Improved Detection of Focal Liver Lesions with Contrast Enhanced Ultrasound

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Abbreviations

CEUS	Contrast enhanced ultrasound
CT	Computed tomography
FLL	Focal liver lesion
HCC	Hepatocellular carcinoma
IOUS	Intraoperative ultrasonography
IO-CEUS	Intraoperative contrast-enhanced ultrasound
MRI	Magnetic resonance image

3.1 Introduction

- Conventional ultrasound is the most frequently used imaging modality as the first-line imaging of abdominal organs, including the liver, but is reported to be less sensitive than CECT, CEMRI, or intraoperative ultrasound in the detection of focal liver lesions (FLL).
- CEUS has dramatically increased the capability of conventional ultrasound for detection of FLL, especially those invisible on conventional ultrasound.
- CEUS has a considerably higher sensitivity of up to 80–90% in detecting liver metastases, comparable to that of CECT and CEMRI [1].
- CEUS is of particular useful in detecting liver metastases ≤10 mm.

3.2 Reasons for Focal Liver Lesions Not Detected on CEUS

- Despite of its high detection rate and diagnostic accuracy in FLLs, CEUS still faces the challenges in the detection of some indistinctive lesions, especially when the diameter of lesion is less than 10 mm.
- In the background of liver cirrhosis, some early or recurrent HCCs may be isoechogenic with indistinctive margins, or show hyperechoic similar with those of cirrhosis nodules.
- After molecular targeted therapy for colorectal liver metastasis, some lesions' volume may shrink and become isoechoic. These lesions are so-called occult tumors since they cannot be detected on CEUS or even on CECT.
- In the condition of sever fatty liver, hemotherapy-induced steatohepatitis, hepatic sinus obstruction, liver structure changes after repeated surgical procedures and local ablative treatment or residual or recurrent lesions located adjacent to treatment area, FLLs might be difficult to be detected by ultrasound.
- Specific tumor location, such as too deep or close to diaphragm, subcapsular tumors affected by rib occlusion or abdominal wall reverberation, may result in difficulties in tumors detection.

3.3 Detection of Liver Primary Malignancies

- CEUS have improved detection and characterization of HCC. Homogeneous hyperenhancement during the arterial phase and mild wash-out are indicative for HCC in liver cirrhosis.
- The incident rate of recurrent HCCs ranging from 45.2% to 60.0% after HCC hepatectomy. The CEUS enhancement pattern of recurrent HCCs including hyper- or iso-enhancement during arterial phase, with no wash-out in portal or late phases (Fig. 3.1).

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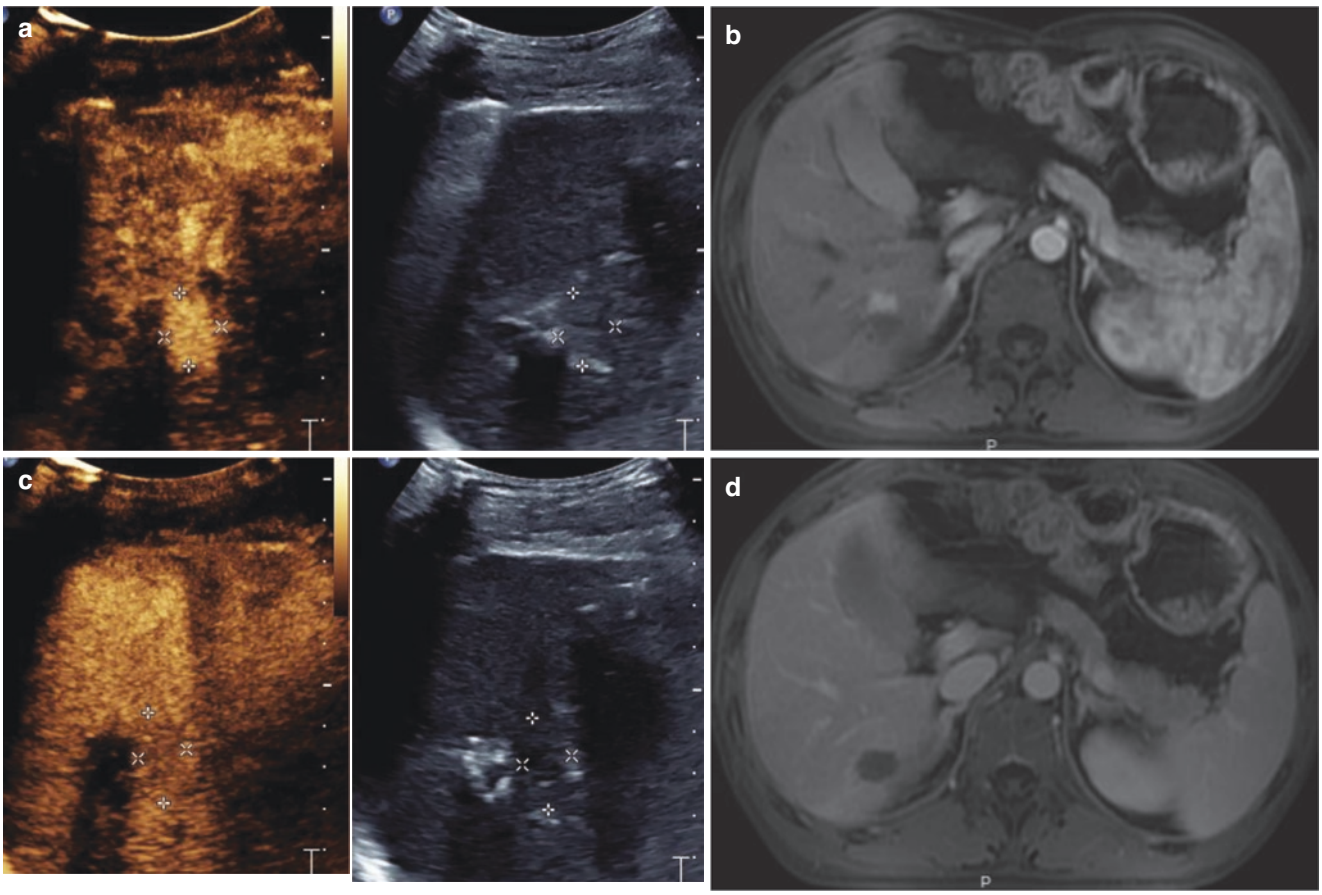


Fig. 3.1 Recurrence of hepatocellular carcinoma (HCC). A 44-year-old man with liver cirrhosis and recurrence of HCC. The lesion on VI hepatic segment beside the primary lesion that had surgical excised 6 months before. The lesion could not be detected on B mode ultrasound (**a**). During arterial phase of contrast enhanced ultrasound (CEUS), the lesion was hyperenhanced (**a**), also on MRI image (**b**). During late phase, the lesion was hypoenhanced (**c**, **d**)

- With the injection of Sonazoid, scanning the entire liver at 10 min or later after injection helps to detect malignant nodules since typical HCC shows as an enhancement defect (Fig. 3.2).
- During late phase scan of the whole liver, intrahepatic cholangiocarcinoma (ICC) wash-out rapidly regardless of the appearance in the arterial phase. This may be helpful for detection of satellite nodules adjacent to a larger lesion that were not visualized on conventional ultrasound (Fig. 3.3).
- Comparing with other imaging modalities, a distinguishing advantage of CEUS is the real time scan with a higher temporal resolution, which makes it possible to observe the dynamics enhancement pattern of lesions in detail [2].

3.4 Detection of Liver Metastases

- The typical CEUS appearance of liver metastases is focal contrast wash-out area by scanning the whole liver segments during portal venous and late phases (Figs. 3.4 and 3.5).
- A second injection of contrast agent can be used to confirm the malignancy of focal areas of contrast wash-out by observing hyperenhancement during arterial phase.
- According to a recent meta-analysis, overall sensitivity of CEUS for diagnosis of liver metastases was 91% (95% CI: 87–95%).

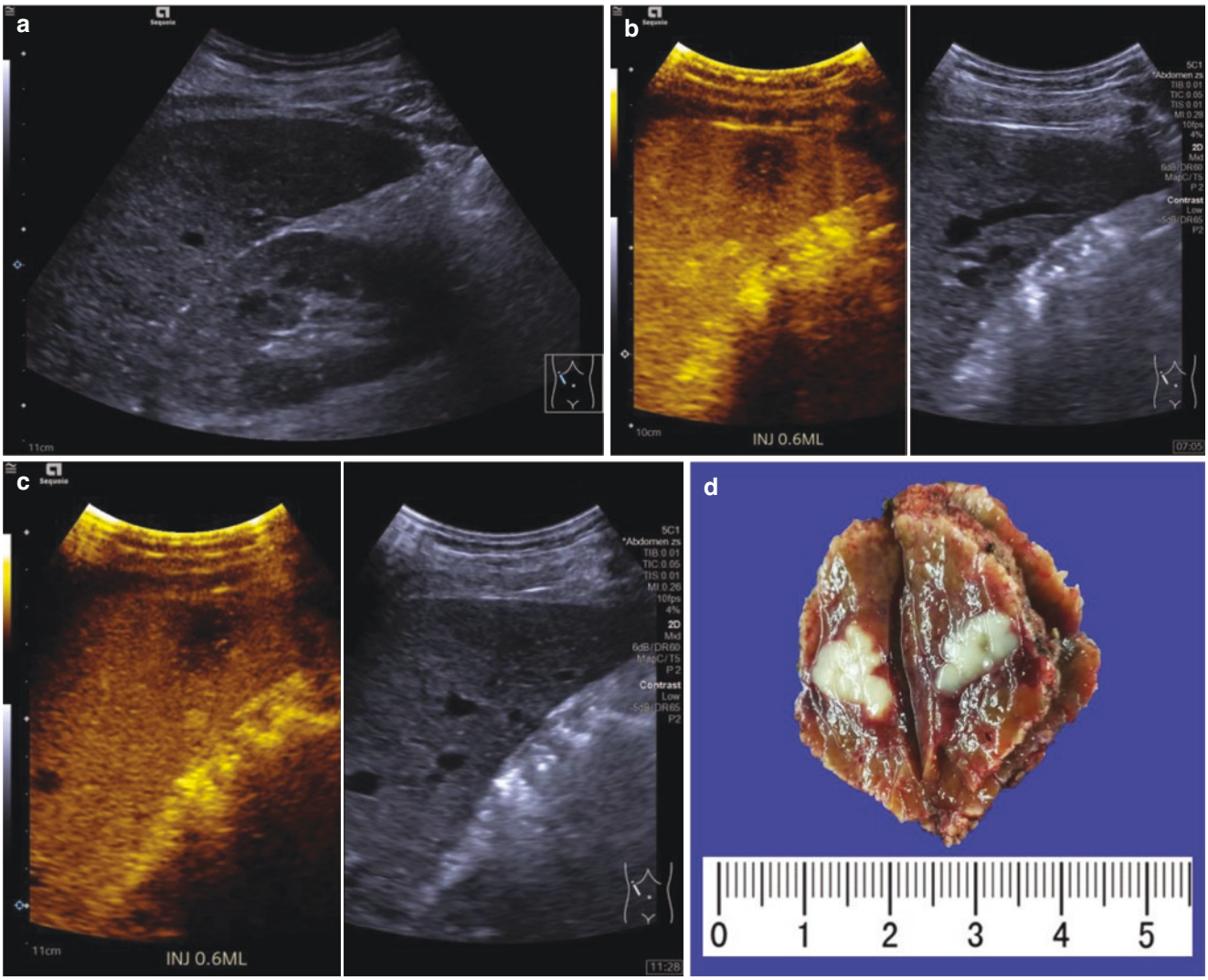


Fig. 3.2 Detection of hepatocellular carcinoma (HCC) lesions that were not visualized on conventional ultrasound. A HCC lesion was suspected on right lobe of liver, while its not distinctive on B mode ultrasound (**a**). After injection of Sonazoid, the lesion could be detected as hypoenhanced area during late phase (**b**) and Kupffer phase (**c**). The final diagnosis was confirmed by surgery and histopathological results (**d**)

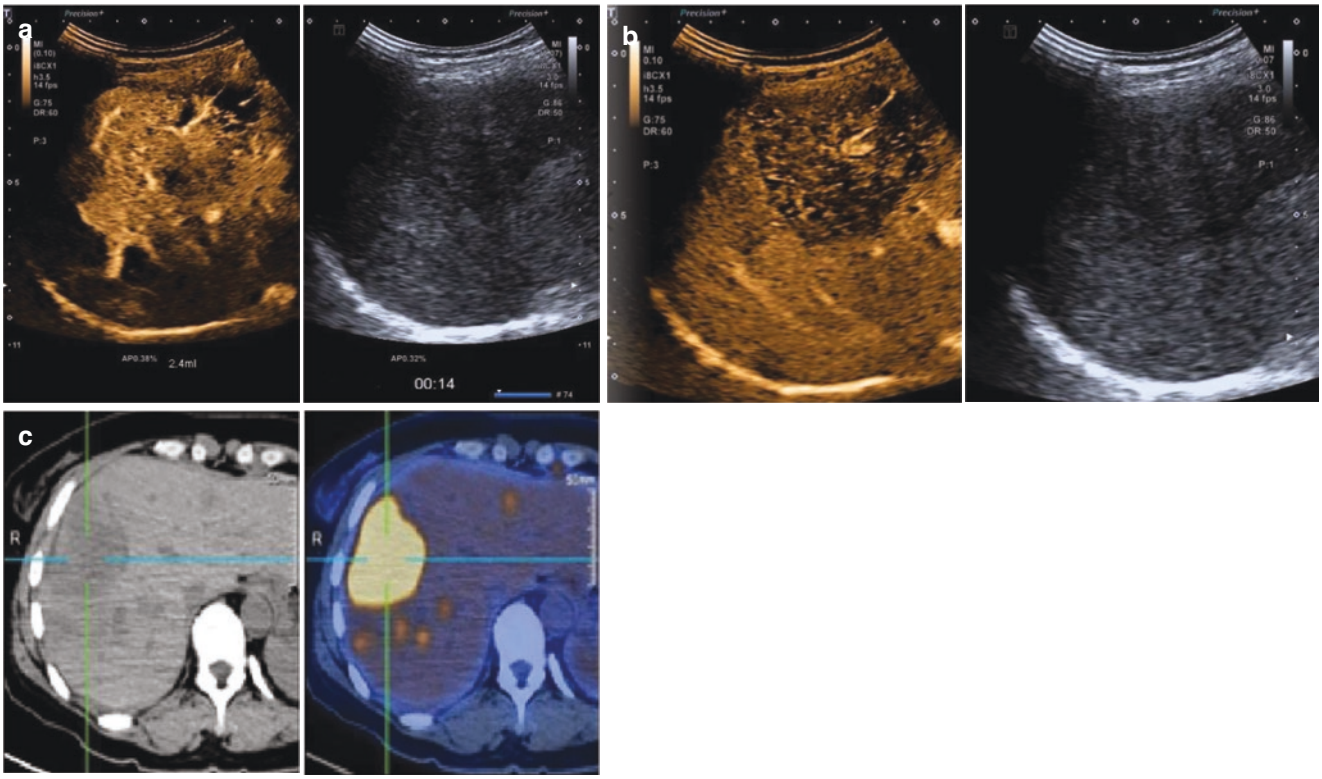


Fig. 3.3 Detection of satellite nodules adjacent to a large intrahepatic cholangiocarcinoma (ICC) lesion that were not visualized on conventional ultrasound. A large ICC lesion located in the left lobe of liver showed hyperenhancement during arterial phase (**a**). Multiple satellite nodules could be detected during late phase scan (**b**). PET-CT showed similar multiple small lesions (**c**)

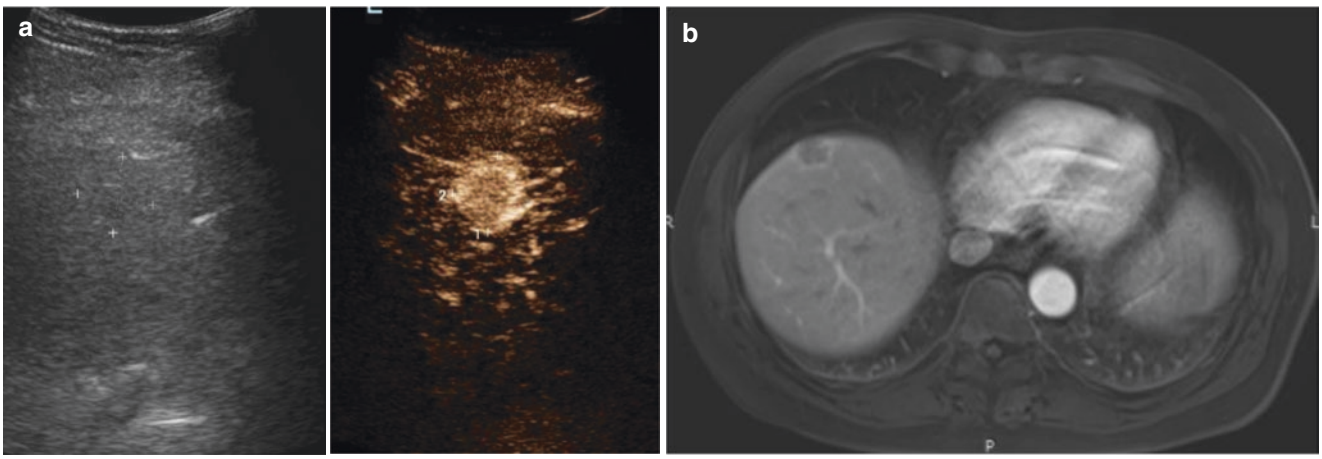
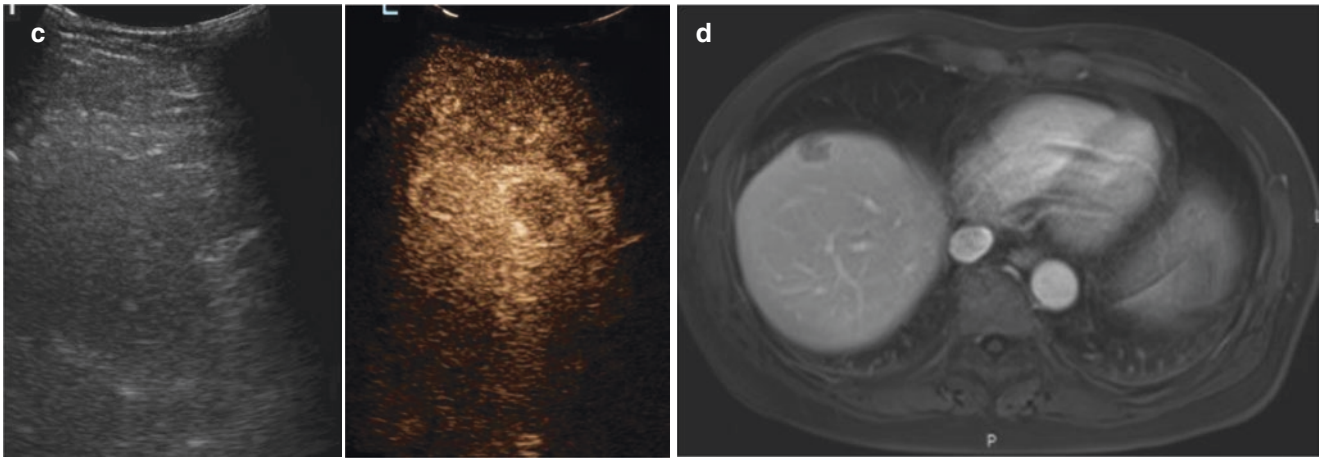


Fig. 3.4 An isoechoic liver metastasis lesion from rectal cancer in a 58-year old. The lesion showed complete hyperenhancement during arterial phase both on contrast enhanced ultrasound (CEUS) (**a**) and on MRI images (**b**). During portal venous phase, the lesion showed hypoenhancement both on CEUS (**c**) and on MRI (**d**)



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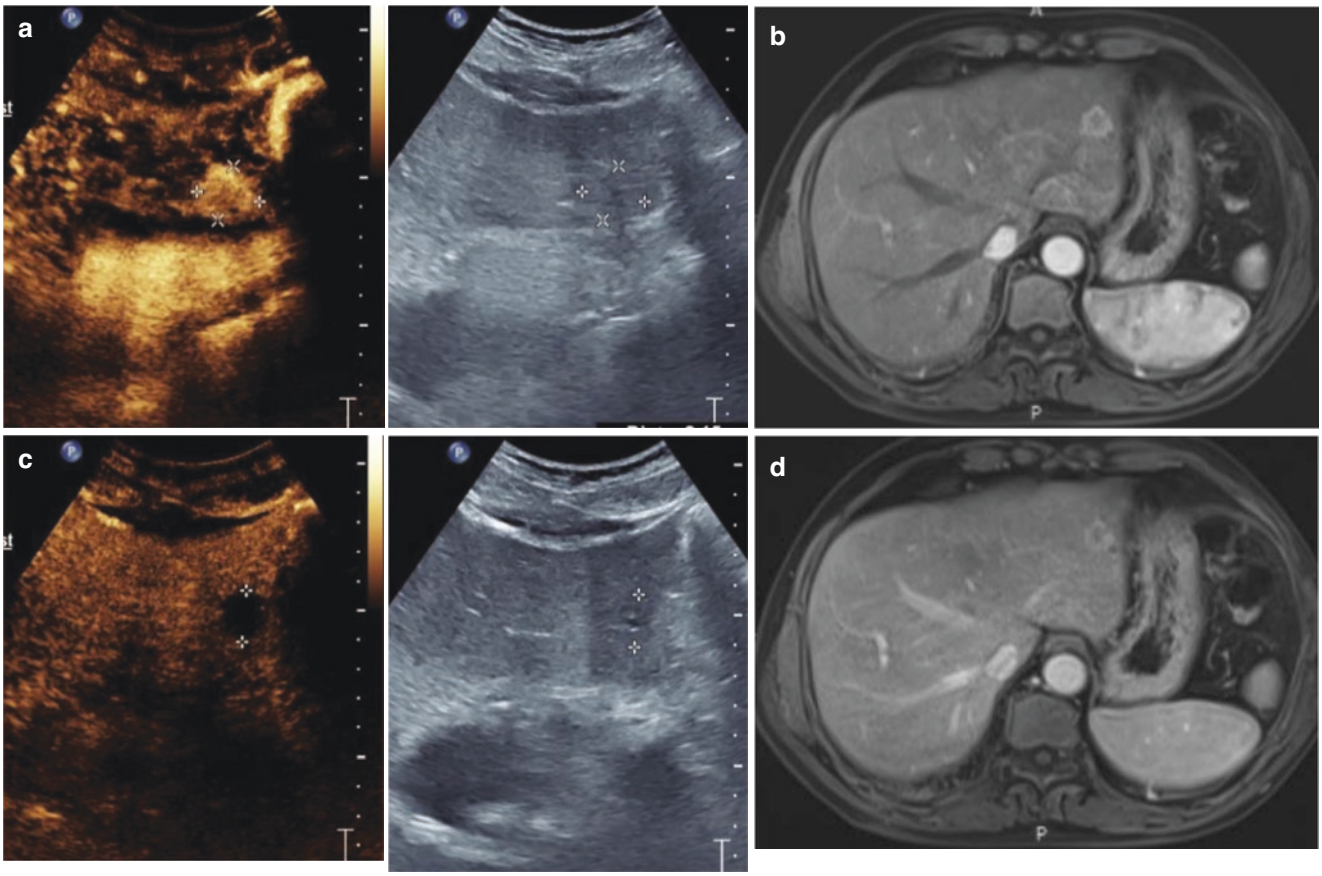


Fig. 3.5 A 59-year-old man with history of surgery of rectal cancer. Multiple liver metastases were suspected. During arterial phase of contrast enhanced ultrasound (CEUS) (**a**) and MRI (**b**), multiple hyperenhanced lesions could be detected in the whole liver. While on portal venous phase, all those lesions showed punched wash-out both on CEUS (**c**) and on MRI (**d**)

3.5 Detection of Superficially (Subcapsular) Located FLLs

- Compared to the usual low frequency abdominal convex transducers (1–5 MHz), the utilization of high frequency 7–9 MHz (or even higher) linear transducers offers important advantages such as high resolution and better near field investigations.
- On imaging with high-frequency linear transducer, the details of FLLs, including echogenicity, size, boundary, and blood flow, can be more distinct, which can facilitate the identification and differentiation between benign and malignant FLLs.
- With high frequency linear transducers, it is helpful to improve the detection of liver surface nodularity or for the detection of small FLLs as deep as 4–5 cm.
- CEUS performed with high-frequency linear transducer is more sensitive in demonstrating tiny blood vessels within the lesion and nuance difference between small lesion and liver parenchyma, which is more helpful to make the plan of surgery and local treatment [3] (Fig. 3.6).

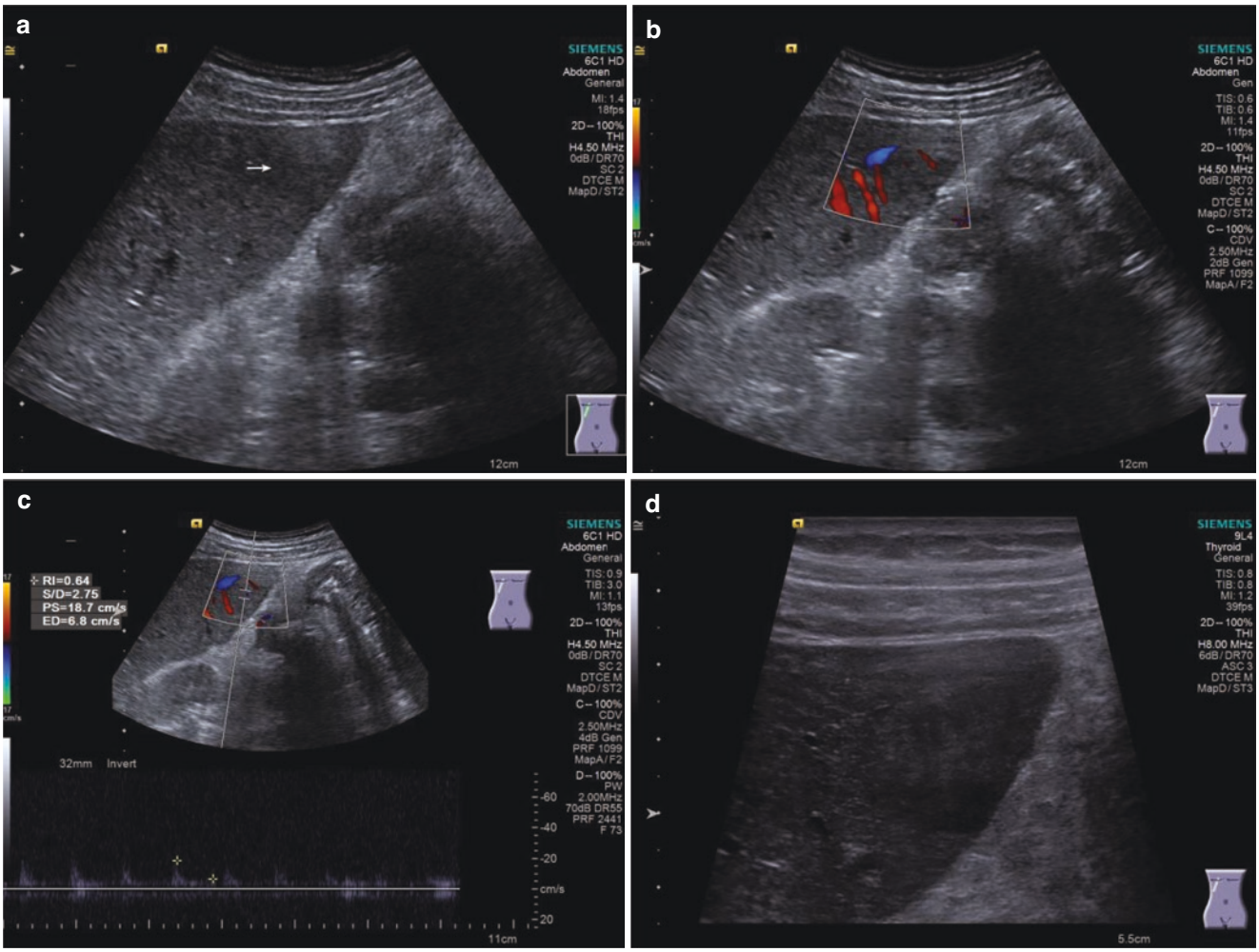
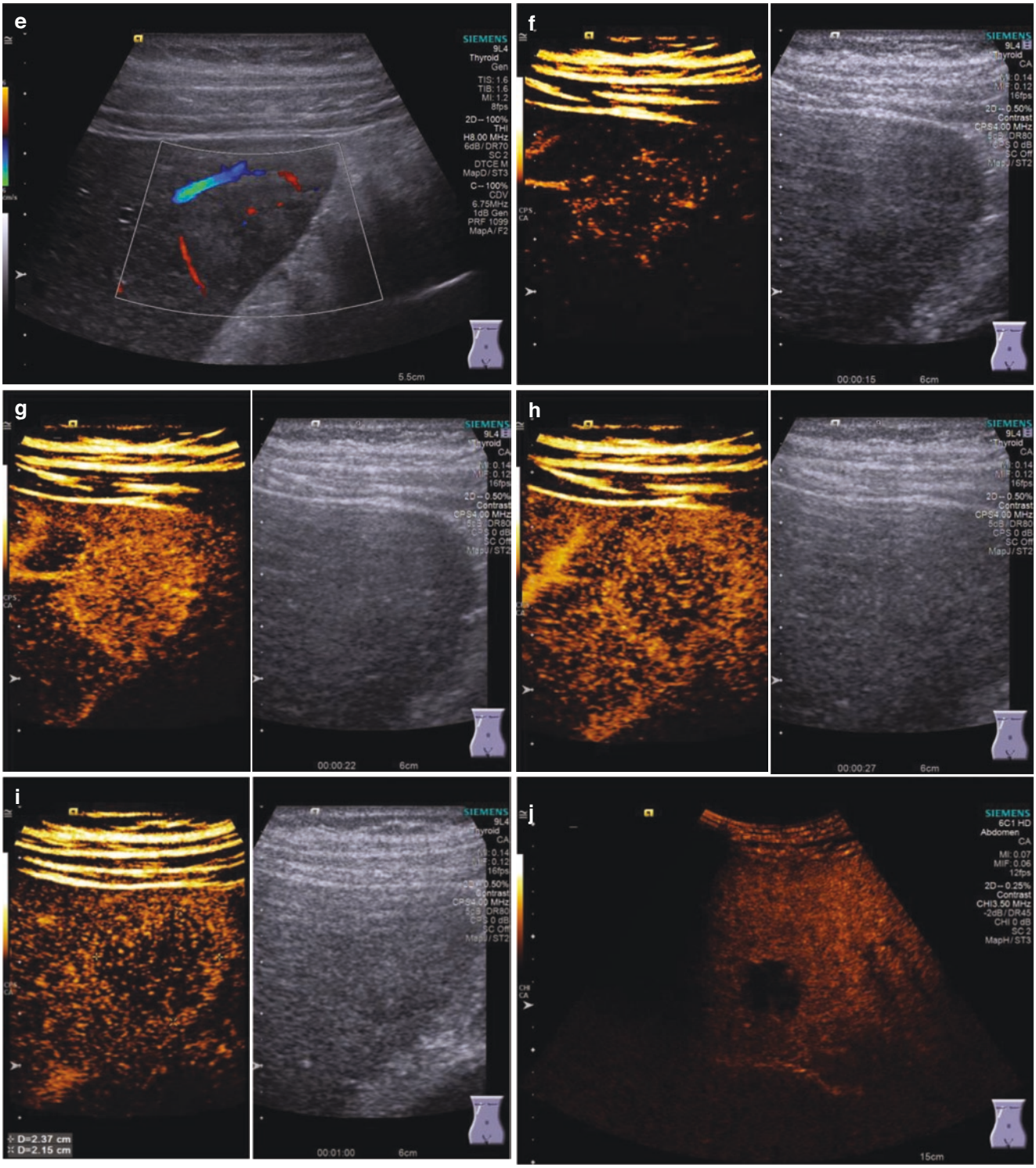


Fig. 3.6 Colon polyps were found by endoscopy half a month ago in a 55-year-old man and confirmed by pathology as malignant tumor. Liver metastasis was suspected by CT scan. The lesion could not be detected on B mode ultrasound (BMUS) (**a**). Color flow signals can be detected in the peripheral area of the lesion (**b**). Arterial Doppler spectrum with resistance index (RI) as 0.64 was measured (**c**). On BMUS ultrasound performed by high frequency linear transducer, the boundary of the lesion was clear (**d**) and more color flow signals can be detected (**e**). In arterial phase of CEUS, it showed rapid and complete hyperenhancement (**f**, **g**). At 27 s after injection of contrast agent, wash-out could be observed in the center area of the lesion (**h**). The lesion showed punched hypoenhancement in portal venous phase (**i**). By scanning the whole liver during late phase, more metastasis lesions could also be detected (**j**)



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3.6 Detection of FLLs Before Local Ablation Therapy

- As confident visualization of a target lesion is important for successful and safe RFA, image-guided RFA is gaining increasing acceptance in clinics.
- During local ablation therapy, ultrasound is the most commonly used imaging technique to offer real-time display and guidance of the insertion of needle. However, targeting of invisible or poorly visualized lesions may be great challenge.
- In some primary hepatic malignancies, progressive liver cirrhosis may cause heterogeneous liver background, which mimics the malignant lesion in the surrounding hepatic tissues. Repeated ablative treatment will also make primary or secondary hepatic malignancies indistinctive at ultrasound.
- CEUS guided ablation therapy is a promising technique for targeting and improving the efficiency of treatment of hepatic malignancies that are indistinctive on B mode ultrasound [4, 5] (Fig. 3.7).

3.7 Detection by Intraoperative Contrast Enhanced Ultrasound (IO-CEUS)

- Contrast enhanced intraoperative US (CE-IOUS) has become a potential imaging method, which enhances tumor detection and allows to assess the region for resection, especially for small, isoechoic, superficially located FLLs not detected at preoperative imaging.
- During the surgical procedure, CE-IOUS is performed with a high frequency intraoperative transducer, which, may require a higher dosage of ultrasound contrast agents.
- During CE-IOUS scan of the whole liver, all the hypoenhanced focal liver lesions during portal venous and late phases were considered to be malignancies.
- CE-IOUS could detect more small metastases <10 mm, with sensitivity up to 100% [6] (Fig. 3.8).

3.8 Tips to Increase the Detection Rate of CEUS

- Similar with conventional ultrasound, CEUS is highly operator dependent. The operator should have rich experience in ultrasound examination, and be familiar with liver anatomy as well as tumoral characteristics.
- It is particularly important to have a comprehensive understanding of the disease before CEUS, including the size, number, and location of the lesions, referring to the other imaging examinations.
- During portal venous phase and late phase, the whole liver needs to be thoroughly scanned to improve the detection rate of the lesions.

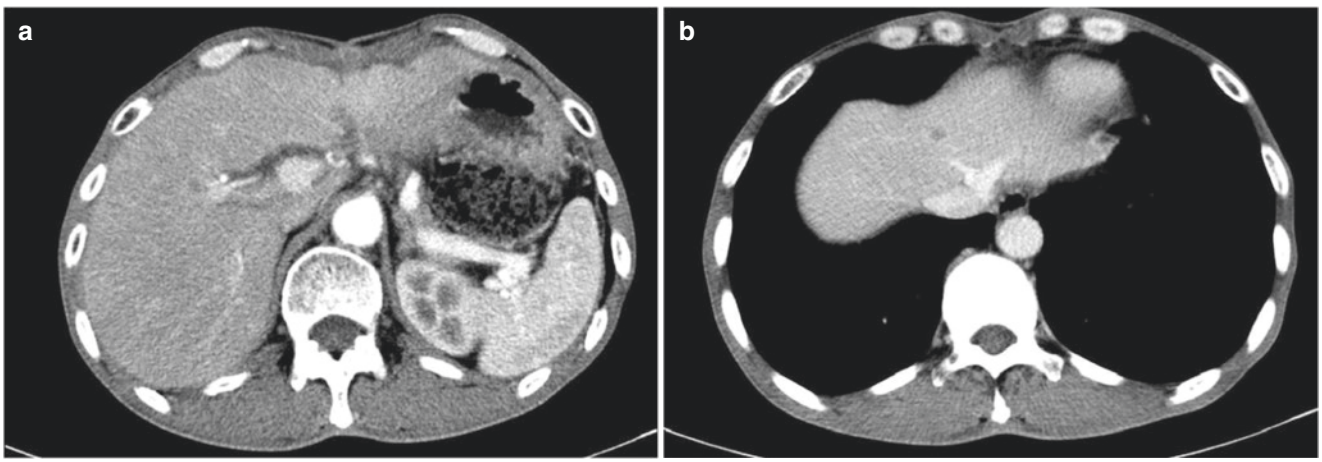
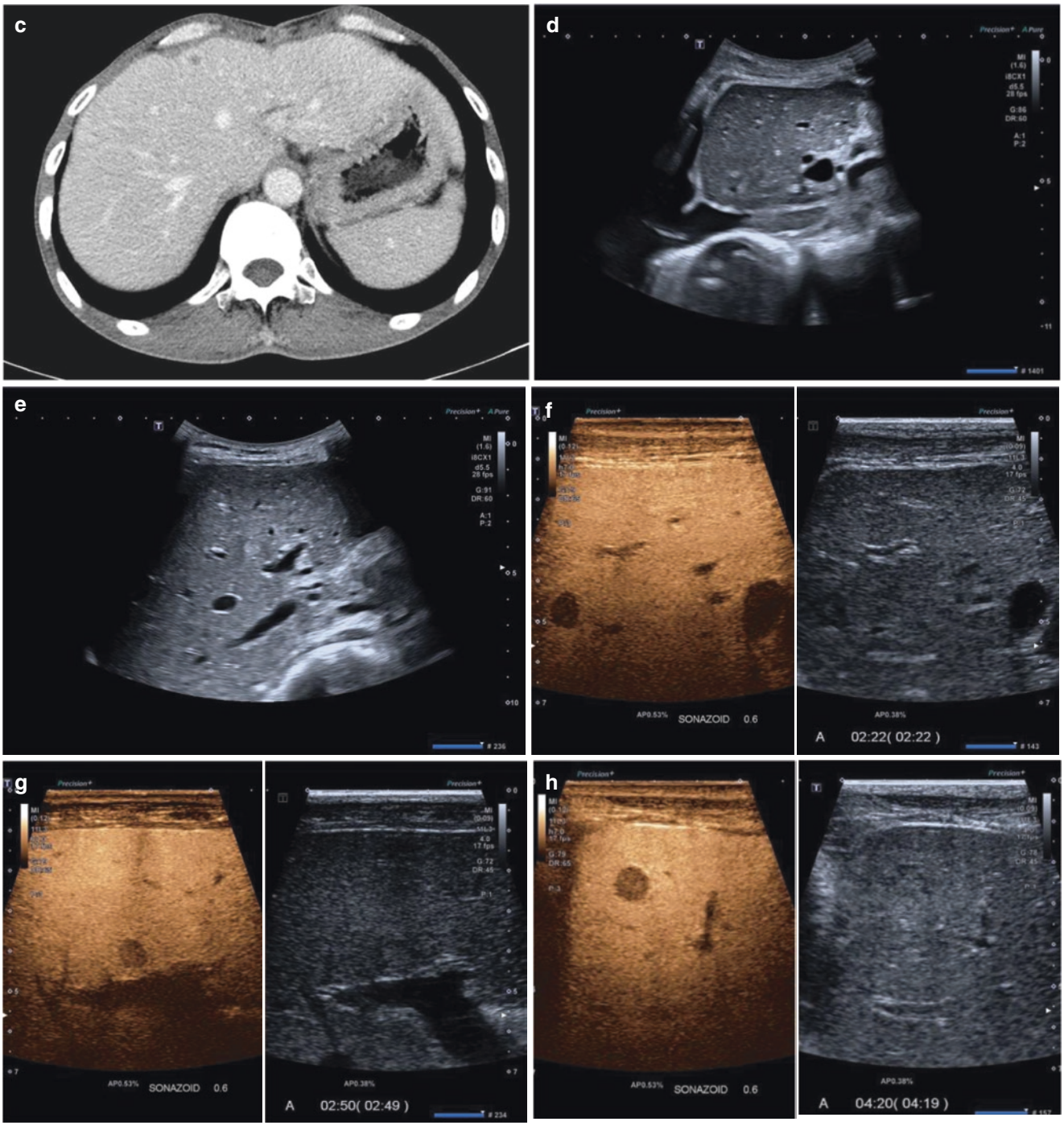


Fig. 3.7 Detection of multiple liver metastases before radiofrequency ablation (RFA). Multiple small liver metastases from pancreatic cancer was detected by CT in both right (**a**) and left liver lobes (**b**, **c**). Those lesions were indistinctive on B mode ultrasound (**d**, **e**). After injection of Sonazoid, multiple hypoenhanced lesions could be detected in right lobe during portal venous phase (**f**), and in left lobe during Kupffer phase (**g**, **h**). Additionally, another small lesion (5 mm), which was superficially located near the surface of left lobe, was also detected during Kupffer phase (**i**)



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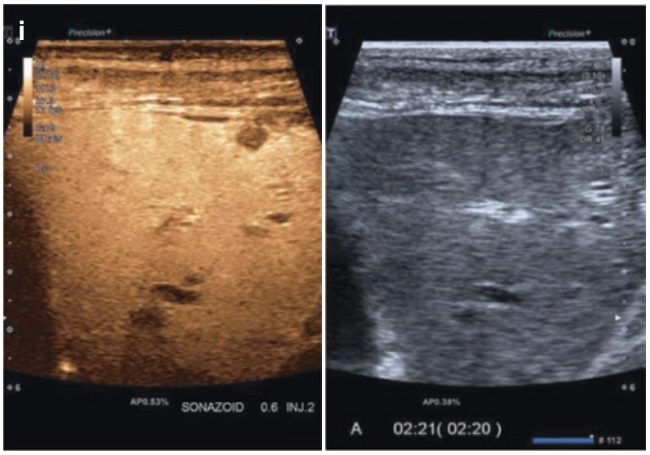

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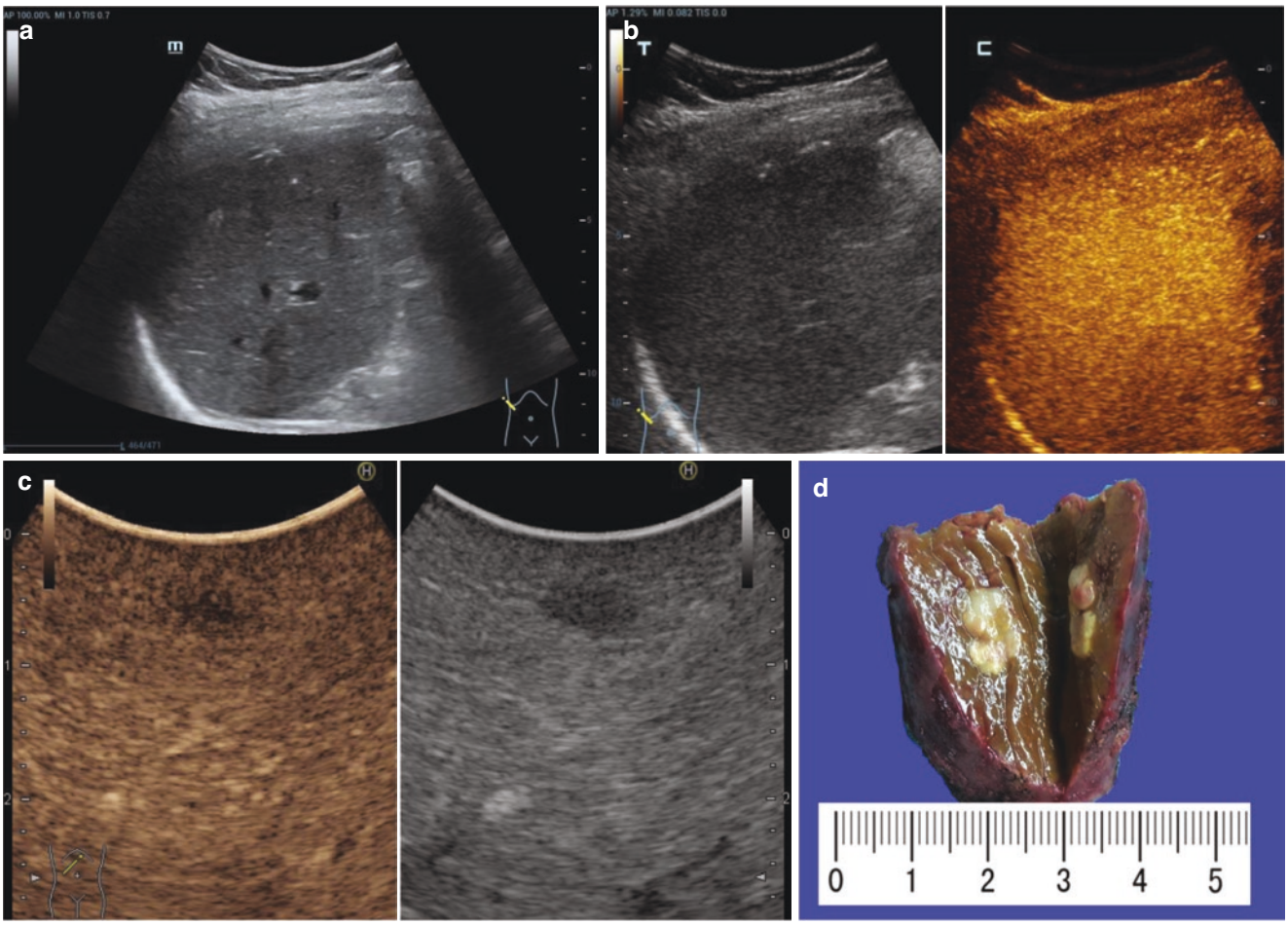

Fig. 3.8 Detection of invisible HCC recurrence by intraoperative contrast enhanced ultrasound with injection of Sonazoid. A suspected recurrent HCC could not be detected by B mode ultrasound (**a**), neither by contrast enhanced ultrasound scan (**b**, **c**). During surgical operation, a small (6 mm) lesion was identified (**d**)

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