Basic Principles of Intraoperative Ultrasound Applied to Brain Tumor Surgery

Javier A. Jacobo¹, Javier Avendaño¹, Sergio Moreno-Jimenez¹, Santiago Nuñez¹, Rocio Mamani¹

¹Department of Surgical Neuro-Oncology, National Institute of Neurology and Neurosurgery, Mexico City, Mexico

Address for correspondence Javier A. Jacobo, Department of Surgical Neuro-Oncology, National Institute of Neurology and Neurosurgery, Insurgentes Sur 3877, La Fama, Mexico City 14269, Mexico (e-mail: jacoboncx@gmail.com).

Abstract
Intraoperative ultrasound (US) has been shown to possess great value in assessing tumor volume and localization, especially for primary resection of gliomas and metastatic lesions. Given that US is a technology that is highly user dependent, many surgeons have encountered problems with the usage of this technology, as well as interpretation of intraoperative US images, limiting its full potential. This article focuses on the basic knowledge a neurosurgeon must acquire to properly use and interpret intraoperative US to improve tumor localization and extent of resection during brain tumor surgery.

Keywords
► basic principles
► ultrasound
► neurosurgery
► neuro-oncology

Introduction
Ultrasound (US) was first introduced in the 1920s by Loomis and Wood, who described its biological effects on living tissue.¹ Since then, this technology has been applied to multiple fields of medicine including neurosurgery.

The first US usage in neurosurgery was reported by the Dussik brothers, who attempted to use it to identify brain tumors.² It was not until 1978 that ultrasonography was first used to aid in the surgical resection of a central nervous system (CNS) tumor.³ Advances in ultrasound imaging have made it popular in the common practice in recent years, making it a very valuable tool for identifying the tumor and aiding in its total resection.⁴⁻⁵

This article will focus on the basic principles and techniques a neurosurgeon must know to perform an adequate US-guided surgery for the resection of a brain tumor, based on the experience acquired by the group of Surgical Neuro-oncology in the National Institute of Neurology and Neurosurgery.

Basic Principles of Ultrasound
Sound is created when a vibrating source comes in contact with a medium, causing it to vibrate. The mechanical energy, which is generated from the vibrations, travels in a longitudinal wave through the medium, generating cyclical areas of high and low pressure, known as compressions and rarefactions. US is considered as the frequencies that exceed the limits of human hearing, or 20 kHz. Modern US systems typically use frequencies between 2 and 10 MHz.⁶ Frequencies differ when different tissues are targeted; greater frequencies offer better imaging at the surface, while lower frequencies are used when a target lies deeper within the tissue.⁷

Sound travels at different speeds through different media. In diagnostic US, human tissue is the medium in which sound travels. By comparison, the propagation velocity of air is quite slow, 440 m/s, and in bone, it can be as high as 5,000 m/s. The basis of diagnostic US is the pulse-echo technique in which small bursts of sound are transmitted into the tissue, and the reflected echoes are then measured.⁷⁻⁸

As previously mentioned, US relies on echoes emitted by a transducer, which are then reflected by various tissue interfaces of different density. The intensity of the echo received by the same transducer is used to calculate the brightness of the specific reflector, whereas the position and space is defined by the time sound needs to travel from emission to reception. This means that the image recreated on the screen is the result of calculations done by the software of the machine, rather than a photograph being projected.⁷⁻⁹
The received echoes can be displayed in the following two modes: A-Mode which is projected in a linear graph, or the so-called brightness mode or B-Mode, which displays the brightness of the echoes throughout an entire section; fast image update in a real-time fashion provides a film-like presentation of a cross-sectional view of the imaged region.\(^9\)

**Indications for Intraoperative Ultrasound**

Just like many other technologies, intraoperative US should be used with rationale and applied to specific cases.

In neuro-oncology, there are three main applications: tumor localization, evaluation of the extent of resection, and assessment of vascular supply or patency of venous sinuses.

All of these indications will be discussed in detail as the article goes on.

**Imaging Interpretation and Technique for Adequate Image Acquisition**

The echogenicity of the tissue refers to the ability to reflect or transmit US waves in the context of surrounding tissues.\(^10\) Whenever there is an interface of structures with different echogenicities, a visible difference in contrast will be apparent on the screen. Based on echogenicity, a structure can be characterized as hyperechoic (white on the screen), hypoechoic (gray on the screen), and anechoic (black on the screen).\(^11\) In the gray spectrum that appears on the screen on B-Mode, the softer the medium is, the darker the image will appear (\(\text{Fig. 1}\)). This way, it is possible to differ from cystic lesions all the way to calcified lesions within the brain parenchyma.

Some structures are easily recognizable because of their distinct echogenicity: naturally hyperechoic structures are the dural folds, choroid plexus, and pineal gland (depending on degree of calcification). Normal brain tissue will be isoechoic. Hypoechoic and anechoic structures include the brainstem and cerebrospinal fluid (CSF)-filled cavities.

One must keep in mind that during surgery, abnormal tissue will be encountered. Lesions like solid tumors, calcifications, and some gliomas will appear hyperechogenic in relation to healthy tissue on the screen (\(\text{Fig. 2}\)). Cystic lesions or the necrotic part of a glioblastoma will appear hypoechoic in relation to healthy tissue (\(\text{Fig. 3}\)).\(^{12-14}\)

Adequate technique and placement of the transducer is of crucial importance to reliably discriminate the images obtained through the procedure.

Choosing of the probe for the desired space and lesion is important; the most commonly used probe in cranial surgery is a 30 × 12 mm probe with frequency of 7 MHz, as this provides a good balance between resolution and penetration.\(^12\) It is important to state that the craniotomy should be of a large enough size to accommodate the probe and facilitate the technique.

Before starting, some default settings are helpful in obtaining a better image during the procedure. Initiate by activating the “tissue harmonic intensity” option to improve image quality, then adjust image gain until the region of interest shows optimal brightness; finally, adjust the zoom on the device, start with zoom out, and then gradually zoom in until the image on the screen is large enough.\(^12\)

After choosing the adequate probe and the US setting is in place, the next step is to adequately place the transducer.
It should be held so that the external notch is facing the patient’s anatomic right in a cross-sectional view or toward the head in a longitudinal view. In this way, the surgeon can reliably assess where the lesion is displayed in the B-Mode and also make adjustments during the procedure.

An important concept to keep in mind is the angle of incidence; this is the angle at which the waves encounter the surface of the examined tissue. The more perpendicular the transducer is placed to the surface of the brain, the less waves will be scattered and the better the image will be seen on the screen. Image resolution can be improved by tilting the transducer, thus adjusting the angle of incidence.

The morphology of the image will change depending on the position of the transducer in relation to the surface of the brain. The scanning planes are similar to the familiar anatomical planes; if the transducer is placed in a horizontal position in the lateral convexity of the brain, the obtained image will resemble that of an axial view in the magnetic resonance imaging (MRI). If the transducer is positioned vertically in the lateral convexity, a somewhat coronal view will appear on the screen. Finally, to obtain a sagittal view, the transducer would have to be located parallel to the sagittal sinus in the superior convexity of the surface of the brain.

The depth of the target lesion within the brain is a variable that must be considered in choosing the right probe for the study. High-frequency probes will give better resolution for superficial structures, while low-frequency probes are better suited for examining deeper structures, for example, when assessing periventricular lesions.

Probe manipulation is another important skill that should be mastered to properly perform an intraoperative ultrasonography.

In addition to adequately placing the transducer to obtain the desired plane of view, as it was previously mentioned, there are additional movements that will help to better visualize the target lesion and improve localization.

First, depending on the anatomical site being evaluated, slight pressure on the surface can improve image quality. It affects the echogenicity of the tissue and shortens the distance to the structure of interest.

Sometimes, the lesion is not perfectly aligned with the initial plane of view, that is, while realigning the probe on the surface may allow for a better image, this can be achieved by sliding or rotating the probe until the image seen on the screen is sufficient to proceed with the procedure.

Finally, tilting the probe may also improve the quality of the image by achieving a view of the short axis of the lesion in question, and this may also give a clue for the surgical route.

**Discussion**

**Intraoperative Ultrasound in Neurosurgery**

The use of US for the resection of brain tumor was implemented since the 1980s; one of the first reports of tumor visibility in US was done by Le Roux et al in 1992, who described that most tumors, including high- and low-grade gliomas, were visible during surgery using common US probes.

As it is known, one of the primary goals for tumor surgery is gross total resection (GTR) of the lesion, as it has been established that resection over 95%, or even 75% of the enhanced lesion, will result in improvement in overall survival (OS) and progression-free survival (PFS).

Intraoperative navigation technology has aided immensely in this field, providing better accuracy in tumor location
and providing tumor margins to both improving grade of resection and preserving healthy tissue. These benefits can be limited however by brain-shift, in which structures change shape and position as a result of intraparenchymal swelling, gravity, tumor resection, CSF drainage, and other factors; this shift has been estimated to be as much as 11 to 12 mm.26 One of the many strategies to improve accuracy during navigation is the use of intraoperative US.

Intraoperative US has been proven to be of great value in assessing tumor volume, and localization, especially for primary resection of gliomas and metastatic lesions.20,21

In addition to providing a reliable real-time image of the surgical field, intraoperative US can also be used to estimate brain-shift and provide correctional strategies to the surgery.22

Petridis et al performed a retrospective study to show the importance of intraoperative US in locating tumors. Thirty-four patients who were taken into surgery for a low-grade glioma were studied. The authors reported that 100% of the tumors were located using a combination of intraoperative US and MRI neuronavigation.5

Another way that tumor localization by US is of value is the capacity to perform needle biopsies. US-guided biopsies can be performed even in deep locations because the real-time image provided will help to place the needle safely in the place of interest.23

The extent of resection (EOR) can also be improved using intraoperative US. Historically, great discrepancy has existed between surgeon estimate of the EOR and actual EOR measured by postoperative MRI, which states that the EOR is overestimated by the surgeon in most of the cases.24 This is why intraoperative aids such as US have gained much attention in the past few years.

In one study comparing assessment of residual tumor using intraoperative US and intraoperative MRI, it was revealed that intraoperative US could reliably detect up to 1 cm of residual tumor, and by doing so, improve the EOR.25 Another study with 45 patients concluded that US can be used to maximize EOR, given that it could detect residual tumor with high-sensitivity.21 Even so, intraoperative US for assessing EOR should be used with care, given that many variables could affect image quality and give false imaging as a result of acoustic enhancement artifact from saline and clotted blood in the resection cavity, both of which can appear hyperechoic on US.26 Another study showed up to 89% concordance with histopathology in hyperechoic areas, which clearly extended into the isoechogenic brain parenchyma, but only 56% concordance along the hyperechoic rim of the resection cavity.26 These results show that although US is a valuable tool to improve the EOR, it should be interpreted carefully and aided by other technologies.

With regard to EOR, a recent meta-analysis that included several studies with a total of 739 patients showed an average EOR of 79%, stating important heterogeneity among the studies. Statistical analysis showed concordance of 89% between postoperative MRI and intraoperative US, with false-positive and false-negative results of 9%.27

A second meta-analysis by Zhang et al included 37 articles, mainly developed in China, and established the sensitivity and specificity for intraoperative US to detect residual tumor of 89% and 91%, respectively.28

Table 1 shows a summary of the published articles that study the impact of intraoperative US on EOR.

Recently, a study was published by Munkvold et al that found several factors associated with the capacity of intraoperative US to detect residual tumor during surgery. They determined that tumor volume and tumor depth were the main factors that influenced the sensitivity for intraoperative US to detect residual tumor; small superficial tumors being more likely to be completely resected.29

One can infer that the impact of the usage of intraoperative US on the clinical course of patients with brain tumors is related to the ability to locate and better resect these lesions.

One study attempted to show the impact of intraoperative US on the OS of patients with high- and low-grade gliomas. The overall conclusion was that the usage of intraoperative US had a positive impact on OS of patients with both high- and low-grade gliomas.27

The neurosurgical applications of US will most likely vary in the future. With the development of new US transducers, contrast agents, and processing systems, this technique will most likely be used more frequently and in more ways than today.

Contrast-enhanced US is one of these new developments, and has been used widely in other fields such as surgery for the liver and kidney.30 This technique involves the injections of microbubbles that comprise an inert gas, such as perfluorocarbon or nitrogen, encapsulated in a layer of protein or polymers. These microbubbles are not affected in the lung

### Table 1: Impact of intraoperative ultrasound on the extent of resection

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number of patients</th>
<th>Mean % of extent of resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerganov et al</td>
<td>2009</td>
<td>25</td>
<td>80.8%</td>
</tr>
<tr>
<td>Chacko et al</td>
<td>2003</td>
<td>35</td>
<td>71.4%</td>
</tr>
<tr>
<td>Wang et al</td>
<td>2012</td>
<td>137</td>
<td>81.8%</td>
</tr>
<tr>
<td>Solheim et al</td>
<td>2010</td>
<td>142</td>
<td>74.5%</td>
</tr>
<tr>
<td>Liang et al</td>
<td>2013</td>
<td>80</td>
<td>86.2%</td>
</tr>
<tr>
<td>Tian et al</td>
<td>2009</td>
<td>88</td>
<td>76.7%</td>
</tr>
<tr>
<td>Sweeney et al</td>
<td>2018</td>
<td>260</td>
<td>81%</td>
</tr>
</tbody>
</table>
circulation and are able to cross into the arterial circulation, allowing to act as a contrast agent depending on the tumor vascularity and perfusion. Recently, many studies have been performed to establish the role of microbubbles in the field of brain tumor surgery; significant information has been obtained by a few studies, which showed that contrast-enhanced US can be used safely and allows for superior image quality.\textsuperscript{12-14}

Strain elastography is another feature of US technology that evaluates tissue macrostructure, as it compares characteristics of the ultrasound beam through tissue before and after compression, and so it is able to map tissue stiffness. Using this technology in combination with B-Mode US, a better differentiation of tumor and normal brain tissue can be achieved.\textsuperscript{31,35,36}

Although intraoperative US has been proved to be a very valuable tool, given its versatility, cost-effectiveness, and efficiency, it has limitations that cannot be ignored.

As it is well known that US is very user-dependent, image quality and restricted field of view are issues that limit accurate interpretation, especially for surgeons who lack proper training.\textsuperscript{31} Small lesions may also be challenging to detect. In addition, blood and hemostatic agents within the resection cavity can confound image interpretation.\textsuperscript{37}

Nevertheless, as previously mentioned, improvement in technology will lead to better image resolution and probe features; together with research into image analysis, it is anticipated that these hurdles will be overcome.

**Conclusion**

Intraoperative US is a very valuable tool that improves tumor location and resection in the field of neurosurgery; however, it is very important to understand the basics of US and the proper technique to obtain the benefits of this technology.

Given its versatility and cost-effectiveness, intraoperative US should be a tool that every neurosurgeon involved in the field of neuro-oncology should master to provide better care to patients.

**Conflict of Interest**

None declared.

**References**

1. Wood RW, Loomis AL. The physical and biological effects of high frequency sound waves of great intensity. Philos Mag Ser 7 1927;4(22):417–436
10. Pollard BA, Chan VW. Introductory Curriculum for Ultrasound-Guided Regional Anesthesia. Toronto, Canada: University of Toronto Press Inc; 2009


33 Wu DF, He W, Lin S, Han B, Zee CS. Using real-time fusion imaging constructed from contrast-enhanced ultrasonography and magnetic resonance imaging for high-grade glioma in neurosurgery. World Neurosurg 2019;125:e98–e109


