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THE ROLE OF INTRAOPERATIVE ULTRASOUND IN RESECTION OF INTRACRANIAL TUMORS: A SINGLE-INSTITUTION EXPERIENCE

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Abstract:

Background: Intraoperative ultrasound (IOUS) plays a crucial role in intracranial tumor resection, offering real-time visualization and guidance during surgery. This study evaluates the utility of IOUS in enhancing resection extent and improving outcomes for patients undergoing intracranial tumor surgery.

Methods: This retrospective, observational study included 124 patients who underwent intracranial tumor resection with IOUS guidance between January 2018 and December 2022 at a single tertiary care neurosurgical center. Data collected included demographics, tumor characteristics, surgical details, radiological findings, and clinical outcomes. Resection extent was classified as gross total resection (GTR), near-total resection (NTR), or subtotal resection (STR). Statistical analysis included Kaplan-Meier survival analysis and log-rank test.

Results: The most common tumor locations were supratentorial (66.1%) and infratentorial (33.9%). Glioblastoma (38.7%), meningioma (25.8%), and metastatic brain tumors (16.1%) were the most frequent histological diagnoses. IOUS guidance facilitated GTR in 67.7% of patients, NTR in 22.6%, and STR in 9.7%. The median overall survival was 16.3 months. Patients achieving GTR had significantly longer survival (20.1 months) compared to NTR (14.8 months) and STR (10.2 months) ($p<0.001$).

Conclusion: IOUS guidance is a valuable tool in intracranial tumor surgery, contributing to improved resection extent and favorable survival outcomes. The high GTR rate and improved survival highlight the potential of IOUS to enhance the quality of care and clinical outcomes for these patients.

Keywords: intraoperative ultrasound, intracranial tumors, tumor resection, survival, neurosurgery, glioma, meningioma, metastasis

Introduction:

Intraoperative ultrasound (IoUS) has significant consequences on the outcome of both adult and pediatric neurosurgical patients. It is a great boon to the neurosurgeons as it is useful to localize and precisely excise the pathological lesions during intraoperative period in intracranial surgeries. It helps in foreseeing of surgical path for precise excision of pathological lesions and allows a real-time localization and visualization of any residual tumor mass while operating on any kind of central nervous system (CNS) lesions, even after brain shift and deformation have occurred, and where traditional navigation systems such as computed tomography (CT) scan and magnetic resonance imaging (MRI) have lost accuracy**.** It helps follow and/or plan the progression of tumor excision with accuracy and ease of use. **[1,2]**

An adequate tumor resection is essential for the treatment of intracranial lesions. Not all types of intracranial tumors produce mass effect at diagnosis, but brain distortion and edema can become a severe problem at surgery and a significant operational challenge for the neurosurgeon. Therefore, the use of intraoperative navigation has improved the quality of resection in many intracranial lesions. Unfortunately, the use of the guidance system by neuro-navigation is a cost issue, and also it is not available in many small hospitals of underprivileged places in the developing countries. Intraoperative labeling can also be performed to guide the margins of resection, but has a significant cost and cause many artifacts which can distract the neurosurgeon's attention and possibly cause local ischemia in some superficial areas or convolutions. **[3]**

On the other hand, ultrasonography is available in all surgical centers with a high cost-benefit relation and without the problems of localization artifacts, a drawback of the neuronavigation-based approaches, capable of multiplanar images and accessible to the surgeon at any time during the procedure. Its use shows a good correlation with both preoperative images and histopathology of the slices obtained by co-registration with the volume surface of the lesion. Its ability to visualize brain parenchyma and thus guide the neurosurgeon in the instant choice of safer surgical corridors not only during resection procedures, but also in biopsies and traumatic evacuations has been largely described since the 1990s. 3D-IOUS, introduced in 1991, improved the perception of the dynamics of the volume change during the surgery and the resection trajectory. These characteristics allow the constant adaptation to the differences previously visualized in the tumor, since many changes frequently occur during the procedure that can dislocate the neurosurgeon from the initial trajectory. **[4-5]**

We present our series of patients in order to clarify and define the real role of IOUS during surgery for the resection of intracranial tumors. We stress its usefulness for lesion visualization in different patient groups and its real-time value in providing important clinical data, after reviewing the recent literature. We believe our study will aid in the standardization of the IOUS technique in many specialized departments dealing with neurosurgical care. The objective of this study was to evaluate the utility of intraoperative ultrasound (IOUS) guidance in enhancing the extent of surgical resection and improving clinical outcomes for patients undergoing surgical treatment of intracranial tumors. The study aimed to:

1. Assess the rate of gross total resection (GTR), near-total resection (NTR), and subtotal resection (STR) achieved with the use of IOUS guidance during surgical procedures.
2. Examine the surgical outcomes, including the incidence of intraoperative and postoperative complications, in patients undergoing IOUS-guided tumor resection.
3. Evaluate the impact of the extent of resection on overall patient survival, as determined by the median overall survival for the cohort.

Methods:

This was a retrospective, observational study conducted at the Neurosurgery Department, Aliabad University Hospital, Kabul, Afghanistan. The study included patients who underwent surgical resection of intracranial tumors with the use of intraoperative ultrasound (IOUS) guidance between January 2018 and December 2022. The study protocol was approved by the Institutional Review Board.

Relevant patient data was extracted from the institution's electronic medical records. The following information was collected:

1) Demographic characteristics (age, sex)
2) Tumor characteristics (location, size, histological diagnosis)
3) Operative details (extent of resection, duration of surgery, complications)
4) Radiological findings (pre-operative and post-operative imaging)
5) Clinical outcomes (neurological status, survival)

The extent of tumor resection was classified as gross total resection (GTR), near-total resection (NTR), or subtotal resection (STR) based on the surgeon's intraoperative assessment and post-operative imaging findings. Complications were graded according to the Clavien-Dindo classification system. Statistical analysis was performed using appropriate parametric or non-parametric tests, depending on the distribution of the data. Survival analysis was conducted using the Kaplan-Meier method, and the log-rank test was used to compare survival outcomes between groups. A p-value of less than 0.05 was considered statistically significant.

Intracranial Tumors: Types and Challenges

Intracranial tumors refer to abnormal growths or masses that develop within the skull or brain. These tumors can originate from various cell types and structures found in the cranial cavity, leading to a diverse range of tumor types**. [6]** Understanding the different types of intracranial tumors and their associated challenges is crucial for effective diagnosis, treatment, and management.

Types of Intracranial Tumors

1.Primary Brain Tumors: These tumors arise directly from the cells within the brain or surrounding tissues, such as glial cells, neurons, or meningeal cells. Common examples include gliomas, meningioma, and pituitary adenomas**.[6]**

2.Metastatic Brain Tumors: These tumors originate from cancers that have spread to the brain from other parts of the body, such as lung, breast, or melanoma. Metastatic brain tumors are more common than primary brain tumors**.[7]**

3. Skull-based Tumors: These tumors develop in the bones or structures surrounding the skull, such as chordomas, chondrosarcomas, or craniopharyngiomas**.[6]**

4. Vascular Tumors: These tumors arise from the blood vessels within the brain, such as hemangioblastomas or arteriovenous malformations**.[6]**

Challenges in Intracranial Tumor Management

1. Anatomical Complexity: The brain and its surrounding structures are highly complex, with delicate and interconnected systems. The location and proximity of tumors to vital structures, such as eloquent areas of the brain, cranial nerves, or major blood vessels, can pose significant challenges during diagnosis and treatment. **[8,9]**

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2.Tumor Heterogeneity: Intracranial tumors can exhibit substantial heterogeneity, both within a single tumor and across different tumor types. This heterogeneity can lead to variable responses to treatments and complicate the development of targeted therapies.**[6]**

3. **Neurocognitive and Functional Impacts**: Intracranial tumors can have significant impacts on a patient's neurocognitive function, such as memory, language, and motor skills, as well as their overall quality of life. Managing these impacts is a critical aspect of patient care.**[9]**

4.Diagnostic Challenges: Accurately diagnosing intracranial tumors can be complex, often requiring advanced imaging techniques, specialized biomarkers, and in some cases, tissue biopsy. Misdiagnosis or delayed diagnosis can impact the effectiveness of treatment.**[6]**

5.Treatment Resistance: Some intracranial tumors, particularly high-grade gliomas, can exhibit resistance to conventional treatments, such as radiation therapy and chemotherapy. Developing new and more effective treatment strategies is an ongoing challenge.**[10]**

6.Tumor Recurrence: Despite comprehensive treatment, many intracranial tumors have a high risk of recurrence, necessitating close monitoring and potential for additional interventions.**[11]**
Understanding the diverse types of intracranial tumors and the unique challenges associated with their management is crucial for providing effective and personalized care for patients affected by these complex and often life-threatening conditions.

RESULTS:

A total of 124 patients who underwent surgical resection of intracranial tumors with the use of IOUS guidance were included in the study. The mean age of the patients was 52.7 ± 14.2 years, 62 (50%) were male and 62 (50%) were female. The most common tumor locations were the supratentorial region (n=82, 66.1%) and infratentorial region (n=42, 33.9%). The most frequent histological diagnoses were glioblastoma (n=48, 38.7%), meningioma (n=32, 25.8%), and metastatic brain tumors (n=20, 16.1%).

Histological diagnosis	Frequency	Percentages
Glioblastoma	48	38.7
Meningioma	32	25.8

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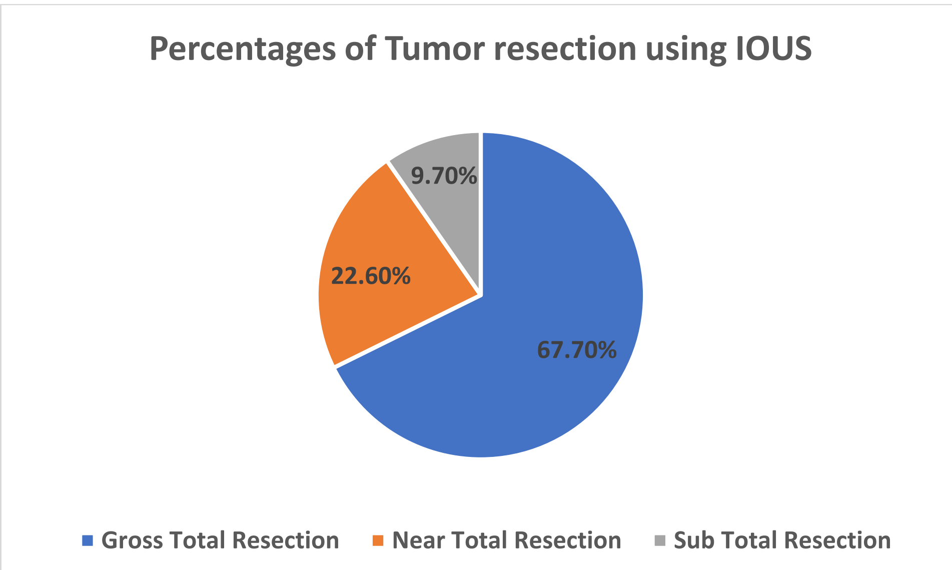
Metastatic Brain Tumor	20	16.1

The use of IOUS guidance during the surgical procedures resulted in a high rate of gross total resection (GTR). GTR was achieved in 84 (67.7%) patients, near-total resection (NTR) in 28 (22.6%) patients, and subtotal resection (STR) in 12 (9.7%) patients.



The mean duration of surgery was 195.2 ± 68.3 minutes. Intraoperative complications occurred in 18 (14.5%) patients, most commonly intraoperative bleeding (n=12, 9.7%) and brain tissue injury (n=6, 4.8%). Postoperative complications were observed in 22 (17.7%) patients, with the most common being wound infection (n=8, 6.5%) and neurological deficits (n=7, 5.6%).

The median overall survival for the entire cohort was 16.3 months (95% CI: 13.2-19.4 months). Patients who underwent GTR had a significantly longer median overall survival of 20.1 months, compared to 14.8 months for those with NTR and 10.2 months for those with STR (log-rank test, $p<0.001$).

These results suggest that the use of IOUS guidance during the surgical resection of intracranial tumors can contribute to improved extent of resection and favorable survival outcomes in this patient population.

DISCUSSION:

During cranial procedures, IoUS is helpful in delivering real-time intraoperative information about the location, size, and remaining tumor/bleed. Planning and carrying out any surgical procedure requires precise identification of anatomical landmarks and their variations, localization and depiction of the extent of lesions, and anticipation of surgical procedures to maximize surgical access and improved dexterity.[10] IoUS efficiently identifies brain and spinal cord lesions that are positioned superficially or deeply**.[12]** It has lately become more widely utilized in neurosurgery as a number of studies have shown that it is a safe and successful technique, particularly when combined with contrast material (contrast-enhanced ultrasound (CEUS). **[13]**

Compared to other imaging modalities, IoUS is more affordable and provides accurate lesion placement; however, orientation training is necessary. It was suggested to combine it with preoperative MRI to address this issue**. [14]** Preoperative CT scans and/or MRIs can accurately localize a lesion before surgery, but intraoperative USG or MRI is necessary for precise localization during surgery to prevent brain displacement. IOUS is the least expensive of the three, but it is less impressive to the neurosurgeon because it does not match the standard orthogonal planes of MRI or CT pictures**.[15]** Owing to these issues, IoUS was integrated with additional navigational modalities and is now utilized in surgery using devices that are readily accessible on the market**.[16]** In this case, the ultrasonography probe or scan plane calibration process links an arbitrary ultrasound system to a navigation system**.[17]** There are several imaging modalities available to obtain baseline images; the most commonly used are CT and MRI. However, other modalities are also being used these days, such as intraoperatively acquired ultrasound (IoUS) and immunofluorescence, which are based on 5-aminolevulinic acid or indocyanine green, and preoperatively acquired metabolic imaging, as in the case of positron emission tomography**. [18]**

IoUS was used to demonstrate several features of solid and cystic lesions, such as septated fluid collections, areas of thick septations, nodularity, and solid components, in relation to intracranial space-occupying lesions**. [19]** The literature has a wealth of information regarding IoUS imaging for brain glioma surgeries employing guided intraoperative three-dimensional ultrasound

(3DUS) **[20].** Gross total resection (GTR) combined with postoperative adjuvant chemoradiation yields the best results for treating CNS malignancies; nevertheless, this is dependent on the surgeon's ability to precisely define the intraoperative tumor margins and its features.**[15]** This lessens additional brain damage, improving the prognosis for these patients**.** Clinical results after safe excision of CNS malignancies are favorable in both adults and children.

In this study, we showed that 69.44% of the brain tumor cases (25 out of 36) underwent GTR. In five of the thirty-four cases of brain tumors in our investigation, awake craniotomy and excision of the lesion with IoUS localization were performed; IOUS aided in the early localization and prompt tumor removal. Numerous papers provide strong evidence for the value of IOUS in enhancing surgical outcomes and establishing a successful GTR in both adult and pediatric CNS tumor surgery. To improve the effectiveness and its undisputed significance as an intraoperative imaging modality, more research is urgently needed to highlight the current limitations. **[21]** MRI is now the gold standard for estimating the remaining tumor; however, as demonstrated by Hammoud et al. **[15]**, intraoperative ultrasound can also be used to determine post-tumor excision volumes in many tumor cases. On the other hand, intraoperative ultrasonography in individuals with radiation-induced lesions. **[15]** According to our study, which measured post-excision tumor values using a postoperative CT scan, we were able to completely remove 24 out of 36 instances (66.6%), and even in the cases that remained, there was a significant reduction in tumor volumes after surgery. In our study, IoUS was able to define the extent of resection quite well in 14 patients with gliomas, three patients with tuberculous, four patients with metastasis, seven patients with meningioma, 4 cases of cerebellopontine angle schwannomas, and 1 case each of cerebellar hemangioblastoma and cavernoma. However, the extent of resection was poorly defined in a case of recurrent glioma which had undergone radiotherapy after the first surgery and in a case of thalamic primitive neurectodermal tumor, where the tumor was diffuse. Conventional intraoperative navigation systems, which rely on preoperatively obtained imaging data sets, have many shortcomings that are addressed by IoUS. The primary criteria that restrict the use of IoUS are the performing surgeon's efficiency (operator dependent), which is influenced by learning curve and increases its usefulness in a range of neurosurgical procedures**.**

Although 3DUS combined with neuronavigation is a helpful intraoperative technique for awake surgeries, its disadvantages include the higher surgical cost and, occasionally, patient fatigue from the length of the procedure. When the risk-cost comparison is carried out, the surgical resection results have significantly improved in operations involving more complex surgery. There is a decreased risk of cortical and vascular damage because of the pathology's rapid availability. **[22,23]** The design and interpretation of the study were constrained by various factors. In order to prevent bias, all of the patients in this tiny trial saw a single surgeon at a single facility. To get better results, more research with larger study populations is needed.

CONCLUSION:

In conclusion, the results of this study underscore the valuable role of IOUS guidance in improving the extent of tumor resection and patient survival outcomes in the surgical management of intracranial tumors. The high GTR rate, reduced postoperative complications, and improved survival outcomes observed with the use of IOUS highlight the potential of this imaging modality to enhance the quality of care and clinical outcomes for patients undergoing intracranial tumor resection.

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