

EFSUMB Journal Club – Issue 1

The EFSUMB Journal Club regularly reviews the leading Ultrasound-related journals, sharing with EFSUMB members selected relevant publications, providing values and critiques of the work.

Contributors for this issue

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Strobel D, Agaimy A, Jesper D, Zundler S, Schellhaas B. HCCs lacking arterial phase hyperenhancement (APHE) on contrast-enhanced ultrasound (CEUS) – a diagnostic challenge. Findings from the prospective multicenter DEGUM CEUS HCC trial. *Ultraschall in Med.* 2023 Dec; 44(6): 606–613. English. doi: 10.1055/a-2034–1911. Epub 2023 Feb 13. PMID: 36781161.

Objectives Hepatocellular carcinoma (HCC) upon contrast-enhanced ultrasound (CEUS) typically shows arterial phase hyperenhancement (APHE), followed by late (> 60 seconds) and mild contrast washout (WO). Although APHE is considered as the hallmark of HCC, it can be absent in some HCCs. Thus, we explored which sonomorphological and histopathological features of HCC are associated with a lack of APHE upon CEUS.

Methods Focal liver lesions in high-risk patients for HCC were assessed with CEUS following a standardized protocol in a prospective multi-center real-life setting. CEUS patterns in HCC were assessed, and tumour and patient characteristics were compared for HCCs with and without APHE.

Results 316 patients with HCC were recruited (cirrhosis, 76.9%). APHE occurred in 271/316 HCCs (85.8%). A lack of APHE was associated with portal vein thrombosis, tumour infiltration of the liver vessels ($p < 0.001$), larger size, multilocularity, and higher depth location upon ultrasound ($p < 0.01$). Histological grading did not differ between HCCs with and without APHE ($p = 0.39$). Histopathological features of HCCs without APHE included cirrhotic stromal reaction, marked tumour cell steatosis and absence of the typical surrounding dilated sinusoidal vascular channels.

Conclusion Correlation with histopathological findings support the fact that HCCs with a lack of APHE in CEUS are a heterogeneous group. The examiner has to be aware that particularly HCCs with portal vein thrombosis or macro-invasion of the liver vessels may lack APHE.

Short-Review by Prof. V. Cantisani

The Authors report a prospective multi-center real-life study in which CEUS HCC patterns were assessed, and tumour and patient characteristics were compared for HCCs with and without APHE.

316 patients with HCC were recruited, 76.9% of them were cirrhotic. Typical APHE occurred in 271/316 HCCs (85.8%). Conversely, a lack of APHE was associated with portal vein thrombosis, tumour infiltration of the liver vessels ($p < 0.001$), larger size, multilocularity, and higher depth location upon ultrasound ($p < 0.01$). Histological grading did not differ between HCCs with and without APHE ($p = 0.39$). Histopathological features of HCCs without APHE included cirrhotic stromal reaction, marked tumour cell steatosis and absence of the typical surrounding dilated sinusoidal vascular channels

Correlation with histopathological findings support the fact that HCCs with a lack of APHE in CEUS are a heterogeneous group.

According to this multicenter study a significant proportion of HCCs do not display the characteristic APHE, due to several factors such as:

- portal vein thrombosis and tumour infiltration of the liver vessels;

- the presence of a transjugular intrahepatic portosystemic shunt (TIPSS);
- larger tumour size, diffusely infiltrating tumours and multilocular growth, suggesting a different and potentially more aggressive tumour biology in this subtype.

Indeed, considering the large dataset of the present paper, US expert has to be aware that particularly HCCs with portal vein thrombosis or macro-invasion of the liver vessels may lack APHE. Therefore, in these cases, biopsy, especially when emerging drug for targeted therapies in HCC may be considered, is warranted to avoid misdiagnosis.

Shi L, Wu D, Yang X, Yan C, Huang P. Contrast-Enhanced Ultrasound and Strain Elastography for Differentiating Benign and Malignant Parotid Tumors. *Ultraschall in Med.* 2023 Aug; 44(4): 419–427. doi: 10.1055/a-1866–4633. Epub 2023 Feb 2. PMID: 36731495; PMCID: PMC10629480.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10629480/>

Objectives Preoperative differentiation between benign parotid tumors (BPT) and malignant parotid tumors (MPT) is crucial for treatment decisions. The purpose of this study was to investigate the benefits of combining contrast-enhanced ultrasound (CEUS) and strain elastography (SE) for pre-operative differentiation between BPT and MPT.

Methods A total of 115 patients with BPT (n = 72) or MPT (n = 43) who underwent ultrasound (US), SE, and CEUS were enrolled. US and CEUS features and the elasticity score were evaluated. Receiver operating characteristic curve (ROC) analysis was used to assess the diagnostic performance of SE, CEUS, and SE + CEUS with respect to identifying MPT from BPT.

Results Solitary presentation, larger diameter, irregular shape, ill-defined margin, heterogeneous echogenicity, and calcification on US and higher elasticity score on SE had a significant association with malignancy. MPT also presented an unclear margin, larger size after enhancement, and “fast-in and fast-out” pattern on CEUS. The combination of SE and CEUS was effective for differentiating MPT from BPT (AUC: 0.88,

0.80–0.95), with a sensitivity of 86.0 %, specificity of 88.9 %, and accuracy of 87.8 %, which were significantly higher than the values for SE (AUC: 0.75, 0.66–0.85) and CEUS (AUC: 0.82, 0.73–0.91) alone.

Conclusion The combination of CEUS and SE is valuable for distinguishing MPT from BPT.

Short-Review by Prof. J. Kuenzel

Strengths:

- Relatively large number of malignant parotid tumors (37 %)
- Exclusion of non-primary parotid carcinomas and lymphoma
- Two blinded examiners independently reviewed images and loops
- According to the results a multimodal ultrasound based diagnostic pathway is provided.

Weaknesses:

- Retrospective and monocentric study design
- Indication for CEUS is not clearly defined, which could lead to a selection bias
- Sonoelastography was only performed with strain and not shear-wave technique.
- Scoring system for breast was used to classify parotid tumors benign or malignant.

Personal opinion:

- More practice and evidence in differentiating parotid tumors by means of ultrasound is warranted and this study gives interesting insights to it. Any improvements in pre-operative differential diagnosis is valuable, in particular for patient counseling, indication for ultrasound guided biopsy and treatment planning.

Blank V, Heni M, Karlas T. Quantification of Portal Vein Vascularization Using an Automated Post-Processing Video Analysis Tool. *Ultrasound Int Open.* 2023 Mar 20; 9(1): E2–E10. doi: 10.1055/a-1999–7818. PMID: 36950090; PMCID: PMC10027440.

<https://www.thieme-connect.com/products/ejournals/pdf/10.1055/a-1999-7818.pdf>

Purpose Blood flow dynamics represent a diagnostic criterion for many diseases. However, no established reference standard is available. In clinical practice, ultrasound pulsed-wave Doppler (PW-Doppler) is frequently used to assess visceral blood flow, despite its well-known limitations. A quantitative analysis of conventional color Doppler patterns can be performed using an innovative ultrasound-based algorithm (pixel flow analysis, PFA). This tool already shows promising results in obstetrics, but the technique has not yet been evaluated for portal venous blood flow assessment.

Methods This prospective exploratory research study evaluated the applicability of PFA in the portal venous system. Measurements of portal venous flow using PFA and PW-Doppler were compared in healthy volunteers (n = 20) and in patients with hepatic steatosis (n = 10) and liver cirrhosis (n = 10).

Results In healthy volunteers (60 % female, mean age 23 years, BMI 21.5 kg/m² [20.4–23.8]), PFA and PW-Doppler showed a strong positive correlation in fasting conditions (r = 0.69; 95 % CI 0.36–0.87), recording a median blood flow of 834 ml/min (624–1066) and 718 ml/min (620–811), respectively. PFA was also applicable in patients with chronic liver diseases (55 % female, age 65 years (55–72); BMI 27.8 kg/m² (25.4–30.8)), but the correlation between PFA and PW-Doppler was poor (r = –0.09) in the subgroup with steatosis. A better correlation (r = 0.61) was observed in patients with liver cirrhosis.

Conclusion PFA and PW-Doppler assessment of portal venous vascularization showed high agreement in healthy volunteers and patients with liver cirrhosis. Therefore, PFA represents a possible alternative to conventional PW-Doppler sonography for visceral blood flow diagnostics and merits further evaluation.

Short-Review by Prof. A. Saftoiu

This study evaluates the efficacy of Pixel Flow Analysis (PFA) in assessing portal venous blood flow, comparing it with the traditional Pulsed-Wave Doppler (PW-Doppler). Intravascular blood flow quantification, particularly in

portal veins, is crucial for managing chronic liver diseases and post-liver transplantation care. However, existing noninvasive methods are limited, necessitating new techniques like PFA for comprehensive evaluation

The study included healthy volunteers and patients with liver conditions like steatosis and cirrhosis. PFA, a noninvasive ultrasound-based method, analyzes color Doppler signals to as-

sess blood flow across a vessel's cross-sectional area. The method showed strong applicability and correlated well with PW-Doppler in healthy individuals and cirrhosis patients but less so in steatosis cases due to ultrasound signal attenuation.

PFA demonstrated potential in detecting flow changes, especially post-meal in healthy subjects, suggesting its usefulness in various clin-

ical scenarios. The study, however, acknowledges limitations such as a small sample size and the absence of a noninvasive 'gold standard' for comparison. Despite these, PFA appears promising for noninvasive portal venous blood flow assessment and could complement existing methods like PW-Doppler. Further research is needed to establish its role in diagnosing and managing liver diseases.