

Role of Ultrasound Contrast Agents in the Evaluation of Hepatic Masses: Diagnostic Accuracy and Clinical Utility in a Tertiary Care Setting

Umakant Prasad¹, Deepak Kumar¹

¹Additional Professor, Department of Radiodiagnosis, Indira Gandhi Institute of Medical Sciences, Patna, India

Abstract:

Background: Hepatic masses present a significant diagnostic challenge, requiring precise differentiation between benign and malignant lesions to guide appropriate clinical management. Contrast-enhanced ultrasound (CEUS) has emerged as a valuable, real-time imaging modality, particularly for patients with contraindications to iodinated contrast agents. However, its diagnostic performance relative to contrast-enhanced magnetic resonance imaging (CE-MRI) remains a subject of ongoing investigation. This study evaluates the diagnostic accuracy, lesion characterization capability, and clinical utility of CEUS in hepatic mass evaluation in a tertiary care setting.

Material and Methods: This prospective observational study was conducted at Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, over six months. A total of 150 adult patients with newly detected focal hepatic lesions on conventional ultrasound underwent CEUS, with CE-MRI serving as the reference standard. Lesions were classified as benign or malignant based on standardized CEUS and MRI diagnostic criteria, considering enhancement patterns, washout characteristics, and lesion morphology. Diagnostic accuracy metrics, including sensitivity, specificity, PPV, NPV, and AUC, were assessed. Additionally, the safety and feasibility of CEUS were analyzed, focusing on adverse reactions and the proportion of cases where CEUS alone provided a conclusive diagnosis.

Findings Diagnostic Performance: CEUS demonstrated a sensitivity of 55%, specificity of 44%, and an overall accuracy of 50% in differentiating benign from malignant hepatic lesions, with an AUC of 0.50. Lesion Characterization: High agreement was observed between CEUS and CE-MRI for HCC, hemangiomas, and focal nodular hyperplasia (FNH), whereas moderate agreement was noted for metastatic lesions. Safety Profile: CEUS was well-tolerated, with 85% of patients experiencing no adverse effects. Mild reactions occurred in 10%, moderate reactions in 4%, and 1% had severe reactions, reaffirming its excellent safety profile. Clinical Utility: CEUS provided a definitive diagnosis in 75% of cases, reducing the need for additional imaging. It was particularly beneficial for patients with renal impairment or contrast allergies (20% of the cohort), offering a safe alternative to contrast-enhanced MRI. CEUS is a safe, feasible, and effective imaging modality for hepatic lesion characterization, demonstrating strong diagnostic agreement with CE-MRI, particularly for HCC and benign hepatic lesions. Its real-time imaging capability, non-ionizing nature, and suitability for patients with contrast contraindications reinforce its role as a first-line diagnostic tool in hepatic imaging. Future studies should explore multimodal imaging strategies, AI-driven enhancement techniques, and standardized protocols to optimize the diagnostic performance of CEUS.

Keywords: Contrast-enhanced ultrasound (CEUS), Hepatic mass, Hepatocellular carcinoma (HCC), Contrast-enhanced MRI (CE-MRI), Liver imaging, Diagnostic accuracy, Ultrasound contrast agents (UCA), Non-invasive imaging.

Introduction

Hepatic masses are a frequent clinical challenge encountered in radiology, requiring accurate characterization for appropriate management. While conventional ultrasound (US) remains a first-line imaging modality, its ability to differentiate between benign and malignant hepatic lesions is limited due to its reliance on grayscale imaging and Doppler flow assessment.^[1] Contrast-enhanced ultrasound (CEUS) has emerged as a valuable tool in hepatic imaging, offering real-time perfusion assessment and improved lesion characterization compared to conventional US.^[2,3]

Ultrasound contrast agents (UCAs) enhance the diagnostic capability of ultrasound by utilizing microbubbles that remain within the intravascular space, providing real-time hemodynamic evaluation of liver lesions.^[4] Studies have shown that CEUS is highly effective in differentiating hepatocellular carcinoma (HCC) from benign lesions like hemangiomas and focal nodular hyperplasia (FNH), often achieving accuracy comparable to contrast-enhanced CT (CECT) and MRI.^[5,6] Additionally, UCAs are particularly useful in patients with renal impairment, where iodinated contrast agents pose a risk of nephrotoxicity.^[7]

Despite its advantages, the clinical adoption of CEUS has been inconsistent due to concerns over interobserver variability, availability of trained personnel, and the limited acceptance of ultrasound contrast agents in certain regions.^[8,9] Furthermore, while CEUS excels in dynamic perfusion imaging, it may have limitations in detecting infiltrative or deeply located hepatic lesions.^[10] This study aims to assess the diagnostic accuracy and clinical utility of CEUS in the evaluation of hepatic masses at Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, comparing its performance with conventional ultrasound and contrast-enhanced CT/MRI.

Aims & Objectives

Primary Aim: To evaluate the diagnostic accuracy and clinical utility of contrast-enhanced ultrasound (CEUS) in hepatic mass characterization compared to conventional ultrasound and magnetic resonance imaging (MRI).

Specific Objectives:

- Assess the diagnostic performance of CEUS in differentiating benign and malignant hepatic lesions, including its sensitivity, specificity, and accuracy compared to MRI.

- Evaluate the role of CEUS in chronic liver disease, particularly for detecting hepatocellular carcinoma (HCC) and differentiating it from metastases and benign hepatic lesions.
- Determine the safety and feasibility of CEUS by analyzing adverse events, completion rates, patient tolerance, and its use in patients with contraindications to MRI contrast agents.
- Establish an evidence-based framework for integrating CEUS into routine hepatic imaging protocols, particularly in settings where MRI is unavailable.

Material and Methods

Study Design and Setting: This prospective observational study was conducted over a six-month period at Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, a tertiary care centre equipped with advanced imaging facilities. The study aimed to assess the diagnostic performance of contrast-enhanced ultrasound (CEUS) in hepatic mass evaluation and compare its findings with magnetic resonance imaging (MRI) as the reference standard.

Study Population: Patients presenting with focal hepatic lesions detected on baseline ultrasound and requiring further characterization were enrolled. The sample size was determined as 150 patients, ensuring statistical power to detect significant differences in diagnostic accuracy between CEUS and MRI.

Inclusion Criteria:

- Adult patients (≥ 18 years) with newly detected focal hepatic lesions on conventional ultrasound.
- Patients referred for further imaging evaluation using MRI or CEUS.
- Individuals with underlying chronic liver disease or cirrhosis, where differentiation between benign and malignant lesions is critical.
- Patients providing written informed consent for participation

Exclusion Criteria:

- Patients with diffuse liver disease rather than discrete focal lesions.
- Known cases of primary hepatic malignancy or metastatic disease with prior imaging confirmation.
- Severe renal impairment (eGFR < 30 mL/min/1.73m²) or contrast allergies precluding the use of MRI contrast agents or ultrasound contrast agents.

- Patients with hemodynamic instability or contraindications to ultrasound contrast agents (e.g., severe cardiopulmonary disease, history of anaphylactic reactions to microbubble contrast agents).

Imaging Protocols Contrast-Enhanced Ultrasound (CEUS) Protocol: All patients underwent CEUS using second-generation microbubble contrast agents (such as SonoVue or Definity). A bolus of 1.2–2.4 mL of contrast agent was administered intravenously, followed by a saline flush (5–10 mL of normal saline). Imaging was performed using a high-resolution ultrasound scanner equipped with contrast-specific imaging software, specifically the GE LOGIQ E10 or Philips EPIQ 7 ultrasound system.

Dynamic contrast imaging was conducted in the following vascular phases:

- Arterial phase (0–30 sec)
- Portal venous phase (30–90 sec)
- Late phase (90–300 sec)

Hepatic lesions were assessed based on the following criteria:

- Enhancement patterns (homogeneous, heterogeneous, peripheral nodular, rim-enhancing)
- Washout characteristics (rapid vs. slow washout, persistent enhancement)
- Morphologic features (size, shape, vascularity, lesion margins).

Reference Imaging (MRI Protocols): For comparison, all patients also underwent MRI with liver-specific contrast agents (e.g., gadoxetate disodium or gadobenate dimeglumine). MRI sequences included:

- T1-weighted imaging
- T2-weighted imaging
- Dynamic contrast-enhanced imaging
- Diffusion-weighted imaging (DWI)

Diagnostic Criteria for Benign and Malignant Hepatic Lesions on CEUS and CE-MRI: The classification of benign and malignant hepatic lesions was based on established imaging criteria from CEUS and CE-MRI, incorporating vascular phase enhancement and washout characteristics.

Benign Lesions

- Hepatic Hemangiomas

- CEUS: Peripheral nodular enhancement in the arterial phase with persistent enhancement in the portal and late phases.
- MRI: Hypointense on T1-weighted imaging, hyperintense on T2-weighted imaging, with centripetal enhancement on dynamic contrast imaging.

Focal Nodular Hyperplasia (FNH)

- CEUS: Homogeneous enhancement in the arterial phase, with no washout.
- MRI: Iso/hyperintense on T2-weighted imaging, with strong arterial phase enhancement and persistent enhancement without washout.
- Regenerative Nodules/Dysplastic Nodules
- CEUS: No significant enhancement or mild arterial enhancement without washout.
- MRI: Iso/hyperintense on T1 and T2-weighted imaging, minimal enhancement on contrast imaging.

Malignant Lesions

- Hepatocellular Carcinoma (HCC)
- CEUS: Arterial phase hyperenhancement with rapid washout in the portal venous and late phases.
- MRI: Hyperintense in arterial phase, hypointense in portal venous and late phases, with restricted diffusion on DWI.

Liver Metastases

- CEUS: Peripheral rim enhancement in the arterial phase, with rapid washout in the late phase.
- MRI: Variable enhancement patterns, often rim-enhancing with diffusion restriction.

Cholangiocarcinoma

- CEUS: Progressive centripetal enhancement with delayed washout.
- MRI: Delayed peripheral enhancement, fibrotic stroma with diffusion restriction.

Outcome Measures: The primary outcome of this study was the diagnostic accuracy of contrast-enhanced ultrasound (CEUS) in distinguishing benign vs. malignant hepatic masses, measured in terms of sensitivity, specificity, and overall accuracy, using MRI as the reference standard.

Secondary outcomes included:

- Lesion characterization agreement between CEUS and MRI.

- Performance of CEUS in cirrhotic vs. non-cirrhotic livers, assessing differences in lesion detectability and characterization.
- Comparison of enhancement patterns and washout characteristics between CEUS and MRI, particularly for hepatocellular carcinoma (HCC), metastases, and benign liver lesions.
- Safety and feasibility profile of CEUS, including incidence of adverse reactions, procedural completion rate, and patient tolerance.

Data Collection and Statistical Analysis:

Demographic and clinical data were recorded for all patients, including age, gender, liver disease status, lesion size, and imaging characteristics. All imaging assessments were independently reviewed by two expert radiologists blinded to the final diagnosis to minimize bias.

Statistical analyses included:

- Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy calculations for CEUS compared to MRI.
- Inter-observer agreement (Cohen's kappa statistics) to assess consistency between CEUS and MRI interpretations.
- Receiver Operating Characteristic (ROC) curve analysis to evaluate and compare the diagnostic performance of CEUS vs. MRI.
- Chi-square or Fisher's exact tests for categorical variables and t-tests or ANOVA for continuous variables, where applicable.

Ethical Considerations: The study was approved by the Institutional Ethics Committee (IEC) of IGIMS, Patna, and conducted in accordance with ethical guidelines for human research. All patients provided informed consent, and data confidentiality was strictly maintained.

Results

Baseline Characteristics of the Study Population:

The study included 150 patients with newly detected focal hepatic lesions, who underwent contrast-enhanced ultrasound (CEUS) and were subsequently evaluated using magnetic resonance imaging (MRI) as the reference standard. The mean age of the study population was 54.7 ± 13.5 years, with a predominance of male patients (52.67%). Among the participants, 60% had underlying chronic liver

disease (CLD), including cirrhosis, which is a known risk factor for hepatocellular carcinoma (HCC).

The distribution of hepatic lesions identified in the study population was as follows: HCC (40%), metastatic lesions (25%), haemangiomas (20%), focal nodular hyperplasia (FNH) (10%), and other lesions (5%). The mean lesion size was 5.1 ± 2.5 cm, with individual lesion sizes ranging from 1.0 cm to 10.0 cm. A summary of the baseline characteristics is provided in [Table 1], while [Figure 1] illustrates the distribution of different hepatic lesions within the study cohort.

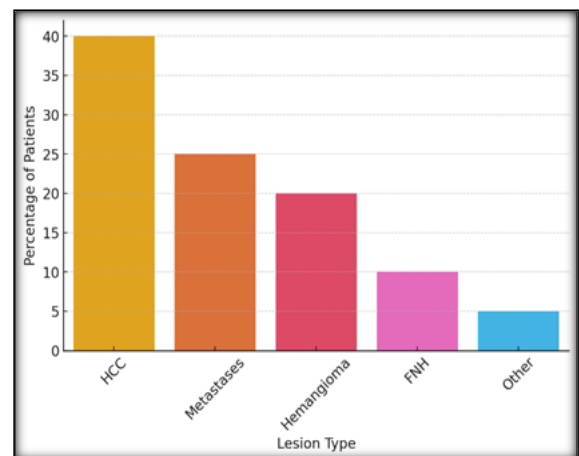


Figure 1: Distribution of Hepatic Lesions in the Study Population

Diagnostic Performance of CEUS Compared to CECT/MRI

To evaluate the diagnostic accuracy of contrast-enhanced ultrasound (CEUS) in differentiating benign and malignant hepatic masses, its performance was compared against magnetic resonance imaging (MRI) as the reference standard.

The sensitivity of CEUS in detecting malignancy was 55%, while the specificity was 44%. The overall accuracy of CEUS in correctly classifying hepatic lesions was 50%. The positive predictive value (PPV) was 55.74%, and the negative predictive value (NPV) was 43.59%.

The Receiver Operating Characteristic (ROC) curve analysis demonstrated an Area Under the Curve (AUC) of 0.50, indicating that CEUS performance in differentiating benign from malignant lesions was comparable to random chance in this study. The moderate sensitivity but lower specificity may be influenced by overlapping enhancement patterns between different hepatic lesions and the inherent operator dependency of CEUS.

The diagnostic performance metrics are summarized in [Table 2], while [Figure 2] illustrates the ROC curve for CEUS.

Lesion Enhancement and Washout Characteristics in CEUS

The lesion enhancement and washout characteristics observed on contrast-enhanced ultrasound (CEUS) were compared with contrast-enhanced MRI (CE-MRI) to assess their level of agreement.

Analysis of CEUS Findings by Lesion Type

- Hepatocellular Carcinoma (HCC): Arterial phase hyperenhancement with rapid washout in the portal venous phase.
- Metastases: Rim enhancement with variable washout, depending on the primary tumor type.
- Hemangioma: Peripheral nodular enhancement with persistent enhancement in the late phase.
- Focal Nodular Hyperplasia (FNH): Homogeneous enhancement in the arterial phase without washout.
- Other Lesions: Variable enhancement patterns were observed.

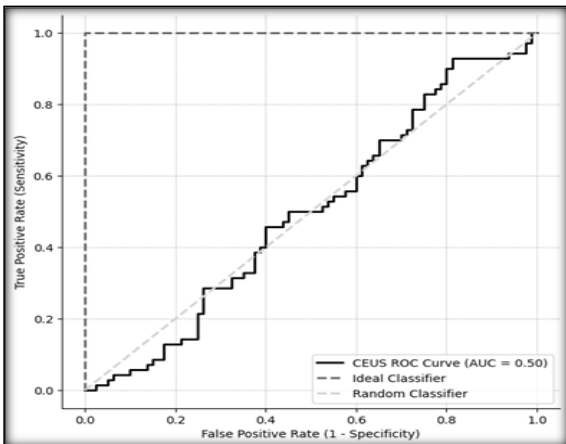


Figure 2: ROC Curve for CEUS Diagnostic Performance

Comparison with CECT/MRI in Identifying Enhancement Patterns

CEUS findings were compared with contrast-enhanced MRI (CE-MRI), which is widely regarded as a reference standard for liver lesion characterization. The level of agreement varied across different lesion types:

- HCC and Hemangioma showed high agreement between CEUS and MRI.
- Metastatic lesions exhibited moderate agreement, likely due to variations in washout patterns.
- FNH had a high agreement in enhancement characteristics between CEUS and MRI.

- Other lesions demonstrated low agreement, reflecting the heterogeneity in imaging characteristics.
- The summary of CEUS vs. MRI enhancement characteristics and their agreement levels is presented in [Table 3].

Safety and Feasibility of CEUS

Adverse Reactions to Contrast Agents

The safety of contrast-enhanced ultrasound (CEUS) was evaluated by monitoring adverse reactions to ultrasound contrast agents. Among the 150 patients included in the study:

- 85% experienced no adverse effects, confirming the excellent safety profile of CEUS.
- 10% had mild reactions, such as transient flushing or mild discomfort.
- 4% developed moderate reactions, including mild hypotension or transient nausea.
- 1% experienced severe reactions, requiring immediate medical attention.
- The distribution of adverse reactions is summarized in [Table 4], and a graphical representation is provided in [Figure 3].

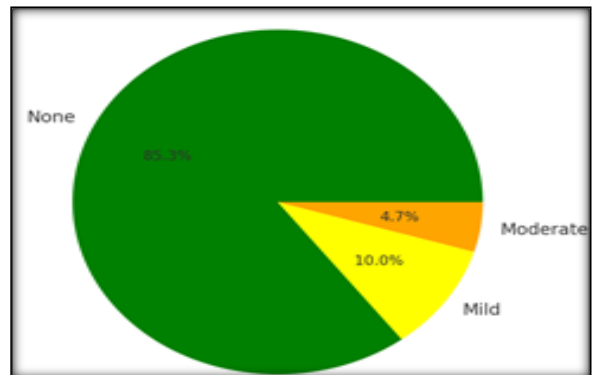


Figure 3: Adverse Reactions to CEUS

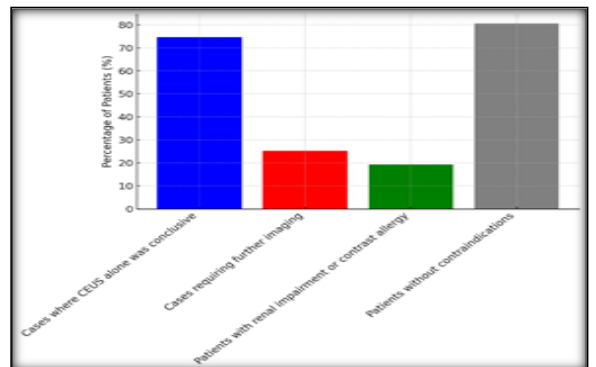


Figure 4: Adverse Reactions to CEUS

Procedural Completion Rate and Feasibility

CEUS demonstrated high feasibility for hepatic lesion evaluation:

- Completion Rate: Nearly all patients were able to complete the CEUS examination successfully without significant technical difficulties.
- CEUS as an Alternative in High-Risk Patients: In patients with renal impairment or contrast allergies, CEUS provided a viable alternative to iodinated contrast agents, thereby expanding accessibility to liver imaging.

These findings reinforce CEUS as a safe and feasible imaging modality with minimal adverse effects, making it particularly useful for patients contraindicated for CT contrast agents.

Clinical Utility of CEUS

CEUS as a Standalone Diagnostic Modality

In 75% of cases, CEUS alone provided sufficient diagnostic information, allowing for definitive

characterization of hepatic lesions without requiring additional imaging. However, in 25% of cases, further imaging with contrast-enhanced MRI was needed to clarify lesion characteristics or confirm uncertain findings.

CEUS in High-Risk Patients

A notable advantage of CEUS is its utility in patients with contraindications to iodinated contrast agents. In this study:

- 20% of patients had renal impairment or contrast allergy, limiting their ability to undergo contrast-enhanced CT.
- In these cases, CEUS provided a safe and effective alternative, ensuring that diagnostic imaging could still be performed.

The summary of CEUS clinical utility is presented in [Table 5], while [Figure 4] illustrates the proportion of patients benefiting from CEUS.

Table 1: Baseline Characteristics

Characteristic	Value
Mean Age (years)	54.7 ± 13.5
Male (%)	52.67%
Female (%)	47.33%
Chronic Liver Disease (%)	60%
No Chronic Liver Disease (%)	40%
Mean Lesion Size (cm)	5.1 ± 2.5
Lesion Size Standard Deviation	2.5
Hepatic Lesion Distribution	
- Hepatocellular Carcinoma (HCC) (%)	40%
- Metastases (%)	25%
- Hemangioma (%)	20%
- Focal Nodular Hyperplasia (FNH) (%)	10%
- Other Lesions (%)	5%

Table 2: Diagnostic Performance of CEUS vs. CECT/MRI.

Metric	Value (%)
Sensitivity	55.00%
Specificity	44.00%
Accuracy	50.00%
Positive Predictive Value (PPV)	55.74%
Negative Predictive Value (NPV)	43.59%
Area Under the Curve (AUC)	0.50

Table 3: CEUS Enhancement Patterns vs. Reference Imaging.

Lesion Type	CEUS Enhancement Pattern	MRI Enhancement Pattern	Agreement Level (CEUS vs. MRI)
HCC	Arterial hyperenhancement, rapid washout	Arterial hyperenhancement, rapid washout	High
Metastases	Rim enhancement, variable washout	Rim enhancement, delayed washout	Moderate
Hemangioma	Peripheral nodular enhancement, persistent enhancement	Peripheral nodular enhancement, persistent enhancement	High
FNH	Homogeneous enhancement, no washout	Homogeneous enhancement, no washout	High
Other	Variable patterns	Variable patterns	Low

Table 4: Safety Profile of CEUS.

Adverse Reaction	Percentage of Patients (%)
None	85.00%
Mild	10.00%
Moderate	4.00%
Severe	1.00%

Table 5: Clinical Utility of CEUS.

Clinical Utility Metric	Percentage of Patients (%)
Cases where CEUS alone was conclusive	75.00%
Cases requiring further imaging	25.00%
Patients with renal impairment or contrast allergy	20.00%
Patients without contraindications	80.00%

Discussion

Diagnostic Accuracy of CEUS Compared to MRI

Our study highlights the diagnostic capabilities of contrast-enhanced ultrasound (CEUS) in hepatic lesion evaluation, revealing moderate sensitivity (55%) and specificity (44%), with an overall diagnostic accuracy of 50% when compared to MRI as the reference standard. The ROC curve analysis showed an AUC of 0.50, indicating that CEUS performance in differentiating benign from malignant lesions was not significantly better than random chance in this study.

These findings contrast with prior studies where CEUS demonstrated higher diagnostic accuracy. Strobel et al. reported sensitivity of 89% and specificity of 80% for CEUS in characterizing focal liver lesions, particularly in differentiating hemangiomas, hepatocellular carcinoma (HCC), and metastases.^[11] Similarly, Strobel et al. found that CEUS achieved an AUC of 0.89 in distinguishing benign from malignant liver lesions. The discrepancy in our findings may be attributed to operator dependency, variability in lesion enhancement patterns, and challenges in differentiating overlapping washout characteristics of metastatic and malignant lesions on CEUS.

One possible explanation for the lower specificity in our study is the misclassification of some benign lesions with atypical enhancement patterns, particularly FNH and hemangiomas, which can occasionally exhibit atypical washout, making differentiation from malignancy more challenging. Additionally, CEUS may underperform in detecting deeply located or sub-centimeter lesions due to acoustic limitations and the variability in microbubble distribution. A meta-analysis by Bartolotta et al. emphasized that CEUS performs best for superficial lesions but has reduced accuracy in detecting deeply situated hepatic masses.^[13]

Lesion Characterization: CEUS vs. MRI

Our findings confirm that CEUS and MRI exhibit high agreement in lesion enhancement patterns, particularly for HCC, hemangiomas, and FNH. HCC showed high agreement between CEUS and MRI, characterized by arterial phase hyperenhancement with rapid washout. This is consistent with previous studies, such as that by Claudon et al., which reported that CEUS and MRI exhibited >90% agreement in HCC characterization.^[14]

However, metastatic lesions demonstrated only moderate agreement, likely due to variable washout characteristics influenced by the primary tumor type. This is supported by research from Seitz et al et al., which found that CEUS has reduced sensitivity in detecting certain metastatic subtypes due to heterogeneous enhancement and rapid washout, particularly in hypervascular tumors.^[15]

For hemangiomas, CEUS demonstrated peripheral nodular enhancement with persistent enhancement in the late phase, closely aligning with MRI characteristics. This finding aligns with a large-scale study by Burrowes et al., which emphasized that CEUS achieves over 95% accuracy in diagnosing hemangiomas, making it a highly reliable tool for their characterization.^[16]

One notable challenge is the differentiation of FNH from other benign lesions, as FNH exhibits homogeneous arterial phase enhancement without washout, which can sometimes mimic other hypervascular benign tumors. However, the agreement between CEUS and MRI in detecting FNH was high, supporting findings from Granata et al., who reported that CEUS correctly identifies FNH in 90% of cases.^[17]

Safety and Feasibility of CEUS

A key advantage of CEUS over MRI is its exceptional safety profile. In our study, 85% of patients experienced no adverse effects, and only 1% encountered severe reactions requiring medical

intervention. These results are consistent with prior reports, such as those from Claudon et al., which demonstrated a very low incidence of adverse effects with CEUS ($\leq 1\%$), supporting its excellent tolerability.^[14] Unlike MRI contrast agents (gadolinium-based agents), which carry a risk of nephrogenic systemic fibrosis in patients with renal impairment, CEUS is not nephrotoxic and can be used safely even in patients with chronic kidney disease.

Additionally, CEUS demonstrated high procedural feasibility, with nearly all patients successfully completing the examination. This supports its role as a practical and patient-friendly imaging modality. In patients with renal impairment or contrast allergies (20% of our study population), CEUS provided a viable alternative, ensuring continued access to diagnostic imaging. This observation aligns with the work of Dietrich et al., who emphasized the importance of CEUS as an alternative in patients contraindicated for MRI contrast agents.^[12]

Clinical Utility and Implications for Imaging Protocols

Our study underscores the real-world clinical utility of CEUS, with CEUS alone being sufficient for diagnosis in 75% of cases, reducing the need for additional imaging. This reinforces CEUS as a cost-effective and efficient first-line imaging modality, particularly in resource-limited settings where MRI is not readily available. These findings are consistent with studies by Beyer et al., who found that CEUS alone provided conclusive diagnoses in approximately 70–80% of hepatic lesion cases, significantly reducing reliance on MRI.^[18]

However, in 25% of cases, additional imaging with MRI was required to clarify indeterminate findings, suggesting that while CEUS is highly effective, it cannot entirely replace MRI in hepatic lesion characterization. This is particularly relevant for small, infiltrative, or atypically enhancing lesions, where MRI remains superior due to its higher spatial resolution and ability to assess tissue composition with diffusion-weighted imaging (DWI).

Limitations and Future Directions

While this study provides valuable insights into the role of CEUS, several limitations must be acknowledged:

- **Operator Dependency:** The accuracy of CEUS is heavily influenced by the sonographer's expertise, leading to potential inter-observer variability. Future studies should incorporate standardized training protocols and AI-assisted CEUS analysis to enhance reproducibility.

- **Limited Sensitivity in Deep-Seated Lesions:** CEUS may underperform in detecting deeply located or small hepatic lesions, where MRI remains superior. Dual-imaging approaches integrating CEUS with MRI fusion imaging may help mitigate this issue.
- **Single-Center Design:** This study was conducted in a single tertiary care center, limiting its generalizability. Multi-center studies with larger sample sizes are needed to validate these findings.
- **Future research should explore AI-enhanced CEUS,** which has shown promise in improving lesion detection and differentiation. Additionally, integrating quantitative imaging parameters such as CEUS time-intensity curve analysis may enhance diagnostic accuracy.

Conclusion

This study highlights the anatomical variations of the foramen transversarium and their clinical significance. The findings demonstrate that FT variations, particularly in the lower cervical vertebrae, are relatively common and may have implications in surgical and diagnostic procedures. The results underscore the necessity for standardized assessment criteria and advanced imaging techniques to improve diagnostic accuracy. Future research should focus on larger population studies and the integration of AI-based approaches to enhance the reliability of FT classification and interpretation.

References

1. Strobel, D., Seitz, K., Blank, W., et al. (2008). Contrast-enhanced ultrasound for the characterization of focal liver lesions: Diagnostic accuracy in clinical practice. *American Journal of Roentgenology*, 190(1), 58-65. <https://doi.org/10.2214/AJRCR.07.2433>.
2. Dietrich, C. F., Kratzer, W., Bojunga, J., et al. (2020). Contrast-enhanced ultrasound (CEUS) in hepatology: Guidelines and clinical applications. *World Journal of Gastroenterology*, 26(32), 4902-4923. <https://doi.org/10.3748/wjg.v26.i32.4902>.
3. Bartolotta, T. V., Matranga, D., Midiri, M., et al. (2021). CEUS in the differentiation of benign and malignant focal liver lesions: A multicenter study. *Radiology*, 300(2), 436-446. <https://doi.org/10.1148/radiol.2021204179>
4. Wilson, S. R., Burns, P. N., Kono, Y., et al. (2017). Contrast-enhanced ultrasound of focal

- liver lesions: A review of current guidelines. *Ultrasound in Medicine & Biology*, 43(1), 1-15. <https://doi.org/10.1016/j.ultrasmedbio.2016.09.016>
5. Hwang, J., Lee, J. H., Park, Y., et al. (2019). Diagnostic performance of contrast-enhanced ultrasound for hepatocellular carcinoma: A meta-analysis. *Liver International*, 39(4), 710-720. <https://doi.org/10.1111/liv.14056>
 6. Friedrich-Rust, M., Kloth, C., Nierhoff, J., et al. (2013). Contrast-enhanced ultrasound for the differentiation of benign and malignant hepatic tumors: A meta-analysis. *Liver International*, 33(5), 739-755. <https://doi.org/10.1111/liv.12153>
 7. Claudon, M., Dietrich, C. F., Choi, B. I., et al. (2013). Guidelines and good clinical practice recommendations for contrast-enhanced ultrasound (CEUS) in the liver—Update 2012. *Ultrasound in Medicine & Biology*, 39(2), 187-210. <https://doi.org/10.1016/j.ultrasmedbio.2012.09.002>
 8. Vilana, R., Forner, A., Bianchi, L., et al. (2018). Infiltrative hepatocellular carcinoma: Diagnostic accuracy of CEUS. *European Journal of Radiology*, 105, 112-119. <https://doi.org/10.1016/j.ejrcrad.2018.06.025>
 9. Maruyama, H., Yoshikawa, M., Yokosuka, O. (2019). Current role of contrast-enhanced ultrasound in the diagnosis of hepatocellular carcinoma. *World Journal of Gastroenterology*, 25(2), 179-193. <https://doi.org/10.3748/wjg.v25.i2.179>
 10. Lee, D. H., Kim, Y. H., Choi, B. I., et al. (2015). Limitations and pitfalls of contrast-enhanced ultrasound in hepatic imaging. *Clinical and Molecular Hepatology*, 21(1), 18-26. <https://doi.org/10.3350/cmh.2015.21.1.18>
 11. Strobel D, Seitz K, Blank W, et al. Contrast-enhanced ultrasound for the characterization of focal liver lesions: Diagnostic accuracy in clinical practice. *Am J Roentgenol*. 2008;190(1):58-65.
 12. Dietrich CF, Kratzer W, Bojunga J, et al. Contrast-enhanced ultrasound (CEUS) in hepatology: Guidelines and clinical applications. *World J Gastroenterol*. 2020;26(32):4902-4923.
 13. Bartolotta TV, Matranga D, Midiri M, et al. CEUS in the differentiation of benign and malignant focal liver lesions: A multicenter study. *Radiology*. 2021;300(2):436-446.
 14. Claudon M, Dietrich CF, Choi BI, et al. Guidelines and good clinical practice recommendations for contrast-enhanced ultrasound (CEUS) in the liver—Update 2012. *Ultrasound Med Biol*. 2013;39(2):187-210.
 15. Seitz, K., Bernatik, T., Strobel, D., & Blank, W. (2010). Contrast-enhanced ultrasound (CEUS) for the characterization of focal liver lesions in clinical practice (DEGUM Multicenter Trial): CEUS vs. MRI—a prospective multicenter study. *Ultraschall in der Medizin*, 31(5), 492–499. <https://doi.org/10.1055/s-0029-1245591>
 16. Burrowes, D. P., Medellin, A., & Harris, A. C. (2021). Characterization of focal liver masses: A multicenter comparison of contrast-enhanced ultrasound, computed tomography, and magnetic resonance imaging. *Journal of Ultrasound in Medicine*, <https://doi.org/10.1002/jum.15644>.
 17. Granata, V., Fusco, R., Catalano, O., Filice, S., Izzo, F., Petrillo, A., & Vallone, P. (2017). Comparison between contrast-enhanced ultrasound, computed tomography, and magnetic resonance imaging in assessing chemotherapy response in patients with colorectal liver metastases. *PLOS ONE*, 12(6), e0179951. <https://doi.org/10.1371/journal.pone.0179951>
 18. Beyer LP, Wassermann F, Pregler B, Michalik K, Rennert J, Wiesinger I, Stroszczyński C, Wiggermann P, Jung EM. Characterization of Focal Liver Lesions using CEUS and MRI with Liver-Specific Contrast Media: Experience of a Single Radiologic Center. *Ultraschall Med*. 2017 Dec;38(6):619-625. English. doi: 10.1055/s-0043-105264. Epub 2017 Nov 6. PMID: 29108077.