

# Contrast-enhanced ultrasound (CEUS+) for Hepatocellular Carcinoma

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## Hepatocellular Carcinoma

Hepatocellular Carcinoma (HCC) is the most frequent primary liver cancer worldwide (80-90% of all primary liver malignancies).<sup>[1]</sup>

Hepatitis B virus and/or hepatitis C virus infection, alcohol, and nonalcoholic fatty liver disease are the most predominant risk factors for HCC worldwide.<sup>[2]</sup> Patients with cirrhosis are particularly considered a high-risk group for the development of HCC and they undergo regular surveillance by means of Ultrasound (US) usually performed every six months.

Unfortunately, Despite technical advance in both spatial and contrast resolution, gray-scale US is still considered a non-specific technique for the diagnosis of focal liver lesions (FLLs), including HCC.<sup>[3]</sup> Doppler examination may provide some clues to the diagnosis; for example, a spoke-wheel pattern associated with the arterial wave form in a pulsed Doppler evaluation may be highly suggestive, although not pathognomonic of focal nodular hyperplasia in otherwise healthy young woman taking oral contraceptives.<sup>[4]</sup> Furthermore, Doppler US can only assess large vessels (i.e., >100  $\mu$ m), and it is prone to motion artifacts.

Hence, once HCC is suspected in a patient with cirrhosis, many international guidelines recommend a diagnostic evaluation for HCC using either multiphasic computed tomography (CT) or multiphasic magnetic resonance imaging (MRI) because both modalities show similar diagnostic performance.<sup>[5]</sup>

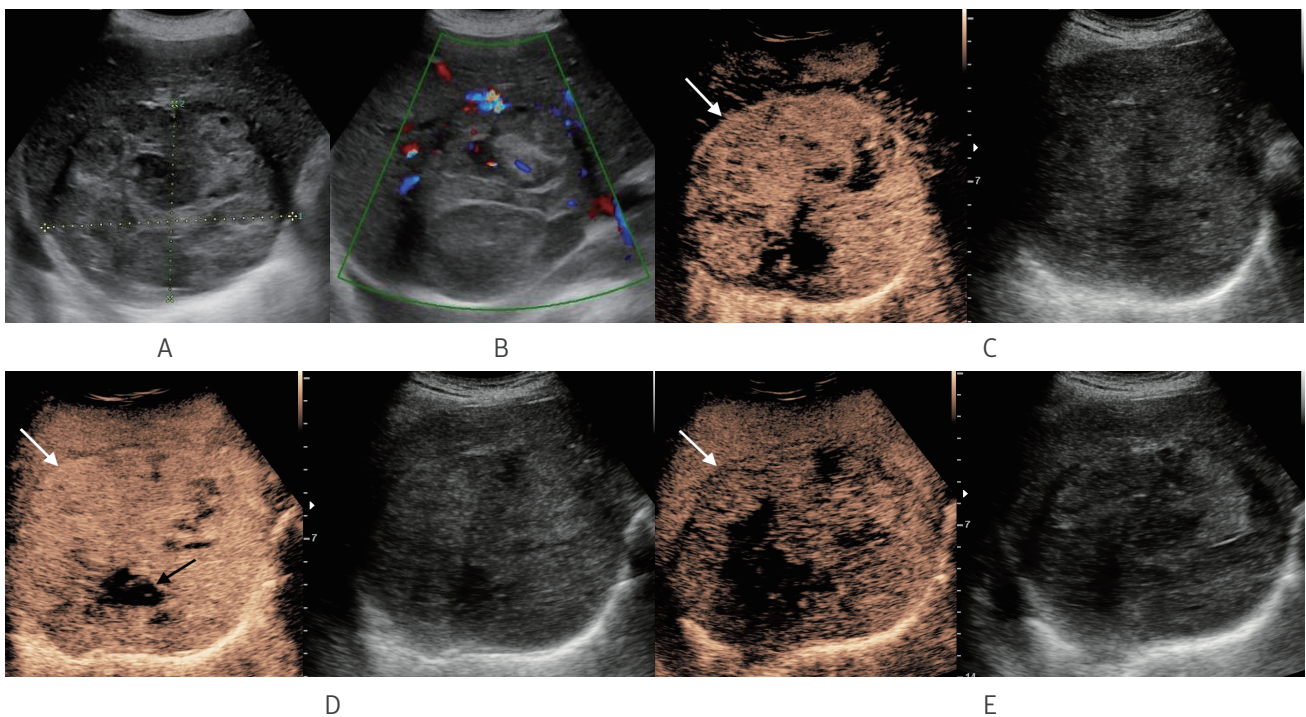
Regardless of the particular strength and short comings of each technique, both CT and MRI require contrast agents, the use of which can be problematic in patients with severely impaired renal function.<sup>[6],[7]</sup>

## Contrast-enhanced ultrasound Diagnosis

Firstly introduced in the late nineties, contrast-enhanced ultrasound (CEUS) is a real-time ultrasonographic technique, which allows to assess non-invasively the contrast enhancement patterns of focal liver lesions (FLLs) throughout the vascular phase, without the use of ionizing radiation and with a much higher temporal resolution than CT and MRI.<sup>[8]</sup> CEUS allowed an accurate depiction of both macro- and microcirculation, which was immediately exploited for the detection and characterization of FLLs, with reported sensitivity and specificity values

approaching those of CT and MRI.<sup>[9],[10]</sup> Several studies have reported the improvement in diagnostic accuracy of US with use of contrast agents in the detection and characterization of FLLS, including HCC, as well as in the guidance and evaluation of response of therapeutic procedures.<sup>[11]</sup> Currently, CEUS is included as a part of the suggested diagnostic work-up of liver FLLs, resulting in better patient management and cost effective delivery of therapy.<sup>[12]</sup>

In the clinical setting of a cirrhotic patient with suspected HCC, CEUS is perfectly able to depict the typical contrast-enhancement pattern of arterial-phase hypervascularity followed by late ( $\geq 60$  s) and mild washout of HCC (Fig. 1). On the other hand, early ( $< 60$  s) and/or marked washout is a major feature for malignancies other than HCC, such as intrahepatic cholangiocarcinoma (Fig. 2).



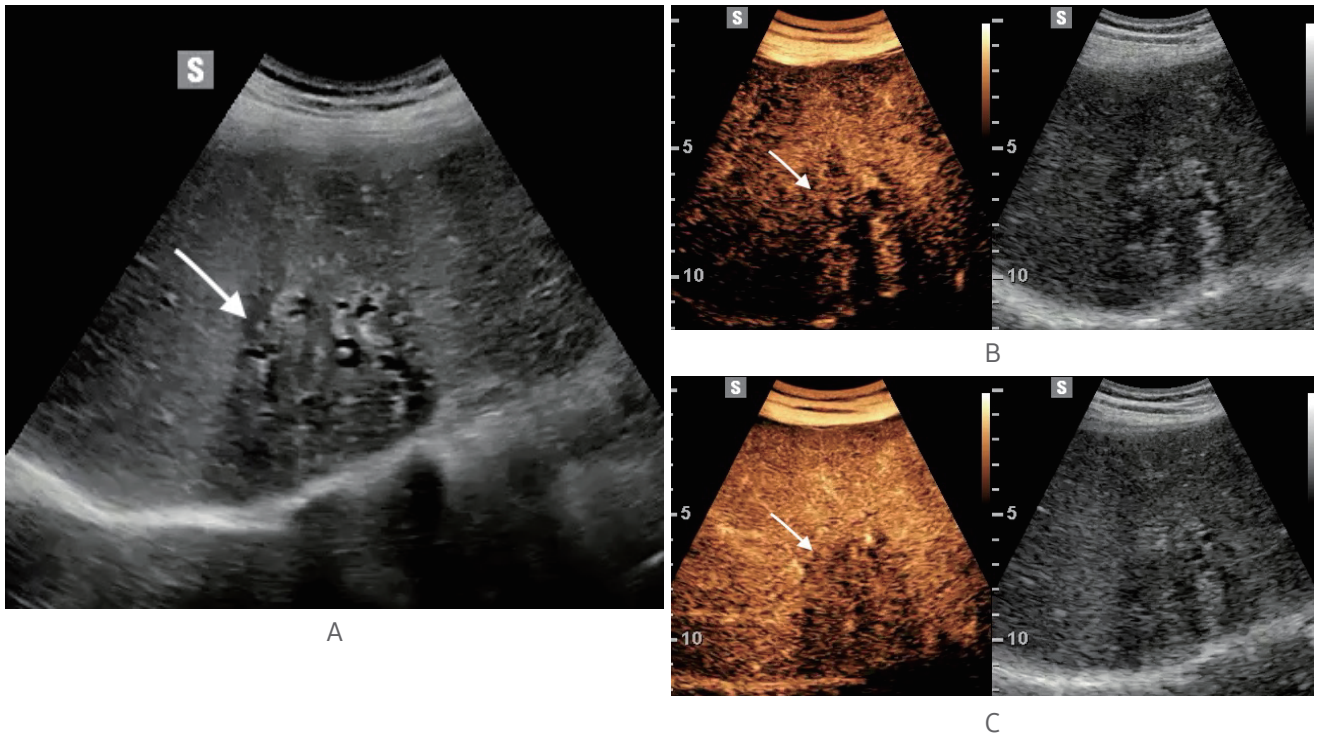
**Fig. 1 HCC in a 70-year-old man with hepatitis C-related cirrhosis.**

A,B: Oblique ascending right subcostal baseline image reveals a markedly inhomogenous lesion sized 9.7 cm in the seventh hepatic segment (calipers) (A) with vascular signal in its context (B).

C: During the arterial phase the mass is highly hypervascular (arrow).

D: During the extended portalvenous phase a slight hyperechoic peripheral rim is evident suggesting a pseudocapsule (white arrow) with necrotic areas inside the mass (black arrow).

E: The lesion shows wash-out sign appearing hypoechoic with respect to surrounding liver parenchyma 5 min after the beginning of contrast medium injection (arrow).



**Fig. 2 Intrahepatic cholangiocarcinoma in a 73-year-old man.** A: Oblique ascending right subcostal baseline image reveals a highly heterogenous lesion with ill-defined margins sized 6.5 cm in the eighth hepatic segment (arrow). B,C: During the arterial phase the mass appears heterogeneously hypervascular (arrow) (B) with rapid (43 seconds after SonoVue injection) wash-out (C).

## Conclusion

Currently, CEUS is increasingly being performed on a routine basis and, in the appropriate clinical setting, is included as a part of the suggested diagnostic work-up of HCC, resulting in better patient management and cost-effective delivery of therapy.<sup>[13],[14]</sup>

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