Contrast Enhanced Ultrasound (CEUS) in the differential diagnosis of FLL

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Why is Contract Enhanced Ultrasound (CEUS) necessary?

- **Medical Imaging methods are *mandatory in our modern medicine*, to solve our daily cases.**
- **Computer –Tomography (CT) and Magnetic Resonance Imaging (MRI) are *used quite always with enhanced substances (CE-CT and CE-MRI).***
- **In this condition *seem normally to use contrast* for ultrasound evaluation (CEUS) *in our daily practice*!**

Why is Contract Enhanced Ultrasound (CEUS) necessary?

- ***Ultrasound became more and more a "Point of Care" (PoCUS) method,*** **used more and more by *clinicians*** **(at least in a good part of the world, like in Germany, Italy, Japan, Romania) *in the room of consultation*, to the end of clinical evaluation, *using Ultrasound method to solve some problems of the case* and than *to propose a therapeutical solution immediately.***
- **We know that Liver ultrasonography (with very good US machine) *is a sensitive method, but is less specific!***

How to improve the specificity of Liver Ultrasound?

- **The answer is very simple!** ***To use a method, that is not expensive, that can be repeated if is necessary, need for evaluation less than 5 minutes and have a high accuracy!***

- **CEUS or Contrast Enhanced Ultrasound have all this characteristics!**

- **Liver CEUS is performed mainly with second generation contrast (*SonoVue*), but in some countries (Japan, South Korea, Norway), *Sonazoid* can be used.**

When to performe a CEUS examination of a FLL?

- First condition is usually **to see the liver lesion in standard US!** (1).
- In some conditions, **when the liver structure is very heterogeneously**, the lesion can be missed in standard US (or not all the liver can be evaluated by CEUS).

1.Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) in the Liver – Update 2012 *A WFUMB-EFSUMB Initiative in Cooperation With Representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS*. M. Claudon, C. F. Dietrich, B. I. Choi, et al. Ultraschall in Med 2013; 34(1): 11-29 doi: 10.1055/s-0032-1325499

Strom et al. Echo Research & Practice (2025) 12:4
https://doi.org/10.1186/s44156-024-00068-7

Echo Research & Practice

GUIDELINE

Open Access

Multi-societal expert consensus statement on the safe administration of ultrasound contrast agents

Jordan B. Strom[1,2*], Andrew Appis[2,3], Richard G. Barr[2,4], Maria Cristina Chammas[2,5], Dirk-André Clevert[2,6], Kassa Darge[2,7], Linda Feinstein[2,2], Steven B. Feinstein[2], J. Brian Fowlkes[2,8], Beverly Gorman[2], Pintong Huang[2,9], Yuko Kono[2,10], Juan Lopez-Mattei[11], Andrej Lyshchik[2,12], Michael L. Main[2,13], Wilson Matthias Jr.[2,5], Christina Merrill[2,14], Sharon L. Mulvagh[2,15], Petros Nihoyannopoulos[2,16], Joan Olson[2,17], Fabio Piscaglia[2,18,21], Thomas Porter[2,17], Arnaldo Rabischoffsky[2,19], Roxy Senior[2,20], Jessica L. Stout[1,2], Maria Stanczak[2,12] and Stephanie R. Wilson[2,14] on behalf of the International Contrast Ultrasound Society with endorsement from

Studies for the value of CEUS in comparison with Standard US

- Wang WP et al (1) – **CEUS vs. standard US for FLL** (gold standard biopsy, MRI or medical history):

- **Indeterminate *diagnosis rate decreased* from 56.7% to 6.1%; CEUS accuracy 88%.**

1.Wang WP et al: Hepatobiliary Pancreat Dis 2009; 8(4): 370-376

CEUS – metastases detection

- Konopke(1) reported an ***increase of the number of lesions detected*** **from 53% in standard ultrasound to 86% in Liver CEUS (+33%).**

- **The study concluded that CEUS should be used as a routine modality for the detection of liver metastases in the follow up of patients with cancer.**

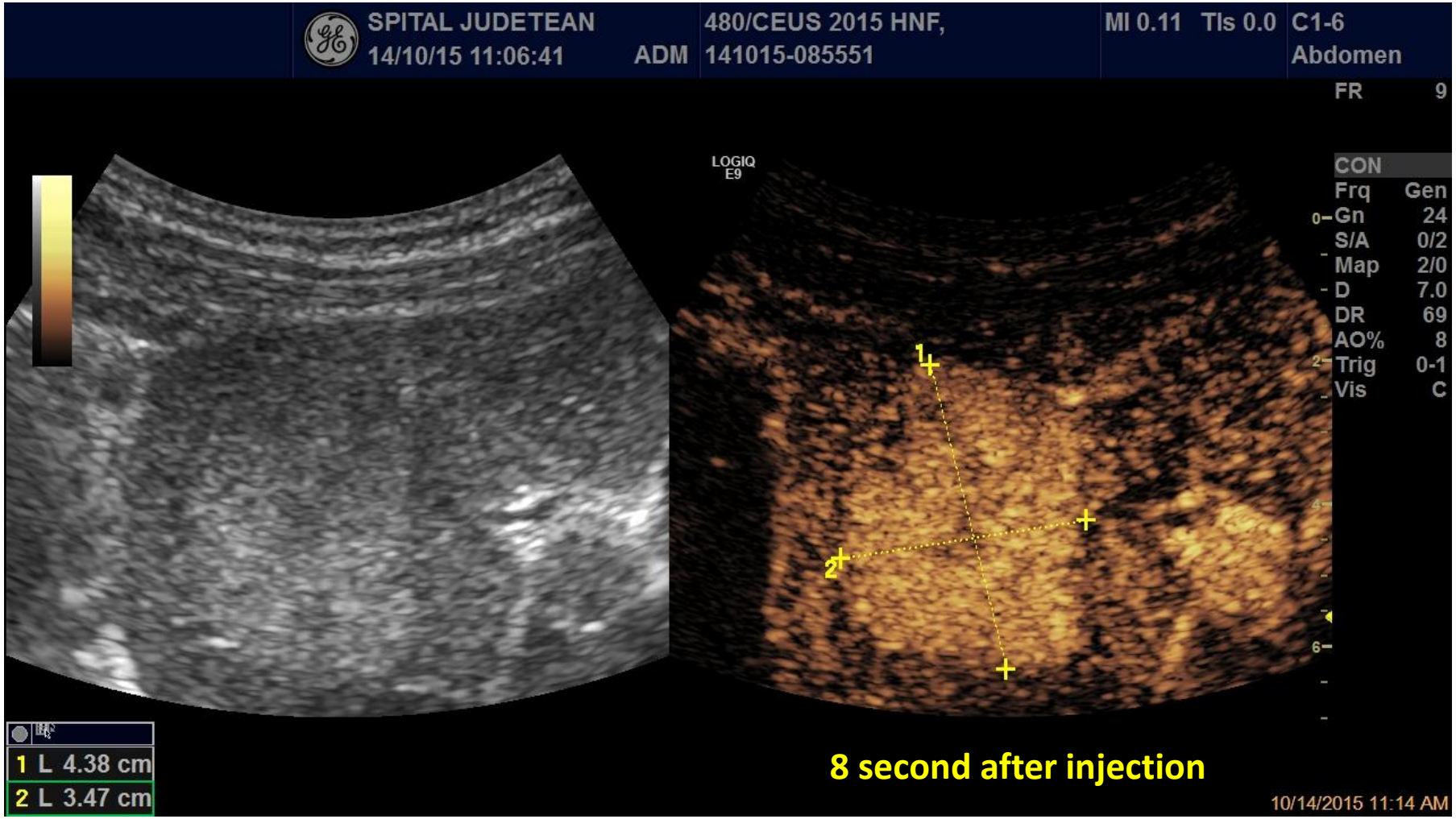
1.Konopke R, Kersting S, Saeger HD et al. Ultraschall Med 2005; 26: 107-113

CEUS – improves detection of metastases

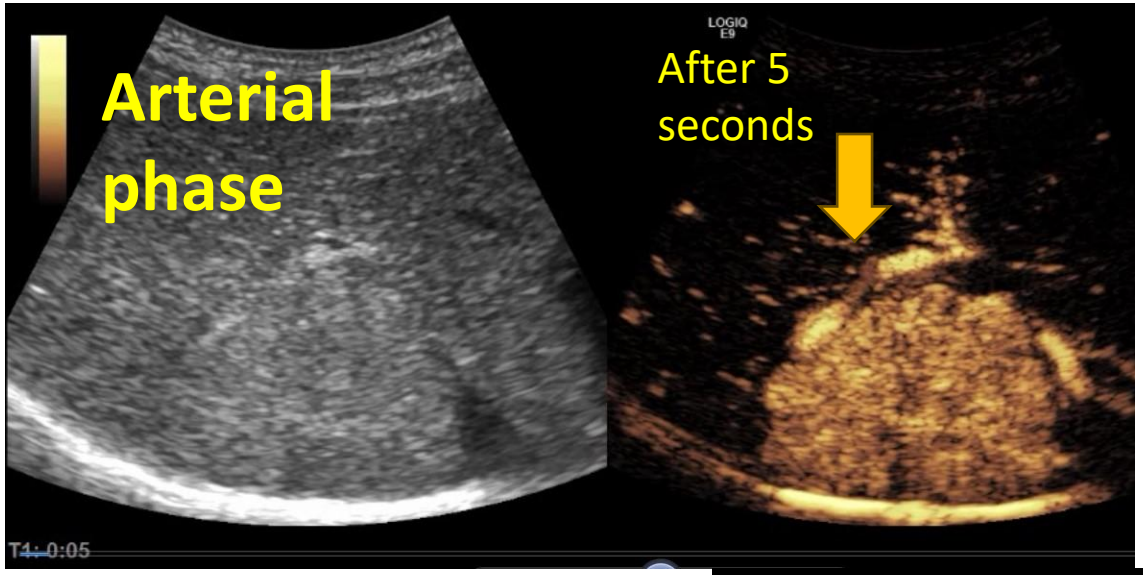
- **CEUS improves detection of liver metastases vs. standard ultrasound (109 lesions studied) (1);**
- Equivalent to CT scan and sometimes superior;
- The late phase is used for detection;
- **CEUS sensitivity as compared to US and CE-CT scan: 95.4% vs. 76.9% and 90.8% respectively.**

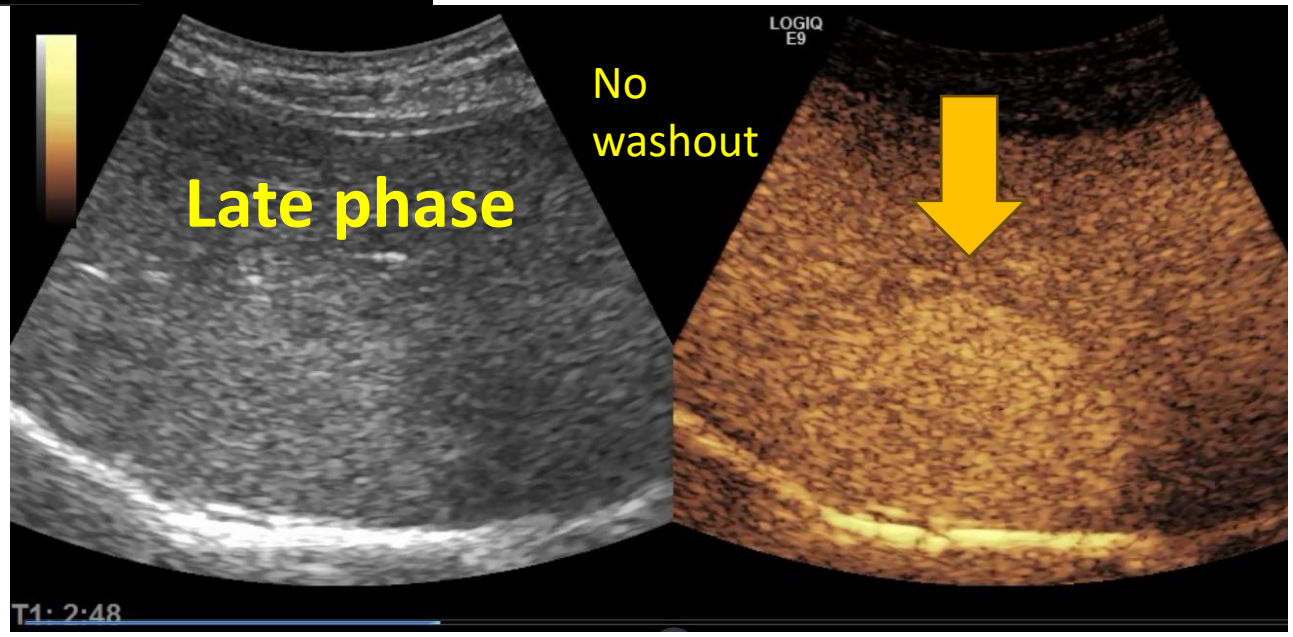
1.Piscaglia F et al – BMC Cancer 2007;7:171

CEUS in FNH: arterial phase



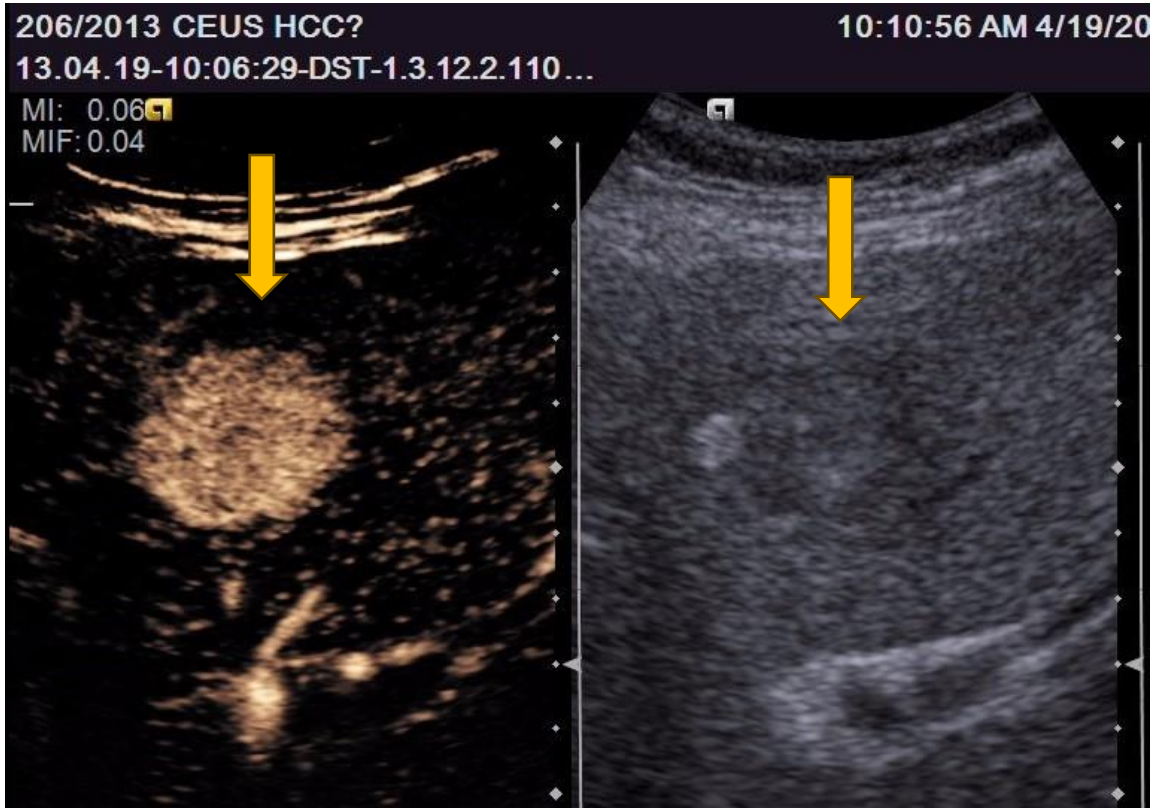
Benign lesions: FNH



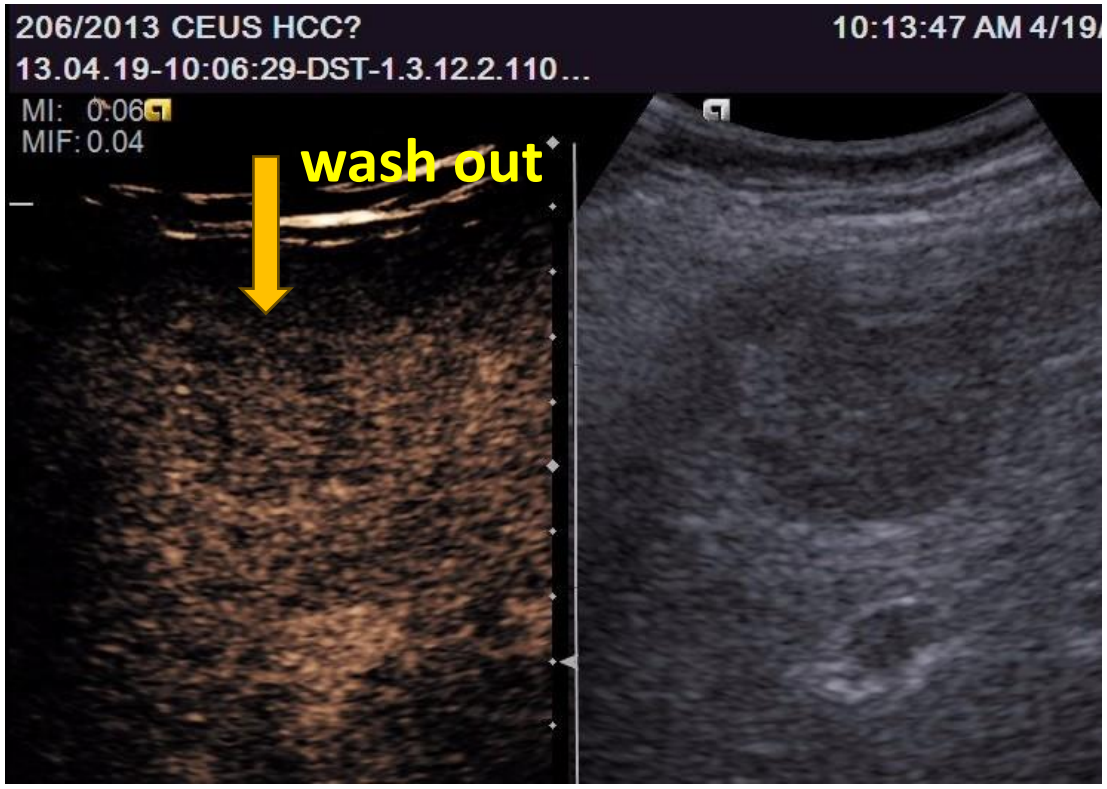


CEUS: HCC

Arterial phase

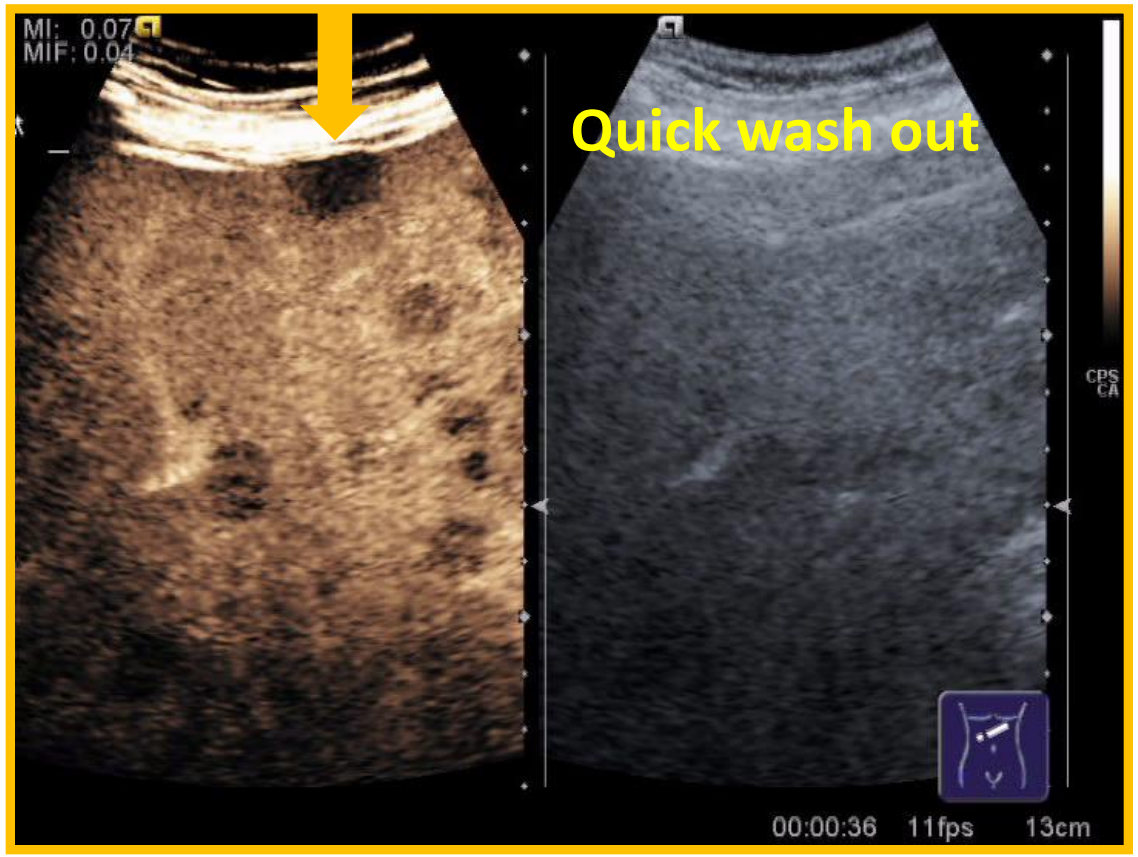


Late phase (wash out)

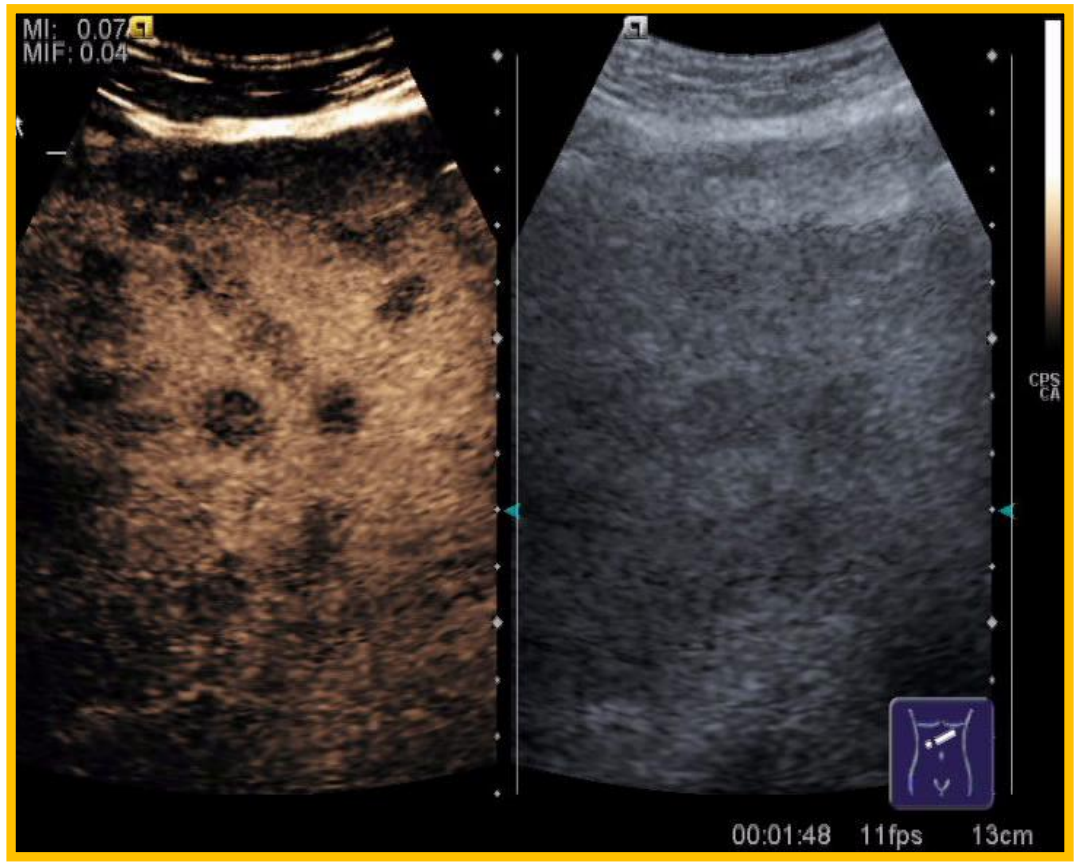


“Wash out” in liver metastasis

Early Portal phase (36 sec.)



Portal phase (1 min.46 sec.)



CEUS in malignant FLLs

- The **vascular pattern during the portal and late phases differentiate benign ("keep" contrast) from *malignant (wash out present) FLLs.***
- **"Wash out" pattern in portal and late phase in malignancy is very typical** and a differentiation criteria from the ***benign FLLs (who "keep" the contrast in the portal and late phases).***

Romanian Multicenter study on CEUS

ORIGINAL PAPER

DOI: http://dx.doi.org/10.15403/jgld-180

Contrast-Enhanced Ultrasound for the Characterization of Malignant versus Benign Focal Liver Lesions in a Prospective Multicenter Experience – The SRUMB Study

Ioan Sporea[1], Daniela Larisa Săndulescu[2], Roxana Șirli[1], Alina Popescu[1], Mirela Danilă[1], Zeno Spârchez[3], Cătălina Mihai[4], Simona Ioanițescu[5], Tudor Moga[1], Bogdan Timar[6], Ciprian Brisc[7], Dana Nedelcu[8], Adrian Săftoiu[2], Viorela Enăchescu[9], Radu Badea[3]

1.Sporea I et al. J Gastrointestin Liver Dis, June 2019 Vol. 28 No 2: 191-196

Structure of the cohort

Parameter			Cohort n=2062
Age (years)			52.4 +/-7.5
Gender	Men: 1148		55.7% 54.7 +/- 7.5 years
	Women: 914		44.3% 50.75 +/- 7.7 years
Chronic liver disease		Yes	727 (35.3%)
		No	1335 (64.7%)

Results

- If we take into consideration only the diagnosis of malignancy, CEUS managed a correct *differentiation of malignant vs. benign lesion in 88.3%* (1820/2062) of the cases.
- For the *lesion-specific diagnosis*, CEUS managed *a correct diagnosis in 81.4%* (1678/2062) of the lesions.

CEUS performance for the most frequent FLLs

good performance → less good performance →

	Sensitivity	Specificity	Accuracy	PPV	NPV
HCC	76.6%	98.4%	91.2%	96.1%	89.4%
Hemangioma	89.2%	99%	96.9%	96.4%	97%
Metastases	90.9%	98.4%	96.9%	93.6%	97.7%
HNF	84%	99.5%	98.8%	89.7%	99.2%
Cholangiocarcinoma	61.4%	99.3%	98.2%	71.4%	98.9%
Abscess	86.6%	99.9%	99.6%	95.1%	99.7%
Adenoma	56.2%	99.9%	99.2%	90%	99.3%

Some comments

- ***Easy to be diagnosed FLL with CEUS: FNH, hemangioma, liver metastasis, abscess.***
- ***More difficult lesions: Adenoma, HCC, Cholangiocarcinoma.***
- **Experience can play a role for the improvement of the accuracy of CEUS liver!**(1)

1. Giesel FL et al. Contrast-enhanced ultrasound for the characterization of incidental liver lesions - an economical evaluation in comparison with multi-phase computed tomography. Ultraschall in Med 2009;30(3):259-68

Meta-analysis of CEUS for FLL

- A total of **45 studies with 8147 focal liver lesions** were included in the analysis.
- Overall **sensitivity and specificity of CEUS for the diagnosis of *malignant* liver lesions** was **93%** (95%-CI: 91–95%) and **90%** (95%-CI: 88–92%) respectively.

1. Friedrich-Rust M et al.Contrast-Enhanced Ultrasound for the differentiation of benign and malignant focal liver lesions: a meta-analysis. Liver International 2013: 33: 739–755

The diagnostic performances of CEUS, CE-CT and CE-MRI in a meta-analysis in patients with FLLs.

25 studies included:

- 1.The pooled estimate **Sensitivity and Specificity** for **CEUS studies** were **87% and 89%** respectively.
- 2.**CE-CT studies: Sensitivity and specificity were 86% and 82%** respectively,
- 3.**CE-MRI studies: Sensitivity and specificity were 85% and 87%** respectively.
- **Conclusion: The diagnostic *performance of CEUS for FLLs is not significantly different than that of CE-CT and CE-MRI*.** CEUS is a highly specific and sensitive diagnostic modality in detecting FLLs and ***should be considered as the first evaluation of a new US lesion.***

1.Xie L et al: Diagnostic value of CEUS, CT and MRI for focal liver lesions: a meta-analysis. Ultrasound in Med. & Biol. 2011; 37 (6) : 854–861

Meta-analysis with 21 studies

- In an other meta-analysis (1) what compared CEUS with CE-CT and CE-MRI In **21 studies**, shown:
- **SonoVue-enhanced ultrasound studies, sensitivity was 88% and specificity was 81%;**
- **CE-CT studies, sensitivity was 90% and specificity was 77%;**
- **CE-MRI studies, sensitivity was 86% and specificity was 81%.**

- ***In conclusion in this comparison, SonoVue enhanced ultrasound had no significant difference compared with CE-CT and CE-MRI.***

1.Guang Y, Xie L, Ding H.Diagnosis value of focal liver lesions with SonoVue®-enhanced ultrasound compared with contrast-enhanced computed tomography and contrast-enhanced MRI: a meta-analysis. J Cancer Res Clin Oncol. 2011 Nov;137(11):1595-605

Meta-analysis with 57 studies and >10,000 lesions

- A comprehensive meta-analysis by Wu et al. (57 studies, >10,000 lesions)(1) reported pooled sensitivity of 0.92 and specificity of 0.87 for CEUS in differentiating malignant from benign FLL, confirming high overall accuracy.
- The analysis also showed that second-generation UCAs significantly outperformed first-generation Levovist, and that Sonazoid had particularly high diagnostic performance.

1.Wu M, Li L, Wang J, et al.Contrast-enhanced US for characterization of focal liver lesions: a comprehensive meta-analysis. Eur Radiol. 2018 May;28(5):2077-2088.

A 2025 published Meta-analysis

- **A 2024 meta-analysis of Sonazoid-enhanced CEUS (SZ-CEUS) reported high diagnostic accuracy for differentiating benign from malignant FLL, again with pooled sensitivity and specificity above 90% (1).**
- **This analysis reported high pooled sensitivity (~94%) and specificity (~84%) for Sonazoid-CEUS in differentiating benign and malignant lesions, demonstrating strong overall diagnostic performance.**

1.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. 2025 Mar-Apr;53(3):510-524.

Lesions that remained indeterminate after CT/MRI/PET

- **In a published paper (2025) the study focused on lesions that remained indeterminate after CT/MRI/PET and *showed that CEUS could correctly reclassify most of these FLL as benign or malignant*, with high positive and negative predictive values, underlining its role as a "problem-solving" modality (1).**

- 1.Lyshchik A, Kuon Yeng, Escalante C,; CEUS LI-RADS Trial Group; Contrast-enhanced US of High-Risk Indeterminate Focal Liver Observations Categorized as LR-4 or LR-M at CT/MRI. Radiology. 2025 Jan;314(1):e240916.

Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) in the Liver – Update 2020

WFUMB in Cooperation with EFSUMB, AFSUMB, AIUM, and FLAUS

Aktualisierte Leitlinien und Empfehlungen für die gute klinische Praxis für CEUS der Leber

Authors

Christoph F. Dietrich[1,2*], Christian Pállson Nolsøe[3*], Richard G. Barr[4], Annalisa Berzigotti[5], Peter N Burns[6], Vito Cantisani[7], Maria Cristina Chammas[8], Nitin Chaubal[9], Byung Ihn Choi[10], Dirk-André Clevert[11], Xinwu Cui[12], Yi Dong[13], Mirko D'Onofrio[14], J. Brian Fowlkes[15], Odd Helge Gilja[16], Pintong Huang[17], Andre Ignee[18], Christian Jenssen[19], Yuko Kono[20], Masatoshi Kudo[21], Nathalie Lassau[22], Won Jae Lee[23], Jae Young Lee[24], Ping Liang[25], Adrian Lim[26], Andrej Lyshchik[27], Maria Franca Meloni[28], Jean Michel Correas[29], Yasunori Minami[30], Fuminori Moriyasu[31], Carlos Nicolau[32], Fabio Piscaglia[33], Adrian Saftoiu[34], Paul S. Sidhu[35], Ioan Sporea[36], Guido Torzilli[37], Xiaoyan Xie[38], Rongqin Zheng[39]

Good Guidelines for practice!

How to perform Contrast-Enhanced Ultrasound (CEUS)

OPEN ACCESS

Authors

Christoph F. Dietrich[1], Michalakis Averkiou[2], Michael Bachmann Nielsen[3], Richard G. Barr[4], Peter N. Burns[5], Fabrizio Calliada[6], Vito Cantisani[7], Byung Choi[8], Maria C. Chammas[9], Dirk-André Clevert[10], Michel Claudon[11], Jean-Michel Correas[12], Xin-Wu Cui[13], David Cosgrove[14], Mirko D'Onofrio[15], Yi Dong[16], John R. Eisenbrey[17], Teresa Fontanilla[18], Odd Helge Gilja[19], Andre Ignee[13], Christian Jenssen[20], Yuko Kono[21], Masatoshi Kudo[22], Nathalie Lassau[23], Andrej Lyshchik[17], Maria Franca Meloni[24], Fuminori Moriyasu[25], Christian Nolsøe[26], Fabio Piscaglia[27], Maija Radzina[28], Adrian Saftoiu[29], Paul S. Sidhu[30], Ioan Sporea[31], Dagmar Schreiber-Dietrich[32], Claude B. Sirlin[33], Maria Stanczak[17], Hans-Peter Weskott[34], Stephanie R. Wilson[35], Juergen Karl Willmann[36], Tae Kyoung Kim[37], Hyun-Jung Jang[37], Alexandar Vezeridis[38], Sue Westerway[39]

Journal of *Personalized Medicine*

MDPI

Article

Multiparametric Ultrasound Approach Using a Tree-Based Decision Classifier for Inconclusive Focal Liver Lesions Evaluated by Contrast Enhanced Ultrasound

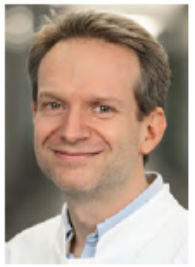
Tudor Voicu Moga [1], Ciprian David [2], Alina Popescu [1], Raluca Lupusoru [1,3,*], Darius Heredea [1], Ana M. Ghiuchici [1], Camelia Foncea [1], Adrian Burdan [1], Roxana Sirli [1], Mirela Danilă [1], Iulia Ratiu [1], Teofana Bizerea-Moga [4] and Ioan Sporea [1]

2024

Ultrasound Diagnosis of Hepatocellular Carcinoma: Is the Future Defined by Artificial Intelligence?

Ultraschalldiagnostik des hepatozellulären Karzinoms: In Zukunft nur mit künstlicher Intelligenz?

Future development of Liver CEUS can be with Artificial Intelligence!



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Artificial intelligence assists identifying malignant *versus* benign liver lesions using CEUS

- **In a cohort of 574 patients, AI performance** was evaluated by ***comparison with radiologists with varied levels of experience. To identify malignant versus benign FLLs, AI achieved an AUROC of 0.934 (95% CI 0.890–0.978), with an accuracy of 91.0%.***
- ***AI outperformed residents* (82.9–84.4%, *P* = 0.038) and *matched the performance of experts radiologists* (87.2–88.2%, *P* = 0.438).**
- **With the *assistance of AI, radiologists exhibited a sensitivity improvement* of 97.0–99.4% (*p* < 0.05) and an accuracy of 91.0–92.9% (*P* = 0.008–0.189), which was comparable with that of the experts (*p* = 0.904).**

1.Hu HT, Wang W, Chen LD et al. Journal of Gastroenterology and Hepatology 2021; 36: 2875–2883

Research Article
Innovative Diagnostics, Modelling and Digital Hepatology

JOURNAL
OF HEPATOLOGY

Contrast-enhanced ultrasound-based AI model for multi-classification of focal liver lesions

2025

Authors

Wenzhen Ding, Yaqing Meng, Jun Ma, …, Jie Yu, Ping Liang, Kun Wang

- In **total 3,725 FLLs (from 52 centers) AI model** ***achieved significantly better performance (accuracy from 0.85 to 0.86) than junior CEUS radiologists (0.59-0.73), and comparable performance to senior CEUS radiologists (0.79-0.85) and senior MRI radiologists (0.82-0.86)***.

- ***Conclusions: "CEUS-based Model-DCB provides accurate multi-classification of FLLs. It holds promise for a wide range of populations, especially those in remote areas who have difficulty accessing MRI."***

Cost-efficiency of Contrast Enhanced Ultrasound (CEUS)

- **In an Italian multicenter study the classic patient work-up (baseline US followed by contrast CT or MRI) was *compared to a new strategy in which CEUS was performed after conventional US.***
- **The study included 485 subjects with 575 FLLs.**
- **The cost of the classical work-up was 134,5 Euros, while in the *strategy including CEUS the total cost was 55,6 Euros, leading to total savings of 78,9 Euros.***

- Romanini L, Passamonti M, Aiani L, et al. Economic assessment of contrast-enhanced ultrasonography for evaluation of focal liver lesions: a multicentre Italian experience. Eur Radiol. 2007 Dec;17 Suppl 6:99-106

Cost-efficiency of Contrast Enhanced Ultrasound (CEUS)

- **Performance of CEUS for the diagnosis of FLL *in a systematic review were that CEUS had similar diagnostic performance to contrast CT and contrast MRI*, for the differential diagnosis of FLLs detected during US surveillance of cirrhosis, for the detection of liver metastases in colorectal cancer and for the characterization of incidentally detected FLLs.**
- **Another *important conclusion was that CEUS was cost-effective vs. MRI in all situations and that CEUS vs. CT was cost-effective for cirrhosis surveillance and for the differential diagnosis of incidentalomas*, with similar costs and effects for the detection of liver metastases from colorectal cancer.**

Westwood ME, Joore MA, Grutters JPC et al. Contrast-enhanced ultrasound using SonoVue® compared with contrast-enhanced computed tomography and contrast-enhanced magnetic resonance imaging for the characterisation of focal liver lesions and detection of liver metastases: a systematic review and cost-effectiveness analysis. Health Technol Assess 2013;17(16)

Cost-efficiency of Contrast Enhanced Ultrasound (CEUS)

- ***An interesting a cost-minimization analysis*** was performed by Giesel et al (1).
- In this study, ***CEUS was compared to multi-phase CT*** **as the diagnostic standard for diagnosing incidental FLLs**.
- **The conclusion was that CEUS was the more cost-effective, only if it was performed in *specialized centers*: 122.18-186.53 Euros vs. 223.19 Euros for CT.**
- ***If CEUS would be performed in non-specialized centers, the cost would be much higher, reaching 407.87 Euros.***

1. Giesel FL et al. Contrast-enhanced ultrasound for the characterization of incidental liver lesions - an economical evaluation in comparison with multi-phase computed tomography. Ultraschall in Med 2009;30(3):259-68

Why not more CEUS in practice?!

Editorial

Med Ultrason 2016, Vol. 18, no. 1, 5-6
DOI: 10.11152/mu.2013.2066.181.isp

Why isn't Contrast Enhanced Ultrasound for Focal Liver Lesions used more in daily practice?

Ioan Sporea

2016

In Romania

Department of Gastroenterology and Hepatology, Romania

The benefits of CEUS and why we don't use more CEUS in clinical practice in the United Kingdom

2026

Gibran Timothy Yusuf, BSc (hons), MBBS, FRCR ✉, Paul Singh Sidhu, BSc MBBS MRCP FRCR DTM&H FCIRSE FAIUM

In UK

British Journal of Radiology, tqag025, https://doi.org/10.1093/bjr/tqag025
Published: 03 February 2026 **Article history** ▾

Green Medical Imaging

Editorial

Blank V et al. "Green Medical Imaging"... Ultraschall in Med 2025; 46: 530–535

Thieme

"Green Medical Imaging" – Ultrasound rediscovered as a resource-saving future technology in clinical imaging

„Green Medical Imaging" – Ultraschall als ressourcenschonende Zukunftstechnologie in der klinischen Bildgebung

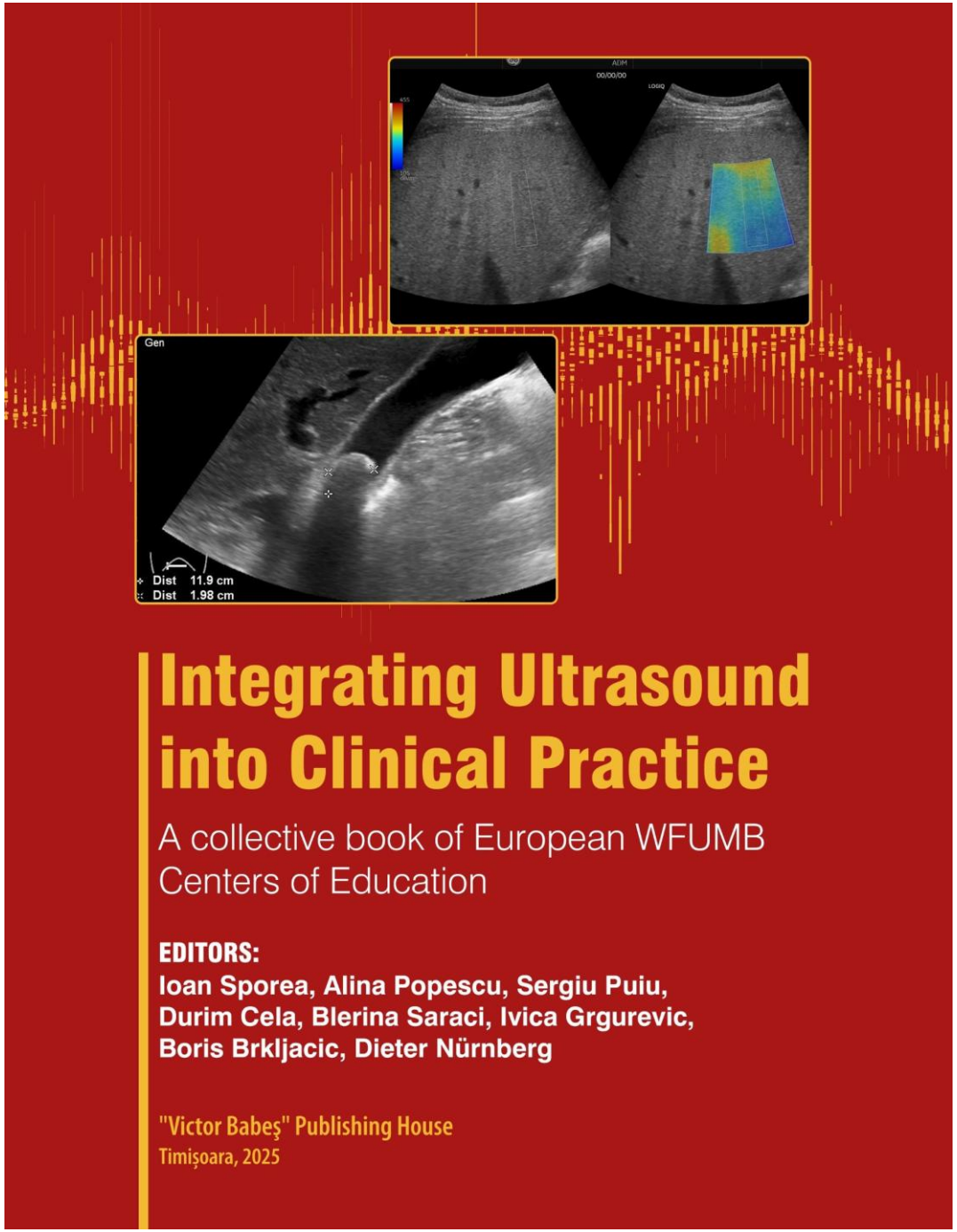
Dr. med. Valentin Blank

Prof. Dr. med. Deike Strobel

Prof. Dr. med. Thomas Karlas

In Conclusion

- Liver CEUS is easy to be performed, including like a PoCUS method,
- Is a cheap technique in comparison with CE-CT or CE-MRI,
- No side effects for this method,
- Good discrimination between benign and malign liver lesions (around 90%) and for a specific lesion (more than 80%),
- Some FLL are easy to be diagnosed, others more difficult!
- Experience play a role for the method, and CEUS is method cost-efficient.
- New technologies and AI can help the diagnosis in the future!



E-book, Free download

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