Editorial

High-grade gliomas – Is radical resection needed? Is radical resection possible? Is surgery necessary?

In Nature's infinite book of secrecy

A little I can read.

-William Shakespeare Antony and Cleopatra (Act 1, Sc 2, 11).

Real knowledge is to know the extent of one's ignorance.

High-grade gliomas (glioblastomas [GBMs]) are the most common malignant primary brain tumors. Identification of such a tumor in an individual spells doom and signals impending neurological sequel, progressive functional decline, and eventual death. The patient seeks treatment in a quest for relief from symptoms and attempts toward increasing longevity and improving the quality of life. Any kind of treatment that affects or threatens existing functions can have devastating implications both for the patient and the family. While complications can follow every neurosurgical endeavor, the challenge is pronounced in surgery for GBMs as any minor or major complication can seriously affect or cripple the remaining "short" lifespan of the patient, with little or no possibility or time for improvement. From my 40-year experience in the subject of neurosurgery and dealing with a number of complex neurosurgical issues, I observe that complications following surgery for GBMs are "significantly" common and can happen after attempted radical tumor resection, after partial tumor resection, or even after a biopsy.

The current standard of treatment of high-grade gliomas is attempt toward maximal and safe resection, radiation treatment, and concomitant temozolomide, followed by maintenance temozolomide for 6–12 months. The median overall survival for patients with newly diagnosed GBM is 12–18 months. Despite extensive research, the ultimate clinical outcome has not changed much.

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Our recent studies identify that gliomas arise from and grow along a named white fiber tract. [1-3] The adjoining tracts are displaced by the growing tumor and are functionally affected by virtue of deformation and pressure and not by destruction or transgression. The compartmentalization or "fencing" formed by the adjoining tracts is "impermeable." The tumor grows by expansion and displacement and not by destruction. [1-3] The tumor color, consistency, and vascularity allow differentiation from adjoining normal brain. Accordingly, a well-defined plane of surgical dissection can be developed between the tumor and the normal brain, and the tumor can be resected in an *en-masse* fashion. [3] Both low- and high-grade gliomas have a similar pattern of origin and extension and are different only in their growth characteristics and physical nature.

Surgery for low-grade gliomas has significantly evolved in the past few decades.^[3] The role of surgery in affecting relief from symptoms, reducing tumor burden, improving quality and increasing the longevity of life, and delaying the potential malignant transformation is now convincing. On the other hand, surgery for high-grade glioma presents a discrete scenario.

In general, surgery for GBMs forms an important cohort wherein the younger neurosurgeons train and hone their skills in tumor resection and the art of achieving hemostasis. It has been a general understanding that the more radically a neurosurgeon can resect a GBM, the more effective he is as a neurosurgeon. The terms "complete" and "radical" tumor resection sound rather enticing to a surgeon. Such surgical attempt provides an opportunity to test the personal level of surgical skills, have the pleasant satisfaction of seeing postoperative imaging that is free of tumor, and finally showcase the imaging result in professional meetings.

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Conventionally, surgery is advised whenever the tumor is safely amenable and significant tumor bulk resection is possible. The aim of surgery for GBMs is to obtain a tissue diagnosis and profile the tumor for adjuvant treatment and tumor resection with the aim of symptomatic relief and an attempt toward improving the quality of remaining life. Relief from symptoms after tumor resection is obvious and frequently significant. More recently, radical and "supratotal" resections of such tumors have been recommended, and the currently published opinion is that such surgery is best suited to delay the recurrence and improve the lifespan of the patient. To achieve radical resection of the tumor, apart from gross morphological features of the tumor, the current trend is to use intraoperative imaging like ultrasound, magnetic resonance imaging, and computed tomography scan, awake-and-asleep neurophysiological monitoring, and use dyes like 5-aminolevulinic acid to maximize tumor resection.

While complications following adjuvant treatment are possible, they are relatively rare and less intense or disabling. Complications following surgery for high-grade gliomas are "frequent" and are probably underreported. Complications can be due to tumor-related factors such as handling of the critical tumor – adjoining brain, inability to identify the tumor – normal parenchyma border, high and abnormal vascularity, brain edema, and several such factors.

"I cannot do everything, but I can do something. But I will not let what I cannot do interfere with what I can do."

Can the natural course of malignant tumor growth be changed by surgery in general and attempts toward radical tumor resection in particular? Can such surgical attempts increase both longevity and quality of life? Can such surgery increase the possibility of complications? The issue is that is a surgical procedure that poses at least some or significant threat of affecting function justified when surgery on high-grade glioma is in question.

The generally agreed aim of glioma surgery, in general, and GBMs, in particular, is to maximize tumor resection, attempt toward relief from symptoms, and aim toward the improvement of function. Whenever any functional compromise is even "remotely" anticipated, it is mandatory that the surgeon backs away. As a complication that is even mild or moderate will impact the whole remaining "short" life span of the patient, deprive him/her of function, and greatly burden the family and caregivers. The impact of surgical complications can be "huge" and should be understood by the operating surgeon. It is also possible that the family blames the surgeon for the rest of the patient's life.

The cause/course/cure of any tumor is not only not known but also unlikely to be known. [4] The so-called surgical cure is more appropriately "surgical care," the dream of the total removal of any tumor – benign or malignant, in my view, is illusory. Even if the tumor was removed totally, the adjoining "normal" cell can throw a malignant tantrum, and then, the process starts all over again.

All malignancies can be classified into good or bad, only in retrospect. Evaluation after a waiting period reveals the true colors of the tumor. A surgeon can remove the tumor, the whole tumor, and nothing but the tumor, but without removing the tumor diathesis or ability to form the tumor. Considering the real possibility of complications in surgery on high-grade gliomas, it is better to shy away from these tumors rather than aggressively attempt to alter the natural disease course.

Moreover, the surgeon must realize the "infinite potential to harm." The surgical philosophy for all tumors, benign or malignant, is to remove the tumor radically and then pray and wait for it not to recur.^[4] It is better that the blame of tumor-related neurological deficit is on its growth pattern rather than on surgery conducted with unrealistic aims.

The terms "radical and total resection" must be defined and clearly understood. One must realize that "once a tumor, always a tumor." A tumor is a spatial problem, demanding a spatial solution. The success of the surgery will be maximum space creation, maximum bulk removal, and safe outcome. The complex terrain of a GBM makes the likelihood of complications greater. Abnormal and friable blood vessels in the tumor increase the possibility of hemorrhagic complications. The recurrence depends more on the growth pattern of the tumor and is independent of the extent of tumor resection.

Therein lies a message for the surgeons: "Less is more." [4] Any operative or cytolytic procedure that is offered to the patient is pure palliation, a treatment concept that has not changed in its limitation. Each tumor is unique. It is not the treatment but the cellular behavior that decides the outcome. The answer to surgical treatment of GBMs may be safe resection in a safe brain area to obtain symptom-free time for the patient.

Much sophistry has evolved in the art of neuro-oncology, from the pioneering times of Macewan, Cushing, and Penfield. [5] The advances have been gadgetry but hardly conceptual. Gadgets provide easier access – visual and operative – to the tumor, but all sophistication ends there. The best imaging techniques and the most evolved operative microscopes do

not in any way alter the basic character of a neuraxial tumor in general and high-grade gliomas in particular.

A benign or malignant tumor occurs as a newly spawned tissue, which is why it is also known as a neoplasm. Its chief aim is slowly and silently to seek space. The adverb "silently" is significant because most tumor growth occurs before being detected by the clinician or before "disease" affects the patient. As long as the body accords space to the newcomer, it makes no noise; this accounts for the fairly widespread presence of tumors before identification. As and when the available space is no longer adequate for the neoplasm, it causes symptoms of obstruction and pressure. Brooke called this phase of tumorigenesis its "discreet silence."

The cardinal need for physicians is to be humble and accepting, and let the disease be, as it may, hopefully in the least harmful way. All modes of therapy – surgery, radiation, chemotherapeutic agents, hormones, and immunologic agents – are at best palliative.

Sir Harold Gillies and Ralph Millard, in their classic *The Principles and Art of Plastic Surgery*, have aphorized that not much has gained in the art of surgery after the first abscess was incised by a flint stone, and the first wound sutured by horse hair.^[4] Today, we have incredibly fast-moving drills and saws, as well as extraordinarily sophisticated imaging and navigation systems. However, our results barely excel those of pioneers in surgery like Macewan, Horsley, and Cushing.

I believe that more than ever before, in the face of growing hubris engendered by more and more sophisticated techniques, neurosurgery is in need of humility and awe before the wonders of nature. Far more than new machines, we surgeons need to be informed and guided by new concepts and philosophy of nature, as well as of nature and the miracle of the human body foremost. While technology surges ahead, the philosophy of neurosurgery should not lag behind. Technology can make you bold without being wise. While technology is easier to change, ideology is not. It should not happen that the attempts of heroics and showmanship during surgery and chasing uncertain and unrealistic goals land the patient in a clinical situation that spells misery.

Surgery on glioblastomas in more critical areas of the brain such as the insula, speech and motor area, thalamus, and left parietal brain, should be offered with caution. Surgery is more often a thankless job in these cases. If symptoms are not compelling, surgery can be avoided. Radical surgery can be successful in some but can be devastating on occasion. Such occasions are necessarily avoided in surgery for GBMs.

Everyone says surgery is the easy way out, but going under the knife is never the easy way out. You don't know if you're going to come back out of it and whether there will be complications.

-Rosie Mercado

My personal experience in the field suggests that while the future of treatment for low-grade gliomas will be radical tumor resection, it will be nonsurgical in cases with high-grade gliomas.

Patients do not place their trust on monitors and dyes, they place their trust in you and there are times when there is no place for a scalpel.

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