12 Surgical Management of Glioblastoma

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Abstract: Malignant gliomas are characterized by their propensity to invade surrounding brain parenchyma. The median survival of patients is less than 2 years with maximal surgical resection, chemotherapy, and radiotherapy. Although there have been controversial arguments about the role of surgical resection, there is increasing evidence that a safe and radical removal of malignant glioma is associated with a better survival outcome. Surgery is still essential to obtain brain tissue for pathological analysis, and reduce mass effect. Intraoperative magnetic resonance imaging, neuronavigation, ultrasonography, and fluorescence-guided surgery are the most used tools worldwide. 5-Aminolevulinic acid surgery, combined with Stupp protocol, produces a median survival of 15 months. The objectives of perioperative positioning are to enhance optimal exposure, prevent injury related to position, and maintain normal body alignment without excess flexion, extension, or rotation. Advances in surgical techniques have contributed to enhanced recovery after tumor resection, improved postoperative functional status, and decreased length of stay in the hospital. This chapter presents the current literature related to the surgical management of high-grade gliomas.

Key words: Extent of resection; Fluorescence-guided surgery; High-grade glioma

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Introduction

The annual incidence of malignant glioma is about 5.26 cases per 100,000 people (1, 2). Malignant astrocytomas are the most common malignant primary central nervous system tumors in adults (3). Glioblastoma accounts for approximately 60–70% of malignant glioma (1, 3, 4). The number of patients is expected to increase with the aging of population, the peak incidence being within the fifth and sixth decades of life (2, 4). The most common symptoms of glioblastoma include headache, focal neurologic deficits, and other nonspecific changes such as altered mental state or gait alteration (5). The classification of brain tumors has been based largely on concepts of histogenesis that label tumors according to their microscopic similarities with putative cells of origin, their presumed differentiation level, and the degree of tumor as a prognostic factor (6, 7). According to clinical characteristics, glioblastomas can be divided into primary and secondary subtypes. Primary glioblastomas emerge from *de novo* process whereas secondary glioblastomas develop progressively from low-grade astrocytoma, over a period of 5–10 years (8) Recently, the Cancer Genome Atlas Network classified glioblastoma into proneural, neural, classical, and mesenchymal, and established an integrated multidimensional genomic data based on patterns of somatic mutations and DNA copy number (9) (Table 1).

Adult neural stem cells, in the subventricular zone and on the walls of the lateral ventricle (LV), generate young neurons and oligodendrocytes under nonpathologic conditions (10). This unique region, which harbors neural stem cells, appears to be more susceptible to tumorigenesis (10). Tumors bordering the LV and patients with subependymal-spreading tumor may be associated with decreased survival. Chaichana et al. reported that the median survival time of patients with LV tumors is less than those with non-LV tumors (8 months vs. 11 months; $P = 0.02$) (11). Glioblastoma progression is thought to be driven by a subpopulation of cancer stem cells, and *in vitro* studies show that these cells are chemoresistant and radioresistant (12). However, Nestler et al. were not able to support the theory of malignant glioma developing in the periventricular stem cell region (13). Most tumors (89%) were in contact with brain cortical regions,

TABLE 1 Comparative Table of the Molecular Classification of Glioblastoma

Phillips et al. (14)	Proneural		Proliferative	Mesenchyme
Verhaak et al. (9)	Proneural	Neural	Classic	Mesenchyme
Genetic signature	Olig2/DLL#/SOX2	MBP/MAL	EGFR/AKT2	YKL40/CD44
Mutation	TP53 PI3K PDGFRA		crom7 (gain) crom10 (lost) PDGRFA	NFkB NF1
Clinical characteristic	Little response to chemotherapy		Favorable prognostic to TMZ and RT	Favorable prognostic to TMZ and RT

whereas only half of glioblastomas (52%) involved the ventricular wall (13). Older age, poor performance status, motor or language deficit, and periventricular tumor location independently predict poor survival in patients with glioblastoma (15). Infiltration and invasion of malignant astrocytoma often involve eloquent areas (4). Historically, surgery has been the initial therapeutic approach for tumor debulking (decompressing mass effect) as well as for obtaining tissues for diagnosis (16, 17). Walter Dandy, in 1928, studied a series of patients undergoing hemispherectomy for invasive high-grade glioma (17, 18). The case series included a patient surviving three and a half years following surgical resection. High doses of corticosteroids (usually dexamethasone 8–16 mg/day) allowed fast decrease of tumor-associated edema and improved clinical symptoms, which were rapidly tapered according to individual needs (4, 19, 20). This chapter provides an overview of surgical management of high-grade gliomas.

PREOPERATIVE EVALUATION

Signed informed consent is mandatory for all surgical candidates in Mexico and in most surgical centers worldwide before going into the operating room (OR). Abstinence from both alcohol and cigarette for 1 month is recommended when appropriate and feasible (21). Preoperative intracranial tumor evaluation should include the assessment of neurological and general status. Current treatments such as steroids and osmotic diuretics must be considered. Assessing status of intracranial pressure (ICP) is the primary aim of evaluating neurological status. Seizures secondary to direct mass effect can also occur in about 60% of cases (22). Antiepileptic drug for seizure prophylaxis is decided by assessment of individual risk factors and careful discussion with patients (22). Preoperative administration of steroids helps to control ICP by reducing peritumoral edema. Patients with symptomatic high-grade tumors (HGTs) or with poor life expectancy can be maintained on dexamethasone 0.5–1 mg daily. The side effects of steroids are common, and their frequency and severity increase with higher dose and therapy duration. Patients must be monitored for endocrine, muscular, skeletal, gastrointestinal, psychiatric, and hematological complications (19). Brain relaxation can be achieved using either hypertonic saline (HS) or mannitol. A recent meta-analysis pointed out that HS could increase the odds of satisfactory intraoperative brain relaxation (OR: 2.25, 95% CI: 1.32–3.81; $P = 0.003$) (22).

INTRAVENOUS ANESTHETICS

Barbiturates have four main actions in the brain: (i) hypnosis, (ii) depression of cerebral metabolic rate (CMR), (iii) reduction in cerebral blood flow (CBF) by increasing cerebral vascular resistance (CVR), and (iv) anticonvulsant activity. All of these actions are able to produce significant hypotension. Propofol has a relative short half-life (1–2 h) but causes hypotension with marked reduction in cerebral perfusion pressure (CPP) (24). Opioids (synthetic opioids: fentanyl, sufentanil, alfentanil, and remifentanil) attenuate ventilator response to hypercarbia and enable the ventilator response to hypoxia, increasing CBF through an increase in $PaCO_2$. Most opioids (except meperidine) are vasotonic, so they can lead to bradycardia; in patients with brain tumors, it is important to distinguish this effect from Cushing's reflex (25). Dexmedetomidine is a highly selective alpha-2 adrenergic receptor agonist.

Clinical effects are both sedative-hypnotic and analgesic by activating alpha-2 adrenergic receptors in the locus coeruleus and the spinal cord. This sedation is useful for awake craniotomy because of the mild increase in $PaCO_2$ (26, 27).

MUSCLE RELAXANTS

Neuromuscular blocking agents (NMBAs) do not have direct effect on CMR, ICP, or CBF. Pancuronium can increase heart rate and mean arterial pressure (MAP). Succinylcholine can increase ICP in brain tumor patients, secondary to the cerebral activation associated with fasciculation and enhanced muscle spindle activity; however, when coadministered with the intravenous agent propofol, ICP can be alleviated (28).

EXTENT OF RESECTION

Cytoreductive surgery for malignant glioma has been performed for decades, from lobectomies to hemispherectomies (17, 29). The purpose of resection is to remove as much tumor as possible to alleviate mass effect and to obtain brain tissue for pathological analysis (class I evidence) (30).Tumor recurrence occurs within a 2-cm margin of the primary site in 90% of the cases (31–33). Evidence to promote brain tumor resections in the current literature are as follows: Ia: 0(0%), Ib: 0(0%), IIa: 1(0.8%), IIb: 7(5.8%), IIc: 0(0%), IIIa: 16 (13.3%), IIIb: 63 (52.5%), IV: 13 (10.8%), and V: 20 (16.8%) (31). Post hoc analysis of 243 patients, randomized for extent of resection in a trial of 5-Aminolevulinic acid (5-ALA) versus white light in newly diagnosed HGG, suggested a positive correlation between complete resection and survival benefit (HR 0.54, 95% CI 0.41 to 0.71) (5). Once the diagnosis for malignant glioma is established, fractionated focal radiotherapy (60 Gys) and chemotherapy are continued. The first-line of choice for chemotherapy is temozolomide (TMZ 75 mg/m^2), administered daily around 1 and 1.5 h prior to radiotherapy during the initial phase. For the maintenance phase, the dosage increases to 150–200 mg/m^2, 5 days a week, every 28 days (29).

Intraoperative Technologies

Emerging imaging technologies facilitate the extent of resection while minimizing the associated morbidity profile (16). Novel assisting technologies require expensive equipment along with prolonged surgical time; more evidence is necessary to justify such adjuncts (34).

FLUORESCENCE-GUIDED SURGERY

5-ALA is a natural amino acid biosynthesized from glycine and succinyl-CoA in the mitochondria. Following systemic administration, ALA in tumor cells is metabolized into protoporphyrin IX (PpIX), a photosensitizing porphyrin (35). The reason for the selective PpIX accumulation in malignant glioma is not fully understood. It is highly specific (98%) in areas of infiltrating tumor, and

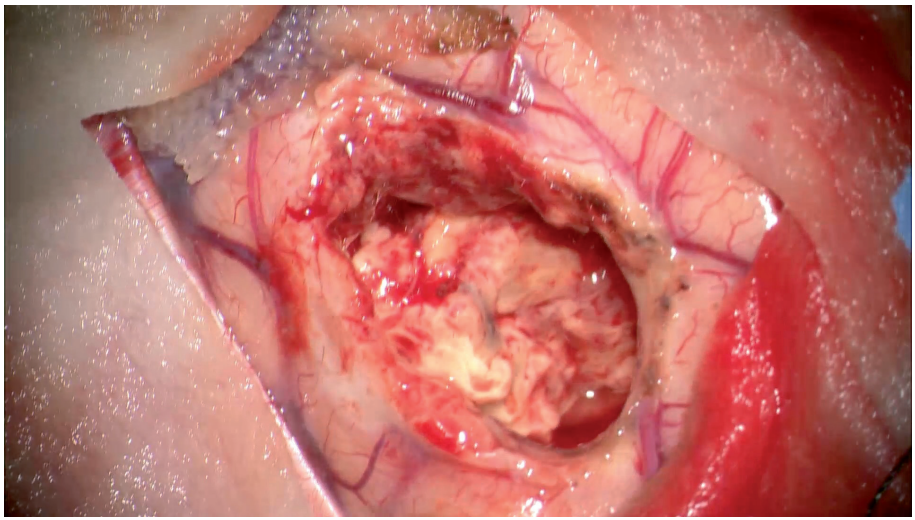
TABLE 2 Commercially Available Fluorophores for Fluorescence-Guided Surgery

	5-ALA	Fluorescein	ICG
Fluorophores	Protoporphyrin IX (PpIX)	Sodium Fluorescein	ICG tricarbocyanine
Localization	Intracellular	Extracellular/ Intravascular (43)	Intravascular
Range of photo-stimulation	409 ± 10 nm	540–690 nm	790–835 nm
Sensitivity & specificity	0.87 (IC 95%, 0.81–0.92) 0.89 (IC 95%, 0.79–0.94) (44)	NA	Correlation >90% Digital Angiographic Subtraction
Dose	20 mg/kg	8–10 mg/kg 20 mg/kg	0.3 mg/kg
Administration route	Orally	Intravenous	Intravenous (45)
Adverse reactions	Photosensibility, nausea, hypertension	Nausea and vomit, anaphylaxis, death (7, 46)	None
Auto fluorescence	Yes	No	No (45)
Contraindications	Porphyria	NR	Iodine allergy, pregnancy, liver disease, uremia, and history of anaphylaxis

PpIX-levels in tumor tissue are highest at 6 h after administration (36) (Table 2). 5-ALA is an orally administered product used for visualization of high-grade glioma tissue during surgery, allowing a safer and more extensive tumor resection. Under blue light excitation (400–410 nm), the tumor tissue appears red, whereas normal tissue (including edema) does not show fluorescence (37) (Figure 1). Another fluorophore is fluorescein sodium; the major disadvantage is that the fluorescence depends on blood–brain barrier integrity, making it less specific. Fluorescein concentration will be high in all perfused tissues and vessels. If tissue is perturbed by surgery, there is unspecific extravasation of fluorescein unrelated to tumor (38). After patient intubation and before skin incision, patients receive 5–10 mg/kg of a 20% solution of sodium fluorescein, administered intravenously using a modified microscope with wavelength range of 560 nm (39) (Figure 2).

INDOCYANINE GREEN

Angiography with indocyanine green (ICG) was first developed for ophthalmology purposes in 1956 to evaluate choroidal microcirculation; other uses are to assess hepatic function, live blood flow, and cardiac output (40). Near-infrared ICG videoangiography was introduced in the neurosurgical field to visualize cerebral vessels for aneurysm clipping, bypasses, and vascular malformations. Superficial avascular areas in HGT have been seen during pre-resection



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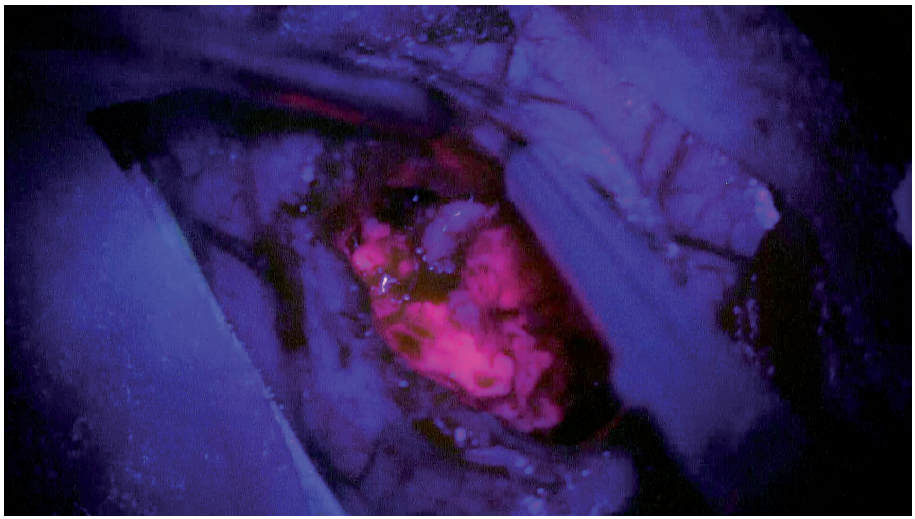


(b)

Figure 1 (a) Brain tumor resection using regular white light and (b) blue excitation light (400–410 nm) using 5-ALA; the tumor tissue appears red, whereas normal tissue shows no fluorescence. (Courtesy of Prof. Walter Stummer.)

ICG videoangiography (41). Neovascular architecture; alterations of the caliber, morphology, and course of vessels; and the hemodynamic patterns can be observed. The dye does not penetrate the membrane and therefore is unable to define the margins of the tumors (42). ICG helps to avoid injury by preserving small caliber vessels during brain tumor surgery (Figure 3).

Figure 2 Brain tumor resection using fluorescein. The whole brain parenchyma and tumor tissues were colored and fixed; the blood–brain barrier had been damaged, making it less specific. (Courtesy of Prof. Walter Stummer.)

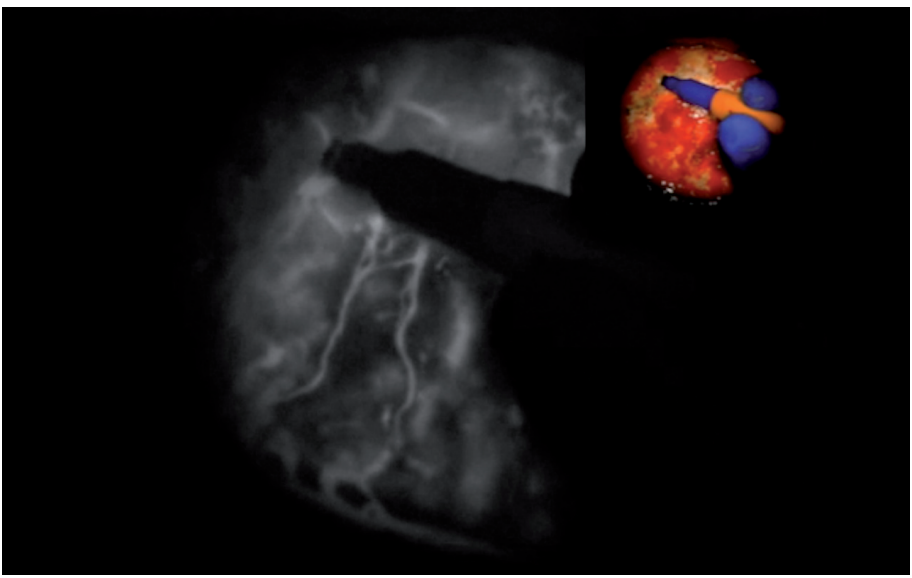


Figure 3 Intraoperative videoangiography in the arterial phase with combined white-light visualization to localize major vasculature and avoid medium and small vessel injury. (Courtesy of Prof. Alfredo Quiñones-Hinojosa.)

NEURONAVIGATION

Neuronavigation systems have been developed for image-guided neurosurgery to aid accurate lesion localization in the brain. Before craniotomy, the patient's head is secured to a head holder with head pins; this fixation might cause skin displacement (skin shift) and reduce accuracy which could be corrected using intraoperative imaging systems (CT and/or magnetic resonance imaging, MRI) (43). The most-widely used tracking systems utilize dual infrared camera that tracks the position of a probe relative to a fixed reference frame. Electromagnetic tracking systems are the major commercially available alternatives to optical tracking systems. Electromagnetic navigation relies on the tracking probe within an electromagnetic field, created by a field generator in a fixed location. Using MRI, the positional accuracy is within 2–3 mm during surgery. Clinical factors that cause shift of the brain or a lesion, such as cerebrospinal fluid loss, cyst decompression, and cerebral edema, may diminish navigational accuracy (44). Neuronavigation is most useful as an adjunct to other brain-mapping techniques such as awake mapping and electrocorticography in the resection of lesions within eloquent motor and language areas (45). Intraoperative MRI has become more widespread and the evidence supporting the use of intraoperative MRI to maximize resection has also grown. A systematic review of existing data on the use of intraoperative MRI for glioma surgery revealed 12 high-quality studies providing level II evidence for the use of intraoperative MRI to improve the extent of resection, quality of life, and survival in glioma patients (46).

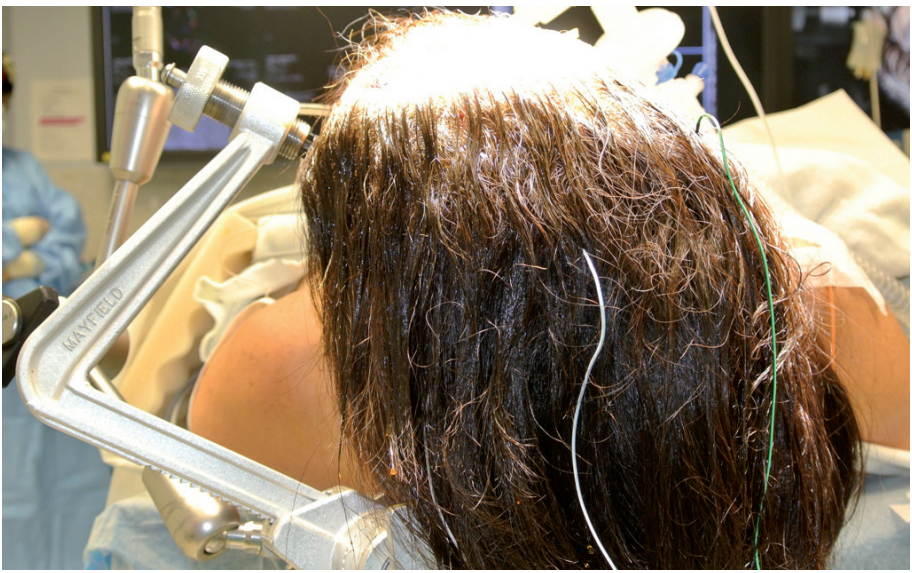
Patient Position

Patient positioning is an essential element before the surgical procedure. Patient's safety is the responsibility of all team members. The objectives of perioperative positioning are the following: optimal surgical exposure; preventing injury; and maintaining normal body alignment without too much flexion, extension, or rotation (47). The operating table is situated in the central area of the OR. Control consoles (monopolar and bipolar coagulation, suction, and drills) are located at the foot of the operating table. An electrophysiological technician is involved when neurophysiological monitoring is indicated. The surgical microscope should be used carefully in accordance with the manufacturer's recommendations. All hardware (optic attachments, eyepieces, mouthpiece, and video-recording device) must be checked before the surgical procedure and adjusted to the surgeon's specifications. When possible, neuronavigation systems can be synchronized to the microscope with the focal point of the surgeon's microscopic view (48). Maintaining normothermia is essential; peripheral vasoconstriction following anesthesia is often common and can result in peripheral hypoperfusion and cell hypoxia (47, 49). Other measures include minimizing skin exposure, using a temperature-regulating blanket or forced-air warming device, and controlling the OR ambient temperature. Neurosurgical procedures are known for extended surgical time, thus increasing the risk of pressure ulcers. Tissue hypoperfusion, ischemia, and necrosis can occur. Soft devices (i.e., gel pad, cotton roll) have to be placed between the patient and any hard surface. The use of graduate compression

stocking and intermittent pneumatic compression is recommended in craniotomy patients to prevent venous thromboembolism (50, 51). Routine use of anticoagulants is not recommended (20, 51). Burn prevention, from electrosurgical tools, can be achieved by ensuring that the patient's skin does not rub against any metal surface (47). *Staphylococcus aureus* is responsible for 32% of the surgical site infections after craniotomy (52). Proper head position allows optimal exposure for surgical access. The use of the three-pin skull clamp can firmly fixate the head in the desired position. Pins should be placed in a band-like distribution on the head. They are often coated with antibiotic ointment before pinning the head. Thin bones, for example, the temporal bone squamous portion, frontal sinus, and mastoid sinus should be avoided. Prior placed shunt, cranial defects, and thick temporalis muscle may cause unstable fixation (53). The practice of shaving before surgery has not proven to reduce surgical site infection. Most surgeons choose to perform a small (<1 cm) strip parallel to the skin incision (21).

SUPRATENTORIAL APPROACHES: SUPINE POSITION

Supine position is often used in neurosurgery because it offers good exposure to (i) anterior and middle fossae of the cranium, (ii) anterior aspect of the neck, and (iii) anterior, medial, and lateral aspects of the upper and lower extremities. Patients' arms should be flexed less than 90° from the long axis to avoid intravenous drop obstruction, injury to the brachial plexus, and compression or occlusion of the subclavian and axially arteries (54) (Figure 4). Preoperative MRI is obtained with skin markers (fiducials when needed), and a surgical trajectory is planned,



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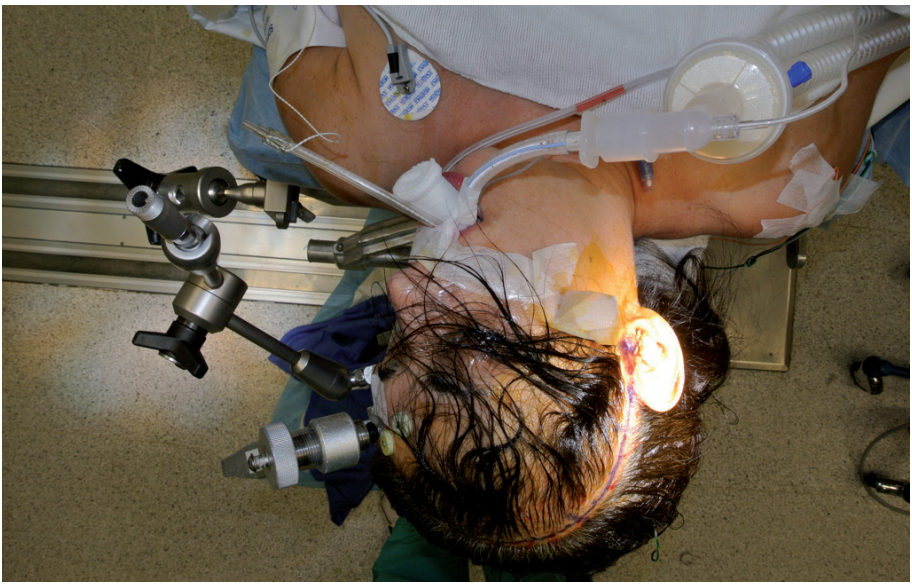

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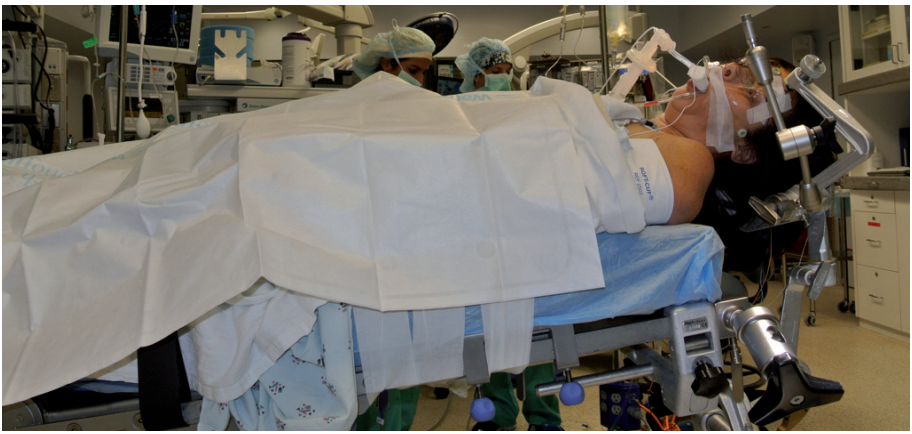


(c)

Figure 4 Head-fixation system is recommended when the neuronavigation system is used. The head clamp must be firmly secured to the skull. Special attention is required when awake craniotomy is performed (a). Head rotation should be limited to the patient's cervical spine condition and to avoid reducing venous return (b). The head must be maintained above the heart level to reduce bleeding (c). (Courtesy of Prof. Alfredo Quiñones-Hinojosa.)

avoiding corticospinal tracts or any other eloquent area. After head fixation, the tumor plane is aligned perpendicular to the floor. The head is kept above the level of the heart. The skin incision is planned based on the location of the lesion. Eyebrow or eyelid incisions can be selected in patients with anterior lesions (55, 56). The craniotomy entry point depends on tumor location; one burr hole is often

sufficient for small craniotomies using a high-speed drill. Dural opening is adjusted to specific needs using either a cruciate or a C-shaped fashion. Trans-sulcal approach can be used for intra-axial lesions in the subcortical space underlying an evident sulcus. For deep tumors in the subcortical space (>1 cm), it may allow an easy access for resection while minimizing disruption of the overlying cortical tissue. The arachnoid overlying the sulcus is incised sharply and is usually opened where the subarachnoid space is the largest. Arteries and veins running within the sulci that supply and provide venous drainage to surrounding gyri must be preserved and bipolar cautery should be used only if bleeding occurs. Use of brain retraction system must be carefully evaluated to avoid pressure-related iatrogenic injury to the surrounding cortical tissue. Once the tumor is identified, it can be resected en bloc or by piecemeal fashion. The tumor can be debulked in such a way that edges are moved inward and removed. Transcortical approaches could be used for subcortical tumors that neither underlie an obvious sulcus nor involve eloquent cortical regions. Corticectomy should be performed in a linear fashion for small tumors. For larger tumors, circumferential corticectomy is preferred (57). For deep intra-axial lesion, tubular retractor system could be useful, as it creates a controlled surgical corridor with minimal brain retraction and damage to the surrounding brain tissue, to reach lesion in the basal ganglia, insular cortex, lateral and/or third ventricle, pineal region, and the thalamus (58). The craniotomy must be large enough to fit the tubular retractor. The initial approach might be transcortical or trans-sulcal. The navigation probe is conducted through the brain parenchyma and the tubular retractor is gently pushed down into the white matter. The retractor is opened to create the surgical corridor to access the lesion (59).

INFRATENTORIAL APPROACHES

Infratentorial approaches have been used since the 1990s for posterior fossa lesions using either craniotomy or craniectomy, usually using the asterion as a constant bone landmark, extending the resection down into the foramen magnum (60). Numerous approaches including anterior petrosectomy, posterior petrosectomy, translabyrinthine, and transcochlear have been developed. A key element to reduce surgical complications is the correct position of the patient, as it will provide a good surgical corridor minimizing brain tissue retraction. Lesions of the cerebellar-pontine angle, whether emerging extra-axially or intra-axially, are challenging due to surrounding vascular and eloquent neural structures. Furthermore, bone anatomy limits access to the ventral surface of the brain stem. Most surgeons begin with the surgical exposure of Dandy's point for potential intraoperative intraventricular catheter placement (61).

PRONE POSITION

Prone position provides good exposure to the dorsal surface of the body. It allows access to the posterior head, neck, and spinal column. For occipital and suboccipital lesions, chest rolls are required. Areas on the patient's body with excess pressure or traction are to be protected using a thick foam pad. The suboccipital craniotomy is used for most lesions in the posterior fossa, for example, tumors (meningiomas, ependymomas, gliomas, medulloblastomas, acoustic neuromas, and metastatic lesions), vascular lesions (aneurysm, cavernous malformations, arteriovenous

malformations, and intraparenchymal hemorrhages), and development anomalies (Chiari malformations). Patients with cervical spine disease with limited flexion and rotation movements should be excluded from this position (62).

SITTING POSITION

In 1931, De Martel introduced the sitting position for patients undergoing neurosurgical procedures (63). Posterior fossa tumors can be reached with good exposure using the sitting position. Although it has lost its popularity, it is still used in some surgical centers. Major disadvantages of this approach include venous air emboli (6–76%), pneumocephalus, and bradycardia (63). Preoperative cardiology evaluation, cardiac Doppler ultrasound, and intraoperative neurophysiology monitoring are essential. Intraoperative transesophageal echo or precordial Doppler monitoring can be used to track any air embolism, while a right atrial central venous pressure line can be placed to aspirate the air embolism. Patients with patent foramen ovale are in higher morbidity risk, so an alternative surgical position should be considered. Anesthesiological monitoring also includes a central venous catheter placed in the right atrium, continuous invasive blood pressure measurement with an arterial catheter (radial artery most of the times), electrocardiogram, pulse oximetry, and capnography with end-tidal CO_2 (64) (Figure 5).

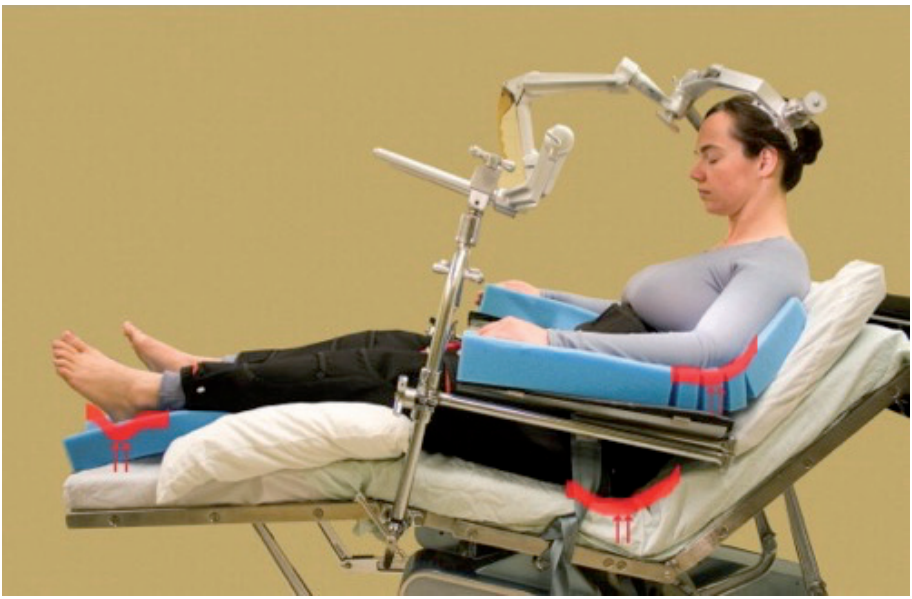


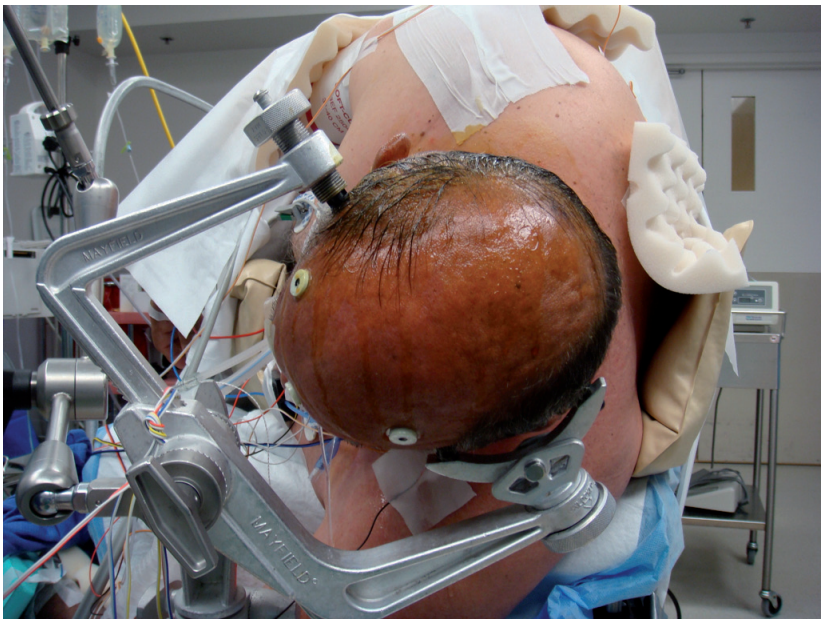
Figure 5 Although it has lost its popularity, sitting position is still used in some surgical centers. Attention must be paid to avoid pressure points (red arrows). The head is partially flexed and the neck turned to lesion side. All care must be taken to prevent neural injury of the spinal cord or the brachial plexus with continuous neurophysiological monitoring. Air embolism detection is essential to avoid complications. Used with permission from the original copyright holder, Elsevier.

PARK BENCH POSITION

Park bench position is the modification of the lateral position and is very commonly used for more laterally positioned lesions, including the lateral cerebellar hemisphere and cerebellopontine angle. The head is flexed and the vertex of the head is tilted toward the floor. Excessive neck flexion and/or side bending may prevent venous return. Patient is well padded to avoid pressure injuries, especially to the ulnar nerve, brachial plexus, and popliteal fossa (Table 3; Figure 6).

TABLE 3 Advantages and Disadvantages of Prone and Sitting Positions for Posterior Fossa Approaches

	Prone position	Sitting position
Air embolism	Less likely	Highly likely
Brain tissue retraction	Highly likely	Less likely
Cervical spine traction	Less likely	Highly likely
Venous sinus thrombosis	Equally likely	Equally likely
Pneumoencephalus	Less likely	Highly likely
Anatomic orientation	Less likely	Highly likely
Cranial nerve preservation (65)	Highly likely	Less likely



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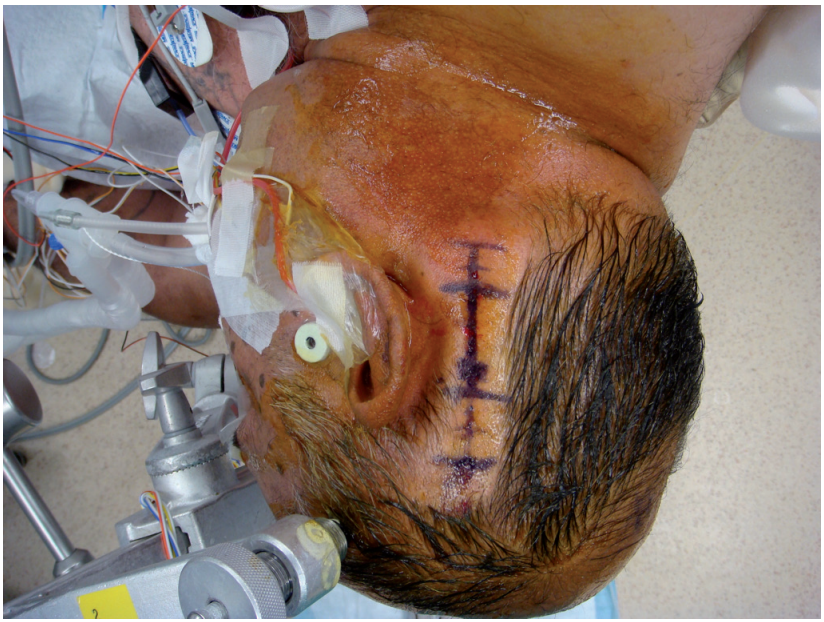

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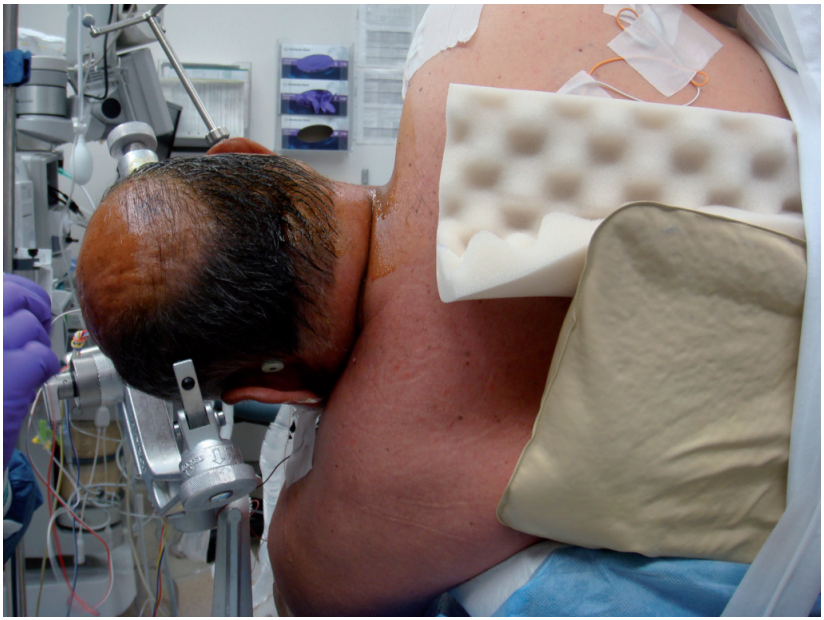

(c)

Figure 6 The park bench position. (a) The face should be facing the floor. Shoulder retractor will allow a more comfortable working area for the surgeon. (b) Cushion paths are placed under the axilla to prevent brachial plexus injury. (c) The incision is planned from above the pinna down to the mastoid process, 2 cm behind the ear. (Courtesy of Prof. Alfredo Quiñones-Hinojosa.)

TABLE 4 Preoperative and Operative Predictors of Extended Length of Hospital Stay Following Craniotomy for Tumor (8 Days)

Variable	OR	95%CI	P
Age over 70 years	1.67	1.41–1.99	<0.001
African American	1.79	1.48–2.17	<0.001
Hispanic	1.54	1.25–1.89	<0.001
Infratentorial	1.42	1.26–161	<0.001
ASA class 3	1.59	1.40–1.79	<0.001
ASA class 4 & 5	2.41	2.03–2.86	<0.001
Diabetes mellitus with insulin treatment	1.50	1.20–1.87	<0.001
Class I obesity	0.84	0.72–0.97	0.02
Preop sodium (mEq/L) <135	1.26	1.08–1.47	0.003
Impaired sensorium	1.69	1.24–2.31	0.001
Hemiplegia	2.40	1.84–3.13	<0.001
Steroid use	0.67	0.58–0.76	<0.001
Anesthesia time >300 min	2.28	1.96–2.65	<0.001
Mechanical ventilation >48 h	11.07	6.56–18.70	<0.001[a]

Source: Adapted from Ref. (66).
ASA = American Society of Anesthesiologists.
[a]All predictors model.

POSTOPERATIVE CARE

Incidence of postoperative complications within 30 days of tumor resection is as follows: stroke (2.1%), myocardial infraction (1.3%), death (2.7%), infection (2.4%), and the need for revision surgery (6.6%). Aiding early hospital discharge for cancer patients expedites chemotherapy and/or radiation therapy and other treatments, potentially improving patient outcomes by decreasing the time period between surgery and resumption of daily activities (20). Bladder catheters are to be removed on postoperative day 1 or as early as possible. Postoperative artificial nutrition is not typically needed for these patients, unless patients are in a prolonged comatose state (>7 days). Early mobilization of patients is encouraged (20) (Table 4). Venous thromboembolic events, pneumonia, and respiratory complications are preventable comorbidities. Urinary tract infections are independently associated with longer hospitalization (67%).

Conclusion

Surgery plays an essential role in the management of glioblastoma. A combination of techniques including intraoperative MRI, neuronavigation, ultrasonography,

and fluorescence-guided surgery has enabled safe and maximal surgical resection, leading to a better survival outcome, and postoperative functional recovery. Despite maximal surgical resection and adjuvant chemoradiation, tumor recurrence occurs within 10 months in many cases, thought to be mediated by resident cancer stem cells. It is imperative that more effective treatment strategies are developed for glioblastoma.

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