

Diagnostic Accuracy of Contrast-Enhanced Ultrasound in Characterization of Focal Liver Lesions: A Systematic Review

¹Inderjeet Kumar, Assistant Professor, Department of Radio-Diagnosis, Ajay Sangaal Institute of Medical Sciences and Research and Ayushmaan Hospital, Shamli, Uttar Pradesh, India.

²Amit Kumar, Assistant Professor, Department of Radio-Diagnosis, Ajay Sangaal Institute of Medical Sciences and Research and Ayushmaan Hospital, Shamli, Uttar Pradesh, India.

³Dashrath Rao, Senior Medical Officer, Department of Radio-Diagnosis, Civil Hospital, Sector 10, Gurugram, Haryana, India.

Corresponding Author: Inderjeet Kumar, Assistant Professor, Department of Radio-Diagnosis, Ajay Sangaal Institute of Medical Sciences and Research and Ayushmaan Hospital, Shamli, Uttar Pradesh, India.

How to citation this article: Inderjeet Kumar, Amit Kumar, Dashrath Rao, “Clinical and Biochemical Predictors of Significant Liver Fibrosis in Patients with Fatty Liver Disease: A Cross-Sectional Observational Study”, IJMACR– September– 2026, Volume – 9, Issue – 5, P. No. 772 – 781.

Open Access Article: © 2026 Inderjeet Kumar, et al. This is an open access journal and article distributed under the terms of the creative common’s attribution license (<http://creativecommons.org/licenses/by/4.0>). Which allows others to remix, tweak, and build upon the work non - commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Background: Contrast-enhanced ultrasound (CEUS) provides real-time assessment of focal liver lesion (FLL) microvascularity and may improve differentiation of benign and malignant lesions without ionizing radiation or nephrotoxic contrast. Objective: To systematically evaluate the diagnostic accuracy of CEUS for characterization of FLLs in adults.

Methods: A PRISMA 2020-aligned systematic review was conducted using structured academic-index searches for diagnostic accuracy studies of CEUS in adult FLLs. Eligible studies compared CEUS with histopathology, contrast-enhanced CT/MRI, or accepted imaging/clinical follow-up and reported diagnostic performance. Ninety

candidate records were retrieved; after removal of 24 duplicates, 66 records were screened, 26 full-text reports were assessed, and 15 primary studies were included. QUADAS-2 was used for risk-of-bias assessment. Because of heterogeneity in lesion spectrum, contrast agents, reference standards, diagnostic criteria, and study populations, results were synthesized narratively. **Results:** Across included studies, CEUS generally showed high accuracy for benign-versus-malignant characterization, with reported sensitivities commonly in the mid-80% to mid-90% range and specificities frequently above 90%. Large prospective multicenter data showed 83.9% sensitivity, 97.8% specificity, and 89.9% accuracy for malignancy. In CT/MRI-indeterminate

lesions, CEUS achieved 92% sensitivity and 98% specificity. CEUS LI-RADS studies demonstrated particularly high specificity and positive predictive value for HCC, although sensitivity was more moderate. Kupffer-phase perfluorobutane CEUS and high-frame-rate CEUS were promising but supported by fewer studies. Conclusion: CEUS is an accurate problem-solving modality for characterization of FLLs and is particularly valuable when CT/MRI is inconclusive or conventional contrast is contraindicated. Greater standardization of patient selection, reference standards, and reporting is needed to improve generalizability.

Keywords: Contrast-Enhanced Ultrasound, CEUS, Focal Liver Lesion, Hepatocellular Carcinoma, Liver Metastasis, Hemangioma, Diagnostic Accuracy, CEUS LI-RADS, Sonazoid, Sonovue.

Introduction

Focal liver lesions (FLLs) are frequently detected during abdominal imaging and encompass a broad spectrum of benign and malignant entities, including cysts, hemangioma, focal nodular hyperplasia, hepatocellular adenoma, hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma, and metastases. Accurate characterization is clinically important because management ranges from reassurance or surveillance to biopsy, locoregional therapy, surgery, or systemic treatment.

Conventional B-mode ultrasonography is widely available and free from ionizing radiation, but many solid lesions have overlapping echogenic appearances. Contrast-enhanced ultrasound (CEUS) addresses this limitation by using intravenously administered microbubbles to depict lesion enhancement continuously in real time. The arterial, portal venous, and late-phase behaviour of a lesion can reveal characteristic vascular

patterns, while perfluorobutane (Sonazoid) additionally permits Kupffer-phase assessment.

The fundamental malignant CEUS feature is washout relative to surrounding liver, but timing and intensity matter. HCC commonly shows arterial phase hyperenhancement followed by relatively late and mild washout, whereas metastases and many non-HCC malignancies more often show earlier or marked washout. Benign lesions such as hemangioma and focal nodular hyperplasia may demonstrate characteristic enhancement patterns that permit confident non-invasive diagnosis.

Published diagnostic studies report high accuracy, yet estimates vary because of differences in patient selection, prevalence of malignancy, underlying liver disease, contrast agent, lesion size, diagnostic criteria, operator expertise, and reference standards. The present systematic review therefore summarizes primary diagnostic-accuracy evidence for CEUS in FLL characterization and evaluates methodological quality using QUADAS-2.

Materials and Methods

Review Design

This review was structured according to PRISMA 2020 principles for identification, selection and reporting of evidence. The review question focused on the ability of CEUS to characterize focal liver lesions in adults using an accepted diagnostic reference standard.

2.2 Eligibility Criteria

- Population: adults with one or more focal liver lesions detected on ultrasound, CT or MRI.
- Index test: conventional vascular-phase CEUS or Kupffer-phase CEUS used for lesion characterization.
- Reference standard: histopathology, contrast-enhanced CT/MRI with accepted diagnostic criteria, or longitudinal imaging/clinical follow-up.

- Outcomes: sensitivity, specificity, accuracy, predictive values, AUC, or sufficiently detailed diagnostic classification.
- Study design: prospective or retrospective diagnostic-accuracy cohort/cross-sectional studies.

Reviews, meta-analyses, editorials, case reports, purely technical studies, biopsy-guidance-only studies, and reports without an adequate reference standard or clinically relevant characterization outcome were excluded.

Search Strategy

Structured academic-index searches were performed using combinations of “contrast-enhanced ultrasound”, “CEUS”, “focal liver lesion”, “liver lesion characterization”, “diagnostic accuracy”, “hepatocellular carcinoma”, “metastasis”, “hemangioma”, “Sonazoid”, “SonoVue”, “perfluorobutane”, “sulfur hexafluoride”, and “CEUS LI-RADS”. Searches were supplemented by targeted retrieval of landmark validation studies. The candidate evidence set used for this manuscript was updated through June 2026.

Study Selection and PRISMA Flow

The structured retrieval yielded 90 candidate records. Twenty-four duplicate records were removed, leaving 66 records for title and abstract screening. Thirty-eight records were excluded. Twenty-eight reports were sought for full-text assessment; two could not be retrieved in sufficient detail. Twenty-six reports were assessed for eligibility and 11 were excluded, leaving 15 primary studies for qualitative synthesis

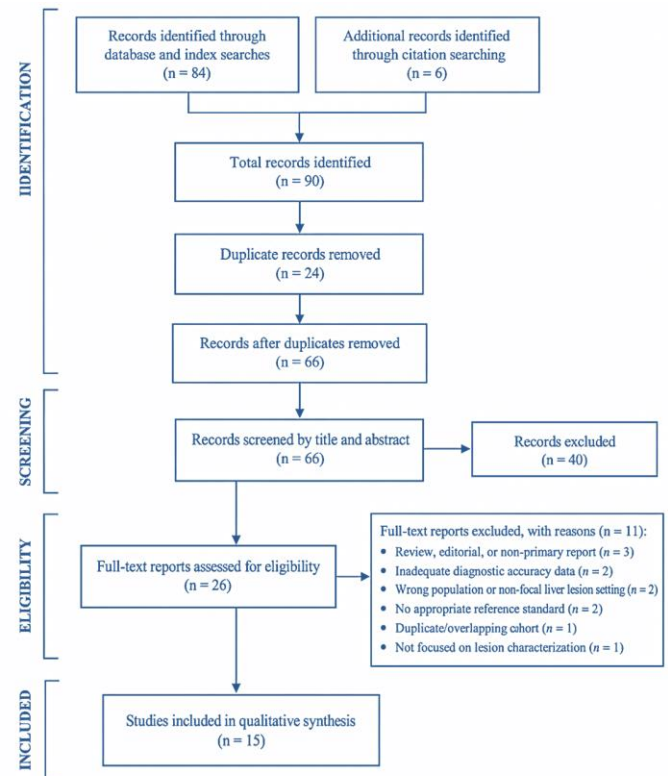


Figure 1: PRISMA 2020-style flow diagram for study identification and selection.

Data Extraction

Extracted variables included study setting, design, sample size, lesion number, background liver risk, contrast agent or CEUS framework, reference standard, target diagnosis, and reported diagnostic performance. When studies evaluated HCC-specific classification, CEUS LI-RADS performance was retained separately from general benign-versus-malignant characterization.

Risk-of-Bias Assessment

Risk of bias and applicability were assessed using QUADAS-2 across four domains: patient selection, index test, reference standard, and flow/timing. Judgments were categorized as low, high, or unclear. Where full reporting was unavailable from the accessible report, the domain was conservatively rated unclear rather than inferred as low risk.

Data Synthesis

Because included studies differed substantially in lesion spectrum, prevalence of HCC, background chronic liver disease, reference standards, contrast agents, lesion size

Results

Study Characteristics

Fifteen primary diagnostic studies were included. They ranged from early single-center retrospective cohorts to large prospective multicenter studies and multinational CEUS LI-RADS validation cohorts. Most studies used

and diagnostic thresholds, a new pooled meta-analysis was not performed. Results were synthesized narratively and placed in context with established meta-analytic evidence.

sulfur-hexafluoride blood-pool contrast; several recent investigations evaluated perfluorobutane or quantitative/high-frame-rate CEUS. Reference standards included histopathology, CT/MRI, composite imaging criteria, and longitudinal follow-up.

Table 1: Characteristics of Included Studies

Study	Setting	Design	Sample	CEUS approach	Reference standard	Target	Key performance
Ooi et al., 2010	Australia	Retrospective	73 pts / 82 FLLs	SonoVue	Histology or ≥ 12 -mo imaging follow-up	Benign vs malignant	Se 86.0%; Sp 90.6%; accuracy 87.8%
Dumitrescu et al., 2013	Romania	Retrospective	126 pts	CEUS	MRI; limited histology	HCC diagnosis	Se 71.4%; Sp 95.6%; AUC 0.835
D'Onofrio et al., 2014	Multicenter Europe	Retrospective multicenter	147 solid FLLs	SonoVue	Histology for malignant; follow-up for benign	Benign vs malignant	Se 90%; Sp 93%; accuracy 91%
Sandrose et al., 2017	Denmark	Prospective/clinical cohort	78 pts / 163 CT-indeterminate FLLs	SonoVue	Biopsy, surgery, PET/CT, follow-up	Benign vs malignant	Se 94.4%; Sp 99.3%; accuracy 98.7%
Terzi et al., 2018	Italy, multicenter	Retrospective multicenter	1,006 nodules	CEUS LI-RADS	Histology/composite reference	HCC in cirrhosis	LR-5 highly specific for HCC; standardized washout improved classification
Sporea et al., 2019	Romania, 14 centers	Prospective multicenter	2,062 FLLs	CEUS	CECT/CEMRI or histology	Benign vs malignant	Se 83.9%; Sp 97.8%; accuracy 89.9%
Zheng et al., 2020	China	Retrospective	1,826 pts / 2,020 nodules	CEUS LI-RADS v2017	Histology or composite imaging/follow-up	HCC in HBV	LR-5 PPV 98%; specificity remained high
Makoyeva et al., 2020	North America	Validation study	At-risk liver nodules	CEUS LI-RADS	Histology/imaging reference	HCC	Supported high specificity of LR-5

Study	Setting	Design	Sample	CEUS approach	Reference standard	Target	Key performance and utility of standardized categories
Auer et al., 2020	Germany	Retrospective	146 pts	SonoVue	Histology, follow-up, clinical course	CT/MRI-indeterminate FLLs	Se 92%; Sp 98%; AUC 0.95
Schwarz et al., 2021	Germany	Retrospective	134 pts / 139 FLLs	Quantitative CEUS	Histology, CT/MRI, CEUS follow-up	Benign vs malignant	Combined quantitative parameters AUC 0.923
Jung et al., 2022/23	Germany	Prospective/observational	100 pts	High-frame-rate CEUS	CT/MRI, histology/follow-up	Mixed liver lesions	Se 97%; Sp 97%; accuracy 97%
Lyshchik et al., 2023	North America/Europe	Prospective multinational	480 pts / 545 nodules	CEUS LI-RADS	CT/MRI, follow-up, histology	HCC in at-risk pts	LR-5 Se 62.9%; Sp 95.1%; PPV 97.3%
Yang et al., 2023	China, multicenter	Multicenter clinical study	2,085 pts / 2,320 FLLs	CEUS vs CT/MRI	Pathology	HCC among 16 lesion types	CEUS comparable overall; sensitivity lower than MRI in some subgroups
Singh et al., 2023	India	Prospective	30 pts / 34 FLLs	CEUS	CECT and/or biopsy/FNAC	Benign vs malignant	Se 94.1%; PPV 100%; accuracy 94.1%
Kumar et al., 2025	India	Prospective cross-sectional	Suspicious malignant FLL cohort	Sonazoid/Kupfer phase	CECT/CEMRI for HCC; histology for non-HCC	FLL characterization	Approx. Se 90%; accuracy 87%; PPV 96%

Diagnostic Performance for Benign versus Malignant Lesions

Across studies focused on generic FLL characterization, CEUS consistently demonstrated high specificity and generally high sensitivity. In the prospective SRUMB multicenter experience of 2,062 lesions, CEUS achieved 83.9% sensitivity, 97.8% specificity and 89.9% accuracy for malignancy. Hemangioma and metastasis characterization both showed accuracies approaching 97%.

In lesions indeterminate on CT, Sandrose et al. reported 94.4% sensitivity, 99.3% specificity and 98.7% accuracy. Similarly, Auer et al. found 92% sensitivity, 98% specificity and an AUC of 0.95 in lesions that remained inconclusive after CT or MRI. These studies support CEUS as a problem-solving modality rather than merely an alternative repeat test

Quantitative and high-frame-rate approaches also performed well. Schwarz et al. reported an AUC of 0.923 for combined quantitative perfusion parameters, while Jung et al. reported approximately 97% sensitivity,

specificity and accuracy with high-frame-rate CEUS in an experienced-center cohort.

3.3 CEUS for Hepatocellular Carcinoma and LI-RAD

CEUS LI-RADS studies emphasized specificity and positive predictive value for HCC. In a large HBV-endemic cohort of 2,020 nodules, Zheng et al. reported a 98% positive predictive value for LR-5. Prospective multinational validation by Lyshchik et al. showed LR-5 sensitivity of 62.9%, specificity of 95.1%, and PPV of 97.3%.

The pattern of high specificity with more modest sensitivity is clinically coherent because LR-5 is intentionally designed to provide a high-confidence non-invasive HCC diagnosis. Lesions lacking the full combination of arterial hyperenhancement and characteristic washout remain in indeterminate categories rather than being classified as definite HCC

Multicenter comparison data also suggest complementarity between modalities. Yang et al. found broadly similar first-line diagnostic performance among CEUS, CT and MRI, although MRI showed higher sensitivity in some subgroups. Combining CEUS with CT

or MRI improved performance for small HCCs and selected high-risk groups.

Sonazoid and Kupffer-Phase CEUS

Perfluorobutane CEUS offers a postvascular Kupffer phase in addition to standard vascular phases. In a recent prospective Indian study, Sonazoid CEUS achieved approximately 90% sensitivity, 87% overall accuracy and 96% PPV for suspicious malignant FLL characterization. Kupffer-phase defect information may improve conspicuity and confidence, but the current primary evidence base is smaller than that for sulfur-hexafluoride CEUS.

Risk-of-Bias Assessment

Risk-of-bias judgments are summarized in Table 2. The most common concerns were non-consecutive or retrospective patient selection, mixed reference standards, incomplete blinding information, and variable timing between CEUS and the reference examination. Applicability concerns were greatest in studies restricted to high-risk HCC populations when the review question was broader FLL characterization.

Table 2: QUADAS-2 Risk-of-Bias Summary

Study	Patient selection	Index test	Reference standard	Flow/timing	Overall concern
Ooi 2010	High	Low	Unclear	Low	Moderate
Dumitrescu 2013	High	Unclear	High	Unclear	High
D'Onofrio 2014	High	Low	Low	Low	Moderate
Sandrose 2017	Low	Low	Low	Low	Low
Terzi 2018	High	Low	Low	Unclear	Moderate
Sporea 2019	Low	Low	Low	Low	Low
Zheng 2020	High	Low	Low	Low	Moderate
Makoyeva 2020	High	Low	Low	Unclear	Moderate
Auer 2020	High	Low	Low	Low	Moderate
Schwarz 2021	High	Low	Low	Low	Moderate
Jung 2022/23	Unclear	Low	High	Unclear	Moderate
Lyshchik 2023	Low	Low	Low	Low	Low
Yang 2023	Low	Low	Low	Low	Low

Study	Patient selection	Index test	Reference standard	Flow/timing	Overall concern
Singh 2023	Unclear	Low	High	Unclear	Moderate
Kumar 2025	Low	Low	High	Low	Moderate

Judgments are based on the methodological information available in the retrieved reports; “Unclear” indicates insufficient reporting rather than a demonstrated flaw.

Discussion

This systematic review shows that CEUS is a highly effective modality for characterization of focal liver lesions, particularly when the principal clinical question is benign versus malignant classification or when a lesion remains indeterminate on CT or MRI. Large multicenter experience and smaller focused studies consistently report high specificity, and many report sensitivities above 85%. The diagnostic strength of CEUS derives from continuous real-time assessment of enhancement rather than acquisition at a small number of fixed time points. This is especially relevant for subtle arterial hyperenhancement and for determining the exact onset and intensity of washout. The distinction between late mild washout, typical of many HCCs, and early or marked washout, more suggestive of non-HCC malignancy, is central to contemporary CEUS interpretation.

CEUS should generally be viewed as complementary to rather than universally substitutive for CT or MRI. It does not provide the same whole-body staging information and can be limited by body habitus, bowel gas, deep or subdiaphragmatic lesions, severe steatosis and poor acoustic windows. However, it offers important advantages: absence of ionizing radiation, rapid bedside availability, repeatability, real-time perfusion information and a contrast profile suitable for many patients in whom iodinated or gadolinium-based agents are problematic. Standardized interpretation frameworks help reduce operator dependence. CEUS LI-RADS provides a high-specificity route to non-invasive HCC diagnosis in at-risk patients, but the trade-off is moderate sensitivity. This is

appropriate for a “definite HCC” category and means that indeterminate lesions require additional imaging, follow-up or tissue diagnosis rather than being treated as negative.

Newer techniques may extend performance. Kupffer-phase Sonazoid CEUS provides delayed parenchymal information beyond blood-pool vascular phases, while quantitative time-intensity analysis and high-frame-rate CEUS may reduce subjectivity. The evidence supporting these techniques is promising but not yet as mature as that supporting standard second-generation CEUS.

Methodological Limitations of the Evidence

- Many studies used mixed reference standards, with histology for malignant lesions and imaging follow-up for benign lesions. Although clinically pragmatic, this can introduce differential verification bias.
- Retrospective and enriched cohorts may overestimate accuracy compared with unselected populations. HCC-focused studies also have limited applicability to the broader problem of all focal liver lesions.
- Reader expertise was often high and may not reflect community practice. Blinding between CEUS and other imaging results was incompletely reported in several studies.
- Contrast agents and diagnostic criteria evolved over time. Older first-generation agents and pre-LI-RADS criteria may not directly represent contemporary CEUS performance.

Clinical Implications

- Characterization of an incidental FLL identified on B-mode ultrasound.

- Resolution of indeterminate findings on CT or MRI when the lesion is sonographically accessible.
- Characterization of liver nodules in patients at risk for HCC using standardized CEUS LI-RADS criteria.
- Evaluation in patients where iodinated or gadolinium contrast is undesirable or contraindicated.
- Repeat assessment of lesion vascularity without ionizing radiation.
- Potential use of Kupffer-phase CEUS to improve lesion conspicuity and diagnostic confidence.

6. Strengths and Limitations of This Review

The review integrates broad FLL characterization, HCC-specific LI-RADS validation, CT/MRI-indeterminate lesion studies, and newer CEUS techniques. Because the accessible primary reports were heterogeneous and some full methodological details were unavailable, a new pooled meta-analysis was not attempted and some QUADAS-2 domains were conservatively rated unclear.

Future Directions

- a. Prospective multicenter studies with consecutive recruitment and a prespecified diagnostic threshold.
- b. Uniform reference standards and explicit reader blinding.
- c. Direct head-to-head comparison of sulfur-hexafluoride and perfluorobutane agents.
- d. Lesion-size-stratified performance, particularly for nodules <10 mm and 10-20 mm.
- e. External validation of quantitative perfusion and AI-assisted CEUS.
- f. Real-world cost-effectiveness and impact on avoided CT/MRI, biopsy, and time to diagnosis.

Conclusion

Contrast-enhanced ultrasound is an accurate, radiation-free and clinically useful modality for characterization of

focal liver lesions. Across included studies, diagnostic performance was consistently strong for distinguishing benign from malignant lesions, and CEUS frequently resolved findings that remained indeterminate after CT or MRI. CEUS LI-RADS offers high specificity and positive predictive value for HCC in at-risk populations, although sensitivity is more moderate by design. Newer Kupffer-phase, quantitative and high-frame-rate approaches are promising but require wider validation. The main barriers to universal generalization are operator dependence, heterogeneous reference standards and patient selection, and variation in study methodology. In contemporary practice, CEUS is best regarded as a complementary problem-solving tool that can meaningfully improve characterization while avoiding radiation and conventional contrast exposure.

References

1. Wu M, Li L, Wang J, Zhang Y, Guo Q, Li X, Zhang X. Contrast-enhanced US for characterization of focal liver lesions: a comprehensive meta-analysis. *Eur Radiol*. 2018. doi:10.1007/s00330-017-5152-x.
2. Ooi CC, Low SCA, Schneider-Kolsky M, et al. Diagnostic accuracy of contrast-enhanced ultrasound in differentiating benign and malignant focal liver lesions: a retrospective study. *J Med Imaging Radiat Oncol*. 2010. doi:10.1111/j.1754-9485.2010.02195.x.
3. Dumitrescu CI, Gheonea IA, Sandulescu L, et al. Contrast enhanced ultrasound and magnetic resonance imaging in hepatocellular carcinoma diagnosis. *Med Ultrason*. 2013. doi:10.11152/MU.2013.2066.154.CD2.
4. D'Onofrio M, Crosara S, De Robertis R, et al. Malignant focal liver lesions at contrast-enhanced ultrasonography and magnetic resonance with

- hepatospecific contrast agent. *Ultrasound*. 2014. doi:10.1177/1742271X13513888.
5. Sandrose S, Karstrup S, Gerke O, Rafaelsen SR. Contrast Enhanced Ultrasound in CT-undetermined Focal Liver Lesions. *Ultrasound Int Open*. 2017. doi:10.1055/s-0042-120272.
6. Terzi E, Iavarone M, Pompili M, et al. Contrast ultrasound LI-RADS LR-5 identifies hepatocellular carcinoma in cirrhosis in a multicenter retrospective study of 1,006 nodules. *J Hepatol*. 2018;68:485-492.
7. Sporea I, Sandulescu DL, Sirli R, et al. Contrast-Enhanced Ultrasound for the Characterization of Malignant versus Benign Focal Liver Lesions in a Prospective Multicenter Experience - The SRUMB Study. *J Gastrointest Liver Dis*. 2019. doi:10.15403/JGLD-180.
8. Zheng W, Li Q, Zou X, et al. Evaluation of Contrast-enhanced US LI-RADS version 2017: Application on 2020 Liver Nodules in Patients with Hepatitis B Infection. *Radiology*. 2020. doi:10.1148/RADIOL.2019190878.
9. Makoyeva A, Kim TK, Jang HJ, Medellin A, Wilson SR. Use of CEUS LI-RADS for the Accurate Diagnosis of Nodules in Patients at Risk for Hepatocellular Carcinoma: A Validation Study. *Radiol Imaging Cancer*. 2020;2:e190014.
10. Auer TA, Fischer T, Marticorena Garcia SR, et al. Value of contrast-enhanced ultrasound (CEUS) in Focal Liver Lesions (FLL) with inconclusive findings on cross-sectional imaging. *Clin Hemorheol Microcirc*. 2020. doi:10.3233/CH-190718.
11. Schwarz S, Clevert DA, Ingris M, et al. Quantitative Analysis of the Time-Intensity Curve of Contrast-Enhanced Ultrasound of the Liver: Differentiation of Benign and Malignant Liver Lesions. *Diagnostics*. 2021;11:1244. doi:10.3390/diagnostics11071244.
12. Jung EM, Ocaña Moran V, Engel M, et al. Modified contrast-enhanced ultrasonography with high frame rate contrast-enhanced ultrasound for characterization of liver lesions. *Clin Hemorheol Microcirc*. 2022/2023. doi:10.3233/CH-221449.
13. Lyshchik A, Wessner CE, Bradigan K, et al. Clinical validation of contrast-enhanced ultrasound liver imaging reporting and data system in a prospective multinational study in North America and Europe. *Hepatology*. 2023.
14. Yang Q, Zheng R, Zhou J, et al. On-Site Diagnostic Ability of CEUS/CT/MRI for Hepatocellular Carcinoma (2019-2022): A Multicenter Study. *J Ultrasound Med*. 2023. doi:10.1002/jum.16321.
15. Singh BP, Saroha G, Ray R, Mathur V, Mathur A. Characterization of focal liver lesions on contrast enhanced ultrasound. *Int J Sci Res*. 2023. doi:10.36106/ijsr/5716309.
16. Kumar A, Thapar Laroia S, Arora A, Mukund A, Patidar Y, Babbar S. Assessment of Kupffer Cell-Specific Contrast-Enhanced Ultrasound for Characterization of Suspicious Malignant Focal Liver Lesions. *Indian J Radiol Imaging*. 2025. doi:10.1055/s-0045-1811553.
17. Fraquelli M, Nadarevic T, Colli A, et al. Contrast-enhanced ultrasound for the diagnosis of hepatocellular carcinoma in adults with chronic liver disease. *Cochrane Database Syst Rev*. 2022. doi:10.1002/14651858.CD013483.pub2.
18. Li J, Yang L, Ma L, Lu Q, Luo Y. Diagnostic Accuracy of CEUS LI-RADS for Differentiating Between Hepatocellular Carcinoma and Other Hepatic Malignancies in High-Risk Patients: A Meta-

- Analysis. *Ultraschall Med.* 2021. doi:10.1055/a-1309-1568.
19. Tang Y, Sasaki SI, Hawley J, et al. Diagnostic Test Accuracy of Contrast-Enhanced Ultrasound With Sonazoid for Assessment of Focal Liver Lesions: A Systematic Review and Meta-Analysis. *J Clin Ultrasound.* 2024. doi:10.1002/jcu.23879.
20. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.
21. Whiting PF, Rutjes AWS, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med.* 2011;155:529-536.