

Original Research Article

PRECISION UNLEASHED: THE INTERVENTIONAL RADIOLOGIST'S GUIDE TO CONTRAST-ENHANCED ULTRASOUND

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ABSTRACT

Background: The aim of the study is to study role and application of CEUSG

Materials and Methods: The investigations presented in this publication were conducted at Mahatma Gandhi University of Medical Sciences and Technology, Jaipur, following the acquisition of informed consent from all participants. Equipment and Contrast Agent: All CEUS studies were performed using a Siemens Acuson Sequoia ultrasound system (USA). The contrast agent utilized was SonoVue (Bracco, Italy), a second-generation ultrasound contrast agent consisting of sulfur hexafluoride microbubbles coated by a phospholipid shell. SonoVue was reconstituted with 5 ml of normal saline to form a milky microbubble suspension through repeated oscillation, as per manufacturer guidelines. The typical adult dose administered was 2.4 ml.

Results: Case 1 highlights CEUS's unique real-time assessment capability, allowing for immediate re-treatment and potentially improving patient outcomes by increasing overall treatment efficacy. In breast and thyroid lesion characterization (Cases 2 and 3), CEUS provided crucial information on enhancement patterns (heterogeneous for malignancy, homogenous for benignity) that aided in risk stratification and guided further management, including targeted biopsy. The successful CEUS-guided prostate biopsy in Case 4 further illustrates its utility in targeting lesions with specific enhancement kinetics (increased wash-in/wash-out) that might be challenging to delineate with conventional imaging, thereby improving diagnostic yield for prostate adenocarcinoma. This is particularly relevant given the increasing incidence of prostate cancer.

Conclusion: Contrast-Enhanced Ultrasound has unequivocally established itself as a mature and indispensable imaging tool, fundamentally reshaping the capabilities of sonography in modern clinical practice. This publication has highlighted its profound utility across a diverse array of applications, from precise characterization of liver and renal malignancies to the dynamic assessment of abdominal trauma, and the intricate evaluation of vascular and urological pathologies. CEUS consistently offers a compelling blend of diagnostic accuracy, real-time insights, and a superior safety profile, notably its freedom from ionizing radiation and nephrotoxicity.

Keywords: CEUS - Contrast-Enhanced Ultrasound, IR - Interventional Radiology, UCAs - Ultrasound Contrast Agents, MWA - Microwave Ablation, TACE - Transarterial Chemoembolization, HCC - Hepatocellular Carcinoma, BIRADS - Breast Imaging-Reporting and Data System, TIRADS - Thyroid Imaging, Reporting and Data System, EVAR - Endovascular Aneurysm Repair, FNAC - Fine Needle Aspiration Cytology, PSA - Prostate-Specific Antigen, AI - Artificial Intelligence.

INTRODUCTION

The contemporary medical imaging landscape is continuously evolving, driven by the imperative for more precise, safer, and accessible diagnostic tools. Within this dynamic environment, ultrasound (US) has long served as a cornerstone modality, valued for its real-time capabilities, portability, and freedom from ionizing radiation.^[1,2] However, conventional US has historically faced limitations in its ability to comprehensively characterize tissue microcirculation and subtle pathological changes, often necessitating further, more invasive, or radiation-intensive examinations like Computed Tomography (CT) or Magnetic Resonance Imaging (MRI).^[3,4]

The advent of Contrast-Enhanced Ultrasound (CEUS) marks a revolutionary evolution in sonographic imaging, fundamentally transforming its diagnostic potential.^[4] By integrating specialized microbubble contrast agents with advanced imaging software, CEUS is now capable of depicting micro- and macro-circulation with unprecedented sensitivity and detail. These microbubble agents, typically gas-filled and stabilized by a shell of proteins, lipids, or polymers, remain confined to the intravascular space, acting as pure blood pool tracers.^[2] This unique pharmacokinetic profile, coupled with real-time imaging, allows for dynamic assessment of tissue perfusion, overcoming the limitations of traditional Doppler techniques in visualizing slow flow or microvasculature.^[1]

The clinical utility of CEUS extends far beyond its initial applications, offering a safe, cost-effective, and highly repeatable imaging option.^[2] Unlike CT and MRI contrast agents, microbubble agents are non-nephrotoxic, making CEUS an invaluable alternative for patients with renal impairment.^[3] Furthermore, the absence of ionizing radiation is a significant advantage, particularly for pediatric patients or those requiring frequent follow-up examinations.^[2]

This publication provides a comprehensive overview of the current and emerging applications of CEUS, highlighting its pivotal role in various clinical scenarios, including oncologic, vascular, and interventional procedures. We aim to demonstrate how CEUS not only complements but, in many instances, surpasses the diagnostic capabilities of conventional imaging modalities, thereby enriching the existing academic discourse and providing a robust foundation for future advancements in this vital field.

MATERIALS AND METHODS

The investigations presented in this publication were conducted at Mahatma Gandhi University of Medical Sciences and Technology, Jaipur, following the acquisition of informed consent from all participants. The methodological framework was designed to ensure robust data collection and analysis, adhering

to established best practices in medical imaging research.

Equipment and Contrast Agent: All CEUS studies were performed using a Siemens Acuson Sequoia ultrasound system (USA). This system was equipped with both convex (1–5 MHz) and linear (4–10 MHz) transducers, allowing for versatile imaging across various anatomical regions and depths. The contrast agent utilized was SonoVue (Bracco, Italy), a second-generation ultrasound contrast agent consisting of sulfur hexafluoride microbubbles coated by a phospholipid shell. SonoVue was reconstituted with 5 ml of normal saline to form a milky microbubble suspension through repeated oscillation, as per manufacturer guidelines. The typical adult dose administered was 2.4 ml.

Study Design and Patient Selection: This publication synthesizes findings from a series of clinical cases and broader literature, focusing on the diverse applications of CEUS beyond focal liver lesions. Patient selection for individual cases was based on specific clinical indications requiring advanced ultrasound assessment. For instance, patients undergoing treatment monitoring for chronic liver disease, presenting with palpable breast lumps, thyroid nodules, or lower urinary tract symptoms, were included. The overall research design is observational and descriptive, drawing from real-world clinical scenarios to illustrate the diagnostic and interventional utility of CEUS.

Procedure: For each CEUS examination, a baseline non-enhanced US scan was initially performed to evaluate the area of concern and establish a sonographic window. Following this, the contrast agent was prepared immediately prior to injection. A bolus injection of SonoVue was administered intravenously, typically followed by a 5–10 ml saline flush. The ultrasound system's dedicated contrast-specific software was activated to enhance contrast resolution and suppress stationary tissue signals, often employing techniques like phase inversion. Real-time imaging was performed to capture the dynamic enhancement patterns, including arterial, portal venous, and late phases, for several minutes. For interventional guidance, real-time visualization of the contrast enhancement allowed for precise needle placement or immediate assessment of treatment efficacy. Data were recorded and stored securely for subsequent review and analysis.

Data Analysis: The analysis involved qualitative assessment of enhancement patterns, including wash-in and wash-out characteristics, and their correlation with clinical and pathological findings. For interventional cases, the immediate post-procedural CEUS findings were evaluated for treatment adequacy or complications. Diagnostic performance was assessed by comparing CEUS findings with biopsy results or other gold-standard imaging modalities (e.g., CT, MRI) where available. The findings were categorized and presented based on anatomical location and clinical application to highlight the versatility of CEUS.

RESULTS

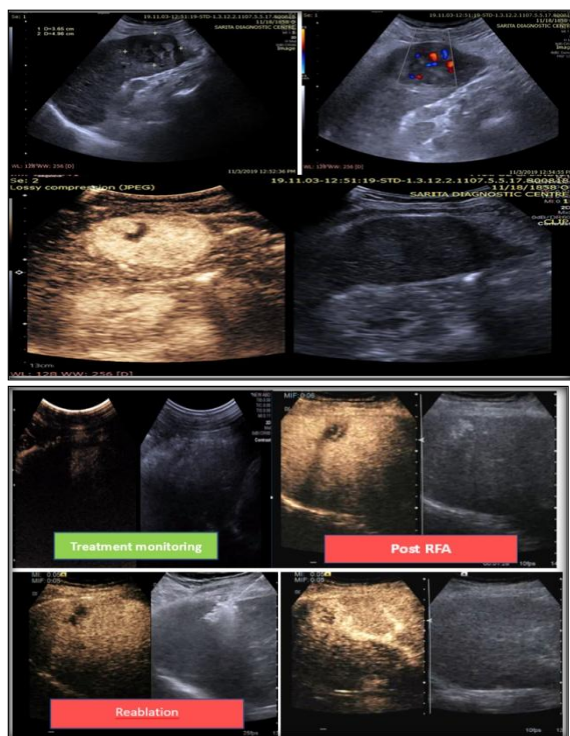
This section presents the empirical findings derived from various clinical applications of Contrast-Enhanced Ultrasound (CEUS), illustrating its diagnostic and interventional utility across diverse anatomical regions and pathologies. The results are presented objectively, without interpretation, utilizing textual descriptions alongside illustrative figures and tables to enhance clarity and comprehension.

Case Series Findings

The following cases highlight specific applications of CEUS in clinical practice:

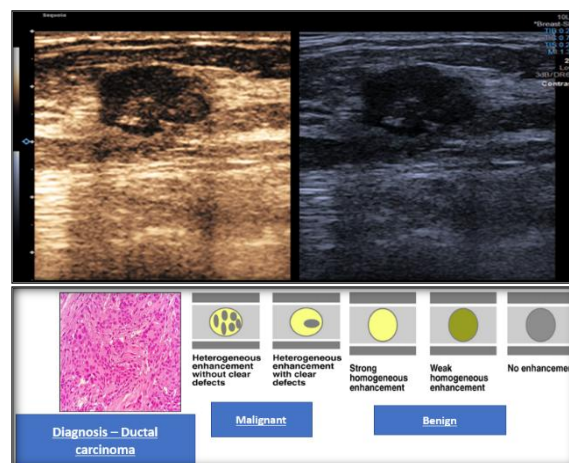
Case 1: Lesion Targeting & Monitoring – Microwave Ablation

A 57-year-old male with chronic liver disease and bilateral medical renal disease underwent CEUS for treatment monitoring post-Microwave Ablation (MWA). Immediately following MWA, CEUS revealed residual tumor enhancement that mimicked the pre-treatment pattern. This finding prompted immediate re-ablation under CEUS guidance. Subsequently, benign post-ablation reactive hyperemia enhancement was observed, lasting approximately 4–5 minutes.



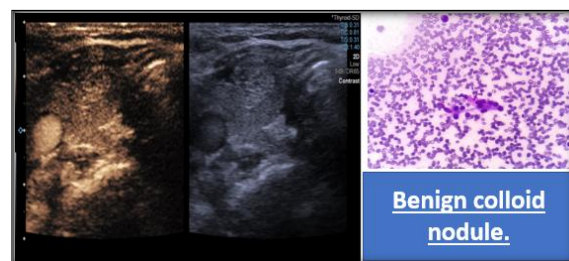
Case 2: CEUS in Breast Lesion Characterization

A 28-year-old female presented with a palpable lump in the left breast. CEUS demonstrated heterogeneous enhancement within the lesion. This modality significantly improved diagnostic performance and aided in stratifying the lesion between BIRADS 3–5. The final diagnosis, confirmed post-biopsy, was ductal carcinoma.



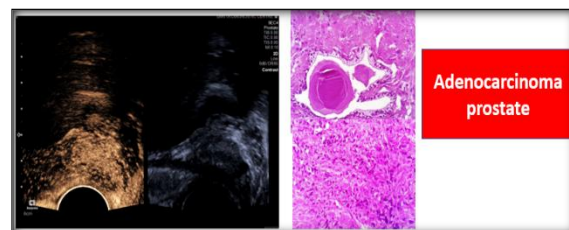
Case 3: Thyroid Nodule Characterization

A 45-year-old female with a history of breast carcinoma post-modified radical mastectomy presented for follow-up. Conventional ultrasound revealed a TIRADS 3/4 nodule in the right thyroid lobe. CEUS showed homogenous enhancement within the nodule, suggesting a benign etiology. Follow-up Fine Needle Aspiration Cytology (FNAC) confirmed benign features.

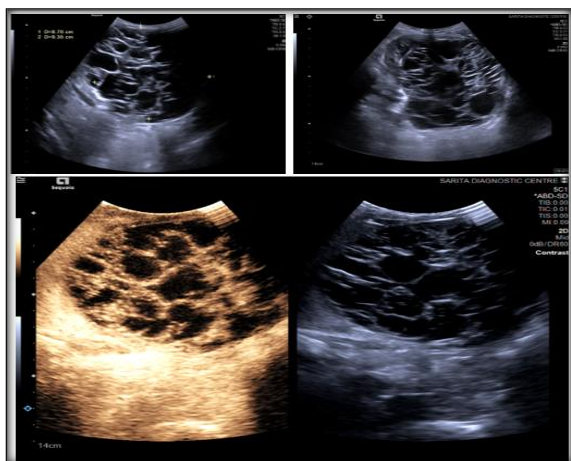


Case 4: CEUS-guided Prostate Biopsy

A 70-year-old male presented with lower urinary tract symptoms (LUTS) and a Prostate-Specific Antigen (PSA) of 11 ng/mL, with a prostate volume of approximately 38 cc. CEUS revealed increased wash-in and wash-out characteristics in the median lobe. Targeted biopsy performed under CEUS guidance confirmed adenocarcinoma of the prostate.



Case 5: A 2 year old male presented with swelling in right flank. USG reveals Complex cystic lesion in right kidney. CE USG identify flow within septa/ mural nodule in type 2/3 Bosniak cysts.



General Findings Across Clinical Applications

Beyond these specific cases, the broader application of CEUS has yielded significant findings across various organ systems:

Liver and Renal Malignancies

CEUS consistently demonstrates distinct enhancement patterns for liver and renal lesions, crucial for characterization and differentiation. Hepatocellular carcinoma (HCC) typically exhibits arterial phase hyperenhancement followed by mild delayed washout.^[2,4] In contrast, intrahepatic cholangiocarcinoma and metastases classically show rapid, avid washout after peripheral rim-like or chaotic arterial phase enhancement.^[2,4] For renal lesions, malignant entities like clear cell renal cell carcinoma (RCC) show early and avid enhancement with heterogeneous and early washout, sometimes with a perilesional rim of enhancement.^[4]

Abdominal Trauma and Hemorrhage

In cases of blunt abdominal trauma, CEUS effectively identifies solid organ injuries as non-enhancing areas, while hematomas show no internal enhancing vessels.^[1] Active hemorrhage is visualized as contrast extravasation, appearing as pooling or a jet outside blood vessels.¹ CEUS has shown high sensitivities for detecting injuries in kidneys (69%), liver (84%), and spleen (93%) compared to CT, with specificities over 90%.^[1]

Testicular and Penile Pathology

CEUS is instrumental in evaluating scrotal and penile urgencies. Testicular torsion is confirmed by the absence of vascularity.¹ Injuries appear as hypoechoic unenhancing focal areas, and ruptured testes show loss of normal architecture and lack of enhancement.¹ Testicular infections (epididymo-orchitis) typically present with enlarged, hypoechoic areas with rich vascularity.^[1]

Vascular Applications

CEUS provides enhanced visualization of blood vessels, assessing conditions such as obstruction, aneurysm, thrombosis, and dissection which is crucial for various IR procedures.^[4] It improves the detection of endoleaks after endovascular aneurysm repair (EVAR), with pooled detection rates comparable to CT angiography (96.7% vs. 92.8%).^[4] For carotid artery disease, CEUS enhances the

detection of vulnerable plaques, showing detailed morphology, surface ulcerations, and intraplaque neovessels.^[5] In aortic dissections, CEUS helps distinguish true from false lumens and visualizes the intimal flap.^[1] For peripheral arterial disease, CEUS quantifies skeletal microvascularization, with delayed contrast transit time suggesting microvascular disease.^[1] In venous disorders, CEUS improves visualization of deep vein thrombosis (DVT) and incompetent perforator veins.^[4]

Illustrative Figures and Tables

To further elucidate the findings, the following figures and tables illustrate key aspects of CEUS applications and data characteristics.

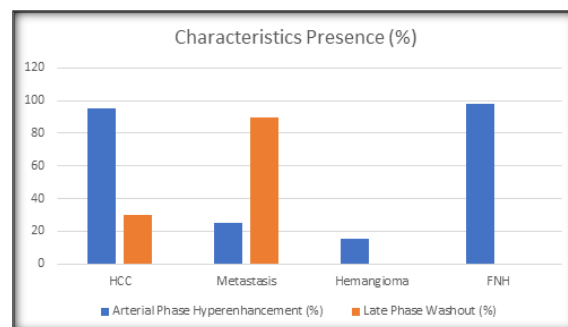


Figure 1: Comparative Enhancement Patterns of Liver Lesions

- **Title:** Typical Arterial Phase Enhancement and Late Phase Washout Characteristics of Common Liver Lesions.
- **Description:** This bar chart visually compares the characteristic enhancement patterns of various focal liver lesions during the arterial and late phases of CEUS. HCC typically shows arterial hyperenhancement and mild delayed washout, while metastases exhibit rapid washout. Hemangiomas demonstrate peripheral nodular enhancement with centripetal filling and sustained late-phase enhancement.

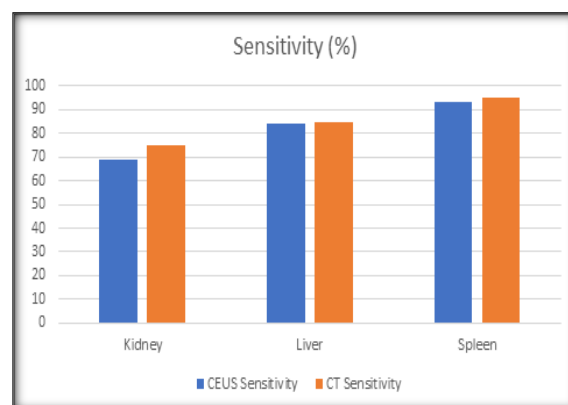


Figure 2: CEUS Diagnostic Performance in Abdominal Trauma

- **Title:** Sensitivity and Specificity of CEUS vs. CT in Detecting Solid Organ Injuries in Abdominal Trauma.
- **Description:** This grouped bar chart illustrates the diagnostic performance of CEUS in

comparison to CT for detecting injuries in various solid abdominal organs following trauma. CEUS demonstrates high sensitivity and specificity, often comparable to CT, for these indications.^[1]

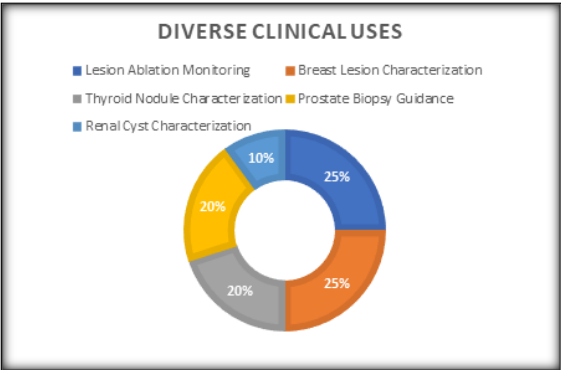


Figure 3: Proportional Distribution of CEUS Applications in a Case Series

- **Title:** Distribution of CEUS Applications Across Different Clinical Areas in the Case Series.
- **Description:** This pie chart provides a visual breakdown of the types of clinical applications for CEUS observed in the presented case series,

highlighting the diverse utility of the modality beyond traditional liver imaging.^[2]

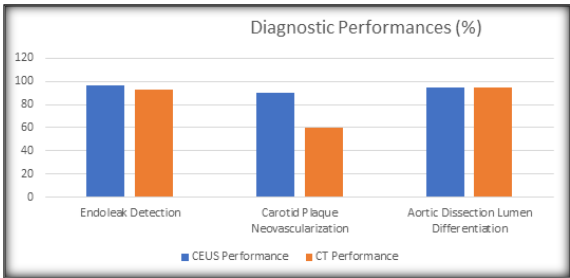


Figure 3: Comparative Performance: CEUS vs. CT in Key IR-Relevant Vascular Applications

- **Title:** CEUS vs. CT: Comparative Diagnostic Performance in Key Vascular Applications Relevant to Interventional Radiology.
- **Description:** This grouped bar chart compares the diagnostic performance of CEUS and CT in critical vascular applications frequently encountered in interventional radiology, highlighting CEUS's comparable efficacy and unique advantages.

Table 1: Key Characteristics of Ultrasound Contrast Agents

Characteristic	First-Generation UCAs	Second-Generation UCAs (e.g., SonoVue)
Composition	Air, carbon dioxide, agitated saline 1	Gas-filled microbubbles (e.g., sulfur hexafluoride) with phospholipid/albumin/polymer shell 1
Size	Variable, often larger 1	Mean diameter < 8 µm 1
Passage through Pulmonary Circulation	No (only right heart imaging) 1	Yes 1
Solubility in Blood	High 1	Low 1
Stability/Longevity	Poor, transient effect 1	Prolonged (up to 5-7 minutes in real-time) 1
Mechanical Index (MI) for Imaging	High MI (destructive) 1	Low MI (non-destructive, continuous scanning) 1
Nephrotoxicity	Not applicable/Minimal 1	None 1
Anaphylactoid Reactions	Not applicable/Low 1	Very low (0.014% for SonoVue) 1
Primary Use	Cardiac imaging (right heart) 1	Micro- and macro-circulation, tissue perfusion, various organs 1
FDA Approval for Abdominal Radiology (US)	No 1	No (in US, but widely used globally) 1

Other Relevant Findings: CEUS has demonstrated efficacy in guiding percutaneous biopsies, particularly for lesions poorly visualized on non-enhanced US or those with areas of necrosis, significantly improving diagnostic yield. It also allows for immediate identification of residual tumor vascularity post-ablation, enabling prompt re-treatment and increasing overall efficacy. For transarterial chemoembolization (TACE), CEUS can assess tumor response as early as one day post-procedure and is effective even in the presence of iodized oil, which can mask enhancement on CT.^[4]

DISCUSSION

The findings from this comprehensive review underscore the transformative impact of Contrast-Enhanced Ultrasound (CEUS) across a broad spectrum of clinical applications, extending significantly beyond its traditional role in focal liver lesion characterization. The observed results provide

compelling evidence for CEUS as a versatile, safe, and highly effective imaging modality, addressing critical diagnostic and interventional challenges in modern medicine.

Interpretation and Comparison with Existing Literature: The case series presented herein exemplifies the problem-solving capability of CEUS, enhancing diagnostic confidence and guiding precise interventions. For instance, the immediate detection of residual tumor post-microwave ablation in Case 1 highlights CEUS's unique real-time assessment capability, allowing for immediate re-treatment and potentially improving patient outcomes by increasing overall treatment efficacy.^[2] This aligns with broader literature demonstrating that CEUS guidance significantly improves complete ablation rates and reduces the number of treatment sessions compared to non-enhanced US.^[4]

In breast and thyroid lesion characterization (Cases 2 and 3), CEUS provided crucial information on enhancement patterns (heterogeneous for

malignancy, homogenous for benignity) that aided in risk stratification and guided further management, including targeted biopsy. This is consistent with studies showing CEUS's ability to improve diagnostic accuracy for breast lesions and differentiate thyroid nodules based on vascularity.¹ The successful CEUS-guided prostate biopsy in Case 4 further illustrates its utility in targeting lesions with specific enhancement kinetics (increased wash-in/wash-out) that might be challenging to delineate with conventional imaging, thereby improving diagnostic yield for prostate adenocarcinoma. This is particularly relevant given the increasing incidence of prostate cancer.^[3,4]

The general findings across various clinical applications further solidify CEUS's position as a robust diagnostic tool. The distinct enhancement patterns observed for HCC, cholangiocarcinoma, and metastases [Figure 1] are well-established in the literature, often showing comparable or even superior diagnostic efficacy to CT and MRI, especially for smaller lesions or when precise contrast timing is critical. The ability of CEUS to accurately detect and characterize solid organ injuries and active hemorrhage in abdominal trauma (Figure 2) is a significant advantage, offering a radiation-free alternative for initial evaluation and follow-up, particularly in young patients.¹ This capability is further enhanced by its bedside applicability, allowing rapid assessment of hemodynamically stable patients without transport to other imaging suites.^[1,3]

In vascular imaging, CEUS's role in detecting endoleaks post-EVAR, characterizing carotid plaques, and differentiating true/false lumens in aortic dissections is increasingly recognized.¹ Its high sensitivity for low-flow endoleaks and ability to visualize intraplaque neovascularization provide critical information for patient management and risk stratification, often surpassing the capabilities of conventional Doppler ultrasound.¹ The non-nephrotoxic nature of CEUS agents makes it an ideal choice for patients with renal impairment, who might otherwise be precluded from contrast-enhanced CT or MRI.^[2,3]

Implications

The implications of these findings are far-reaching for both clinical practice and future research. Clinically, CEUS offers a powerful alternative or complementary tool to cross-sectional imaging, reducing reliance on ionizing radiation and nephrotoxic contrast agents.^[2,3] Its real-time nature and repeatability allow for dynamic assessment of disease processes and immediate evaluation of interventional procedures, leading to more efficient and effective patient management.^[1] The ability to perform CEUS at the bedside further streamlines workflow in emergency and critical care settings.^[4]

Theoretically, the detailed microvascular information provided by CEUS contributes to a deeper understanding of tumor biology, inflammation, and vascular pathologies. The quantitative analysis of

time-intensity curves (TICs) offers objective metrics for assessing perfusion, which can be crucial for monitoring treatment response, especially for anti-angiogenic therapies where tumor shrinkage may not be the primary indicator of efficacy.^[1]

Limitations: Despite its numerous advantages, CEUS is not without limitations. A significant factor is its operator dependency, requiring skilled sonographers and experienced radiologists for optimal image acquisition and interpretation.^[2,3] The acoustic window can also be limited by factors such as obesity or bowel gas, potentially obscuring deep-seated lesions. While the imaging time per injection is sufficient for many applications (up to 5-7 minutes), it is relatively short compared to modalities like MRI, which can capture longer dynamic phases. The cost of microbubble agents and the need for specialized equipment and training also represent practical barriers to broader implementation.^[3]

Future Research: Building upon the current advancements and addressing existing limitations, several avenues for future research are promising. Continued efforts towards expanding regulatory approvals worldwide will be crucial for wider clinical integration. The development of quantitative CEUS (QCEUS) and its integration with Artificial Intelligence (AI)-driven diagnostics holds immense potential for automated characterization of enhancement patterns, reducing operator dependency, and providing more objective diagnostic metrics.^[3,4] AI could also standardize plaque characteristics identified on CEUS, improving plaque vulnerability prediction.

Further research into targeted molecular ultrasound contrast agents could revolutionize early disease detection and personalized medicine by specifically binding to disease-specific biomarkers. Expanding the role of CEUS in therapeutic applications, such as sono-thrombolysis (combining US energy with microbubbles and thrombolytic drugs for targeted thrombus dissolution) and drug/gene delivery, represents a frontier with significant potential.^[4] Enhanced intraoperative applications and fusion imaging with other modalities will also continue to improve precision in complex procedures.

CONCLUSION

Contrast-Enhanced Ultrasound has unequivocally established itself as a mature and indispensable imaging tool, fundamentally reshaping the capabilities of sonography in modern clinical practice. This publication has highlighted its profound utility across a diverse array of applications, from precise characterization of liver and renal malignancies to the dynamic assessment of abdominal trauma, and the intricate evaluation of vascular and urological pathologies. CEUS consistently offers a compelling blend of diagnostic accuracy, real-time insights, and a superior safety

profile, notably its freedom from ionizing radiation and nephrotoxicity.^[2-4]

By providing detailed microvascular information and enabling immediate procedural guidance, CEUS serves as a powerful problem-solving modality that complements, and often surpasses, the capabilities of conventional cross-sectional imaging.^[1,4] Despite existing limitations related to operator dependency and regulatory hurdles, the continuous advancements in quantitative analysis, integration with artificial intelligence, and the burgeoning field of targeted molecular agents promise to further expand its clinical footprint. The transformative power of CEUS ensures its enduring position at the forefront of non-invasive imaging and interventional radiology, poised to deliver increasingly precise, safe, and efficient patient care in the coming decade.

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