Original Article

Awake Craniotomy Under Local Anaesthesia and Monitored Conscious Sedation for Resection of Brain Tumours in Eloquent Cortex – Outcomes in 20 Patients

David Low,[1] *MBBCh, MRCS, MMed*, Ivan Ng,[1] *MBBS, FRCS (Surg Neurol)*, Wai-Hoe Ng,[1] *MBBS, FRACS (Neurosurg)*

Abstract

Introduction: Resection or even biopsy of an intra-axial mass lesion in close relationship to eloquent cortex carries a major risk of neurological deficit. We review the safety and effectiveness of craniotomy under local anaesthesia and monitored conscious sedation for resection of mass lesions involving eloquent cortex. Materials and Methods: We performed a 3-year retrospective review of patients who underwent awake craniotomy under local anaesthesia at the National Neuroscience Institute, Singapore. All patients had tumours in close proximity to eloquent cortex, including speech areas in the dominant hemisphere as well as primary sensory and motor cortex in either hemisphere. Brain mapping was performed by direct cortical stimulation using the Ojemann stimulator to identify a safe corridor for surgical approach to the tumour. Intraoperative physiological monitoring was carried out by assesment of speech, motor and sensory functions during the process of surgical resection. All resections were evaluated and verified by postoperative imaging and reviewed by an independent assessor. Postoperative complications and neurological deficits, as well as extent of tumour resection, were evaluated. Results: A total of 20 patients underwent stereotactic resection over a period of 3 years from July 2003 to August 2006. There were 7 male patients and 13 female patients, with a mean age of 39.8 years. The average length of stay was 5.5 days. There were no major anaesthetic complications and no perioperative deaths. Postoperative neurological deficits were seen in 6 patients (30%) and this was permanent in only 1 patient (5%). The degree of cytoreduction achieved was greater than 90% in 58% of patients and a further 21% had greater than 80% cytoreduction. Conclusion: Tumour surgery with conscious sedation in combination with frameless computer stereotactic guidance is a safe technique that allows maximal resection of lesions in close relationship to eloquent cortex and has a low risk of neurological deficit.

Ann Acad Med Singapore 2007;36:326-31

Key words: Awake craniotomy, Brain tumour, Cortical mapping, Cytoreduction, Tumour resection

Introduction

The aims of surgical management in the resection of brain tumours are to obtain an accurate histological diagnosis, achieve maximal resection with minimal morbidity, relieve intracranial hypertension and improve neurological symptoms. Mass lesions in close proximity to eloquent cortex represent a significant surgical challenge and the surgeon has to balance the theoretical benefits of an aggressive resection with the anticipated postoperative neurologic morbidity. Preoperative MRI imaging with contrast and functional MRIs, together with intraoperative computerised stereotactic guidance, are commonly used to aid in maximal resection of tumours without encroaching into eloquent brain tissue. However, in tumours within or adjacent to eloquent brain, anatomical localisation alone is insufficient. Precise localisation of areas responsible for critical neurological functions are necessary to avoid postoperative neurological deficits.

The use of awake craniotomy has become frequently used in the management of tumours located in eloquent brain and has been shown to be a safe technique with a low risk of new neurological deficit.[1,2] The use of awake craniotomy can result in considerable reduction in resource utilisation without compromising patient care by minimising intensive care time and hospital stay.[3]

The aim of our study was to perform a retrospective review of awake craniotomy cases performed at our institution since 2003 and analyse the outcomes achieved. We wanted to assess the reliability of technique of brain mapping and resection in preventing postoperative deficit.

[1] Department of Neurosurgery, National Neuroscience Institute, Tan Tock Seng Hospital, Singapore
Address for Correspondance: Dr Ng Wai Hoe, Department of Neurosurgery, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.
Email: wai_hoe_ng@nni.com.sg

Secondly, we aimed to determine how often substantial or complete resection could be achieved using our techniques. Lastly, we wanted to see if there were any specific anaesthetic or surgical complications associated with this procedure.

Materials and Methods

Patient Population

The operative data records of the National Neuroscience Institute over the past 3 years were reviewed to identify craniotomies for tumour resection in eloquent brain performed with monitored conscious sedation. These locations included speech areas in the dominant hemisphere as well as primary sensory and motor cortex in either hemisphere. The patients selected for this surgery had to be cooperative and physically able to tolerate awake surgery. The hospital and clinic records of the selected patients were thoroughly reviewed using a predetermined method. The details of the preoperative condition, indications for surgery, surgical procedure, extent of intraoperative brain mapping, anaesthetic drugs used, and record of the intra- and postoperative courses were recorded. The records were carefully scrutinised to assess each patient's postoperative neurological state and complications (if any).

Anaesthetic and Surgical Technique

In the operating room, the anaesthetist established intravenous access, placed an oxygen mask and monitored the patient with pulse oximetry and end-expiratory CO_2 concentration via nasal prongs. Blood pressure was monitored via radial arterial lines in most cases and cardiac monitoring was done via 3-lead electrocardiography. Intravenous sedation was commenced prior to insertion of a urinary catheter using lignocaine gel. Patients were supine in all of our cases. Efforts were made to ensure each patient was secured in a comfortable position, with all pressure points well padded, and pneumatic calf pumps were used for deep venous thrombosis prophylaxis. Local anaesthesia which comprised a combination of 0.5% bupivicaine and epinephrine (1:200,000) was infiltrated around skin margins where pin sites were expected to be placed and the Mayfield head-frame was applied. The frameless stealth system was registered and the tumour location was mapped to facilitate the planning of the skin incision. After routine shaving, skin preparation and draping, the area of incision and nerves supplying the area were anaesthetised using the above preparation. Sterile draping was arranged to give the anaesthetist constant access to the patient's face, arm and leg. A microphone was placed beside the patient so that the surgeon could converse with the patient while operating. Intravenous mannitol, dexamethasone, antibiotics and anti-convulsants were administered prior to skin incision. Patients were kept deeply sedated during the incision and craniotomy. The dura was anaesthetised with topical and intradural local anaesthetic in some cases. After the dura was opened, intravenous sedation was tailed down and the location of the lesion was confirmed via the stereotactic system with the imaging probe. Direct cortical stimulation was performed using the Ojemann stimulator (Radionics, Burlington, MA).

Brain Mapping and Physiological Monitoring

The region of exposed cortex was systematically stimulated with careful attention to the region of the lesion. Stimulation began with a low current of 0.2 to 3 mA of a 60-Hz biphasic square wave. If there was no effect such as movement, sensory changes or speech arrest, the stimulation voltage was increased. Language testing involved observation of the patient for interference with counting or object naming during the stimulation. In mapping the somatosensory and motor regions, we requested that the patient report any sensations or movements that occurred during stimulation. The anaesthetist acted as an observer and also performed neurological examinations during the stimulation. A corticortomy was made, avoiding all sites identified as eloquent cortex after cortical mapping. Resection was started circumferentially around cortical margins and progressed gradually into underlying white matter. During resection, intermittent physiological monitoring of speech, sensory and motor function was carried out and resection was stopped if the patient developed any signs of worsening neurological deficit from baseline. Repetitive stereotactic localisation checks were also used to give the surgeon assessment of accuracy in location where resection was being carried out. In some cases, subcortical stimulation was also used to identify eloquent white matter during resection. After tumour resection was completed, the patient was sedated more deeply again during closure. Postoperatively, the patient was generally awake and able to be examined prior to leaving the operating room. The majority of patients were usually kept overnight at the high-dependency unit for monitoring while some patients were sent directly to the general ward postoperatively.

Quantitative Assessment of Cytoreduction

Most postoperative scans were performed within 48 hours to eliminate the potential problem of postoperative inflammatory changes as well as early tumour progression, hence facilitating the assessment of extent of resection. Evaluation on extent of resection was carried out by an independent assessor. Resection was deemed to be macroscopically complete if there was no enhancement on the postoperative scans. In the case of non-enhancing tumours, criteria was based on evaluating the degree of resolution of T2 hyperintensity. The assessment was done via volumetric analysis of the MRI scans using GE

Healthcare Advantage Window Version 4.2 (Milwaukee) operating system. The software used was the Volume View Plus Voxtool 5.5.4 paintbrush method.

Results

Patient Characteristics

Twenty consecutive patients with brain lesions located in close proximity to eloquent cortex underwent stereotactic resection over a period of 3 years from July 2003 to August 2006. In 3 patients, surgery was performed for recurrent tumours. Two awake craniotomies were performed for 1 patient. During the initial surgery for this patient, cortical stimulation resulted in the loss of motor activity and only a biopsy was done, yielding inconclusive histological results. Two weeks later, repeat surgery was performed, and confirmed the diagnosis of metastatic adenocarcinoma.

Most of the patients were young, with patient ages ranging from 10 to 73 years. The mean age was 39.8 years. There were 7 male patients and 13 female patients. The patients presented most frequently with seizures followed by symptoms of headache and hemiparesis. The presenting symptoms and frequency of occurrence are as shown in Table 1. The majority of the patients did not suffer from any significant comorbid conditions. Two patients had a history of hypertension with left ventricular hypertrophy seen on electrocardiogram, 1 patient was a smoker with chronic obstructive lung disease and 1 patient was seropositive for HIV. The preoperative Karnofsky performance scores for 19 of the patients were 80 to 90 and 1 patient had a score of 60 due to neurological impairment resulting from a previous road traffic accident.

Table 1. Symptoms at Presentation in 20 Patients

Symptom	% of patients
Seizure	55
Headache	35
Cognitive deficit	10
Speech deficit	15
Motor deficit	35

Table 2. Histological Classification of Mass Lesions in 20 Patients

Histological classification	No. of patients
Glioblastoma multiforme (WHO grade 4)	4
Anaplastic astrocytoma (WHO grade 3)	1
Oligoastrocytoma (WHO grade 3)	1
Astrocytoma (WHO grade 2)	2
Pleomorphic xanthoastrocytoma (WHO grade 2)	2
Oligodendroglioma (WHO grade 2)	3
Anaplastic ependymoma (WHO grade 3)	1
Dysembryplastic neuroepithelial tumour	1
Tumour metastasis	4
Cerebral toxoplasmosis	1

Tumour Characteristics

There were a total of 12 left hemispheric tumours and 8 right hemispheric tumours. The distribution of tumours by lobe is shown in Table 2. The various histological diagnoses are reflected in Table 3. The diagnosis of cerebral toxoplasmosis was made in the patient who was seropositive for HIV.

Anaesthesia and Surgery

The choice of anaesthetic agents used comprised a combination of midazolam, propofol, fentanyl or remifentanyl. A combination of 2 or 3 agents was usually used. The usual combination used was that of propofol together with either fentanyl or remifentanyl. Intraoperatively, there were no major anaesthetic complications. Minor anaesthetic complications occurred in 6 cases, as shown in Table 4. These complications were transient and managed with appropriate medications. During resection, intraoperative neurological deficits developed in 2 patients. These 2 patients had tumours located adjacent to the primary motor cortex and developed motor weakness while resection was being performed, hence further surgical resection was discontinued. The duration of surgery ranged from 1 hour 25 minutes to 4 hours 35 minutes. The average operating time for the 21 operations performed was 2 hours and 45 minutes.

Postoperative Care

Most patients were observed in the high-dependency unit

Table 3. Location of Lesions in 20 Patients

Location	Left	Right	Total
Frontal	3	3	6
Temporal	5	-	5
Parietal	2	2	4
Fronto-parietal	1	3	4
Parieto-temporal	1	-	1

Table 4. Minor Anaesthetic Complications

Complication	No. of patients
Hypertension	3
Confusion	1
Agitation	1
Pain	2
Transient desaturation	1

overnight before being transferred to the general ward the following day. In 2 of the cases, they were directly sent to the general ward at the surgeons' discretion. The average length of stay after surgery was 5.5 days, with a range of 3 to 11 days in 16 of the cases performed. In the remaining 5 cases, there was prolonged length of stay due to discharge problems relating to home caregiver issues or because there was a need to wait for the availability of nursing home placement.

Incidence of Morbidity and Mortality

In this group of 20 patients, there were no perioperative deaths. Nine postoperative complications occurred in 8 patients, as reflected in Table 5. Postoperative neurological deficits were seen in 6 patients (30%) and this was permanent in 1 patient (5%). Four patients developed transient hemiparesis postoperatively, all of which resolved within 2 weeks. One of these patients had pre-existing weakness and developed further weakness intraoperatively; the weakness returned to the preoperative level after 48 hours. The patient with permanent deficit had no pre-existing weakness but developed weakness in the distal upper limb during resection. Postoperatively, she had only minimal movement of her hand and at 1-year follow-up, she had mild residual weakness of finger flexion and extension (grade 4). One patient who underwent cortical stimulation for tumour resection adjacent to the speech area developed dysphasia postoperatively, but this was self-limiting and resolved after 24 hours. Nosocomial infection occurred in 1 patient and was treated with intravenous antibiotics without further complications. One patient developed postoperative haematoma in the tumour cavity, which was identified on postoperative MRI scan. It was managed conservatively and was not associated with any neurological deterioration or new deficits.

Degree of Cytoreduction

The percentage reduction in tumour volume was assessed in 19 of the 20 patients. In 1 patient, assessment could not be carried out as computerised radiological images were unavailable for volume calculation. Table 6 shows the location, histological diagnosis and degree of cytoreduction achieved. Eleven patients (58%) had greater than 90% resection of their tumour volume and 4 patients had greater than 80% reduction.

Table 5. Complications and Adverse Effects in 20 Patients

Complication	No. of patients
Hemiparesis	
Transient	4
Permanent	1
Temporary dysphasia	1
Nosocomial infection	1
Postoperative haematoma (not requiring surgery)	1
Postoperative seizures	2

Discussion

Benefits of Aggressive Tumour Resection

The published neurosurgical literature remains unclear on the correlation between the extent of surgical resection and survival.[4] While no randomised prospective trials have been performed, a large amount of retrospective data suggest that the median survival time and time to recurrence are improved in patients who undergo the aggressive resection of tumours.[5-9] Lacroix et al,[10] in their retrospective analysis of 416 patients, found that resection of 89% or more of tumour volume was necessary to improve survival after surgery. In addition, there was a significant survival advantage in patients with resections of 98% or more of tumour volume. These patients had a median survival of 13 months, as compared to 8.8 months for resections of less than 98%.

In addition to improved survival, increased extent of resection also offers a diagnostic advantage. Malignant gliomas are heterogenous in nature and stereotactic biopsy alone or minimal resection carries a risk of sampling error. Sawaya[11] reported a consecutive series of 64 patients where craniotomy and maximal resection was performed for patients who had previously undergone stereotactic biopsies at other institutions. The diagnosis was subsequently modified in a meaningful way in more than 50% of the patients. Jackson et al[12] demonstrated in their series of 81 consecutive patients that diagnosis based on biopsy or resection differed in 49% of the cases.

Aggressive surgical resections can, however, leave a patient with serious postoperative neurological deficits. Therefore, in order to preserve neurological function, it has been felt that patients with tumours in eloquent areas should only undergo biopsy procedures or partial resection. In patients where aggressive surgical resection is advocated, the use of preoperative functional MRI as well as intraoperative computerised stereotaxis has been used to improve the accuracy of surgical resection and minimise damage to eloquent brain tissue.

Use of Awake Craniotomy

The rationale for awake craniotomy in tumour resection is that it allows for brain mapping, which facilitates maximum resection and minimises the risk of postoperative neurological deficits. Precise cortical localisation of areas involved in critical neurological functions can vary significantly among individuals. The identification of the

Table 6. Degree of Cytoreduction in 19 Patients

Location	Pathology	T1/T2	Gd Vol (cm^3)	% reduction
Lt Temporal	GBM	T1	12.55	81.11
Lt Temporal	GBM	T1	30.43	93.30
Lt Temporal	GBM	T1	40.83	80.00
Lt Temporal	GBM	T1	83.55	95.66
Lt Frontal	Astrocytoma (Gd3)	T1	9.88	70.85
Rt Fronto-parietal	Astrocytoma (Gd2)	T1	9.85	71.47
Rt Fronto-parietal	Astrocytoma (Gd2)	T2	11.81	85.10
Lt Parieto-temporal	Oligoastrocytoma (Gd3)	T1	58.51	91.27
Rt Frontal	Oligodendroglioma	T1	1.60	100
Rt Parietal	Olidodendroglioma	T1	39.88	90.31
Lt Temporal	Oligodendroglioma	T2	70.11	81.71
Lt Frontal	Ependymoma (Gd3)	T1	41.16	95.16
Rt Parietal	PXA	T2	17.92	93.25
Lt Fronto-parietal	PXA	T1	67.92	63.27
Lt Frontal	Metastatic carcinoma	T1	2.35	97.15
Lt Parietal	Metastatic adenocarcinoma	T1	6.50	95.85
Rt Fronto-parietal	Metastatic adenocarcinoma	T1	4.10	74.15
Rt Frontal	Metastatic adenocarcinoma	T1	25.63	99.20
Rt Frontal	Cerebral toxoplasmosis	T1	10.98	90.62

GBM: glioblastoma multiforme; Gd: grade; Lt: left; PXA: pleomorphic xanthoastrocytoma; Rt: right; Vol: volume

central sulcus and motor/sensory cortex can be difficult intraoperatively and this is especially so when there is distortion of the normal anatomy secondary to tumour infiltration and vasogenic oedema. In addition, the primary motor area can extend more than 20 mm anterior to the central sulcus in the presence of an intra-axial lesion.[13] Localisation does not always conform to classic anatomic location and resection within 1 cm of the primary centres carry a risk of postoperative morbidity.[14] In language localisation, primary language centres have been demonstrated to occur across a wide area over the fronto-parieto-temporal cortex and is organised in a mosaic pattern about 1 to 2 cm^2, with 67% of patients having 2 or more such mosaics.[15] With the use of brain mapping, together with intermittent intraoperative physiological monitoring of speech, sensation and motor function by the anaesthetist, we were able to confidently identify a safe corridor for tumour resection and hence were able to achieve more than 80% cytoreduction in 79% of the cases performed.

The anaesthetic regimen for awake craniotomy was associated with minimal intraoperative complications and good patient tolerance. It allowed maximal comfort for patients during initial positioning and craniotomy and did not interfere with the ability for interaction with the patient during brain mapping. Minor anaesthetic complications that occurred intraoperatively could be managed expeditiously by our anaesthetic colleagues without any delay in surgery.

There was no increase in the use of resources as compared to conventional craniotomy for tumour resection and patients did not require intensive postoperative care management. This translated to both cost savings for the patient as well as a decrease in resource utilisation for the department. Our mean duration of hospital stay was 5.5 days, as opposed to other series, whose mean reported lengths of stay ranged from 1 to 3.7 days. The longer length of stay can be accounted for by the fact that patients were usually kept in hospital for their repeat MRI scan 48 hours postoperatively and they often underwent a short period of physiotherapy or occupational therapy before discharge. The majority of patients were surgically fit for discharge from hospital within 2 days postoperatively but had extended stays due to problems relating to home caregiver issues or having to wait for the availability of nursing home placement.

Surgical Outcomes

Postoperatively, patients did not develop any major surgical or anaesthetic complications. Neurologically, all

20 patients had a Glasgow Coma Scale of 15 at presentation and their scores remained similar postoperatively on discharge from hospital. Preoperatively, 19 patients had Karnofsky scores of 80 to 90. On evaluation of their postoperative Karnofsky scores, 14 patients (70%) had no change in their scores on discharge from hospital, with 90% of the patients being discharged with Karnofsky scores of 80 and above. One patient had a preoperative score of 60 due to a prior road traffic accident and his score remained unchanged. One patient suffered permanent hemiparesis and had a drop in score from 80 to 70. Postoperative neurological deficits occurred in 6 patients but resolved completely in 5 of them within 2 weeks. Two of the patients with postoperative neurological deficits developed hemiparesis intraoperatively and this was a strong predictor of postoperative neurological deficit.

Transient neurological deficits have been well described in other series. This is thought to be due to the removal of the supplementary motor cortex, arterio-venous damage during resection or damage to white matter tracts beneath eloquent cortex. The latter could be minimised through more judicious use of subcortical mapping during resection. Permanent neurological deficit occurred in 1 patient (5%), which was comparable to the rates of 4% and 4.5%, as reported by 2 larger series.[2,3]

Conclusion

Tumour surgery under conscious sedation, in combination with frameless computer-guided stereotaxis and cortical stimulation with repetitive neurologic and language assessments, is a safe and reliable technique that allows maximal resection of lesions in close relationship to eloquent cortex. This procedure could be carried out without any additional usage of hospital resources and overall patient tolerance was good, with a low risk of postoperative neurological deficits or surgical complications. Further incorporation of intraoperative imaging with the current tools could help to achieve better results in tumour debulking.

REFERENCES

1. Meyer FB, Bates LM, Goerss SJ, Friedman JA, Windschitl WL, Duffy JR, et al. Awake craniotomy for aggressive resection of primary gliomas located in eloquent brain. Mayo Clin Proc 2001;76:677-87.
2. Danks RA, Aglio LS, Gugino LD, Black PM. Craniotomy under local anaesthesia and monitored conscious sedation for the resection of tumors involving eloquent cortex. J Neurooncol 2000;49:131-9.
3. Taylor MD, Bernstein M. Awake craniotomy with brian 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.
4. Hess KR. Extent of resection as a prognostic variable in the treatment of gliomas. J Neurooncol 1999;42:227-31.
5. Vecht CJ, Avezaat CJ, van Putten WL, Eijkenboom WM, Stefanko SZ. The influence of the extent of surgery on the neurological function and survival in malignant glioma. A retrospective analysis in 243 patients. J Neurol Neurosurg Psychiatry 1990;53:466-71.
6. Simpson JR, Horton J, Scott C, Cuwan WJ, Rubin P, Fischbach J, et al. Influence of location and extent of surgical resection on survival of patients with glioblastoma multiforme: results of three consecutive Radiation Therapy Oncology Group (RTOG) clinical trials. Int J Radiat Oncol Biol Phys 1993;26:239-44.
7. Shaw EG, Scheithauer BW, O'Fallon JR, Davis DH. Mixed oligo-astrocytomas: a survival and prognostic factor analysis. Neurosurgery 1994;34:577-82.
8. Scerrati M, Roselli R, Iacoangeli M, Pompucci A, Rossi GF. Prognostic factors in low grade (WHO grade II) gliomas of the cerebral hemispheres: the role of surgery. J Neurol Neurosurg Psychiatry 1996;61:291-6.
9. Jeremic B, Grujicic D, Antunovic V, Djuric L, Stojanovic M, Shibamoto Y. Influence of extent of surgery and tumor location on treatment outcome of patients with glioblastoma multiforme treated with combined modality approach. J Neurooncol 1994;21:177-85.
10. Lacroix M, Abi-Said D, Fourney DR, Gokaslan ZL, Shi W, DeMonte F, et al. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection and survival. J Neurosurg 2001;95:190-8.
11. Sawaya R. Extent of resection in malignant gliomas: a critical summary. J Neurooncol 1999;42:303-5.
12. Jackson RJ, Fuller GN, Abi-Said D, Lang FF, Gokaslan ZL, Shi WM, et al. Limitations of stereotactic biopsy in the initial management of gliomas. Neurooncol 2001;3:193-200.
13. Uematsu S, Lesser R, Fisher RS, Gordon B, Hara K, Krauss GL, et al. Motor and sensory cortex in humans: topography studied with chronic subdural stimulation. Neurosurgery 1992;31:59-72.
14. Haglund MM, Berger MS, Shamseldin M, Lettich E, Ojemann GA. Cortical localization of temporal lobe language sites in patients with gliomas. Neurosurgery 1994;34:567-76.
15. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. J Neurosurgery 1989;71:316-26.