TOSHIBA MEDICAL

Medical Review

Modern Liver Imaging Techniques – A New Era in Liver Ultrasound

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Introduction

HCC Epidemiology

Hepatocellular Carcinoma (HCC) is the 6th most common cancer worldwide and the 2nd leading cause of cancer death globally [1]. In the United States, HCC is the fastest growing cause of cancer mortality, growing by 2.7% per year from 2003 to 2012. At this rate, there will be an estimated 78,000 new cases in the United States in 2020 [2]. Worldwide, the major risk factors for HCC are Hepatitis B (54%) and HCV (31%), which is the #1 cause in the United States [3]. Cirrhosis of any etiology is associated with HCC, and nonalcoholic steatohepatitis (NASH) continues to increase with high prevalence of obesity and metabolic syndromes in the United States [4]. Reducing mortality, by diagnosing HCC while the disease is still amenable to medical or surgical treatment, requires effective surveillance tools.

HCC Screening and Surveillance Recommendation

Ultrasound is a non-invasive imaging modality widely used to evaluate liver disease. The American Association for the Study of Liver Diseases (AASLD) published practice guidelines on the management of HCC and recommended at-risk groups such as patients with cirrhosis of any etiology or specific hepatitis B carriers to be entered into a surveillance program. Ultrasound is the preferred surveillance tool based on a large randomized controlled trial and the recommended surveillance interval is 6 months based on doubling time of HCC [5].

Semiannual US surveillance recommendation is also supported by cost effective analysis. It is the only cost-effective modality for HCC surveillance [6].

Importance of Image quality

One of the main challenges for ultrasound in HCC surveillance is the variability of sensitivity. The pooled sensitivity of ultrasound to detect early HCC with a size smaller than 5cm was reported to be 63%, with a range from 23% to 91% [7]. Ultrasound is operator dependent, equipment and its software can affect image quality, and patient body habitus is also an important factor for the quality. The increased high BMI trend in patients in the United States is a concern. We conducted a retrospective study reviewing 297 ultrasound examinations performed for HCC surveillance, evaluated the image quality and investigated its affecting factors. We found nearly half of the ultrasound examinations (49.3%) of with inadequate quality, and multivariate analysis showed BMI to be the largest affecting factor. A one-unit increase in BMI leads to a 30.8% increase in the odds of having an inadequate image ratings (Kono Y. et al. unpublished data).

Toshiba Aplio™ i-series systems is designed to deliver outstanding clinical performance with enhanced resolution and penetration to improve clinical precision, diagnostic performance and productivity. With the implementation of advanced architecture, iBeam forming technology and Intelligent Dynamic Micro-Slice technology (iDMS) allows the formation of a shaped, uniform and thin slice beam that offers clinical images with higher resolution, more homogeneity, and fewer artifacts. The latest technology offer improvement in contrast resolution, temporal resolution and spatial resolution in all three aspects: axial, lateral and elevation.

Aplio i-series is equipped with a newly developed iDMS ultra-wideband convex transducer, PVT-475BX. The 2-in-1 ultra-wideband transducer is designed to cover the frequency range normally covered by two transducers, in order to provide both high resolution and penetration.

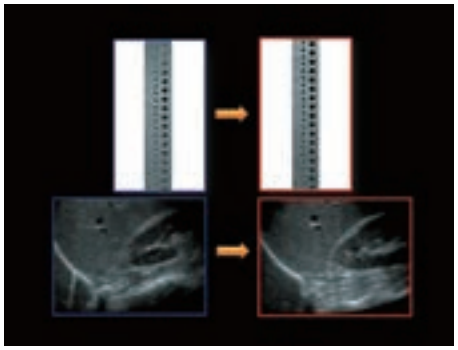

Figure 1. iBeam forming technology generates clinical images with higher resolution, more homogeneity and fewer artifacts.

Figure 2. Intelligent Dynamic Micro-Slice (iDMS) technology provides high-flexibility electronic focusing in the lens direction and improves the elevation resolution.

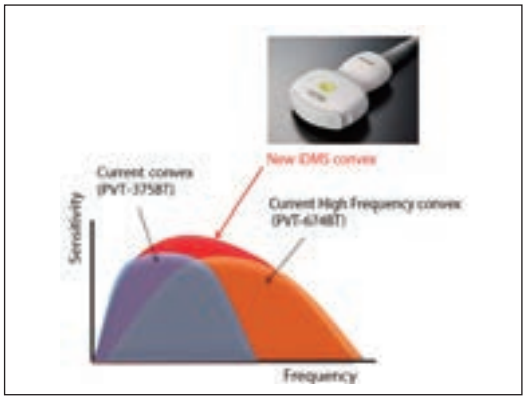

Figure 3. Ultra-wideband iDMS convex transducers

CASE STUDIES

Case 1: Obese patient without known liver disease (BMI 30)

Aplio i-series provides grayscale images with higher resolution, contrast and penetration. With iDMS technology that generates thin-slice beams, homogeneous images throughout the depth can be provided. The increased sensitivity of Doppler images can be demonstrated through Superb Micro-vascular Imaging (SMI). SMI delineates low-velocity minute flows and the detailed vascularity can be visualized.

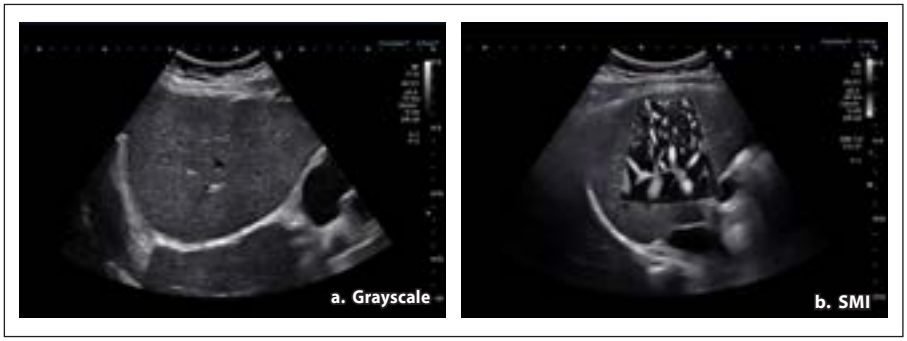

Figure 4.

Case 2: Technically difficult patient with morbid obesity (BMI 40)

The improvement in penetration and image homogeneity ensures high resolution in the technically difficult patient. The back of the liver and texture of the liver parenchymal can be clearly visualized.

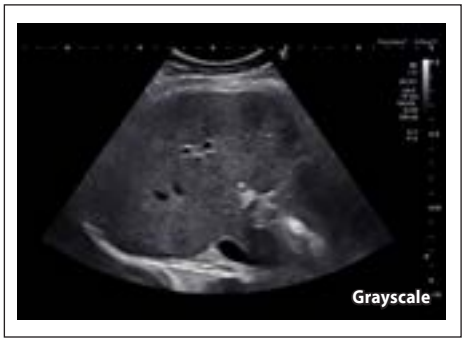

Figure 5.

Categorization of Focal Liver Lesions using Contrast Enhanced Ultrasound (CEUS)

Contrast Enhanced Ultrasound (CEUS) is capable to provide real time, high-resolution perfusion information and is one of the state-of-art technologies for differentiation of focal liver lesions. The contrast agents are microbubbles of a few µm in diameter and stable enough to circulate in the body with intravenous injection. Modern ultrasound technology with contrast specific imaging is very sensitive to detect circulating microbubbles, and can visualize dynamic contrast enhancement in a real time manner. In Aplio i-series, spatial resolution, penetration and tissue suppression have been improved for easy observation and accurate diagnosis for categorization of focal liver lesions. Contrast medium Lumason® (Bracco, Italy), (A.K.A. SonoVue® in Europe and elsewhere) was recently approved for characterization of focal liver lesions in adult and pediatric patients in the United States.

CEUS LI-RADS®

The American College of Radiology (ACR) endorsed LI-RADS® (Liver Imaging Reporting and Data System) for standardized reporting and data collection of computed tomography (CT) and magnetic resonance (MR) imaging for HCC in 2011. With the recent approval in the United States of microbubble-based agents for US liver imaging, LI-RADS® has been expanded to include CEUS in August 2016. The LI-RADS imaging criteria are used to classify 'liver observations on high-risk patients' from 'definitely benign' (LR-1) to 'definitely HCC' (LR-5) based on imaging criteria [8]. We expect a categorization algorithm with well-defined CEUS criteria would reduce imaging interpretation variability and errors, and improve communication with referring clinicians and facilitate quality assurance and research. Please note LI-RADS only applies to high-risk patients for HCC.

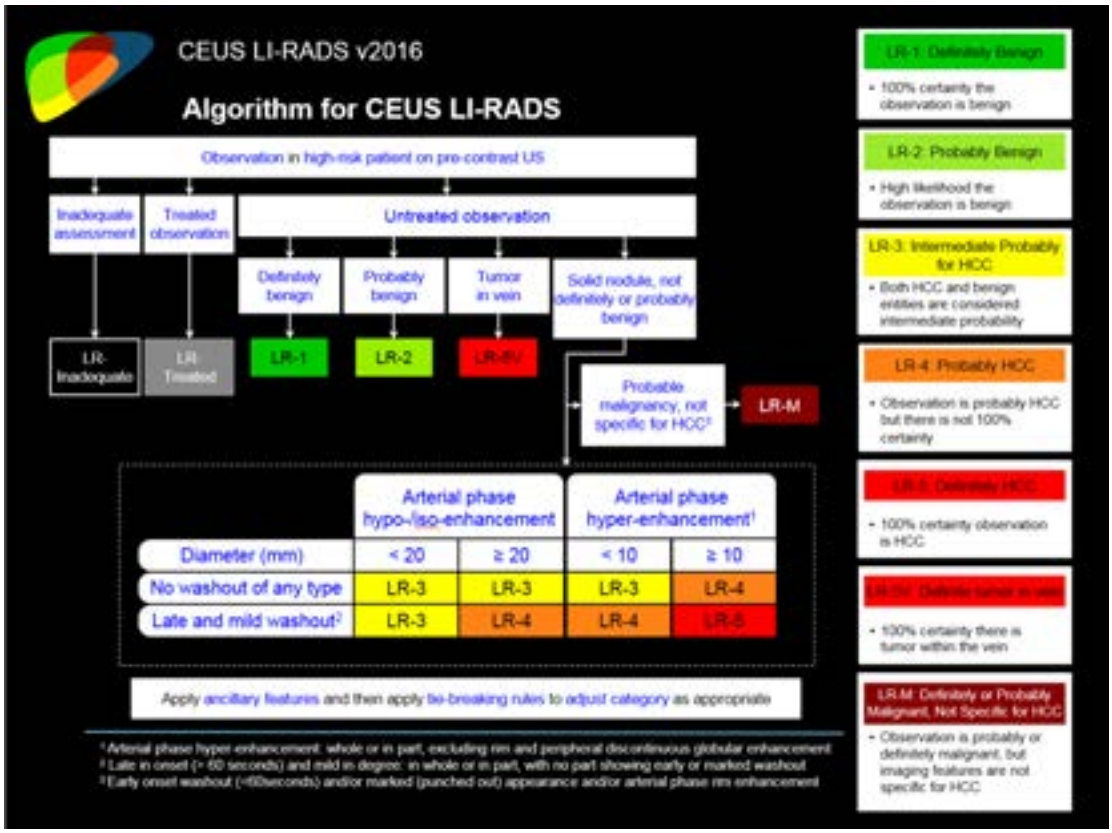

Figure 6. Algorithm and categorization of CEUS LI-RADS®

CASE STUDIES

CEUS is a very powerful tool to observe perfusion pattern of focal liver lesions in real time during arterial phase, portal venous phase and delayed phase, which enables characterization.

Hemangioma

Hemangioma is one of the most common benign liver lesions. The grayscale image from a 50 year-old male shows a heterogeneous hypoechoic lesion in the left hepatic lobe, measuring 3.6 cm in diameter. In the grayscale image, the border and the internal structure of the lesion is clearly depicted. Utilizing SMI, low-velocity minute vessels inside the lesion can be visualized at high frame rates (47fps) and the lesion demonstrated high vascularity. Focal liver lesions can be clearly seen on non-contrast ultrasound with good image quality. Vascularity can be evaluated to some extent. However, diagnosis cannot be made without the use of contrast agent. This is no exception for CT or MRI, both require multiphasic imaging with contrast injection for diagnosis.

The lesion showed a typical enhancement pattern for a hemangioma with an initial peripheral nodular enhancement and centripetal enhancement pattern in the arterial phase. The perfusion of the lesion can be seen clearly based on improvements in tissue suppression with Aplio i-series. The hemangioma continues to show complete hyper-enhancement in the portal venous phase, and become iso-enhancement in the delayed phase. This is a typical pattern of a benign lesion without any type of washout in the portal venous phase or delayed phase.

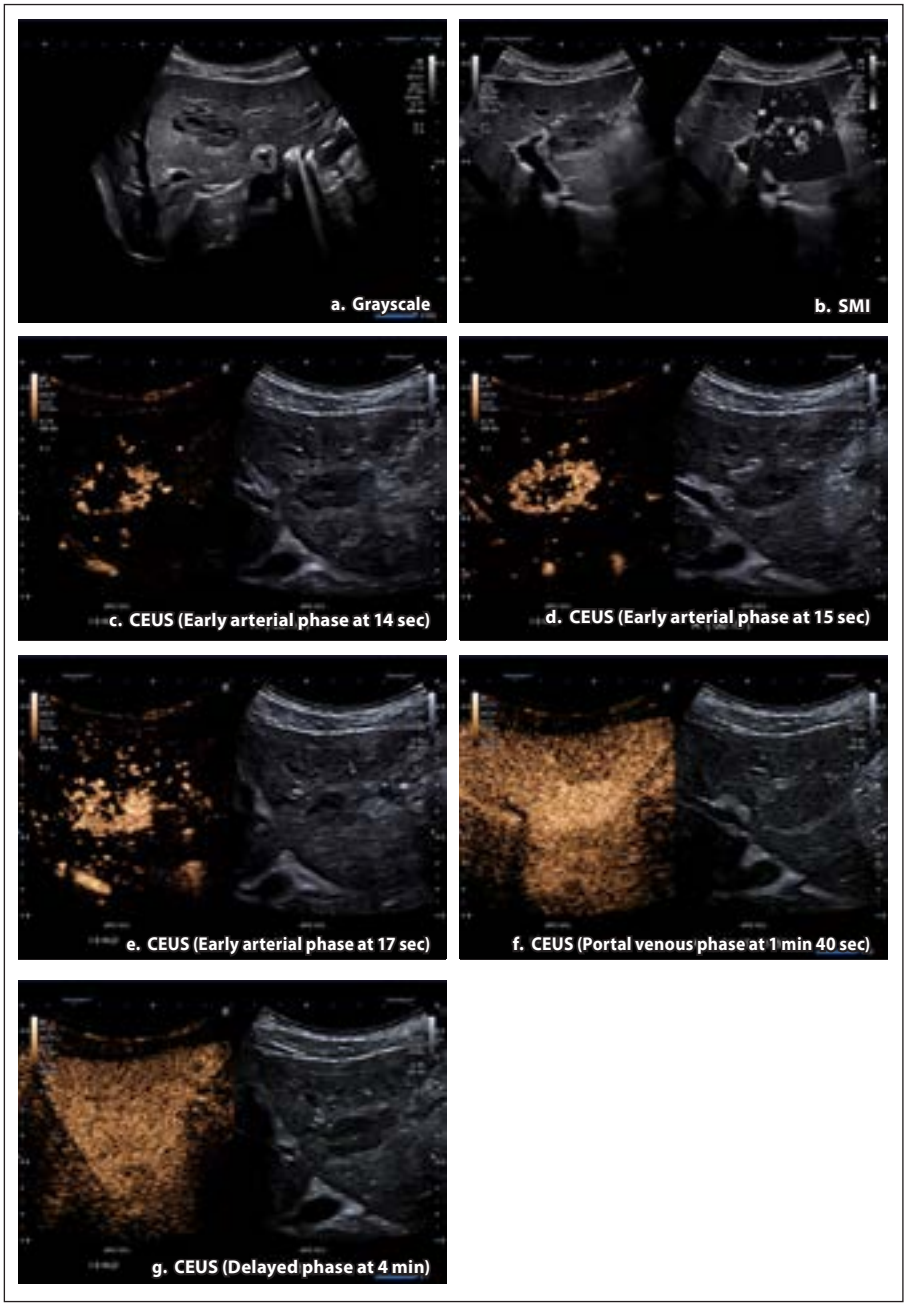

Figure 7.

Hepatic Adenoma

This case is a 25 year-old female with multiple hepatic adenomas. The largest lesion is 3.5cm in diameter, located in segment 6. Although the lesion locates deep at 10cm and is nearly isoechoic to the parenchymal, the image quality in grayscale allows clear observation of the lesion. At a depth of 10cm, the arterial phase hyper-enhancement, and its vascular pattern can be easily visualized with a peripheral, diffuse pattern towards the lesion center. It is an important diagnostic point to distinguish a hepatic adenoma from a benign focal nodular hyperplasia (FNH) as FNH has similar imaging appearances but enhances from inside to outside. Iso-enhancement in the portal venous phase and delayed phase demonstrate the lesion is benign. Lesions with iso-enhancement can be difficult to track during the late portal venous or delayed phases, however, the clear visualization of the lesion in the grayscale image helps confident tracking of the lesions.

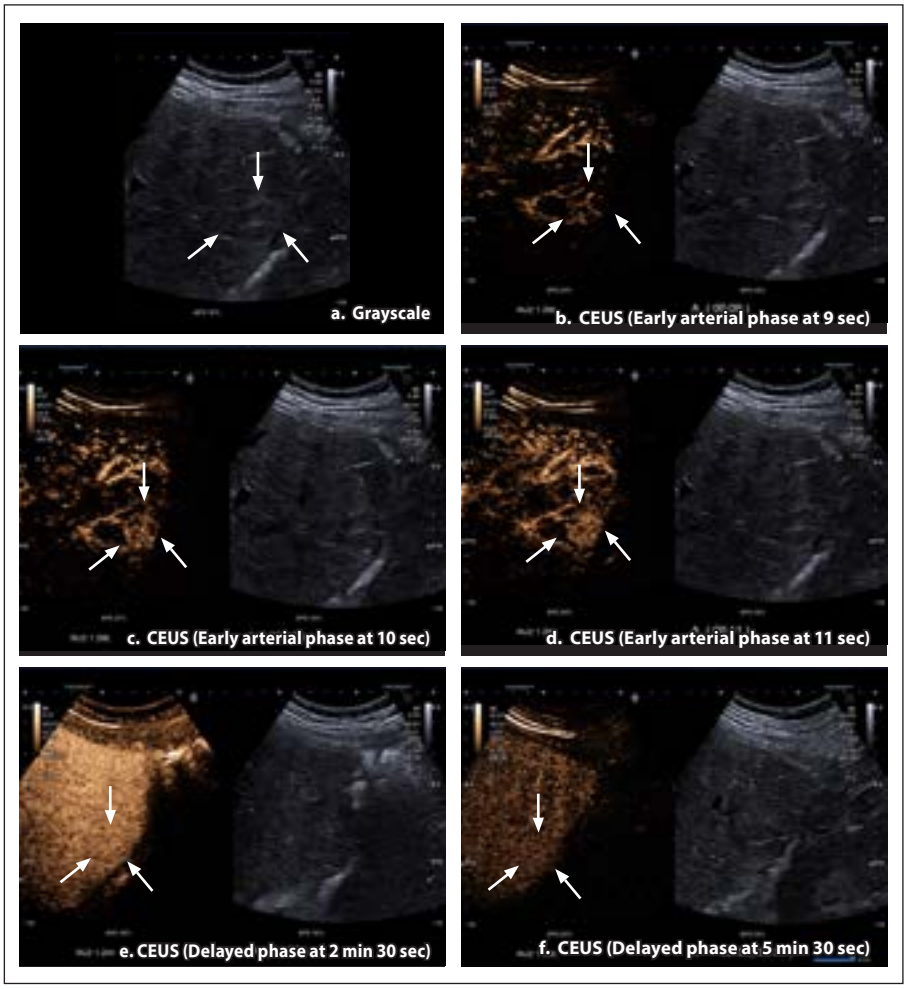

Figure 8.

LI-RADS 5 HCC

A 63 year-old female with alcoholic cirrhosis presented with a 3cm liver lesion. The boundary of the isoechoic lesion and its hypoechoic halo can be clearly depicted on a grayscale image. Using color Doppler, intra-tumoral vascularity can be detected. Rich vascular structure can be delineated with SMI and distorted vessels can be shown, suggesting malignant lesion. After contrast injection, in the arterial phase, the lesion shows homogeneous hyper-enhancement, associated with the feeding vessels. No washout is seen at 1 minute and at 2 minutes. In the delayed phase at 3.5 minutes, mild washout can be observed. Washout slowly progresses and more clear at 5 minutes. Late (≥ 60 sec) and mild washout is one of the major features for LI-RADS 5, and is very important to differentiate from LI-RADS M which shows early (<60 sec) and/or marked washout. As a result, the lesion is categorized as CEUS LI-RADS 5. The CEUS LI-RADS categorization corresponds to the LI-RADS on CT.

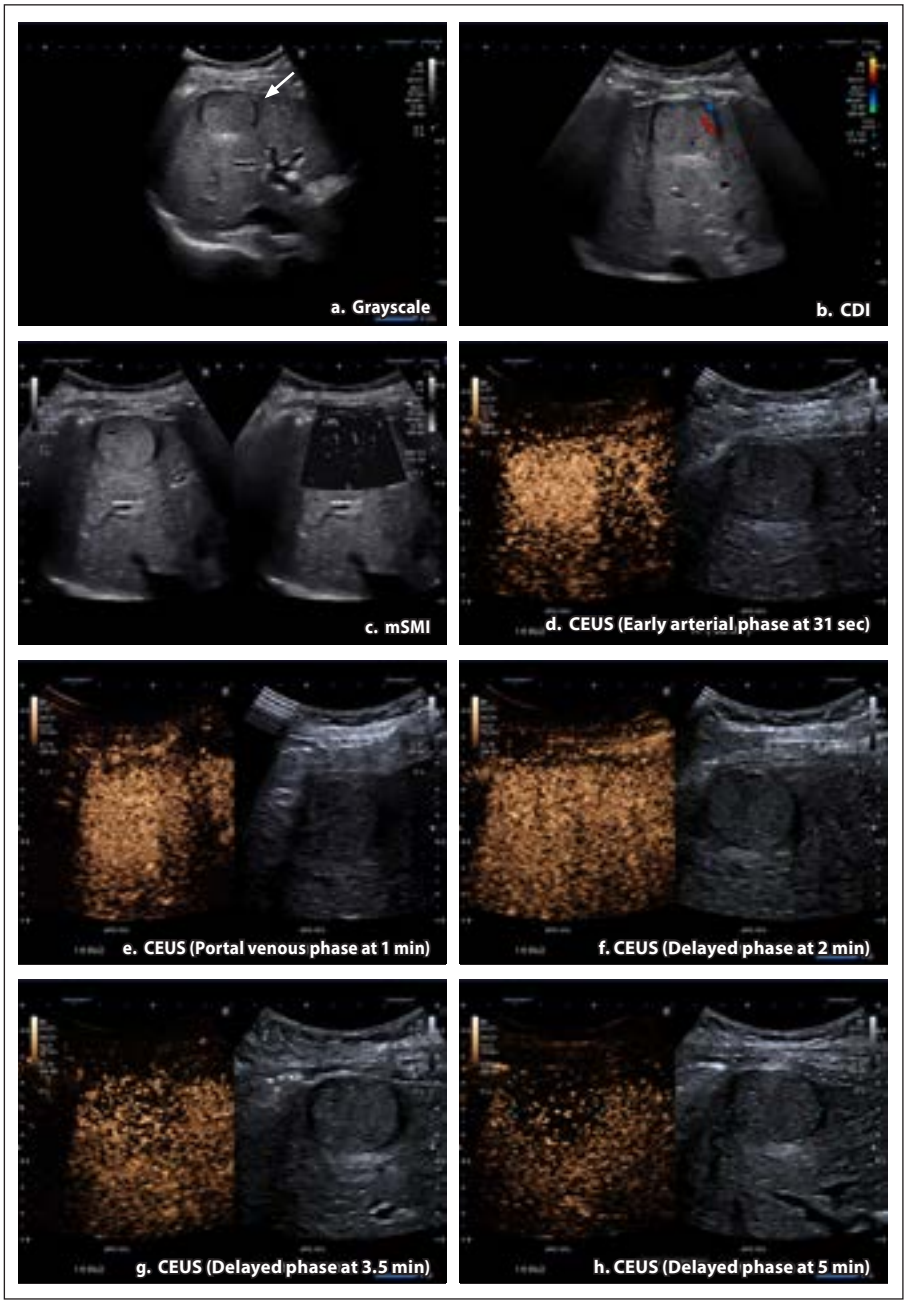

Figure 9.

HCC post treatment assessment

A follow-up exam was performed on a 79 year-old male with hepatic B cirrhosis complicated with HCC after trans-arterial chemoembolization (TACE) therapy. A new lesion was detected adjacent to the post-TACE lesion. On the grayscale image, the new lesion is clearly seen, but it is difficult to detect the HCC recurrence in the post-TACE lesion. Using the color-coded SMI (cSMI), rich vascularity can be seen inside the new lesion. CEUS was performed to evaluate the treatment outcome. By using CEUS, both new lesion and HCC recurrent in the post-TACE lesion can be investigated easily. The new lesion shows arterial phase hyperenhancement and no washout up to 5 minutes, therefore, it is a LI-RADS 4 lesion, probable HCC by LI-RADS criteria. Feeding vessels can be observed clearly in the early arterial phase. For the post-TACE treated lesion, majority of the lesion does not enhance, however, hyper-enhancing area were observed in the arterial phase at the upper side of the treated lesion, indicating the HCC recurrence.

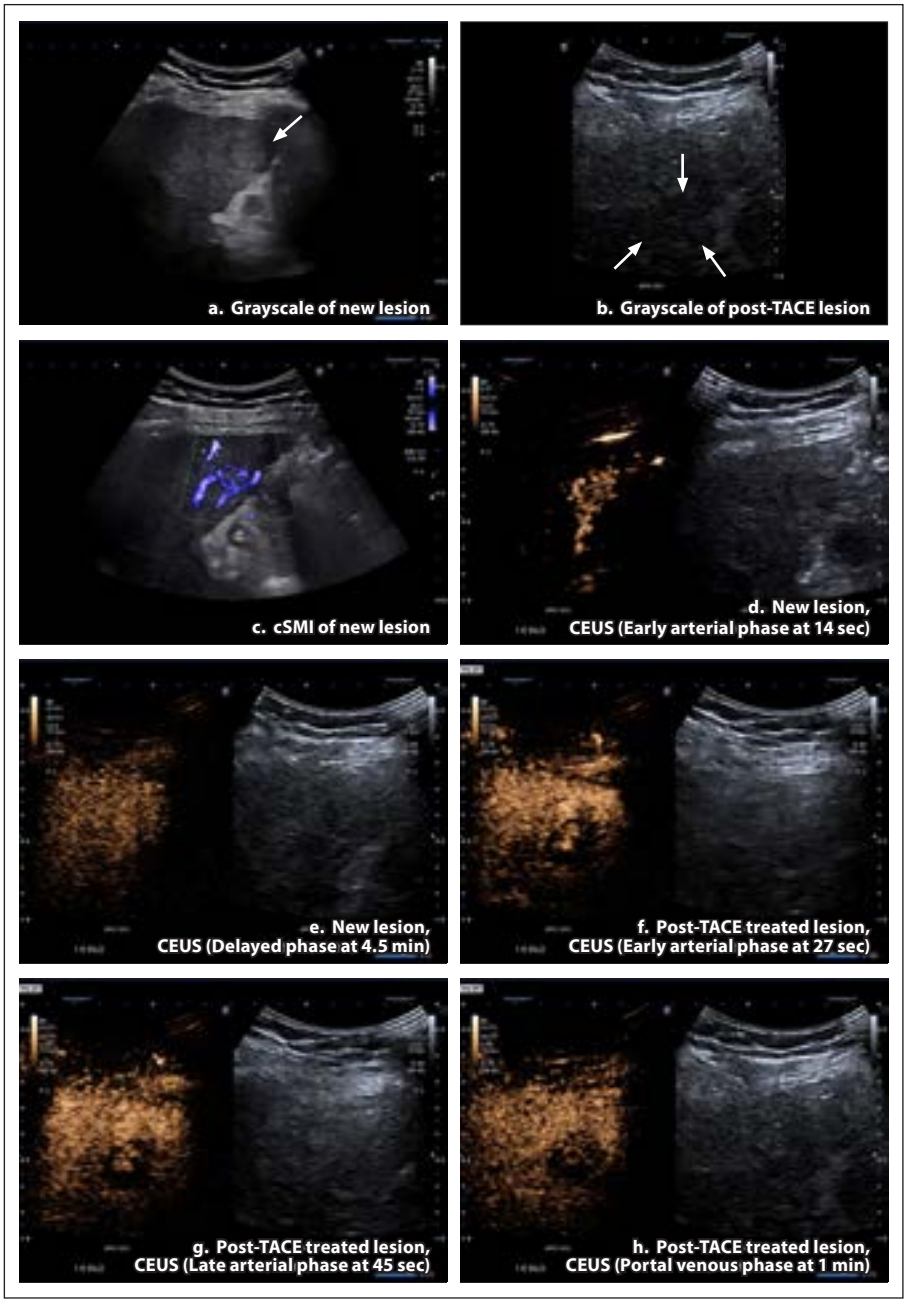

Figure 10.

LI-RADS 4 multiple HCCs

This is a case of a 60 year-old female with decompensated HCV cirrhosis with ascites. In the grayscale image, two lesions, 21mm and 10mm respectively, located in segment 5 can be detected. Since Toshiba shear wave is performed by push pulse, shear wave examination can be performed on patients with ascites to determine the fibrosis stage. In the early arterial phase, homogeneous hyper-enhancement can be observed in both lesions. The lesions are isoechoic in the portal venous and late phases, no washout was observed at 6 minutes post injection, therefore these lesions were categorized as LI-RADS 4, probable HCC. It is important to know LI-RADS 5 is an HCC with 100% certainty, and it does not require biopsy. Significant numbers of LI-RADS M (probably or definitely malignant, but not specific to HCC) and LI-RADS 4 (probable HCC) are actually HCC.

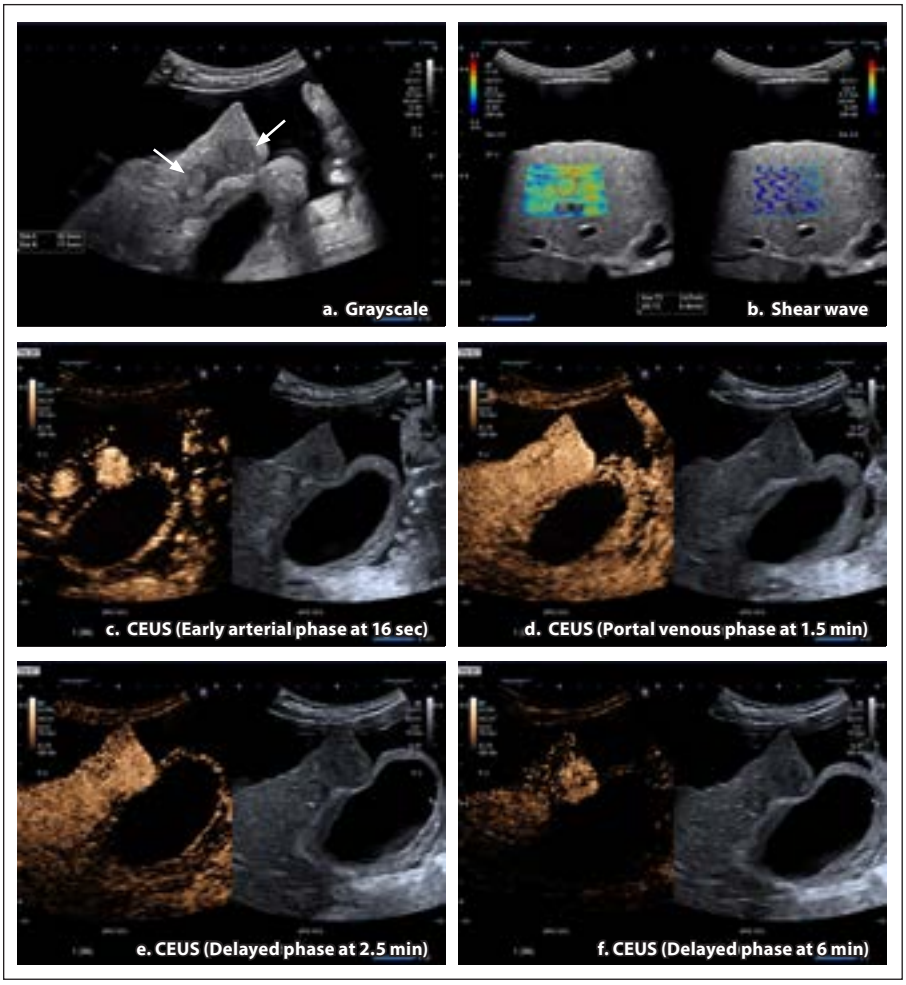

Figure 11.

LI-RADS 5 multiple HCCs

A 23 mm lesion was detected in the right hepatic lobe of a 70 year-old female with HCV cirrhosis. Detailed vascular structure and the feeding vessel are clearly depicted with CEUS in the early arterial phase and during portal venous phase, and the lesion is iso-enhancing. This lesion is a typical LI-RADS 5 lesion for its size, hyper-enhancement in the arterial phase and late and mild washout seen at 3 minutes post injection.

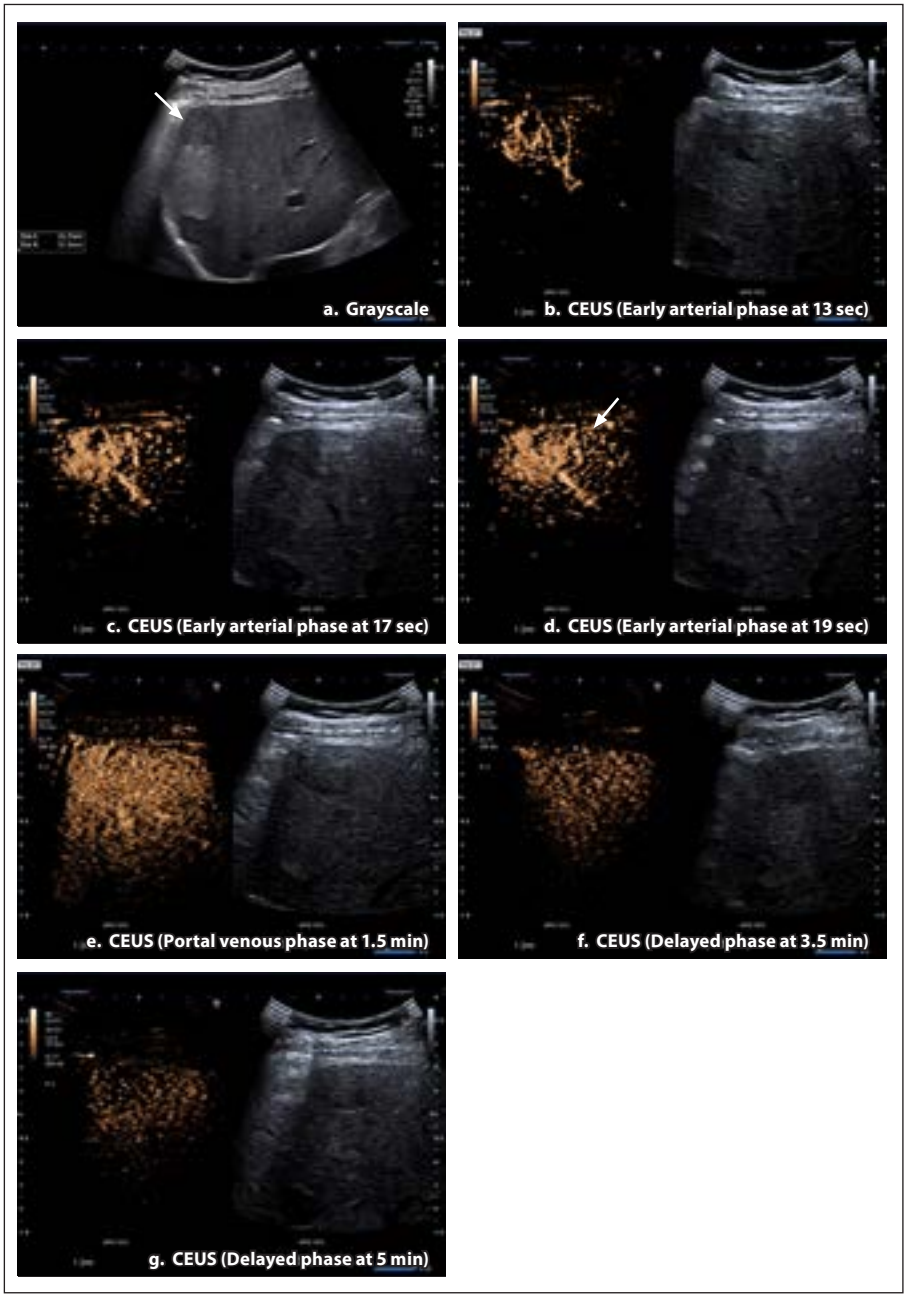

Figure 12.

Conclusion

Aplio i-series systems provide unprecedented imaging clarity and definition while significantly enhancing penetration to overcome difficulties in imaging obese patients and small HCCs. Better image quality even on obese patients is critical to improve HCC surveillance outcome.

The enhanced tissue suppression enables precise and fast diagnosis on differentiating the malignancy of focal liver lesion and CEUS LI-RADS® categorization can be diagnosed accurately. Diagnostic performance and productivity are highly improved based on the high image quality. In addition, the newly designed workflow and system design which offer excellent ergonomic for operators.

CEUS is a cost-effective method for categorization of focal liver lesions without ionizing radiation in adult and pediatric patients. For patients with acute and chronic kidney injury, there is high risk of contrast induced nephropathy by CT contrast agents, and nephrogenic systemic fibrosis by Gadolinium-based MRI contrast agents, and CEUS is a safe alternative as there is no nephrotoxicity. Health care reform is transforming the United States from a volume- to value-based health care system. As that transition continues, CEUS for characterization of focal liver lesions can emerge as an example of a cost-effective and high-value clinical tool.

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