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# Intraoperative contrast-enhanced ultrasound in traumatic brain surgery☆

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ABSTRACT

**Objective:** The objective was to assess intraoperative contrast-enhanced ultrasound (CEUS) in traumatic brain surgery. **Methods:** We prospectively performed intraoperative conventional ultrasound (IOUS) and CEUS in 32 patients who underwent emergency surgery for the treatment of traumatic brain injury (TBI). Sonographic appearance including echogenicity, border, and size of the traumatic lesion and adjacent brain tissue on CEUS were compared with those on IOUS using surgical results as the gold standard. The differences in the size and contrast enhancement parameters of the lesions between IOUS and CEUS were analyzed with a paired *t* test. **Results:** The accuracy of CEUS in assessing TBI was 100%, whereas IOUS was 51%. The absolute peak intensity (API) varied depending on the severity of brain injury. Lower API was observed in severely damaged brain tissue, whereas high API was seen in normal brain tissue or the brain tissue with mild injury. The border of the trauma lesion was more clearly defined on CEUS when compared to IOUS. The size of the lesions measured on CEUS was significantly larger than that on IOUS ($P<.01$). Importantly, small vessels supplying blood to the tissue in traumatic lesions, as an indication of possible brain vitality, were optimized on CEUS during the surgery. Based on the parameter of time intensity curve and appearances of the lesions on CEUS, the severity of lesions was reclassified and surgical intervention was redesigned in 21 (21/32, 66%) cases. **Conclusion:** Intraoperative CEUS improves accuracy in classification of traumatic brain injury, which helps neurosurgeons to effectively remove hematoma, preserve normal brain tissue, and prevent damaging the vessels during surgical intervention.



## 1. Introduction

Traumatic brain injury (TBI) is a common neurosurgical emergency, and it is the second most common injury in trauma medicine. Notwithstanding, TBI has the highest death rate and incidence of posttrauma disability of all traumatic injuries [1]. The number of TBI cases as a cause of neurosurgical emergency has increased following the increase in the incidence of automobile collisions in recent years. Approximately 100,000 brain trauma patients (1:6 of TBI) die each year, representing a cost of about 1 billion dollars in China in 2004 [1].

TBI is divided into primary injury that occurs at the time of brain trauma and secondary injury that develops after the primary injury, including ischemia, cerebral edema, and mass effect from hematoma. Based on anatomic location, the hematoma can be classified as epidural hematoma, subdural hematoma, intracerebral hematoma, and subarachnoid hematoma [2]. Modern neurosurgical care is intended to minimize secondary insults through early detection and effective prevention [3–5]. However, the condition in patients with TBI is usually critical, and the type of brain injury is often complex. Although most cases with TBI can be diagnosed by preoperative computed tomography (CT), the characteristic of a trauma lesion during the surgery may be significantly different from that on acute preoperative CT because progressive and extensive secondary brain damage results from active bleeding and/or compression by a hematoma following primary brain injury [3–6]. Moreover, it is difficult for neurosurgeons to accurately assess the type and affected region of brain damage for removing dead brain tissue and hematoma and preserving normal brain tissue during the surgery without intraoperative imaging guidance. It is known that both preserving normal brain tissue and removing hematomas are important for improving successful rates of TBI treatment not only in brain surgery but also in postoperative recovery [6–10]. Therefore, the intraoperative assessment of trauma lesion is considered both crucial and challenging.

CT and magnetic resonance imaging are useful imaging techniques for preoperative TBI classification and postoperative follow-ups. However, they are not practical during surgery due to risk of radiation exposure and relative high cost.

Notably, contrast-enhanced ultrasound (CEUS) has several important advantages including portability, being iodine-free and radiation-free, and relative low cost. Its application has been

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extended to the diagnosis of diseases, evaluation of treatment, and guidance for interventional procedures [11–19]. Importantly, enhancement patterns and perfusion in trauma lesions on CEUS are considered to be important indicators for tissue viability [11–13]. The goal of our study was to assess the usefulness of intraoperative CEUS during neurosurgery treatment of TBI and assess effectiveness of CEUS vs. intraoperative conventional ultrasound (IOUS) for improving classification of TBI.

## 2. Material and methods

### 2.1. Patients

An institutional ethics committee in Capital Medical University, Beijing, China, approved this study, and a written informed consent was obtained from the legally authorized representative of all enrolled subjects.

Between September 2009 and April 2012, we prospectively enrolled 32 patients (18 men and 14 women, age range 22–46 years, mean age 31 years) who underwent emergency neurosurgery for the treatment of TBI in our institution. The time from brain trauma to surgery ranged between 2 to 96 h (mean 12$\pm$16 h). Board-certified neuroradiologists interpreted all preoperative head CTs in all 32 cases. All neurosurgeries were performed by licensed neurosurgeons in Tiantan Hospital, Capital Medical University.

Indications for using intraoperative CEUS include the severity, classification, and the size of the lesion on the IOUS differed from those on preoperative CT. The size of bone flap window was $>$3 cm $\times$ 1 cm, which allowed us to place the intraoperative ultrasound transducer on brain surface to image the trauma lesion.

Exclusion criteria included patients being under 18 years of age, patient with a history of heart failure, and the size of bone flap window was $<$3 cm $\times$ 1 cm, as well as instances where informed consent was not obtained.

### 2.2. Intraoperative conventional ultrasound

Aloka ($\alpha$-10, Aloka, Japan) ultrasound scanner equipped with UST-9133 (transducer surface 3.0 cm $\times$ 1.0 cm) curved linear array intraoperative transducer (6–8 MHz, maximal depth 18 cm) and coded phase-inversion harmonic ultrasound was used for the study. Ultrasound output mechanical index was 0.10–0.12.

Under general anesthesia, the neurosurgeon shaved the hair and cleaned the skin in the surgical area. The neurosurgeon then made an incision through the scalp at the location of the brain trauma lesion according to preoperative head CT. Brain trauma surgery was performed through the bone flap after opening the skull.

The intraoperative ultrasound probe was placed into a sterile transducer cover (Surgical Sterile Protective Ship-cover, 3L Medical Products Group Co., Ltd., Jiangxi, China) and was then inserted into the bone flap to image the brain trauma lesions after opening the calvarium and tenting the dura. The pressure on the brain was minimized as much as possible.

We initiated with IOUS imaging to observe the location, shape, size, border, internal echogenicity, and vascularity of traumatic lesions in the brain [6–10]. The classification of TBI was determined based on ultrasound characteristics, which were compared with preoperative head CT. For grayscale imaging, total gain, dynamic range, and focal zone were adjusted in each case depending on the depth of the lesion. Color Doppler property settings (total color gain, PRF, and filter) were also manually changed according to flow status of the vessels within and near the traumatic brain lesion.

Scanning of multiple sections of the brain was performed using the preoperative CT as a reference. Ultrasound scanner setting was switched to CEUS when the traumatic brain lesion was displayed on real-time grayscale image.

### 2.3. Contrast-enhanced ultrasound

Intraoperative CEUS was applied in 32 patients. CEUS analysis software was installed into the ultrasound scanner.

A second-generation contrast agent, $SF_6$ microbubble 2.5 μm in diameter (SonoVue, Bracco, Milan, Italy), was used for CEUS. Contrast agent (25 mg) was mixed in 5 ml 0.9% saline and was then administered (0.025 ml/kg, rapid bolus) through a femoral vein or brachial vein followed by 10 ml saline. The timer on ultrasound scanner was started at the time of contrast agent injection. The characteristics of enhancement in trauma lesion and surrounding brain tissue during the administration of ultrasound contrast agents were observed in real time for 2 min. The results including the size and characteristics of the trauma lesions on real-time CEUS were reported to a neurosurgeon as reference for determining surgical plan. The real-time images of CEUS were stored on cine loops and static images. The borders and internal enhancement patterns of each lesion on CEUS were compared with those on the IOUS images. The size (area=length $\times$ anterior–posterior dimension) of the lesion was measured at the peak intensity and was automatically analyzed by CEUS software. We measured the maximal area (maximum sagittal dimension $\times$ maximum transverse dimensions) of each particular traumatic brain lesion on both IOUS and CEUS in all 32 cases, and the measurement on CEUS was considered accurate.

To classify the type of TBI, time–intensity curves were used to analyze contrast enhancement in traumatic lesions including the types of the enhancement and absolute peak intensity (API). Using contrast enhancement in the normal brain tissue as a reference standard, the contrast enhancement in the brain trauma lesion was classified into four grades: (a) no enhancement was considered when the echogenicity of the lesion on CEUS was the same as before administrating contrast agent; (b) mild enhancement was considered when the echogenicity of trauma lesion was slightly more echogenic than that on precontrast image and it was lower than the enhancement in normal brain tissue; (c) equal enhancement was considered when the echogenicity in trauma lesion was the same as the enhancement in normal brain tissue; and (d) high enhancement was considered when the echogenicity of the lesion was higher than that in normal brain tissue [20].

The size of the region of interest (ROI) for measuring API in normal brain tissue and trauma lesion was standardized as a round area 0.3 cm in diameter. It seemed that ROI was small; however, vessels and/or fissures of the brain could be excluded in the measurement by setting a small region of inclusion. In other words, a relatively large ROI ($>$0.4 cm) may result in over- or underestimation of API in trauma lesion. Therefore, using ROI 0.3 cm as the standard for measuring API in all brain trauma lesions throughout the study may potentially minimize bias. The administration of contrast agent was also standardized including the speed of injection and the dose of the contrast agent used for imaging since all subjects had normal cardiac function with left ventricle ejection fraction $>$55%. We measured CEUS parameters including time to initiation of enhancement, time to peak enhancement, and peak intensity. API was calculated with the following equation.

$$\text{API} = \text{peak intensity} - \text{baseline intensity}$$

### 2.4. Statistical analysis

SPSS 13.0 (SPSS, Chicago, IL, USA) was used to perform statistical analysis. All variables including the size and API were expressed with mean and standard deviation. An unpaired two-tailed $t$ test was applied to test the difference in API (enhancement) in varied types of traumatic brain injuries. A paired $t$ test was used to analyze the difference in assessing those parameters in each particular trauma