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Intraoperative Ultrasound in Glioma Tumors

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Abstract:

Background: ***Glioma tumor is the most common primary brain tumor and extent of resection of this tumor plays a significant role in the survival rate of the patients. Intraoperative ultrasound (IOUS) has become a convenient technique in brain tumor surgery due to its non-invasiveness, affordability, and real-time imaging capabilities, making it appealing to neurosurgeons, and assists neurosurgeons in identifying the tumor's location and adjacent structures during surgery.***

Materials & Method: This study was done prospectively, in Rasul Akram and Shahada-ye-Haftam Tir hospitals, Tehran, Iran, and evaluated IOUS's use in 20 patients with brain glioma between 2019 and 2022. Simple random sampling was used to select patients. The resection was performed using IOUS, and the extent of resection was assessed through imaging. We used SonoSite convex ultrasound probe with bandwidth of 10-3 MHz and scan depth of 3 to 18 cm.

Results: The study found that with ultrasound guidance, the average mass resection rate was 89.3%. The use of ultrasound during surgery improved the resection rate compared to previous studies. Motor complications observed in 15% of patients after surgery included paralysis and verbal deficits, while the rate of meningitis was low. The average length of hospitalization for patients was 10 days, and the average intraoperative bleeding was 344 cubic centimeters.

Conclusion: Ultrasound can be a valuable tool in resection of brain glioma as it provides real-time imaging and assists in tumor resection, and detect adjacent structures. However, it should be used in conjunction with other monitoring modalities. Further studies are necessary to explore the full potential and limitations of IOUS in neurosurgery.

Keywords: Intraoperative Ultrasound, Glioma Tumor, Resection rates

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Introduction:

Glioma tumor is the most common primary brain tumor, which is divided into different categories from grade 1 to grade 4[1]. The extent of resection of this tumor plays a significant role in the survival rate of the patients. In contrast, the greater extent of resection can be associated with increased complications[2]. Therefore, the localization of the lesion and not entering the healthy tissue adjacent to the tumor becomes extremely important. According to studies, the resection rate above 95% and the residual tumor below 2 cc is related to reducing the risk of death in patients with glioma[3].

Intraoperative ultrasound (IOUS) is a widely used technique in medicine. Neurosurgeons find IOUS appealing due to its non-invasiveness, affordability, and the potential for repeated use during surgery without significant time consumption[4]. The first reported use of IOUS in neurosurgery was in 1982 by Chandler et al.[5]. However, one limitation of ultrasound is its reduced efficacy in areas with a thick skull[6].

Despite the notable challenges associated with IOUS usage, one of its advantages is real-time imaging of the lesion. Given the nature of brain tumors, tissue movement can occur at each step of the surgery (including opening dura and beginning resection). Therefore, real-time intraoperative ultrasonography assists surgeons in identifying the current location of the mass and neighboring structures, such as ventricles and the falx cerebri[7]. Since the introduction of Intraoperative MRI (iMRI) to the field of neurosurgery, part of this problem has been solved, although MRI during surgery has limitations that make its use in all surgeries impossible[8].

Different ultrasound techniques have different uses in tissue diagnosis. For example, doppler ultrasound can

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help the surgeon by identifying vessels in the surgical field [6].

Materials and methods:

This study was done prospectively, in Rasul Akram and Shahada-ye-Haftam Tir hospitals, which work under the supervision of Iran University of Medical Sciences. Researchers evaluated patients with brain tumors between 2019 and 2022. Two neurosurgeons and an emergency medicine specialist with a degree in ultrasound worked together to perform the resection. To select the samples, they initially chose 33 patients with intra-axial brain tumors. Then, the decisions of two neurosurgeons were collected regarding the possibility of gross total resection of tumors in these cases. As a result, 3 patients were excluded from the study, and 30 patients were included. Simple random sampling was used to select patients that had inclusion criteria. The conditions of the study and the procedures performed for the patient during and after surgery were explained to patients and their families, and written consent was obtained from the patients. According to the type of study, $\alpha = 0.05$ and power $(\beta\text{-}1) = 0.95$ were considered. Due to its similarity of Peterdis et al. research with our study, this research was chosen as a criterion for calculating the sample size (2). With Cochran formula, the sample size considered for this study was determined to be 20 people. The study plan approved in University Research Ethics Committee and relevant code was obtained (IR.IUMS.FMD.REC.1399.592). To collect data, a form was designed to record cases in pre-made forms. After checking and recording the data, statistical analysis was performed using SPSS software.

Ultrasound device features:

We used SonoSite convex ultrasound probe with bandwidth of 10-3 MHz and scan depth of 3 to 18 cm. The advantages of the convex ultrasound probe are wider field of view and possibility of observing deep structures.

Imaging review and treatment strategy:

The patient with a brain tumor was admitted, and initial imaging was conducted. Before the surgery, the approximate location of the lesion on the skin was determined based on MRI. A skin incision and craniotomy were then performed. At this stage, the ultrasound probe with a sterile cover was entered into the surgical field before opening the dura. The exact location of the tumor was determined over the dura, and then the dura was opened. The location of the lesion was determined with the ultrasound guide, and the resection of the lesion started. Then, ultrasound was performed during removal of tumor to determine the tumor borders, and surgery continued until gross total resection of the lesion based on IOUS. After the resection based on ultrasound, hemostasis was performed, and the dura and surgical site were closed. Within 72 hours after the surgery, an MRI was performed to assess the extent of resection.

Calculation of tumor volume:

MRI images were evaluated to measure the tumor volume. The tumor area in all MRI imaging slices was added together and multiplied by the slice distance. The amount of resection was calculated by comparing the volume of the tumor before and after surgery (Figure 1) [9,10].

Results:

Twenty-three patients were selected for the study. Three patients died after surgery and during hospitalization, so they were not included in the study. The characteristics of the patients are listed in table 1. In this study, there were 7 women and 13 men, with an average age of 45.3 years. Most of the patients were middle-aged adults. Regarding the alertness and functional status of the patients, the average Glasgow Coma Scale (GCS) was 13, and the median GCS of the samples was 15. The minimum GCS was 9, corresponding to a 58-year-old man with recurrent glioblastoma. Additionally, the median Karnofsky Performance Status (KPS) of the patients was 80.

Most of lesions were observed in the frontal lobe, predominantly on the left side. In 35% of patients (7 patients), the tumor was located in the eloquent area, and the lesion had an ill-defined margin in 18 patients (90%).

In alive patients, the average length of surgery was 3 hours, with a minimum of 1.5 hours and a maximum of 5 hours. The average intraoperative bleeding was 344 Cubic Centimeters (cc). Also, in examining the consciousness, the average GCS was 10 one hour after surgery, 12 six hours after surgery, and 13 twenty-four hours after surgery. The average length of hospitalization for alive patients with intra-axial mass was 10 days.

The size and amount of tumor resection were calculated based on pre- and post-surgical imaging. The mean size

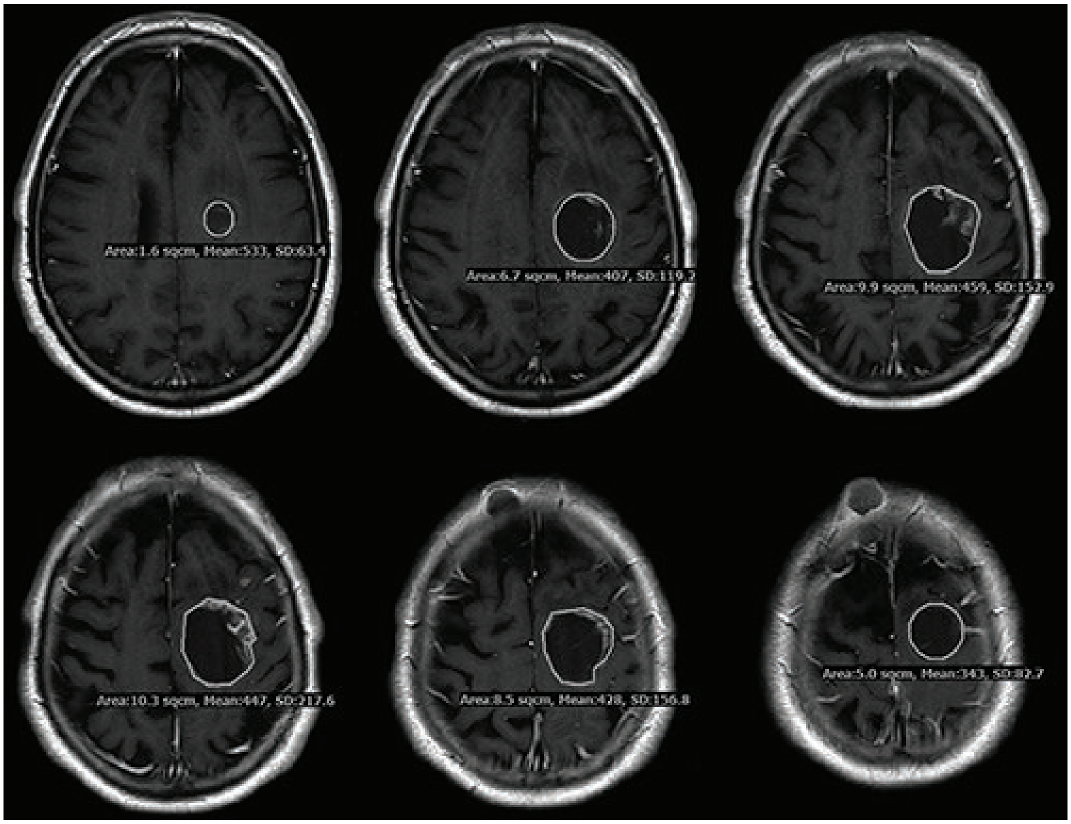

Figure 1: *To calculate the tumor volume, the tumor areas in consecutive sections were added together, and then multiplied by the distance between the cuts. For example, in the bellow patient, the sum of the tumor areas was 42 square centimeters, and the distance between cuts was 0.6 centimeters. Therefore, the volume of the tumor was 25.2 cc.*

of the tumor in pre-surgical imaging was 31 cc. The smallest tumor was 1.5 cc in a 52-year-old woman with complaints of convulsions, whose lesion was located in the left frontal lobe and had glioblastoma pathology. No lesions were observed in imaging after surgery. The largest tumor was 74 cc in a 52-year-old man with agitation and urinary incontinence. Imaging showed butterfly glioma of the frontal lobe. In the post-surgery imaging, 56.5% of the tumor was resected.

In the post-surgical imaging, the average tumor size was 4.5 cc. In evaluation of extension of resection, an average of 89.3% of the tumor was resected. The largest residual tumor, measuring 32 cc, was found in a patient with a butterfly glioma in the frontal lobe.

The amount of resection was divided into three categories based on the extent of resection: gross total resection (GTR) with a removal rate of over 95%, subtotal resection (STR) with a removal rate between 80 and 95%, and partial resection (PR) with a removal rate below 80% (11). According to this classification, there were two patients with partial resection in the study.

Fourteen patients were extubated in the operating room, while the reason for non-extubation in other patients was low GCS. We found that GTR is related to the amount of dysphagia experienced by the patient after surgery (Table 2). Furthermore, the study revealed that women had a higher rate of extubation compared to men. All 7 alive women in the study were extubated in the operating room, whereas only 7 out of 13 alive men were extubated during surgery. The study did not find any significant correlation between overall complications and amount of tumor resection and bleeding, and hospitalization of patients, which could be due to the small number of samples (Table 3). However, more studies are necessary to conduct a more comprehensive investigation.

Table-I

Characteristics of patients and tumors

Characteristics	Alive	Expired
Patients	20	3
Gender		
……… Male	13	2
……… Female	7	1
Age	45.3 ± 15.9	54.6 ± 15.2
……… Male	49.3 ± 16.1	48 ± 14.1
……… Female	37.7 ± 13.4	68
GCS *		
…….. Preoperative	13 ± 2	10 ± 1
…….. Postoperative (after 24 hours)	12 ± 3	8.3 ± 2
Primary KPS †	77 ± 22	50 ± 10
Duration of operation (Minutes)	182 ± 54	173 ± 91
Operation bleeding volume (cc ‡)	344 ± 137	516 ± 275
Eloquent area tumor (Number of patients)	7	2
Tumor Volume (cc)		
………. Preoperative	31.2 ± 22.7	49.1 ± 5.9
………. Postoperative	4.5 ± 7.4	9.6 ± 5.7
Tumor resection percentage	89.3 ± 9.7	80.1 ± 12.9
Extend of resection		
………. GTR § (over 95%)	6	0
………. STR ** (over 80% & under 95%)	12	2
………. PR †† (under 80%)	2	1

* Glasgow Coma Scale
† Karnofsky Performance Status
‡ Milliliter
§ Gross total resection
** Subtotal resection
†† Partial resection

Table-II

Surgery outcome and complications in alive patients

Number of patients	20
Dysphagia	2
Paresia or Plegia	4
Hematoma	0
Cardiac complications	0
Meningitis	1
Seizures	3
Deep vein thrombosis	0

Table-III

Relation of tumor resection extension and new neurological deficit, intraoperative bleeding and hospitalization day

		Residue of tumor < 1.5 cc	Residue of tumor > 1.5 cc	p value
New FND*	No	6	11	0.306
	Yes	2	1	
Intraoperative bleeding	< 300 cc	5	7	0.852
	> 300 cc	3	5	
Hospitalization day	< 7 days	3	7	0.361
	> 7 days	5	5	

* Focal neurological deficit

Discussion:

This study involved 20 patients diagnosed with glioma, who underwent gross total resection with ultrasound-guided surgery. In patients with glioma, average mass resection under ultrasound guidance was 89.3%. A study by Kaisorn et al. involving patients with GBM who underwent surgical resection with the help of intraoperative mapping and navigation found a mass resection rate of 91.7% (12). In Ammirati et al.'s study, 31 patients underwent surgical resection of glioblastoma and anaplastic astrocytoma. In their study, 61% of patients had a resection of more than 90%, which was considered as GTR, while in the current study, 70% of patients had more than 90% resection of the mass (13). Additionally, in Simpson et al.'s study, which involved 645 patients, GTR was performed in 19% of patients (3). These results showed that the use of ultrasound during surgery can improves the resection rate of glioma tumors.

Regarding complications after surgery, Kaisorn's study found that patients who underwent surgery with the help of intraoperative mapping and navigation had motor deficits observed in 2% of patients and verbal deficits in 1% of patients (12). In the current study, new paralysis, and speech defects following resection were found in 15% of patients. According to Vives et al.'s study, new defects in glioma surgery without intraoperative monitoring and navigation have been reported between zero and 19% (14). In the current study, the rate of meningitis after surgery was one case, and the patient was discharged after treatment. According to Jackson's study, the rate of meningitis after surgery has been reported between 0.5 and 1% (15). Also, in Jackson's study, the overall rate of infection was reported to be 1 to 3%. No other infection occurred in the current study. Based on these results, the neurological complications of surgery under ultrasound guidance are higher than surgeries under intraoperative mapping guidance.

In Kaisorn's study, where patients underwent surgery with the help of intraoperative mapping and navigation, the average number of days the patients stayed in the hospital was 4 days (12). In the current study, the average stay of patients was 10 days, which was significantly different from Kaisorn's study ($p<0.05$). The patients in this study had an average of 344 cc of bleeding during the surgery, and the duration of the surgery was 180 minutes. In contrast, in Rajagopalan et al.'s study, which investigated the effect of bleeding on surgical results in brain tumor patients, the average bleeding was 915 cc. Additionally, in Rajagopalan study, the average duration of surgery was 331 minutes (16). The reason for the decrease in operation time and bleeding can be attributed to the localization of the opening of the dura and determining the location of the tumor, which causes the surgical field to be smaller than usual, and thus the amount of bleeding and surgery time are reduced. But this difference was not significant, which could be due to the small number of samples.

One of the uses of intraoperative ultrasound is to detect the ventricles located on the periphery of the tumor and prevent accidental entry into the ventricle during surgery. This helps to avoid significant complications, such as ventriculitis. One reason why complete resection was not possible in some patients was the long time between preoperative imaging and surgery, which caused some tumor foci to be missed during surgery.

Conclusion:

Ultrasound can be used as a modality in brain tumor surgery due to its ease of use, affordability, and ability to identify surrounding areas of the tumor. However, it should not be considered a replacement for other monitoring modalities during surgery. Nonetheless, its use can be advantageous for the patient.

Conflict of interest

The Authors declare that there is no conflict of interest.

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