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Research Article

Real-Time Intraoperative Ultrasound Imaging in Intrinsic Brain Lesions; Enhancing the Surgeon, Benefiting the Patient: Literature Review and Case Series

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Abstract

Background and objective: Neuronavigation image guidance; an essential part of most neurosurgical operating room. Real-time intraoperative use of ultrasound imaging to localize nervous system lesions by neurosurgeons is becoming popular as a vital tool in neurosurgical manipulations, due to its efficiency and no known immediate or delayed harm to the human organism. It has over the years shown its advantages in imaging, low cost, minimal footnote and localizing Central nervous system lesions while minimizing damage to eloquent structures of the nervous system. Aim of this study is analysing the benefits of IoUS imaging in localizing lesions, enhancing maximum resection, with minimal or no neurological deficit, while overcoming post craniotomy brain shift, reporting 3 of our case experience.

Method: Literature search and 3 of our case experience using IoUS reported.

Result: IoUS made localization, resection and postoperative extent of resection in intrinsic brain lesion efficient and effective, enhancing the surgeon's efficiency, overcame unnecessary brain probing, saved time and overcame post craniectomy brain shift.

Conclusion: A clear understanding of normal and pathological ultrasound anatomy in the brain, how this anatomy changes over the course of surgery is critical to effective use of intraoperative ultrasound. It saves time, minimize damage to the nervous tissues, enhance maximum resection of brain lesion, having a small intraoperative footprint and cost efficient. Future improvements in ultrasound technology and research into image analysis will help to overcome the limitations, allowing maximum benefit of IoUS.

Keywords: Artefact; Brain lesions; Brain shift; Central nervous system; Contrast; Intraoperative; Magnetic resonance imaging; Neuronavigation

Abbreviations

AVMs: Arterio-Venous Malformation; B mode: Bright Mode; CEIoUS: Contrast Enhanced Intraoperative Ultrasound; CEUS: Contrast Enhanced Ultrasound; CNS: Central Nervous System; CSF: Cerebrospinal Fluid; EEG: Electroencephalogram; EFSUMB: European Federation of the Societies for Ultrasound in Medicine and Biology; GTR: Gross Total Resection; iMRI : Intraoperative Magnetic Resonance Imaging; IoUS : Intraoperative Ultrasound; MRI: Magnetic Resonance Image; SONAR: Sound Navigation And Ranging; US: Ultrasound; 2D: Two Dimension; 3D: Three Dimension

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Introduction

History of ultrasound; The development of Sound Navigation and Ranging (SONAR) dates back to the early 19th century when Jean-Daniel Colladon and Charles Sturm in 1826 researched sound navigation and ranging. Ultrasound research went through phases of development, it was practically test-used during the 1st and 2nd world wars in detection of submarines and ships, but not until the late 1930s that Karl Theodore Dussik a psychiatrist and neurologist and his brother Friederich Dussik a physicist began to study ultrasonography in relation to medicine [1-5]. It's striking to note that, the first reported use of ultrasonography on a human was on the nervous system. The Dussik brothers used a 1.5 MHz transmitter to scan the human brain, although up until the 1950s ultrasound went through phases of development. 1950s to 1970s was an important period in ultrasound technological evolution [4,5]. Before the introduction of computer tomography ultrasound was used to perform mid-line encephalography to detect epidural hematoma in patients with traumatic brain injury [1,6]. Ultrasound has been used as an intraoperative instrument since the 1980s, in contrast to intraoperative Magnetic Resonance Imaging (iMRI), the most important advantage of IoUS is that it provides inexpensive image data in real time, saves time [1,7-10].

Materials and Methods

Published literatures on the use of IoUS were reviewed and 3 of our numerous clinical cases reported.

Benefits of IoUS in neurosurgery

The use of IoUS to localize and resect CNS lesions, is gaining popularity to become a standard in neurosurgical suits around the globe pointing its benefits. IoUS has managed the most significant drawback of other intraoperative neurosurgical navigation system which is 'intraoperative brain shift', standing as the most challenging factor to neurosurgeons when correlating preoperative and intraoperative image. Great technology progress in the development of ultrasound machines with clearer and real-time images have made it of great importance. There is no immediate or future harm done to the human organism by the use of this machine in diagnosis [8,11-14]. Modern IoUS transducers range: 5 MHz-10 MHz provide pixel resolutions of 500 µm-1,100 µm at depths of 2 cm to 8 cm from the transducer. High-frequency transducers go up to 25 MHz providing maximum pixel resolutions of 100 µm-600 µm with depths of 2 cm to 4 cm from the transducer [14]. Choice of transducer and acquisition frequency depends on the location, sonographic properties of the lesion, size of the craniotomy, surrounding anatomy, surgeon's preference, and other factors. B-mode of structures in an IoUS image reflects the amplitude of the reflected signal. Acoustic homogeneous tissue generates little signal whereby structures with high grade acousticity generate strong echoes and often times obscure structures from the scanner, see Table 1 [14-17].

IoUS in comparison to other neurosurgical image guiding system

IoUS has overcome some limitations of other image guided neurosurgical systems by giving real time imaging at localization of lesion irrespective of post craniotomy and dura opening brain shift. Comes handy without losing time of procedure, compared to iMRI with a lot of technical fixes as its drawback, pre and post scan evaluation by the surgeon and radiologist, time taken to introduce and evaluate contrast [11,13,18-20]. Brain shift is a problem neurosurgeons experience after initial evaluation using preoperative images, it occurs in deep laying lesions that are not readily seen on the cortex after dura opening, occurs as a result of gravity. On approach to the lesion, neurosurgeon release fluid from the cisterns thereby causing a major brain shift, quantitative analyses show that co-registered IoUS could measure the intraoperative displacement effectively when used with a computable model, with the use of IoUS it's easy to overcome brain shift without losing time [7,11,12,14,18,19,21,22].

IoUS is cost efficient in comparison to an iMRI, has a small footprint, exceptional in puncturing of cystic lesions or biopsy taking in real time. The mobility and equipment size makes it easy to fit into any operating room, needing little skill acquisition by the neurosurgeon to use. With modern IoUS scanner-heads equipped with 2D and 3D scanning and image production abilities, merging preoperative MRI or CT scans into a navigation system is simplified [7,11,18,19,23]. With the development of 2D and 3D image construction in IoUS and the frame-less tracker navigator overcoming artifacts is made easy [17,19,21,22,24].

IoUS is effective in affirming the consistency of lesions, cystic lesions, abscesses are properly differentiated, most brain tumors and their margins are usually hyper-echoic, cisterns, ventricles, cerebrospinal fluid and most cystic tumors are hypo-echoic. Gray matter, white matter (gray matter is brighter than white matter typically), localizing small lesions is made easy, avoiding probing especially lesions on eloquent zones, outdoing significant neurological deficit postoperative, see Table 1 [12,25,26].

The use of IoUS in vascular lesions or when anticipating a major blood vessel in operating field, it stands out with the help of angiosonography, colour doppler (colour flow) and power doppler sonography are able to differentiate an artery from a vein thereby avoiding injury to vessels. This feature helps localize vascular lesions as, AVMs and cavernous malformation of the CNS without risk of over probing or large encephalotomy [15,27,28]. Power doppler ultrasonography is dependent on mechanical energy for facilitation of intraoperative real-time navigation to the tumor making it apparent for assessment of intra-tumoral vasculature, feeding and draining vessels, while color doppler is dependent on flow, making it motion dependent [14,29]. There are more versatile use of IoUS in vascular disorders than we have noted, our scope is more on it's use in intrinsic brain lesion resection.

The multifaceted function of IoUS makes it very effective in biopsy procedures, comparing it to stereo-tactic frame system with pitfalls as dependency on CT for accuracy, exposure to ionizing radiation, it's frame obstructing the operating field, thereby limiting surgical maneuvers and longer duration of procedure. The IoUS guided biopsy or cyst aspiration dealt with the need for repeated CT and recalculation of geometry should a shift occur in cases of cystic lesion aspiration [7,8,13,16,30,31].

Case Presentation

Case 1

A 23-year-old female presented with refractory epileptic seizures, right upper extremity weakness and hypoesthesia, she had been diagnosed with multiple cavernous angioma, was operated 15 years ago micro surgically for the symptomatic cavernous angioma, 4 years ago she underwent radiosurgery procedure for cavernous angioma. For the past 2 weeks she had seizure episodes and progressive right upper extremity weakness, she was referred to our hospital. MRI showed multiple cavernous angiomas and a post radiosurgery necrotic change. EEG specified the epileptogenic lesion of the left parietal lobe, being on the dominant lobe we used IoUS to navigate intraoperative avoiding over probe. Post operative MRI demonstrated GTR without progressive neurological deficit.

Preoperative she was on Levetriacetam 500 mg twice daily and still had seizure episodes. Hospital stay was 4 days, preoperative neurological deficits had a positive dynamics, and histopathology confirmed the diagnosis of cavernous angioma. Follow up a year later, she continued on Levetriacetam 500 mg dose without seizure for 12 months, no neurological deficit and was referred to epileptologist for AEDs dose correction, see Figure 1-3.

Case 2

A 16 years old female presented with refractory epileptic seizures and headache for the past 18 months. MRI shows a cystic lesion of the right frontal lobe, she was on Levetriacetam 500 mg twice daily, EEG confirmed the cystic lesion to be epileptogenic, with small incision and craniotomy with IoUS the lesion was aspirated, no sign of hematoma, no neurological deficit noted, patient was discharged the next day, Histology reported a sterile fluid. Six months follow up, there was no seizure nor lesion regrowth, she was referred to epileptologist for AEDs dose correction. 18th month follow up showed no regrowth and no seizures despite the low dose of AED see Figure 4 and 5.

Case 3

A 53-year-old male presented with complaints of refracted seizures

Table 1: Echoic appearances of structures in IoUS.

Hypoechoic structures	Isoechoic structures	Hyperechoic structures
Ventricles	Brain parenchyma	Falx cerebri
Cysts	Low grade glioma	Sulci
Cisterns		Choroid plexus
Chronic subdural hematoma		Vessel wall
		Hemostatic materials(surgical)
		Meningioma
		Glioblastoma
		Cavernous malformation
		Tentorium cerebelli
		Acute hematoma
		Brain abscess

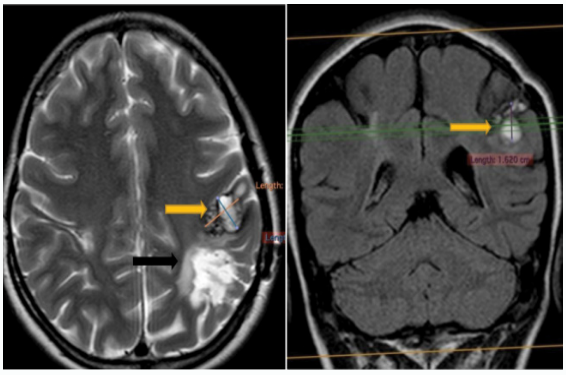

Figure 1: Two dimension view of contrast enhanced Preoperative MRI scan of a 20 years old female, showing cavernous malformations, she presented with epileptic seizures and headache, yellow arrow pointing the lesion on the left parietal region, EEG confirmed it symptomatic, Zabramski type 1. The black arrow is showing changes of cavernous malformation previously treated by radiosurgery.

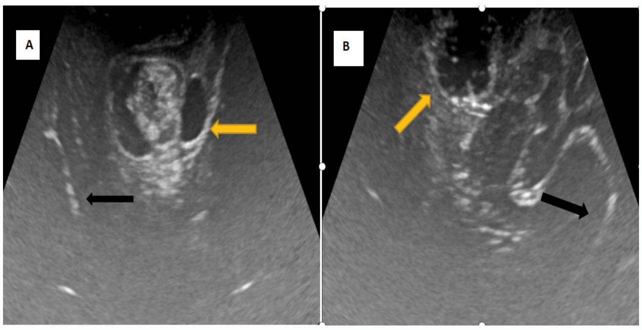

Figure 2: A: IoUS image pre-resection, the yellow arrow showing the cavernous malformation, the black arrow showing cerebral sulcus. B: IoUS image post-resection, yellow arrow showing the post resection cavity, the black arrow showing cerebral sulcus.

and headache for the past 4 months necessitating a brain CT which showed a right parieto-occipital lesion. He was on Carbamazepine 500 mg twice daily, through a moderate craniotomy the lesion was gross totally resected, no neurological deficit postoperative, no postoperative hemorrhage. The patient was discharged 2 days postoperative, histopathology reported metastatic melanoma, and he was referred to Oncologist for further treatment and continued Carbamazepine 500 mg twice daily. Six months follow up, he stopped using AED as recommended by the Epileptologist and there was no regrowth or neurological deficit see Figure 6-8.

We use Hitachi ultrasound Scanner (Arietta S60), with 3 MHz-8 MHz or 4 MHz-10 MHz transducer. From our case experience, IoUS saves time intraoperative, reduce over probing and enable GTR.

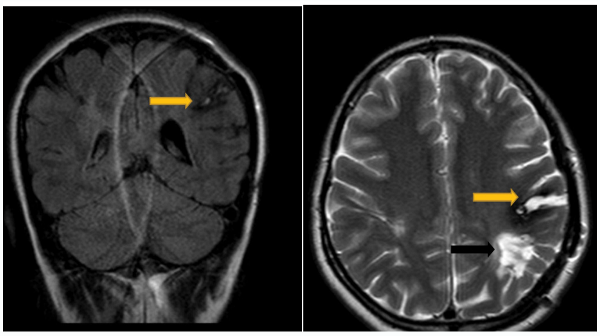

Figure 3: Two dimension postoperative MRI, the yellow arrows showing post-resection cavity, the black arrow showing changes on the cavernous malformation post radiosurgery.

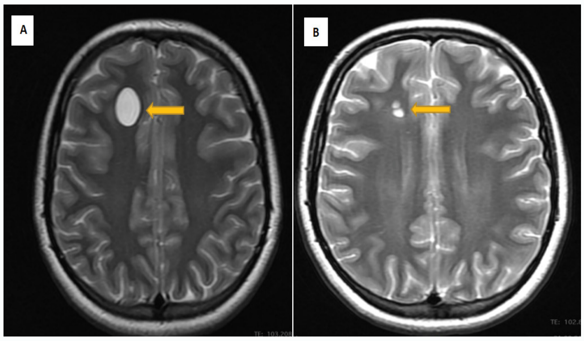

Figure 4: A: Pre-operative MRI scans of a 16 year old female who presented with epileptic seizures, yellow arrow showing the cystic lesion in the right cerebral hemisphere. B: Postoperative MRI scan, yellow arrow showing the aspirated lesion.

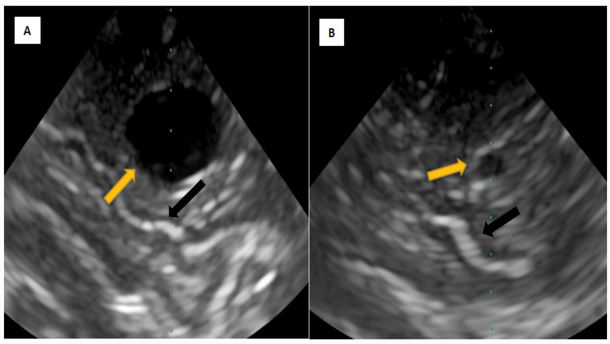

Figure 5: A: IoUS image pre-aspiration, yellow arrow showing the cystic lesion, black arrow showing the cerebral sulcus. B: IoUS image post-aspiration, yellow arrow showing post-aspirated lesion, black arrow showing the cerebral sulcus.

Limitations, overcoming limitations of IoUS in neurosurgery

The use of intraoperative ultrasound in neurosurgery has its drawbacks, noting available technology, although relatively simple to use, the neurosurgeon needs to acquire basic skills for its use, recognizing physiological anatomy and pathological lesions, be able to differentiate them. US image interpretation is user dependent in orientation when navigating [14,19,26].

The transducers are most times bigger than the ideal neurosurgical burr hole for minimally invasive procedures like biopsy, cyst aspiration

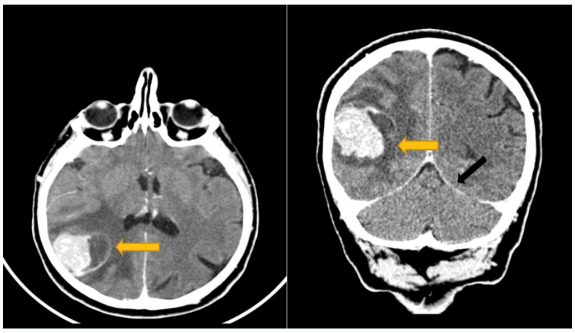

Figure 6: Two dimension pre-operative CT brain scan of a 53 year old male who presented with epileptic seizures and headache, yellow arrows showing the lesion black arrow points the tentorium cerebelli.

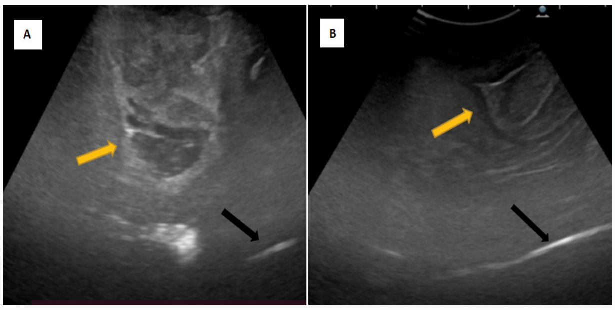

Figure 7: A: IoUS image pre-resection, yellow arrow points the lesion, blue arrow points tentorium cerebelli. B: IoUS image post-resection, yellow arrow points the post resection cavity, black arrow points the tentorium cerebelli.

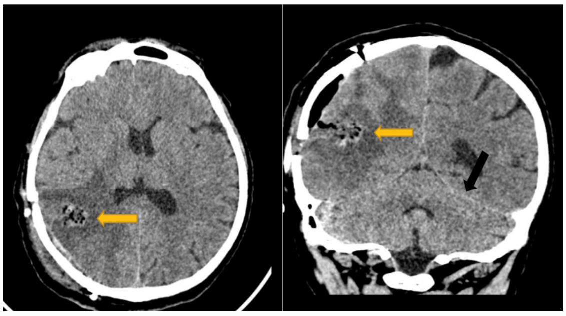

Figure 8: Two dimension postoperative CT scan of brain, the yellow arrows showing the post-resection cavity, black arrow points the tentorium cerebelli.

or ventricular access, if compared to stereotactic, thereby promoting the need for smaller transducers [15,19].

Clear IoUS image acquisition and interpretation can be a challenging for surgeons who lack experience with the technology, training programs in ultrasonographic practice models, and consultation with expert sonographers is of essence to refine surgical technique and avoid artifacts [7,14,15,31].

IoUS in neurosurgery have benefited from the development of new transducers, contrast agents, and processing systems, development in IoUS image quality and increased native 3D will help overcome challenges with tissue differentiation allowing accurate assessment of resection [3,18]. Its integration with neuronavigation preoperative image processing will grant surgeons the ability to measure the extent of resection, brain shift-corrected imaging modalities. Neurosurgeons should be conscious of artefact in IoUS images that may occur in brain tumor resection, techniques to recognize and reduce image artefact are important and should be known to users in brain lesion surgery. Artefact may interfere with the neurosurgeon's interpretation of the image, leading to hyper or hypo resection [15,16,20,26,31].

Discussion

IoUS has a significant edge over other intraoperative modalities of image guidance in neurosurgery, specific in terms of independence, portable and adapting to multiple clinical scenarios. IoUS can independently provide real-time imaging, it is not cumbersome and can be integrated into already existing operating suit infrastructure with little or no disruption to neurosurgical workflow, cost of acquisition and maintenance of IoUS equipment are significantly cheaper compared to any other intraoperative imaging tool, its selective visualization of blood vessels or lesions [20,22,31].

IoUS is a more flexible surgical companion serving more purposes: demonstration of CSF and blood flow, tissue density, peripheral infiltration or other physical properties of lesions excised and immediate visualization of complications as hematoma [31]. Without experience it is difficult to minimize the error of distinguishing between edematous tissue and lesion, especially in cases of hypoechogenic lesions or changes that occur during neurosurgical lesion resection, i.e., hemorrhage, hemostatic materials, increased edema. Post-resection cavity, changes ultrasound characteristics at the margins which are artifacts. Its user dependent, expectations are, that new generation of IoUS be suited with integrated algorithm for image analysis, and by the diffusion of contrast enhanced ultrasound imaging would outpace the already known [32,33]. The introduction of contrast agents in medical radiology is for the purpose of enhancing differences and characteristics of varying organs, vessels, and cavities, simplifying their visualization. Contrast Enhancement in Ultrasound (CEUS) is now an established technique and has been used in many organs; it allows better detection of neoplastic lesions. The use of contrast enhancement in CNS lesions is likely a game changer, allowing real-time evaluation of contrast enhancement and vascularity of lesions during different dynamic phases post injection of an intravenous contrast agent [33,34]. It is possible to identify 4 phases of contrast enhancement in the use of CEIoUS: arterial phase, peak of contrast enhancement, parenchymal phase and venous phase. These phases are dependent on tumor vascularization and perfusion pattern [1,27,35,36]. CEIoUS are extremely informative on tumor biology i.e., high grade glioma, meningiomas are better enhanced than low grade glioma [1,15,29,34,35,36]. CEIoUS eliminates intraoperative anatomical distortions associated with standard neuronavigation and provides quantitative perfusion data in real-time. The use of CEIoUS during neuro-oncological procedures has been recently included in the guidelines from the European Federation of the Societies for Ultrasound in Medicine and Biology (EFSUMB), presenting a paradigm shift for the use of US in neurosurgery [16,29,33,35].

Artefacts is any part of an IoUS image that does not represent the physio-anatomy or the patho-anatomy of the structure being visualized correctly, artefacts arise for various reasons, tissues with high attenuation signal, like bone, might create a masking shadow that decrease the echo signal of tissue behind it, the attenuation coefficient of saline used to fill the resection cavity is lower than that of neural tissue, producing a brightness artefact at the brain/saline interface [14,26,31]. Coagulated blood or hemostatic materials along the walls of the resection cavity also produce a brightness artefact. Artefacts could make the images at the end of surgery difficult to interpret, and could lead to residual lesion or misinterpretation of normal tissues as residual lesion causing more aggressive resection, being aware of these possible artefacts is essential for successful use of IoUS-guided brain lesion surgery [14,16,26]. These drawbacks limit widespread adoption of IoUS in neurosurgery, improved sensitivity and specificity of identifying lesions and residual lesion during resection, integration of real-time IoUS with anatomic imaging, and compensation for intraoperative brain shift should be the technological development of novel IoUS modalities, including 3D reconstruction, merging of tracking neuronavigation preoperative images, in the future. Studies to evaluate the impact of these novel technologies on clinical outcomes for a more effective use of IoUS in neurosurgery are essential [14,16,22,24,27,31].

Conclusion

A clear understanding of normal and pathological ultrasound anatomy in the brain, and how this anatomy changes over the course of surgery, is critical to understanding of intraoperative ultrasound. The use of IoUS imaging in our hospital in localizing lesions saves time and minimize the damage to the nervous tissues while enhancing maximum resection of brain lesion, with minimal or no neurological deficit, overcoming post craniotomy brain shift. Future improvements in ultrasound technology and research into image analysis will help to overcome the few limitations, allowing maximum benefit of IoUS.

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