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Ultrasound-guided versus traditional surgical resection of supratentorial gliomas in a limited-resources neurosurgical setting

Aly Ibrahim, Walid Ahmed Abdel Ghany[*] , Mohamed Atef Elzoghby, Ayman El-Shazly, Hisham Simry and Mohamed Alaa Fakhr

Abstract

Background: Intraoperative ultrasonography (IOUS) represents a cheap and safe alternative to the more expensive intraoperative guidance modalities. In this study, we investigate the impact of introducing IOUS in the surgical management of supratentorial gliomas and compare its use objectively to unguided surgery.

Methods: We conducted a prospective cohort study comparing two groups of patients with supratentorial gliomas amenable to gross total resection. One group was operated using intraoperative ultrasound guidance while the other group was operated using a more traditional approach with no intraoperative image guidance. The main outcomes assessed were the extent of tumor resection (EOR) based on early postoperative MRI, the postoperative Karnofsky performance score (KPS), and the rate of complications.

Results: There were 17 patients in the ultrasound group and 13 in the control group. EOR was significantly better in the IOUS group. Gross total (GTR) and near-total (NTR) resection were achieved in 29% and 24% respectively in the IOUS group, while 0% and 8% respectively in the control group. The mean volumetric EOR was 83% and 66% in the IOUS and the control groups respectively. Ultrasound was able to detect residual tumor after surgeon perceived GTR in 76% of cases. Postoperative KPS was significantly better in the IOUS group.

Conclusion: IOUS guidance is superior to non-guided surgery in terms of EOR. Higher tumor resection confers a survival benefit according to previously published literature. This is particularly useful in a limited-resource setting, where neuronavigation and intraoperative MRI are not available.

Keywords: Astrocytoma, Glioblastoma, Ultrasound, Extent of resection

Introduction

Astrocytomas are the most common primary tumors of the nervous system, and glioblastoma (GBM) is the most common and most aggressive of these tumors [1]. Despite the vigorous basic and clinical research, survival trends have remained largely static for many years, reflecting the general lack of effective therapeutic options for patients with these tumors [2]. Low-grade diffuse astrocytomas (World Health Organization (WHO) grade II) usually progress to malignant variants over years [3]. Malignant astrocytomas are infiltrative lesions, with tumor cells found outside the radiological tumor margin, which makes them surgically incurable [4, 5]. Yet, surgical resection is the mainstay of treatment followed by adjuvant chemoradiotherapy. Current median life expectancy for patients with GBM with optimal treatment is 12–14 months [6]. The most important factors affecting survival include tumor grade, EOR, patient's age, and preoperative KPS, with a worse prognosis for patients more than 60 years of age and for a KPS < 80% [7].

Maximum safe resection remains the primary goal of surgery. A multitude of studies have shown that gross total resection can prolong survival bearing in mind that the extent of tumor resection should not negatively affect the postoperative functional status of the patient

[8–12]. Classic surgical planning relied on preoperative imaging and indirect localization methods. This is limited by the quality of preoperative images, the surgeon's anatomical knowledge, and his accuracy in making preoperative calculations. Even in optimal conditions, classic methods are still hampered by human errors of judgment and difficulty to designate anatomical landmarks with intrinsic lesions, which makes gross total resection, without intraoperative image assistance, an unsafe alternative [13].

The introduction of intraoperative navigation and imaging techniques has improved the neurosurgeons' ability to tackle brain tumors in a safer manner while achieving a higher extent of tumor resection [14, 15]. Magnetic resonance imaging (MRI) has great soft tissue resolution, and thus, its intraoperative use offers an accurate assessment of residual tumor. But MRI is expensive and requires a special setting and extra time for image acquisition [14, 16, 17]. Intraoperative ultrasonography (IOUS) on the other hand is cheap, fast, and flexible but with a poorer image resolution. IOUS images can be better interpreted through some modifications and a learning curve [18, 19]. One of the best advantages of IOUS is that it gives a real-time image, unlike neuronavigation that relies on preoperative images and is liable to the inaccuracy of brain shift [15, 20]. Although IOUS have been introduced in brain tumor surgery a long time ago, to the best of our knowledge, only a few prospective studies have compared it to either guided or unguided surgery. Also, IOUS seems to have fallen in favor of newer, more expensive tools that are not available in every medical center.

The aim of this study was to assess the impact of intraoperative ultrasonography on surgery for supratentorial intra-axial brain lesions represented in astrocytomas. This impact would be particularly important in neurosurgical centers where no other intraoperative imaging modalities are available, which is the case in many medical centers in the developing world. This was assessed through the extent of tumor resection and the patient's postoperative neurological and functional outcomes.

Patients and methods
Patients
The study included patients with supratentorial astrocytomas operated at Ain Shams University Hospitals with or without intraoperative ultrasound guidance. The study was a prospective comparative (cohort) study including two groups: intraoperative ultrasonography (IOUS) group for patients operated with ultrasound guidance and a control group for patients operated without image guidance. The IOUS group represented the first cohort of patients operated using ultrasound guidance at our institution. New patients with suspected supratentorial brain astrocytoma on preoperative magnetic resonance imaging (MRI) and whose tumors were amenable to gross total resection were initially included in the study. Patients who harbored lesions deemed irresectable were excluded from the study; these included, but not limited to, corpus callosum butterfly lesions and thalamic, hypothalamic and basal ganglia lesions. The postoperative histopathological analysis determined the final inclusion. Patients with the following pathologies were included: diffuse astrocytoma (WHO II), anaplastic astrocytoma (WHO III), glioblastoma (WHO IV), and low-grade focal astrocytomas, in addition to mixed astrocytomas. The study was approved by the Research Ethics Committee of the Ain Shams University Faculty of Medicine.

Preoperative assessment
In addition to the preoperative MRI, patients underwent a formal and detailed clinical neurological assessment. Preoperative functional status was described using KPS.

Craniotomy (intervention)
All patients who met the above criteria underwent craniotomy for resection of the mass using standard microsurgical techniques. In the IOUS cohort, ultrasound guidance was added. No neuronavigation or other imaging adjuncts were available. In the IOUS group, ultrasound transducer (LOGIQ Book XP, General electric, USA) was applied to the dura before dural opening. Two probe (transducer) types were used: GE hockey stick probe with frequency range 4–10 MHz and an 8C microconvex probe with 6–10 MHz frequency range. The ultrasound probe was passed through a sterile plastic endoscope sheath, and the tip was put in a sterile surgical glove filled with optic gel.

The intraoperative use of ultrasonography can be divided into three stages. The first stage is the initial scan, better started from outside the dura since this is usually the highest quality image, acquired before release of CSF or introduction of any blood or air into the field. This initial scan confirms the location of the lesion beneath the dura, its depth, and its main anatomical relations, and above all, it acquaints the surgeon with the echogenicity of the tumor and its margins. In this stage, the use of transducers with relatively larger footprint (1–2 in.) is advisable to get a panoramic view of the tumor and its surroundings. Convex or the smaller microconvex transducers are preferred over linear transducer since they can show a wider field from relatively small craniotomy as well as help detect parts of the tumor that may exist underneath the bony edges of the craniotomy. The frequency used should depend on the depth of the tumor through an inverse proportional relation. From our experience, frequencies from 5 to 10 MHz are

generally adequate. Upon opening the dura, in cases where cortical mapping is used, the gyrus immediately overlying the tumor may not be the safest route due to eloquence. In this case, ultrasound can help navigate the way through an indirect route to reach the subcortical tumor.

The second stage starts once the tumor is reached and tumor resection begins; IOUS should be repeatedly used to assess the extent of resection and avoid false passage into unaffected white matter or breach into the ventricle. The color flow mode can help identify important vascular structures, which enhances orientation and probably avoids vascular injury. Finally, once the surgeon is comfortable with the completeness of resection and no further tumor could be clearly seen under the microscope, the third stage of IOUS use includes a systemic scanning of the tumor bed. After initial hemostasis, all hemostatic substance as well as cottonoids should be removed and the resection cavity should be filled with irrigation fluid. A small transducer, burr-hole probe or microconvex probe, is introduced into the cavity and gently used to systemically scan the resection cavity for residual tumor. Residual tumor nodules usually have the same echogenicity as the tumor margins seen on the initial scan and are generally hyperechoic. Note that small clots of blood can sometimes appear as residual tumor. It is advisable to do one final scan after dural closure and before bone flap repositioning; this can help detect an accumulating hematoma in the tumor bed and prompt re-exploration.

In the control group, after dural opening, the location of the tumor was predicted based on a combination of factors including preoperative calculations and abnormally looking gyri. Standard microsurgical techniques were then used to reach and resect the lesion. Circumferential resection was usually attempted first, but in some cases central debulking was done, especially with larger lesions. The extent resection proceeded without image guidance depending on the surgeon's perception of resection under direct microscopic visualization. The field was then irrigated copiously and hemostasis achieved. Closure proceeded routinely. A postoperative MRI of the brain with and without gadolinium contrast was done within the first 48 h after surgery.

Outcome assessment
The primary outcomes of the study were the extent of tumor resection and patient's Karnofsky performance score at 1 month postoperative. The extent of tumor resection was assessed using two techniques: a volumetric and a non-volumetric technique [10, 21]. In the non-volumetric technique, gross total resection (GTR) was defined as no residual enhancement noted on postoperative MRI, near-total resection (NTR) if only rim enhancement of the resection cavity was noted on

postoperative MRI, or subtotal resection (STR) if residual nodular enhancement was noted on postoperative MRI. In grade II gliomas and in some grade III gliomas that did not demonstrate enhancement on preoperative MR imaging, FLAIR/T2WI abnormalities were used to determine residual tumor. In these cases, the postoperative presence of residual nodular FLAIR signal that corresponded to tumor on preoperative MR imaging was classified as STR. Volumetric analysis was also applied. Volumetric analysis was performed on Osirix software (Pixmeo SARL, Geneva, Switzerland). The tumor region of interest (ROI) is manually delineated in each slice (Fig. 1). The software then computes the volume of the tumor using a preset algorithm. For contrast-enhanced lesions (high-grade tumors), the residual volume (RV) is calculated by subtracting the total volume of the hyperintense lesion (total white volume (TWV)) in the postoperative MRI T1-weighted images (T1WI) without contrast from the total volume of hyperintense lesion (TWV) in the postoperative MRI T1-weighted image with contrast (T1WI + C) [21].

$$RV = (TWV\ T1WI + C) - (TWV\ T1WI)$$

The extent of resection (EOR) from preoperative tumor volume (PTV) is then calculated using the following formula:

$$EOR(\%) = \left(\frac{PTV - RV}{PTV}\right) X\ 100$$

For non-enhancing tumors (low-grade tumors), the preoperative tumor volume was calculated in the same manner using the Flair/T2WI images while the residual volume was also assessed using postoperative Flair images. Karnofsky performance scale was used to describe the functional status at 1 month postoperative [22].

Secondary outcomes included the ultrasound characteristics of operated tumors and comparing it with the histopathology. These were the ability to localize and delineate the tumor margins.

Ability of ultrasound to localize the tumor was defined as either well localized or poorly localized [23]: A well-localized tumor is a tumor that was well visualized by IOUS in the initial acquisitions by having a clearly different echogenicity than that of surrounding brain or other structures. A poorly localized tumor was a tumor that is not well visualized by IOUS due to any obstacles after exhausting all means to overcome these obstacles like changing the probe position or the operating table position and changing the transducer frequencies.

Ability to define tumor margin [23] (Fig. 2): the margins were labeled well defined if they can be clearly differentiated from the surrounding brain tissue or edema
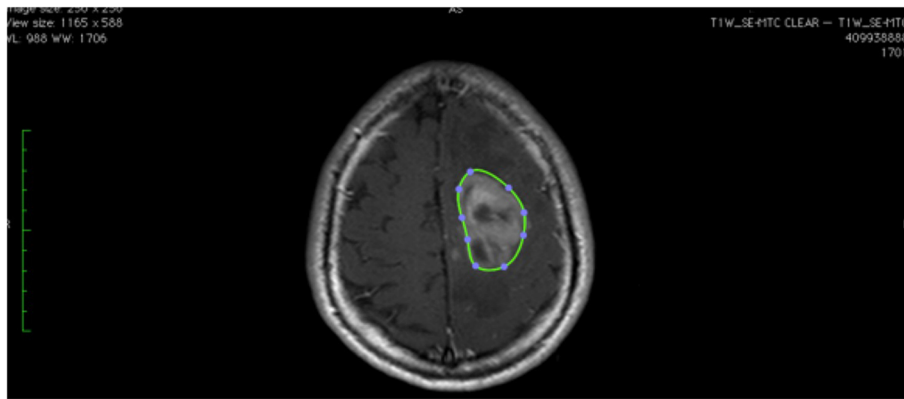
Fig. 1 Screen shot from Osirix software showing delineation of tumor region of interest (ROI) in an MRI slice

or any other structure throughout the whole tumor margin; moderately defined if the margin could be visualized but not clearly differentiated from the brain tissue or edema in certain areas; and poorly defined if they could not be visualized or differentiated from surroundings.

Secondary outcomes also included the rate and type of operative complications.

Statistical analysis

Statistical analyses were performed on MS Excel (Microsoft Corp., Redmond, WA, USA) and XLSTAT (Addinsoft, New York, NY, USA). Parametric tests, including Fisher's exact test and T test were used to compare categorical and continuous data respectively.

Results

Thirty patients fulfilled the inclusion criteria and were enrolled in the study. Seventeen patients (10 males) underwent craniotomy and tumor resection guided by intraoperative ultrasonography (IOUS) while 13 patients (4 males) underwent resection without IOUS (Table 1). Initially, we intended to recruit more patients, but interim analysis showed a clear advantage of IOUS, so recruitment ended and IOUS was recommended for all patients. The mean age and preoperative Karnofsky performance score were 35 years and 81% for the IOUS group respectively while 48 years and 69% for the control group respectively. There was a statistically significant age difference between groups and near significant difference in preoperative KPS, but there were no statistically significant differences in other basic characteristics between groups. The results of postoperative histopathological analysis of tumor specimen are shown in Table 2. The mean tumor size was higher in the control group (80 cm^3) than in the IOUS group (59 cm^3), but the difference was not statistically significant (p = 0.2).

On the other hand, the IOUS group had more tumors in eloquent areas (53%) than in the control group (46%) but this was also not statistically significant (p = 1).
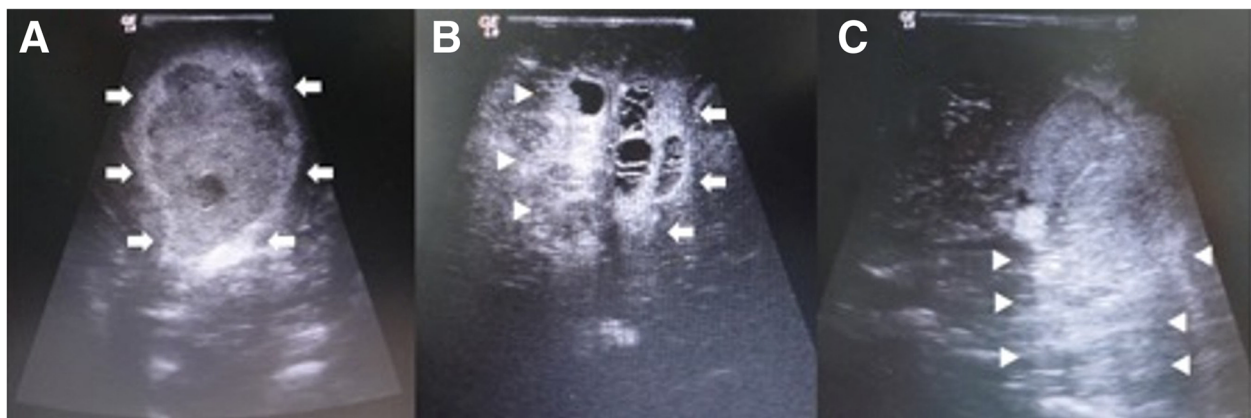

Fig. 2 Ultrasound ability to define tumor margins: **a** well-defined tumor margins, indicated by white arrows. **b** Moderately defined: the tumor margins can be clearly differentiated in some areas (white arrows) but not in other areas (white triangles). **c** Poorly differentiated: the tumor margins cannot be clearly differentiated (white triangles) all around the tumor

Table 1 Patient characteristics

	IOUS	Control	p value
n	17	13	–
Male (%)	10 (59%)	4 (30%)	0.4
Mean age (SD)	35 years (± 19)	48 (± 13.7)	0.04
Mean preoperative KPS (SD)	81% (± 20)	69%(± 15)	0.053
Preoperative seizures (%)	10 (59%)	4 (30%)	0.4
All preoperative neurological deficits (%)	9 (53%)	11 (85%)	0.1
Speech deficit (%)	3 (18%)	2 (15%)	0.6
Motor deficit (%)	8 (47%)	10 (77%)	0.1

IOUS intraoperative ultrasonography, KPS Karnofsky performance score

The extent of tumor resection (Table 3) based on the GTR/NTR/STR method of assessment showed that the IOUS group had statistically significant higher chance of achieving GTR ($p = 0.05$) or GTR/NTR combined ($p = 0.01$) than the control group. All control group cases had STR but one case, while in the IOUS group, gross total, near total, and subtotal resection rates were 29%, 24%, and 47% respectively. When comparing the volumetric analysis of resection, the mean percent resection for the IOUS group and the control group was 83% and 66% respectively ($p = 0.03$).

The postoperative functional outcome and complications are shown in Table 4. The mean Karnofsky performance scores at 1 month were 83% and 68% for the IOUS and the control groups respectively ($p = 0.03$). All complication rate was at 27% including two patients with seizures, two patients with intracranial hemorrhage, and four patients with new or worsened neurological deficit. Two patients in the IOUS group and one patient in the control group had their motor deficit actually improve as compared to preoperative motor exam. In the two patients who had postoperative seizures, the seizure

was quickly controlled and did not recur in the first postoperative month. Both incidences of intracranial hemorrhage occurred in the tumor bed, but no surgical evacuation was done. There was no mortality in the first postoperative month.

The sonographic appearance of various tumors within the IOUS group is shown in Table 5. All GBM ($n = 10$) were well localized using ultrasonography and their borders were well defined in 7 cases and moderately demarcated in 3. Two pleomorphic xanthoastrocytoma, one pilocytic astrocytoma, and one anaplastic astrocytoma tumors were well localized and had well-defined margins. Diffuse astrocytomas WHO II ($n = 2$) were poorly localized and poorly delineated. One case of oligoastrocytoma showed well localization but poor delineation of the margins. In all cases, the degree of contrast enhancement on preoperative MRI was more or less concordant with the echogenicity on IOUS.

The added value of IOUS during surgery is summarized in Table 6. In 13 out of the 17 cases (76%) operated with US guidance, IOUS detected residual tumor after the surgeon could not directly see residual tumor under magnification. In 7 of these cases, the residual was subsequently removed while in the other 6 cases, the surgeon decided not to remove it due to perceived risk of either neurological deficit, breach of the ventricle, or thinking that the echogenicity corresponded to edema rather than residual. In 8 cases (47%), the surgeon thought the image quality of the IOUS was poorer towards the end of the case compared to the initial scans.

Table 2 Tumor characteristics

	IOUS	Control	p value
All gliomas (WHO grade):			
• GBM (IV)	10	10	–
• Anaplastic astrocytoma (III)			
• Diffuse astrocytoma (II)	1	1	–
• Oligodastrocytoma (II)			
• Anaplastic Oligoastro (III)	2	1	–
• Pilocytic Astrocytoma (I)	1	0	–
• PXA (II)			
• Anaplastic PXA (III)	0	1	–
	1	0	–
	1	0	–
	1	0	–
Mean size in cm³	59	80	0.2
Side: left/right (left side %)	9/8 (53%)	8/5 (62%)	0.7
Eloquent (%)	9 (53%)	6 (46%)	1.0

IOUS intraoperative ultrasonography, GBM glioblastoma multiforme, PXA pleomorphic xanthoastrocytoma

Table 3 Extent of tumor resection

	IOUS	Control	p value
GTR (%)	5 (29%)	0 (0%)	0.05
NTR (%)	4 (24%)	1 (8%)	0.3
GTR + NTR (%)	9 (53%)	1 (8%)	0.01
STR (%)	8 (47%)	12 (92%)	0.01
Mean % resection (volumetric)	83%	66%	0.03

IOUS intraoperative ultrasonography, GTR gross total resection, NTR near total resection, STR subtotal resection

Table 4 Postoperative functional outcome and complications

	IOUS	Control	*p* value
Mean 1-month postoperative KPS (SD)	83%	68%	0.03
All new or worsened neurological deficits	1	3	0.29
New speech deficit	1	1	1.0
New motor deficit	0	2	0.17
Other complications • Seizures • Intracranial Hemorrhage • Surgical site infection	2 0 0	0 2 0	0.49 0.17 –

IOUS intraoperative ultrasonography, *KPS* Karnofsky performance score

Color flow mode was used in the majority of cases, and in 3 cases, the surgeon thought that color flow US was helpful in identifying and avoiding injury of important blood vessels. There was no reported damage directly caused by the ultrasound transducer application.

Illustrative case from the series

A 57-year-old male presented with a ring enhancing, well-demarcated intrinsic mass extending in the right parietal and occipital lobes and reaching the ipsilateral ventricle and the splenium of the corpus callosum, surrounded by marked perifocal edema (Fig. 3). His KPS was estimated to be 30 (severely disabled, hospital admission indicated but no risk of death). Initial intraoperative ultrasound scan Showed that the tumor was well localized using IOUS, with well-defined margins, as well as different nearby structures and relations including the ipsilateral and contralateral ventricle and the inter-hemispheric fissure (Fig. 3). The tumor was resected with interval US acquisitions to guide the resection (Fig. 4). Follow-up MRI done on the second postoperative day showed gross total resection of the tumor (Fig. 5). At 1 week postoperative, his KPS was estimated to be 60.

Discussion

Despite many advances in the understanding and treatment of gliomas in general and glioblastoma in particular, this group of tumors still presents a great challenge to clinicians and, above all, to patients and their loved ones. Surgery remains the mainstay of treatment followed by radio-chemotherapy. The aim of surgery is to establish a diagnosis, remove the mass effect, and if possible, achieve a gross total resection of the mass. The latter has proved to be one of the major determinants of survival, along with age, functional status, tumor grade, and more

Table 5 Sonographic appearance of intracranial tumors

Case #	Pathology (WHO grade)	Gd contrast enhancement (intensity and distribution)	US ability to localize tumor (well/poor)	US ability to delineate tumor margins (well/moderate/poor)	Echogenicity
1	GBM (IV)	Strong with patchy non-enhancing	Well	Moderate	Hyper/mixed*
2	PA (I)	Strong patchy	Well	Well	Hyper
3	Oligoastro (II)	Faint patchy	Well	Poor	Iso
4	GBM (IV)	Faint Patchy	Well	Moderate	Hyper/mixed
5	GBM (IV)	Faint Patchy	Well	Well	Hyper/mixed
6	PXA (II)	Enhancing nodule with cyst	Well	Well	Hyper with hypoechoic cyst
7	GBM (IV)	Moderate heterogeneous	Well	Well	Hyper/mixed
8	GBM (IV)	Strong rim enhancement	Well	Well	Hyper/mixed
9	GBM (IV)	Strong with areas of necrosis	Well	Well	Hyper/mixed
10	GBM (IV)	Strong rim enhancement	Well	Well	Hyperechoic borders, less hyperechoic core
11	GBM (IV)	Rim enhancement	Well	Well	Hyperechoic borders, less hyperechoic core
12	Diffuse Astrocytoma (II)	Non enhancing	Poor	Poor	Iso to hyper with homogenous texture
13	GBM (IV)	Strong with areas of necrosis	Well	Moderate	Hyper/Mixed
14	Diffuse Astrocytoma (II)	Non enhancing	Poor	Poor	Iso
15	Anaplastic PXA (III)	Homogenous enhancement	Well	Well	Hyper
16	Anaplastic Astrocytoma (III)	Cyst with enhancing wall and a mural nodule	Well	Well	Hyper (nodule)–Hypo (cyst)
17	GBM (IV)	Thick ring enhancement	Well	Well	Hyper/Mixed

Mainly hyperechoic with areas of lower echogenicity within the core
WHO World Health Organization, *Gd* gadolinium, *US* ultrasound, *GBM* glioblastoma multiforme, *PA* pilocytic astrocytoma, *PXA* pleomorphic xanthoastrocytoma

Table 6 Intraoperative ultrasound added value

	Number of patients (%)
Residual detected	13 (76.5)
Residual removed	7 (41)
Color flow mode helped avoid vascular injury[a]	3 (17.5)
Poorer image quality at end of procedure	8 (47)
Damage caused by probe	0 (0)

[a]Based on surgeon's impression

recently, tumor genotype [7, 24]. The extent of resection (EOR) is probably the only surgeon modifiable factor, and therefore, many tools have been introduced to help surgeons achieve maximum safe tumor resection.

In this study, we revisited the topic of intraoperative ultrasonography (IOUS) as an image guidance modality to help neurosurgeons achieve the goals of surgery. In the time where inflated health care budgets in developing countries are ringing many bells, while developing countries continue to struggle with limited resources, IOUS offers a cost-effective and valuable tool in surgery of intrinsic brain tumors. The aim of this study was to evaluate the impact of introducing IOUS on the ability to safely achieve higher extent of tumor resection (EOR).

Multiple studies have reported on their EOR and its impact on the overall survival in patients with both high- and low-grade gliomas [3, 9, 10, 25]. Modern era neurosurgical series, in which microsurgical techniques in addition to neuronavigation were employed, reported EOR ranging from 87 to 96% for high-grade gliomas with about 25–35% gross total resection rate [9, 21, 26]. Additional intraoperative assisting techniques were able to increase this rate to 50% as shown in the aminolevulinic acid (ALA) study where ALA fluorescence further guided resection [27]. In 2011, Sanai and colleagues challenged the status quo maintained since the late 1990s that only GTR and NTR were beneficial in terms of survival when they demonstrated in a large series of 500 patients that as low as 78% resection was still beneficial in terms of survival, but not as well as higher degrees of resection, arguing that more modest resection goals can be beneficial if met, especially with complex, eloquent tumors [26]. In 2014, Chaichana and colleagues were able to demonstrate a further reduction in that threshold to 70% resection and added another variable which is residual tumor volume (RV) when they showed that RV < 5 cm^3 lead to a better survival irrespective of the EOR [21].

In our IOUS series, and despite the lack of frameless stereotaxy navigation or fluorescence, we were able to achieve a median resection of 83% with a GTR rate of 29% and combined GTR/NTR (resection > 90%) of 53% (Fig. 6). This seems acceptable by international standards, and it was achieved using ultrasound guidance, while the results in the control group were significantly worse with median EOR of 66% and 0% GTR rate. The reason behind this is that surgery without image guidance, depending only on microscopic visualization, usually misses small nodular residuals that can be detected by IOUS and subsequently removed. Despite an adequate microscopic appearance of total resection, small nodular residual tumor scattered in different places along the tumor periphery can easily be missed. These small nodules left behind simply make the resection subtotal and deprive patients from the advantages of a gross total resection.

The study included multiple pathological entities with glioblastoma being the most prevalent (67%). It also included both diffuse and focal low-grade astrocytomas, which enriched the experience gained with the
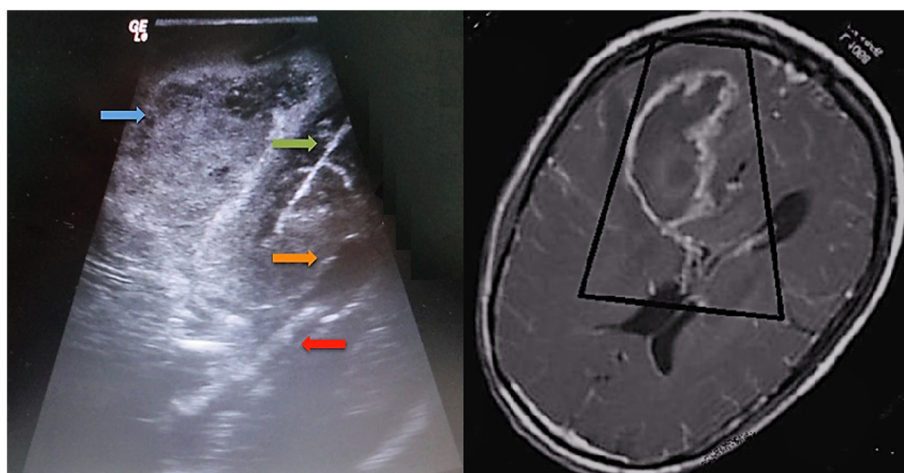

Fig. 3 Illustrative case, ultrasound scan with corresponding MRI slice in the same orientation as the ultrasound transducer. Tumor (blue arrow), interhemispheric fissure (green arrow), contralateral occipital horn (orange arrow), and choroid plexus (red arrow)
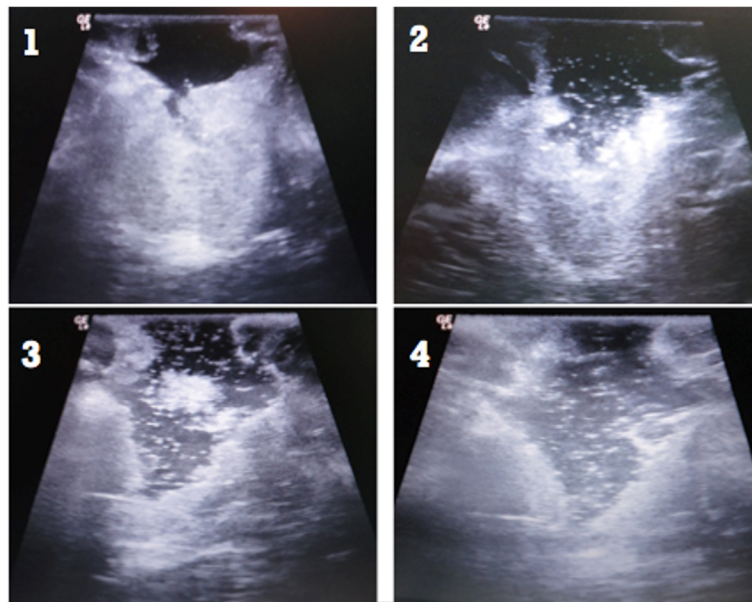
Fig. 4 Stages of tumor resection from 1 to 4 showing ultrasound ability to assess the degree of resection and residual tumor

echogenic differentiation of these various pathologies. Future analysis of survival trends based on long-term follow-up is expected to produce survival benefits in specific entities as the study represents the first cohort in an ongoing prospective registry. After these primary results, we were compelled to stop the control group and to recommend ultrasound guidance in all new patients.

Preoperative KPS is one of the most consistent prognostic factors affecting survival in glioma patients. Studies have shown that KPS of 80% or above was associated with better overall survival following surgery [7]. The preoperative neurological function, better expressed in performance scores, was probably better in the IOUS group than the control group with near statistical significance. The postoperative KPS of IOUS group was significantly better than the control group. It is not clear whether this difference is a true reflection of the IOUS benefit or a bias caused by differences in basic characteristics between groups. On the other hand, the mean postoperative KPS in the IOUS group (83%) was higher than preoperative KPS in the same group (81%), albeit without significant statistical difference, indicating that more radical resection did not have an obvious negative impact on neurological outcomes.

Among tumors operated, 15 (50%) were in eloquent areas. The rate of new or worsened postoperative neurological deficits in the early postoperative period was 13.3% (4 patients), which probably could have been avoided if cortical mapping and awake craniotomy techniques were
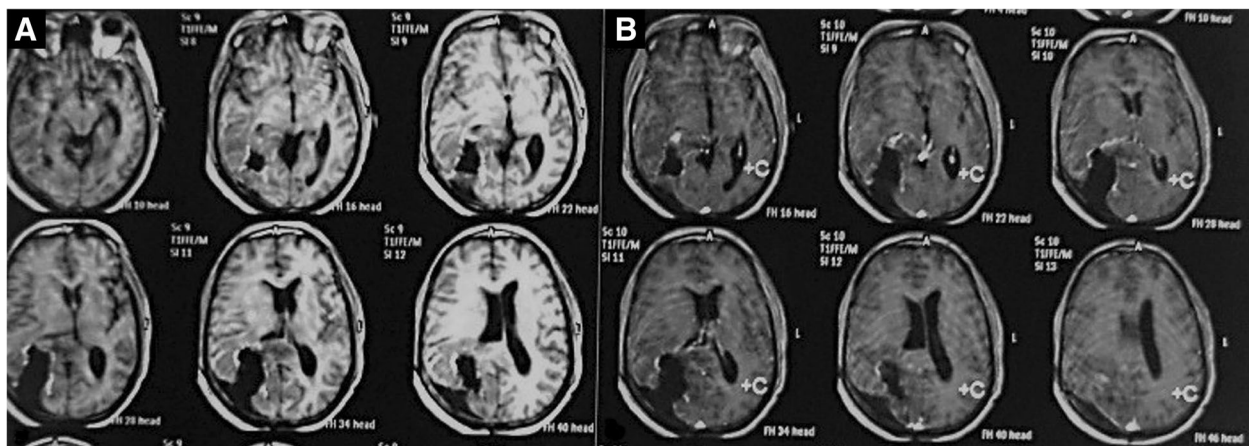

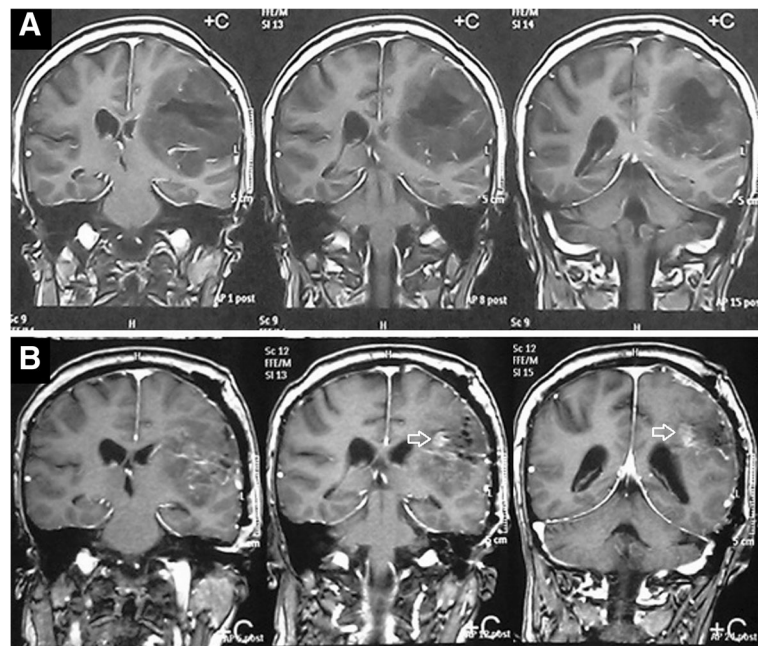**Fig. 5** Illustrative case, postoperative MRI axial T1WI: **a** without contrast and **b** with contrast

Fig. 6 **a** MRI brain, coronal cuts with contrast showing a Lt. temporoparietal recurrent/residual grade III astrocytoma. **b** Postoperative MRI brain, coronal cuts with contrast showing near total resection of the lesion with a very small enhancing residual (white arrow)

used. Within 1 month, 2 patients returned to their baseline making the 1-month postoperative neurological deficit rate 6.7% equally divided between both groups. This general low incidence and the small sample size did not allow to draw any conclusions regarding difference between groups. No patient died within the first 30 days after surgery.

Stummer reported a 7% neurological complication rate while there was around 3% mortality rate within 30 days of surgery of 260 patients [27]. Chaichana reported a 13% neurological deficit rate following surgery for 259 patients [21]. In both studies, the patients were mixed with both eloquent and non-eloquent tumors. Ius and colleagues used cortical mapping and fMRI navigation on 190 patients with LGG in eloquent areas and found an immediate postoperative neurological deficit of 43.7% that dramatically improved to 3.16% in 6 months [3].

One of the important benefits of this study was the steep learning curve of IOUS. After the first few cases, surgeons were more comfortable using and interpreting ultrasound images. Preoperative MRI scans and intraoperative US images where compared in the same orientation to produce a better understanding of the surgical field anatomical landmarks.

There was a clear relationship between MRI contrast enhancement in the preoperative images and the lesion echogenicity intraoperatively. Contrast-enhanced lesions were generally hyperechoic, making them sonographically well localized and with better defined margins. Non-contrasted lesions, like diffuse low-grade astrocytomas, were generally isoechoic, making it difficult to distinguish them from surrounding normal brain. But this does not mean that echogenicity corresponded to tumor grade, since focal low-grade tumors like pilocytic astrocytoma and pleomorphic xanthoastrocytoma that had contrast enhancement did appear hyperechoic with IOUS and were generally well localized. This is an interesting topic that needs further studies, but until then, it is advisable not to rely on IOUS alone when tackling non-enhancing lesions like diffuse low-grade gliomas. Intraoperative MRI guidance seems to be helpful when resecting these tumors, but intraoperative MRI has its considerable cost and special setting [14].

The study had the advantage of being prospective, yet it had some weaknesses. First, there is a lack of patient randomization, which may have contributed to selection bias. Second, the relatively small number of patients, and particularly in the control group, did not allow to draw statistically significant difference, if one does exist, in some comparisons including the rate of complications. Also, a separate pathological examination of residual nodules identified and removed could have strengthened the results. The future goal is to acquire multiple biopsies from the homogenous thin hyperechoic margins thought to be due to edema and that do not show contrast enhancement on postoperative MRI. Despite the weaknesses, the study showed the image guidance advantage of IOUS and helped establish IOUS as a routine tool in our surgeries. It also accelerated the

IOUS learning curve and made surgeons more comfortable using and interpreting IOUS images.

Conclusion

This prospective comparative study has demonstrated that intraoperative ultrasonography (IOUS) is a useful tool in achieving a higher extent of tumor resection (EOR) when operating supratentorial gliomas when compared to unguided surgery. In addition, the postoperative KPS of the IOUS group was significantly better than the control group.

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