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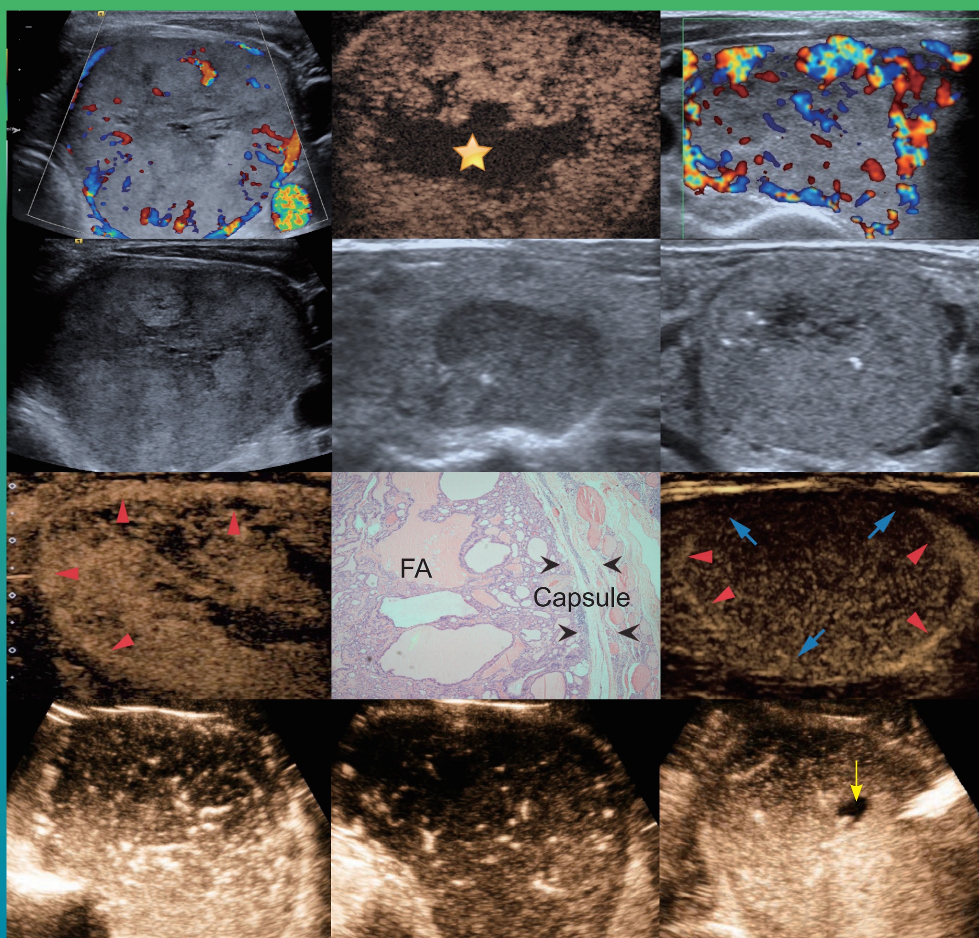


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# Advanced Ultrasound in Diagnosis and Therapy

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REVIEW ARTICLE

# Emerging Applications of Contrast-enhanced Ultrasound in Trauma

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***Abstract:*** The use of contrast-enhanced ultrasound (CEUS) has expanded over the past decade to include a variety of diagnostic and therapeutic applications. These include urgent clinical situations that require timely diagnosis and subsequent treatment. With the introduction of microbubble ultrasound contrast agents (UCAs), CEUS provides increased sensitivity and specificity over conventional ultrasound. Within the trauma setting, CEUS benefits include point of care imaging and an ability to monitor perfusion in real-time. Additionally, UCAs are non-nephrotoxic, and can be used when contrast enhanced CT is contraindicated. In this review, we discuss recent advancements of CEUS within trauma settings.

***Key words:*** Contrast-enhanced ultrasound; Computed tomography; Abdominal trauma; Critical care; Bleeding

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In an emergency room setting, CT remains the gold standard for the rapid detection and grading of neurologic, skeletal, and thoracoabdominal injuries in all cases of high-energy trauma in hemodynamically stable patients. [1]. However, in unstable trauma patients, ultrasound is the preferred screening modality, with the ability to be performed at the bedside without interrupting resuscitative procedures. The FAST (Focused Assessment with Sonography for Trauma) exam has been widely adopted in the early assessment of a polytrauma, owing to its high sensitivity in detecting free fluid (up to 99%) [2]. Its major limitation is its poor sensitivity in detecting traumatic solid organ injuries and low flow bleeds associated with organ lacerations [3]. With the introduction of UCAs, CEUS has been shown to overcome these limitations, increasing sensitivity of low flow detection by over 10-fold relative to traditional Doppler [4]. and increasing the accuracy of detecting traumatic organ lesions.

Following intravenous administration of UCA, solid organ parenchymal enhancement depends on the differences in the organ vasculature [5]. Solid organ injuries are sharply demarcated from well-enhanced healthy tissue, appearing as a non-enhancing defect, best visualized during the venous phase [1]. Specifically, contusions appear as hypoechogenic areas amongst progressively enhancing surrounding parenchyma, lacerations appear as markedly hypoechoic linear bands, often oriented perpendicular to the organ surface, and hematomas as non-enhancing areas lacking internal vessel enhancement [6]. CEUS images blood flow better than color or power Doppler, particularly in parenchymal microvasculature where blood flow may not be easily discriminated from surrounding tissue motion.

## General Abdominal Trauma

CEUS can be employed in clinical practice as an alternative to CT in stable patients with isolated blunt moderate-energy abdominal trauma to rule out solid organ injuries [1]. In a large prospective study, CEUS and CT were used in 133 hemodynamically stable patients following blunt abdominal trauma. CEUS identified 81 of the 84 injuries identified by CT and showed a high

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correlation with CT in the evaluation of lesion volume according to the AAST (American Association for the Surgery of Trauma) classification, seen in Table 1 below [7]. Contrast enhancement is able to last long enough to allow adequate visualization of parenchymal organs in a trauma patient, providing a role for CEUS in the initial evaluation of low-energy injuries in urgent settings.

**Table 1** Lesion dimensions measured by CEUS compared to CT grading. Modified from [7].

| Item | CT grading* | CEUS dimensions (mm) |
|---|---|---|
| Liver (*n* = 21) | Grade I: *n* = 3 | <10 (n = 2) |
| | Grade II: *n* = 13 | <20 (*n* = 4), <30 (*n* = 9) |
| | Grade III: *n* = 5 | >30 (*n* = 5) |
| Spleen (*n* = 48) | Grade I: *n* = 4 | <10 (*n* = 4) |
| | Grade II: *n* = 32 | <30 (*n* = 11), <50 (*n* = 21) |
| | Grade III: *n* = 12 | >50 (*n* = 12) |
| Kidney & adrenals (*n* = 13) | Grade I: *n* = 2 | Not identified |
| | Grade II: *n* = 5 | 10 (*n* = 5) |
| | Grade III: *n* = 6 | >10 (*n* = 6) |
| Pancreas (*n* = 2) | Grade II: *n* = 1 | 10 (*n* = 2) |

* Organ Injury Scale of the American Association for the Surgery of Trauma

In stable patients with isolated blunt abdominal injuries, CEUS has sensitivities for detecting injuries of 69% (kidneys), 84% (liver), and 93% (spleen), with high specificity (over 90%) compared with CT [2]. However, CEUS should not replace contrast-enhanced CT in critically ill patients, and those with multiple injuries.

## Liver Trauma

The liver is one of the most commonly injured organs in both blunt and penetrating abdominal trauma [8]. Active bleeding from liver lacerations is a major cause of death and disability, necessitating early and rapid detection in critically ill patients in order decrease time to intervention. The employment of CEUS greatly improves the quantity and quality of findings with respect to conventional ultrasound in patients with mild isolated abdominal trauma. In 203 patients, CEUS identified a traumatic hepatic lesion in 4 patients, as well as confluent hepatic lesions in 2 others, all of which were missed with conventional ultrasound [9]. With contrast enhancement, peripheral tissue components were more defined, allowing better visualization of lesion margins.

Additionally, CEUS has proven advantageous in the diagnosis of active bleeding from hepatic trauma, with the site of active hepatic hemorrhage appearing as an isolated, hyperechoic band-like region (Fig. 1c), versus the equivocal findings seen on CT (Fig. 1d). In a study of 392 patients with liver and/or spleen injuries, CEUS detection rates for active bleeding were not different from that of contrast-enhanced CT ($P = 0.333$), demonstrating the role of CEUS as an additional tool in establishing bedside diagnoses from traumatic abdominal injuries [10].

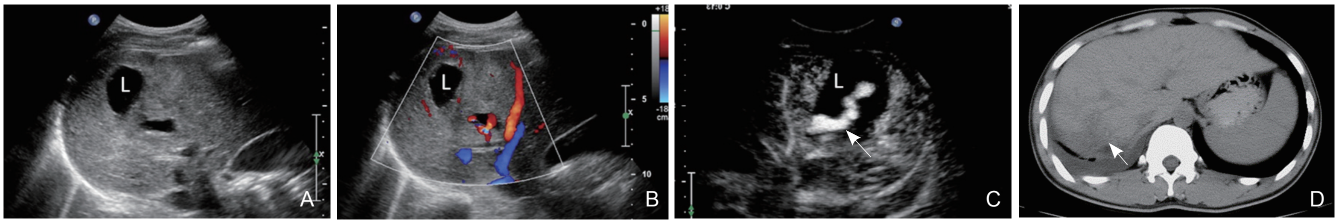


**Figure 1** 17-year-old male admitted 6 hours after abdominal trauma. Grey-scale ultrasound (A) and color Doppler ultrasound (B) showed a cystic lesion (L) within the posterior lobe of the liver. Contrast ultrasound (C) demonstrated the anechoic lesion (L) with active bleeding (arrow) from the wall of the lesion which corresponded with CT findings (arrows) (D). [Provided by Drs. Xiang Jing and Jianming Ding from Tianjin Third Central Hospital]

In an emergency department (ED) setting, ED physicians and trauma surgeons are experienced in using bedside ultrasonography to identify and assess blunt trauma injury using the FAST exam. While radiologists may have more experience with CEUS, a study examining blunt liver trauma in 20 animal models found that, regardless of the degree of trauma, the interobserver agreement between ED physicians and radiologists increased from 0.867 to 0.955 after contrast enhancement on ultrasound [11], demonstrating CEUS permitted a more accurate diagnosis for liver trauma than conventional ultrasound.

CEUS has also been implemented intraoperatively to estimate the degree of liver damage. From a 2019 report of a gunshot wound to the liver in a military mission in Afghanistan, CEUS was performed in the emergency room, following the initial FAST and CT scan. While the wound tract extension could not be estimated upon first CEUS examination, secondary to aerodermectasia, subsequent CEUS after the first operation effectively detected the wound tract, hematoma, and necrotic tissue caused by the gunshot [12]. The application of CEUS may prove to be useful imaging post-operatively and in follow-up, avoiding repeat CT scans.

Extending beyond diagnostic capabilities, CEUS has shown promise as a therapeutic modality in both blunt hepatic and splenic hemorrhagic traumas. A large-scale clinical study in 2013 investigated the efficacy of hemostatic percutaneous therapy of liver and splenic trauma under CEUS guidance in both ED and ICU settings. Percutaneous injection of haemocoagulase atrox and alpha-cyanoacrylate under CEUS guidance successfully controlled hemorrhaging in 86 of 88 patients presenting with traumatic Grade I-IV injuries, as classified according to the AAST Injury Scale [13]. In a clinical setting, many of these injuries could have been treated with more conventional techniques, such as laparoscopy or transarterial embolization, but would have required more complex instrumentation and techniques. The clinical application of CEUS-guided treatment in select hepatic and splenic trauma has proven to be an efficient, convenient, rapid, and minimally invasive alternative.

## Splenic Trauma

In addition to the liver, the spleen is also frequently injured in blunt abdominal trauma. Non-operative management with or without angioembolization and observation is the standard for hemodynamically stable patients. In the context of CEUS, splenic injury is best observed during the venous phase, starting at 40-60s after contrast-media injection, with a duration of about 5-7 minutes. The irregular enhancement of the spleen during the arterial phase, due to contrast media movement within the red and white pulp, makes it difficult to recognize any splenic tissue lesions [14].

CEUS has been shown to be an effective imaging modality useful in assessing splenic injury, with improved boundary definition and visualization of active bleeding over conventional US (Fig. 2), and the ability to assess splenic injury grade. A 2019 prospective study of 101 emergency room patients with CT-diagnosed splenic injury found CEUS to have a diagnostic sensitivity of 96.9%, with a 95.8% concordance between CEUS and CT, according to the AAST-SIS (spleen injury scale) [15]. CEUS was used as follow-up imaging in splenic injury of all grades to assess mean healing time, which could be used clinically in recommendations for contact restrictions in patients presenting with splenic injury.

Following blunt splenic injury managed non-operatively, two main complications can develop: delayed splenic vascular injury (DSVI) and delayed active extravasation (DAE). In a prospective study by Tagliati et al, serial CEUS and CECT (contrast-enhanced CT) showed a diagnostic comparability of 98.6% in detecting delayed splenic injury complications following non-operative management, all diagnosed within the first 7 days after trauma [16]. CEUS was shown to be a valuable imaging modality that can be utilized during follow-up to promptly diagnose splenic injury complications, and reduce radiation exposure, particularly in patients with AAST-SIS grade >2, when complications are more frequently encountered.

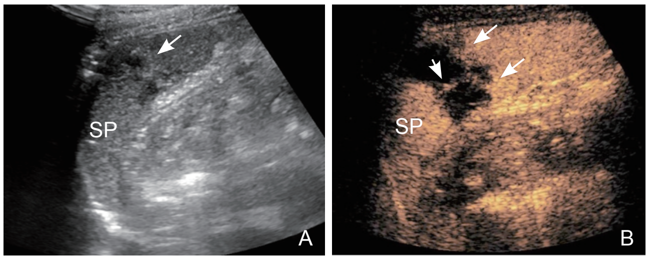


**Figure 2** 25-year-old female involved in a traffic accident. (A) Transverse oblique grey-scale US showed an injury site without clear boundaries in the middle of the spleen (arrow); (B) CEUS obtained from the same region showed the injury site in the middle of the spleen as an anechoic and hypoechoic perfusion defect (long arrows) with active bleeding (short arrow). SP, spleen. [Provided by Dr. Faqin Lv from Third Medical Center of Chinese PLA General Hospital]

Aside from diagnostic applications, CEUS has shown promise in the conservative treatment of blunt splenic trauma. Using an animal model, an experimental study found that CEUS-guided hemostatic injection using haemocoagulase atrox and alpha-cyanoacrylate hemostatic was both effective and safe in the treatment of dogs with grade III-IV splenic injury [17]. Following treatment, CEUS and CT showed that CEUS-guided hemostatic injection was effective in stopping active bleeding, and no complications (splenic hemorrhage, splenic abscess, splenic pseudoaneurysms, intestinal obstruction/adhesions) occurred during 3 weeks of follow-up [17].

## Kidney Trauma

Renal trauma represents about 5% of abdominal trauma, and similarly to CEUS in the liver and spleen, contusions and lacerations appear as hypoechoic areas (Fig. 3), with lacerations being linear and perpendicular to the organ surface. However, the kidneys show differing degrees of enhancement, with the cortex showing immediate bright and even enhancement, while the pyramids diffusely enhance over 30 seconds, from the periphery to the center [18].

In a prospective study between June 2002 and June 2004, among 35 CT-diagnosed abdominal injuries, 10 of which were renal in origin, CEUS sensitivity was 80%, identifying only 8 of the 10 lesions [19]. The two missed kidney injuries were reportedly small and low-grade (CT grade II). Despite the decreased sensitivity for diagnosing renal lesions compared to CT, it did not change the clinical management of the patients, since both lesions resolved without any treatment by the time of follow-up.

A larger, multi-centric, international, prospective study in 2009 evaluated the concordance of conventional ultrasound and CEUS with CT, which included 26 renal parenchymal lesions. Sensitivity and specificity for renal trauma at baseline ultrasound were 36% and 98%, respectively, increasing to 69% and 99%, respectively, following the addition of contrast enhancement [6]. Despite the increased sensitivity of CEUS from conventional ultrasound in the identification of renal injuries, CEUS is unable to identify injuries of the renal collecting system, as microbubbles are not excreted in the urine [20,21]. However, unlike CT and MRI, UCAs are not excreted by the kidneys, and are not contraindicated in patients with decreased renal function.

Research in canine models shows CEUS to be a promising method for monitoring hemodynamic changes in hemorrhagic renal lesions. Following AAST grade III-IV renal injuries, various stages of hypotension were induced through controlled exsanguination in a 2015 canine study [22]. CEUS and CECT had similar detection rates of renal trauma during the various stages of shock, with renal trauma defined as the absence of enhancement or a low-enhanced perfusion defect. With progressive hypovolemia, the flow of the contrast agent significantly slowed, with arteries at all depths becoming increasingly constricted [22]. In the stage of severe shock, renal parenchymal perfusion declines, with decreased intensity of contrast enhancement.

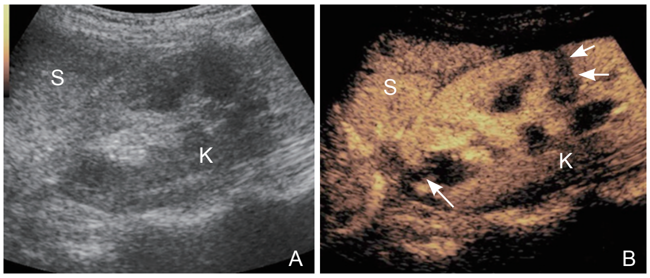


**Figure 3** A male patient with left flank injury was admitted to hospital. Dual grey-scale (A) and contrast (B) ultrasound imaging detect an avascular perfusion defect at junction of mid and low poles which confirmed as kidney laceration at surgery. [Provided by Dr. Faqin Lv from Third Medical Center of Chinese PLA General Hospital]

## Pancreatic Trauma

Pancreatic trauma occurs in < 2% of blunt abdominal trauma, but due to its retroperitoneal location, it has a high mortality rate ranging from 70-80% when injury involves adjacent structures such as the aorta and its branches or the vena cava [5]. Historically, few studies have investigated the role of CEUS in the detection of pancreatic trauma, and the valve of CEUS in pancreatic injuries has not yet been evaluated with double-blind comparisons between CEUS and CECT.

In 2013, blunt pancreatic injury was evaluated in 40 miniature pigs using conventional ultrasound, CEUS, and CECT. CEUS detection rates were significantly higher than conventional ultrasound (85% vs 52.5%, $P < 0.05$), and slightly higher than CECT (85% vs 82.5%, $P > 0.05$) [23]. Lower detection rates were seen in CECT when the depth of the lesion was less than the slice thickness; a problem that can be avoided by using CEUS. A more recent retrospective study conducted in humans reported a CEUS detection rate of 95.5%, diagnosing blunt pancreatic injury in 21/22 patients [24]. With conventional ultrasound, pancreatic injury appears as a heterogenous texture with unclear borders, and the use of contrast agents improves visualization, better delineating the injury (Fig. 4A), with similar features seen on CT (Fig. 4B).

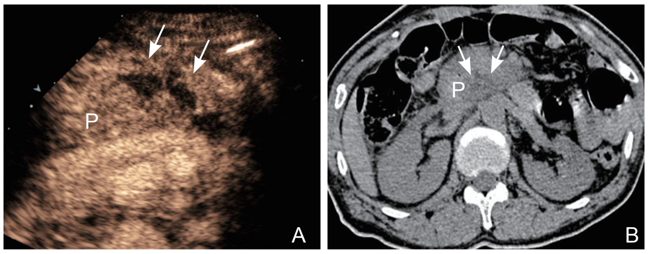


**Figure 4** 55-year-old man involved in a traffic accident. (A) CEUS identified the injury as an anechoic and hypoechoic perfusion defect with irregular borders in the pancreatic body/tail (arrows); (B) CT demonstrated the injury as a heterogenous, low-attenuation region (arrows) in the pancreatic body/tail, consistent with a hematoma and rupture of pancreas (P). [Provided by Dr. Faqin Lv from Third Medical Center of Chinese PLA General Hospital]

While useful as an adjunctive diagnostic tool to CECT, CEUS has similar limitations to conventional ultrasound in the evaluation of pancreatic injury, including patient obesity and subcutaneous emphysema [24]. However, UCAs enable better visualization of the peripancreatic space over conventional ultrasound.

## Scrotal Trauma

Scrotal injury composes approximately 1% of all trauma that present to a hospital [25]. Prompt diagnosis and evaluation of testicular viability is essential in guiding the treatment plan between conservative versus operative management. Unlike assessment of abdominal trauma, ultrasound is considered the gold standard for assessment of traumatic scrotal injury, in both the acute and non-acute setting, particularly when used with high-frequency transducers, such as color and power Doppler [26].

An early study in 2004 identified 8 in 126 cases concerning for acute painful scrotum [testicular torsion (*n* = 6), epididymitis (*n* = 1), testicular trauma (*n* = 1)] in emergency radiology, with CEUS showing no advantage over Doppler ultrasound [27]. Similar findings in a study focusing exclusively on cases of acute painful scrotum found that while CEUS showed no advantage over Doppler ultrasound in diagnosing testicular torsion, in the two cases of epididymitis complicated by abscess, CEUS showed better delineation of the lesions [28].

Doppler ultrasound does have certain drawbacks that can be overcome by CEUS. In cases of incomplete (less than 360-degrees) torsion, the affected side can often maintain some vascularity, making comparison of color Doppler signals with the normal side difficult, enabling CEUS to facilitate a diagnosis in the context of low-flow states [28]. In 2011, CEUS was used to examine 50 out of 613 cases (8.6%) in which ultrasound with color Doppler proved inadequate in reaching a definitive diagnosis, with contrast enhancement providing additional perfusion findings that improved diagnoses [29]. The subset of inconclusive cases with testicular torsion displayed questionable flow artifacts on color Doppler, and an absence of perfusion with CEUS.

Testicular hematomas represent a diagnostic pitfall of conventional ultrasound, since its appearance on ultrasound may mimic other conditions, particularly testicular seminomas. Depending on the time interval between the traumatic event and the time of imaging, there can be overlap between imaging findings. On ultrasound, testicular hematomas present acutely as a focal avascular hyperechoic lesion, with echogenicity decreasing over time [30], while seminomas are usually homogeneously hypoechoic [31]. The addition of CEUS proved useful in a case study of a 19-year-old male presenting with scrotal trauma highlighting this dilemma. The initial scrotal ultrasound showed a mildly hypoechoic, ill-defined area, and follow-up Doppler ultrasound demonstrated no vascular signal, but inadequate evaluation of the testicular capsule in the damaged area [32]. Since MRI was not immediately available, subsequent CEUS was utilized, and clearly demonstrated the integrity of the testicular capsule, supporting the hypothesis of testicular hematoma, a fundamental finding that changed the patient's management [32]. While color Doppler added more information from baseline ultrasound, doubts remained about the extension of the lesion and capsule involvement, which was only identified upon further evaluation with CEUS.

## Musculoskeletal Trauma

Muscle injuries are frequently observed, and diagnostic imaging is often essential in providing an accurate assessment of injury severity. Ultrasound has long been used for the imaging and diagnosis of muscular injuries, but the accuracy in diagnosing minor, low-grade lesions is limited. MRI has been shown to be superior to ultrasound in providing detailed analysis and characterization of intramuscular lesions, but in clinical practice, is often reserved for serious injuries or injuries refractory to treatment.

Early studies suggesting CEUS as a functional real-time biomarker for muscle viability and function [33,34] have resulted in its application in many orthopedic settings. An early 2007 study used CEUS to monitor intramuscular repair processes within 48 hours of injury, and after 20, 40, and 60 days, and allowed estimation of when athletes were able to return to competitive activity [35], but did not use MRI as a reference standard.

A 2015-2016 study investigated the diagnostic value of CEUS compared with conventional ultrasound and MRI in diagnosing muscle injuries of varying severity [36]. Among grade I injuries, no intramuscular lesions were identified on conventional ultrasound, while all were identified following UCA administration. While grade I injuries are typically managed nonoperatively, they may result in muscular weakness and recurrent injury. The role of CEUS in the diagnostic imaging of muscular injuries may provide prognostic information with regard to healing times.

Among shoulder injuries, supraspinatus tendon tears are a common indication for surgical intervention, and despite current predictors of postoperative function using MRI-based parameters and patient's demographic data (age, gender, comorbidities), retear rates remain high. A study in 2020 found that preoperative CEUS-based assessment of supraspinatus perfusion significantly correlated with early postoperative shoulder function ($P < 0.018$) and tender retear ($P < 0.001$) [37]. These findings suggest the implementation of CEUS-based preoperative supraspinatus muscle perfusion to be a potentially beneficial predictor of postoperative outcomes.

Traumatic soft tissue injuries and fractures have a rare, but feared complication of developing acute compartment syndrome, with increased compartmental pressures leading to reduction of local tissue perfusion, and the potential to cause irreversible muscle damage. Perfusion of acute compartment syndrome using CEUS was studied in a small set of 8 patients to monitor changes in microcirculation, and a reduced wash-in of microbubbles was observed in all patients [38], but the sample size was too small to define critical values or correlate reduced perfusion with severity, warranting further investigation in subsequent studies.

In the context of traumatic fracture repair, bacterial infection remains a potentially severe complication, and may lead to adverse outcomes including long bone non-union. A recent study in 2021 used CEUS preoperatively to evaluate hypervascularity at the site of nonunion as a potential parameter for infection. CEUS performed 1-3 days prior to revision surgery reliably predicted the results of intraoperative tissue sample cultures (92.3% sensitivity, 100% specificity), but showed no significant correlation with the results from implant sonication following removal [39]. While CEUS may prove to be a valuable preoperative diagnostic tool that can reliably predict microbiology of tissue culture samples, hypervascularity is only one possible sign of an infection, and may not be present throughout the entire course of an infected nonunion.

## Central Nervous System Trauma

Traumatic brain injury (TBI) is the second most common injury encountered in trauma medicine [40], with a high death rate and incidence of post-traumatic disability. Modern neurosurgical care attempts to minimize secondary insult through early detection and effective prevention, with CT and MRI as useful imaging modalities in preoperative TBI classification and postoperative follow-up. Nonetheless, the characteristics of a traumatic lesion intraoperatively may differ significantly from preoperative CT or MRI, and without intraoperative imaging guidance, it can be difficult to assess the affected region of brain damage in the attempts at preserving normal brain tissue during tissue or hematoma removal. With CEUS, enhancement patterns and perfusion in traumatic lesions are considered to be important indicators of tissue viability.

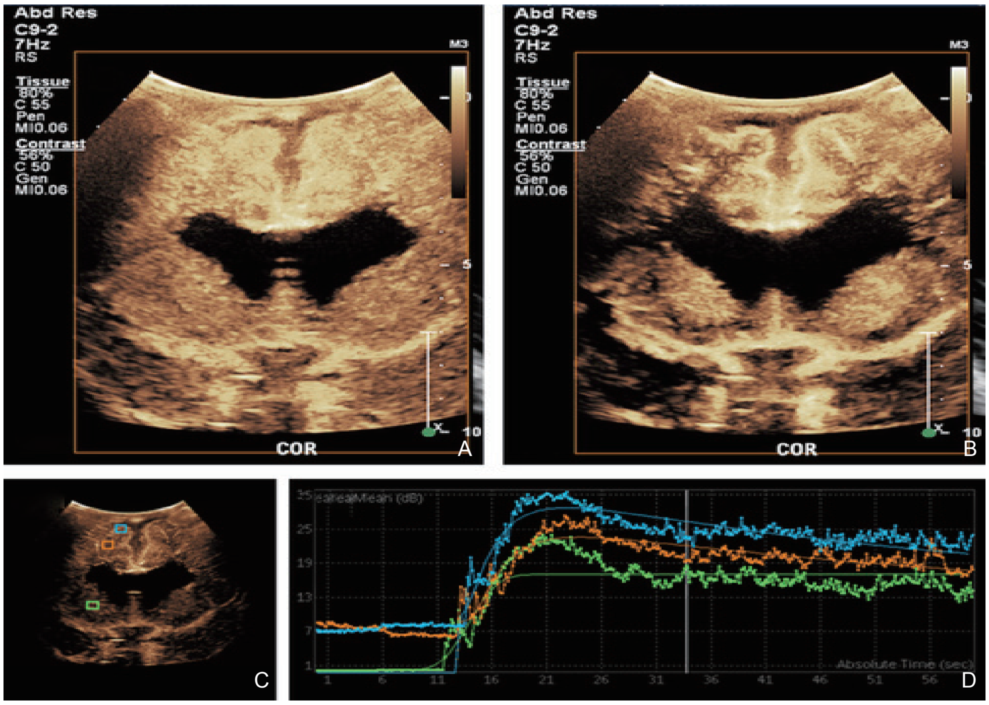


**Figure 5** Time-dependent changes on CEUS imaging using perfusion kinetics in the brain of a 9-month-old following cardiac arrest. (A) a coronal CEUS image 15 seconds after contrast injection, showing avid perfusion to the cortical region; (B) a coronal CEUS image 20 seconds after contrast injection, showing prolonged hyperperfusion to the peripheral gray and white matter; (C) Regions of interest selected; (D) unique perfusion kinetic curves generated in a region-specific manner. Reproduced from [42].

CEUS is a quantifiable technique in which wash-in curves obtained following intravascular microbubble administration are used to obtain perfusion kinetic parameters [41]. The kinetic parameters, including wash-in slope, time to peak, peak intensity, and area under the curve, are demonstrated as time-dependent changes on CEUS imaging, as seen in Figure 5. This technique can enable bedside diagnosis and serial monitoring of brain perfusion abnormalities in hemodynamically unstable patients in which transport to MRI is not feasible. A prospective cohort study of 8 neonates and infants with suspected hypoxic ischemic injury were evaluated with

CEUS, and results showed that the ratios at the peak enhancement, wash-in area under the curve, perfusion index, and maximum wash-in slopes were lower in all of the cases compared to the normal group but was not statistically significant given the small sample size [42]. A larger prospective study evaluating the correlation between CEUS findings and the reference standard of diffusion- and perfusion-weighted MRI is needed to further establish CEUS as a diagnostic tool.

A 2013 study compared intraoperative CEUS with conventional ultrasound in neurosurgical treatment of TBI, with surgical results as the gold standard. The accuracy in localizing TBI and detecting intracranial hematoma was 100% with intraoperative CEUS, compared with 51% using conventional ultrasound [40]. CEUS imaging displayed normal brain tissue as homogenous enhancement, brain contusion as low enhancement, and hematoma as no enhancement. 21 of the 32 cases redesigned their interventional procedure according to difference in size, border between lesion and normal brain tissue, brain perfusion, and vascularity seen on intraoperative CEUS compared to intraoperative conventional ultrasound and preoperative CT [40].

Extensive research has been dedicated to methods of monitoring cerebral perfusion, which is essential in preventing secondary brain damage in patients with acute brain injury [43]. Three different approaches for CEUS have been used to measure cerebral perfusion pressure, which are based on bolus, refill, and depletion kinetics [44]. Bolus kinetics utilizes the increase in acoustic intensity as a bolus of microbubbles is injected, using a time-intensity curve (TIC) to quantify the parenchymal perfusion, whereas refill kinetics focuses on the reappearance of UCA into the plane after complete destruction of the microbubbles using high mechanical index (MI) flashes [45]. Depletion kinetics analyzes perfusion status by destruction curves, and the difference in acoustic intensity before and after UCA destruction [45]. A 2017 systematic review included 43 studies with a total of 861 patients, assessing the tolerability, repeatability, reproducibility, and accuracy of the different CEUS techniques in quantifying cerebral perfusion, finding CEUS to have a sensitivity and specificity ranging from 75-96% and 60-100%, respectively, in the detection of cerebral ischemia [43].

## Emergency & Critical Care

CEUS offers several advantages over other imaging modalities in assessing an acute patient. In an ICU setting, CEUS allows imaging of critically ill patients without the need for transport to other departments or imaging suites, and due the non-nephrotoxic effects of UCAs, examination can be performed without the need for preliminary labs. CEUS is a dynamic technique that can acquire images over time, and unlike CT, is not subject to motion-blurring artifacts. CEUS has several potential applications relevant to critical care and ICU medicine, as seen in Table 2. In one case report, CEUS was used in the ICU at the bedside to identify acute complications following traumatic pathology (liver, spleen, kidney) and hemorrhagic complications following interventional procedures [47]. While CEUS cannot replace CECT, it is sensitive, quickly available at the bedside, and can precisely quantify ischemia in many organs. A 2021 pilot study investigated adjunct CEUS in the surgical assessment of patients evaluated for suspected small bowel ischemia, using delayed enhancement as an indicator of intestinal ischemia [48]. In 12 cases with recent CT imaging suggesting bowel ischemia, CEUS demonstrated simultaneous enhancement in 91.7% (11/12), interpreted to suggest no or subclinical small intestinal ischemia. Importantly, no cases ruled out by CEUS demonstrated ischemia (in the 5 patients that underwent surgery) or failed to resolve with non-operative management, emphasizing the importance of combining imaging techniques with clinical and laboratory findings [48].

**Table 2** Selected indications for point-of-care contrast medium-enhanced ultrasonography. Modified from [46].

| Organ system | Potential indications |
|---|---|
| Cardiac | Left ventricle visualization, myocardial ischemia |
| Abdominal aorta | Abdominal aortic aneurysm (AAA) rupture, aortic dissection |
| Venous | Improved visualization of deep venous system |
| Lung | Differentiation between pneumonia and infarction |
| Kidney | Lacerations, hematomas, infarcts, abscesses, perfusion |
| Liver & biliary | Lacerations, hematomas, acute cholecystitis |
| Spleen | Lacerations, hematomas, infarcts |
| GI tract | Activity of Inflammatory bowel disease (IBD) |
| Scrotum | Testicular torsion/infarct, infections, hematomas |
| Musculoskeletal | Actively bleeding hematomas, compartment syndrome muscle perfusion |

## Summary

In considering the wide spectrum of injuries encountered in trauma, the versatility of CEUS makes it advantageous to use as it can augment or substitute other imaging technologies to identify injuries. In addition, it can be available at bedside and can be employed while resuscitation efforts are ongoing. To date, much of the applications of CEUS are in the early stages of clinical use and require further validation to gain greater clinical relevance. The use of UCAs improves the sensitivity and specificity over conventional ultrasound, making CEUS a useful adjunct in urgent clinical settings, both diagnostically and therapeutically.

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## Conflict of Interest

Authors do not have conflict interests related to this paper to declare.

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