matter fiber tracts (Fig. 1a–d); the remaining cases were asymptomatic. Although there was a mild degree of edema in the tumor resection margins in all cases, this did not cause clinical concern and invariably settled with a weaning course of steroids in the postoperative period.

Discussion

AC with direct electrical stimulation mapping is becoming the “gold standard” procedure for resection of gliomas in eloquent locations. Patients are much more likely to have better functional outcomes than similar patients who undergo general anesthetic for tumor resection. With the increasing evidence that GTR of gliomas results in survival benefit, surgeons are pushing the boundaries of resection to the limit of functional tolerance. The input of SLT/NP during “awake” resection may help guide the surgeon when to stop if they feel that further deficit may permanently harm the patient. Although several larger studies have already highlighted the efficacy and safety of AC in glioma patients, our preliminary experience with SLT/NP input highlights the key role the therapist plays in optimizing neurological function and may serve as a useful guide to other neurosurgical centers considering setting up an AC service.

Comparative analysis with other series

Although we have not performed a direct comparative analysis with similar “matched” cases from our “pre-awake” era, anecdotally, the frequency and severity of postoperative deficits are much less following “awake” debulking compared to previous practices. Our own anecdotal experience is comparable with a single institution study by Duffau et al. who found that 17% of LGG patients developed a severe permanent neurological postoperative deficit with no mapping, compared with 6.5% in a cohort of patients who were mapped functionally. Future studies will be important to formally assess the neurological outcomes and potential survival benefits compared with a case-matched control series from the “pre-awake” era in our institution. It will also be important to assess if ongoing refinements in our technique result in outcomes significantly different from the 10% morbidity of this initial experience.

Length of stay

In comparison with some other AC series, our length of stay (median of 6 days) was relatively long. This perhaps reflects a degree of caution on the part of the authors in setting up a new service, to avoid discharging patients who may have developed a delayed “missed” neurological deficit. Most patients were happy to avail of in-patient therapy while waiting for their pathology report typically given on the day of discharge (5 days postoperatively). With greater experience and recognition of patients who may need additional rehabilitation, the authors hope to reduce the length of stay for uncomplicated patients in future. Indeed, patients with a preoperative deficit tended to develop worsening symptoms in the postoperative period, suggesting that these patients will likely need to remain an in-patient longer than those without a preoperative deficit.

Learning curve

At the outset of our AC program, perhaps eager to avoid any added morbidity from the procedure such as that reported by Gupta et al., tumor debulking was halted at the first hint of a neurological deficit (some of which may have been patient discomfort-related). This is perhaps reflected in the relatively low GTR rates for both high- and low-grade glioma cases in our series compared to other more experienced institutions. It is recognized that patients can be pushed into a mild or moderate neurological deficit to maximize EOR in the knowledge that they will likely rapidly recover function thereafter. With increasing experience, the ability of the therapist to discern a reversible mild intraoperative deficit amenable to rehabilitation from an irreversible deficit, has facilitated more radical resection in latter cases. The enhanced ability of the therapist to detect stimulation-induced responses has also resulted in a reduction in seizure current leading to reduction in intraoperative seizures (one in the last 15 cases). A greater awareness of more seizure-prone areas, for example, supplementary motor areas, will also influence current settings used in future cases.

Our use of a patient questionnaire (supplementary file) has also been helpful in refining our technique. The initial slight problems of dry mouth, urinary issues, and positional discomfort have been reduced. Patient satisfaction ratings of the multi-disciplinary team approach were very high (90%). Time spent during preoperative assessment was greatly appreciated and promoted a sense of confidence in the team.

The role of the therapist in prevention of new deficits

Although many AC centers use a neuropsychologist to perform preoperative cognitive assessments and to assess language intraoperatively, our department has limited access to neuropsychology services. Instead, we have “on-site” access to SLT, which provides the perioperative services outlined above. However, the authors recognize that this specialist role is undertaken in some centers by neuropsychology, which may result in variation between centers with regard to assessments and pre- and postoperative care.

Although language can be tested in many ways during AC, for example, naming and reading tasks, we have found that continuous speech production allows for the full spectrum of language function to be tested during ongoing resection (as opposed to “on-off” resection synchronous with testing) and may facilitate detection of language errors more readily than a single language function task such as object naming.
Indeed, in comparing our SLT experience with that of NP continuous clinical assessment is much easier with speech cases than sensorimotor cases where multi-modality testing (e.g., light touch, pin-prick, proprioception, and motor) is relatively more challenging to perform and monitor. In such cases, an “on-off” resection approach is particularly required at the tumor margin to forewarn the NP of the higher risk of incurred deficit. In preparation for such cases, we now routinely have a preoperative case conference to review the imaging, in particular overlap of tumor and relevant fiber tracts, to help focus the intraoperative therapy assessments.

In many cases, the baseline preoperative assessment by the SLT/NP helped detect deficits that would have been easily missed by the untrained observer. These subtle deficits can then be specifically monitored intraoperatively to ensure that no further worsening of neurological function occurs. It is also in the interest of the relevant therapist to ensure that no new deficits are encountered, as this minimizes the burden of rehabilitation postoperatively and helps minimize delays in subsequent radio/chemotherapy for patients with high-grade tumors. Functional preservation is also an important contributing factor to health-related quality-of-life indices—a key component of any treatment algorithm for glioma patients, given the limited life expectancy of many of these patients.18

The role of the therapist in rehabilitation

The importance of rehabilitation of brain tumor patients is gaining increasing recognition following the publication of the latest version of Manual for Cancer services: Brain and CNS measures, May 2014.19 Having the SLT and NP as key members of the AC team significantly lends itself to meeting these criteria and standards. Patients will in essence have a “key rehabilitation worker” who oversees their rehabilitation needs from the outset to discharge, with a transition to community therapists to ensure that maximal neurological recovery is achieved. Although patients may improve due to brain “plasticity,” active input from the SLT/NP is also likely to yield significant neurological recovery. Indeed, the benefits of early and intense rehabilitation in the setting of brain tumor patient management is increasingly being recognized20 and is also shown to be more cost-effective.21

The role of postoperative imaging in predicting length of follow-up required

Our findings on early postoperative imaging are interesting, although future validation of these findings with a larger patient cohort will be required. The predictive value of the extent of ischemia on diffusion-weighted imaging and the need for a more prolonged rehabilitation program will also need to be studied in greater detail. However, based on our preliminary experience, the presence of significant vasogenic edema and/or peritumoral ischemia in eloquent areas may predict the need for more intense and prolonged postoperative rehabilitation involving community services.

Conclusion

The multidisciplinary approach of our AC service incorporating the expertise of SLT/NP helps to preserve neurological function and is key to delivery of a tailored program of postoperative rehabilitation to ensure optimal patient outcomes. Such a multidisciplinary approach may serve as a helpful guide for other neurosurgical centers considering setting up their own AC service.

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Supplementary material available online

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