Technical White Paper

HiFR CEUS

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1. Overview

Contrast-enhanced ultrasound (CEUS) can be used to obtain dynamic high-contrast images showing the lesions and the blood perfusion status of surrounding normal tissue blood perfusion comparison of lesions and surrounding normal tissue. Taking malignant tumor as an example, compared with normal tissue, micro blood perfusion in the arterial phase of pathological tissue is more abundant, and the metabolic level is higher. For example, the hemodynamics in metastatic hepatic carcinoma is typically shown as fast wash-in and fast wash-out. Currently, in mainstream commercial ultrasound machines, the frame rate of contrast imaging for non-cardiac applications is generally around 10 frame per second (FPS). Due to the increased performance of contrast imaging, the CEUS provides clinicians with more detailed microbubble perfusion information and better vascular structure visualization in the lesions, significantly enhancing the confidence in diagnosis. With the in-depth clinical research, doctors observe that it is a very narrow time window from bubble arrival to full perfusion, which can be observed for minor lesions with abundant blood supply (such as gallbladder polyps and small HCC). With the frame rate of existing contrast imaging, image data is under-sampled so that doctors are not capable of reviewing lesions perfusion in a more detailed way. Consequently, only the rough speed of hyper- and hypo-enhancing can be concluded, whereas the detailed perfusion path inside the lesions is lost as a result of limited frame rate. To capture the complete dynamic perfusion process and provide accurate diagnosis, clinicians impose requirements on an increased frame rate of the contrast imaging.

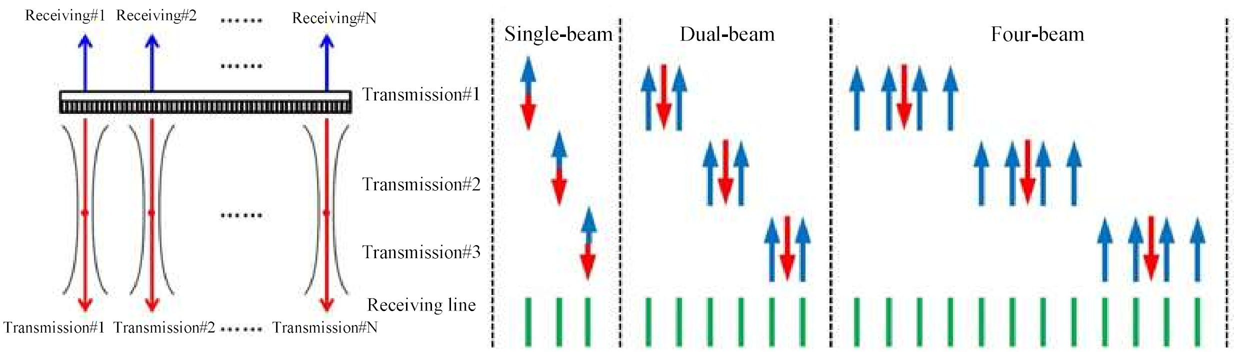
Limited by the focused transmission and line-by-line scanning mode, the maximum frame rate in the traditional CEUS is restricted to a lower value and is difficult to increase. The zone imaging technology is the key to break the limitation. The Mindray Resona 7 platform provides two zone imaging technologies: ZONE Sonography Technology Plus (ZST^{+}) technology and plane wave technology particularly for linear array probes. Based on these two technologies, Mindray develops the high frame rate (HiFR) contrast function with the Resona 7 platform and has applied it in the diagnosis of benign and malignant gallbladder polyps.

2. Introduction to the HiFR CEUS Technology

2.1. Frame Rate of the Traditional Contrast Imaging Technology

The traditional CEUS adopts the focused transmission and receiving mode shown in Figure 1 (a). The imaging area formed in each transmission beam is very small (only a limited area is scanned). Therefore, only one receiving line is acquired for each transmission using the single-beam technology. As shown in Figure 1 (b), with the evolved parallel multi-beam technology, the number of transmissions at the same density of receiving lines is reduced, and the imaging frame rate is increased accordingly. However, the physical width of the transmission beams fundamentally limits increasing the number of multi-beams infinitely.

Table 1 illustrates the contrast imaging frame rates in single-beam, dual-beam, and four-beam modes in a simple scenario with a convex-array probe: the sound velocity is 1540 m/s, the imaging depth is 17 cm, and the number of receiving lines is 192. The amplitude modulation (AM) technique is adopted to obtain the nonlinear echo of microbubbles. The time costs for transmission/receiving initialization and receive-end processing are ignored.



(a) Traditional focused transmission (b) Parallel multi-beam technology

Figure 1 Focused transmission and parallel multi-beam technology (red arrows indicating transmission, blue arrows indicating receiving, and green lines indicating final receiving lines)

Under the above conditions, even in the ideal four-beam mode, the upper limit of the frame rate in traditional convex-array abdominal CEUS is only 32 FPS and is even lower in practical applications. However, if more parallel receiving beams are used, the gap between transmission lines would be enlarged, which compromises the image quality.

Table 1 Frame rates in single-beam, dual-beam, and four-beam modes in traditional contrast imaging

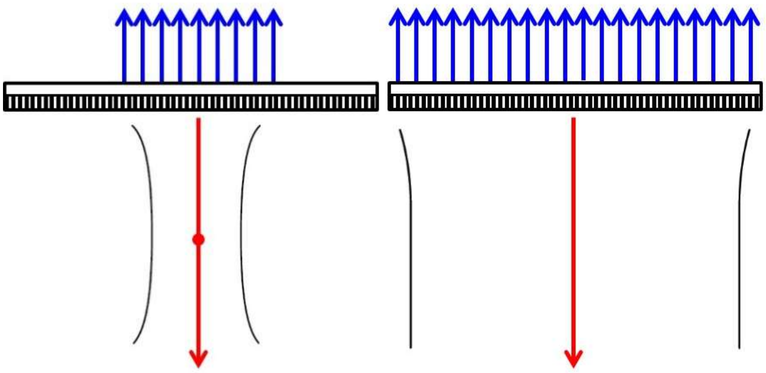
Number of receiving lines	192	192	192
Number of parallel multi-beams	Single-beam	Dual-beam	Four-beam

Number of focused transmissions	192	96	48
Duration for forming one frame of contrast image	0.127s	0.063s	0.031s
Contrast imaging frame rate	8 FPS	16 FPS	32 FPS

2.2. Key to Increasing the Frame Rate: Zone Imaging Technology

The zone image technology can significantly reduce the number of transmissions required for generating one frame of contrast image, greatly increasing the frame rate of contrast imaging. As shown in Figure 2, the Resona 7 platform of Mindray provides two zone imaging technologies: ZST$^+$ technology and plane wave technology. The ZST$^+$ technology adopts the weak focused transmission, generating wider physical beams. The area scanned in each transmission is significantly larger than that in traditional focused transmission. The plane wave technology applies the non-focused whole-zone transmission mode. The entire imaging area is scanned in one transmission. Therefore one frame of image can be generated with one transmission. The plane wave technology can be regarded as the ultimate form of the zone transmission technology, but it can only be used with linear array probes and therefore is only applicable to the superficial tissue. As for high frame rate CEUS in other applications, it is mainly enabled by ZST$^+$ technology.

In addition, due to the weak focused transmission and non-focused transmission modes, the both two zone transmission technologies require post processing at the receive end, to achieve a higher frame rate without compromising the image quality of the contrast imaging.



(a) Multi-beam imaging of the ZST$^+$ technology (b) All-zone imaging of the plane wave technology

Figure 2 Zone transmission technologies of the Resona 7 platform

2.2.1. ZST$^+$ Technology

Figure 3 shows a simple example of the ZST$^+$ technology to illustrate its basic principle. ZST$^+$ is a transmission/receiving technology that adopts weak focused transmission at the front end. As its transmission beam is wider than that of the traditional focused imaging technology, it can excite the entire imaging area with fewer transmissions, which is the key to HiFR CEUS.

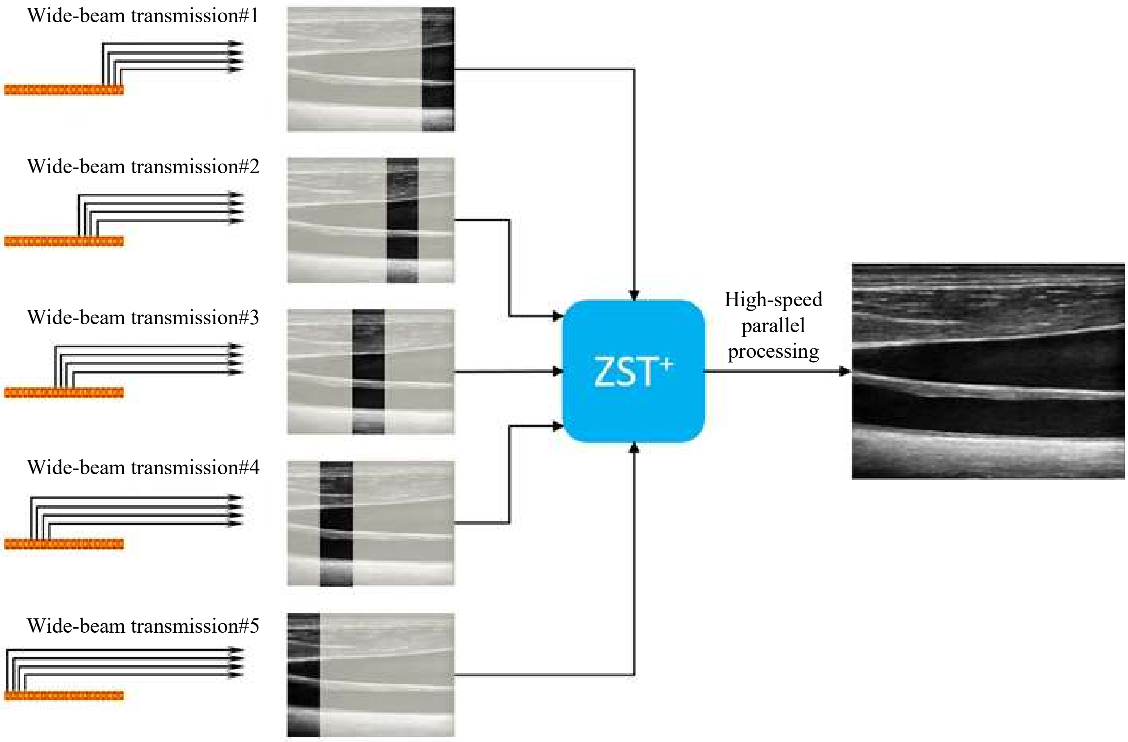
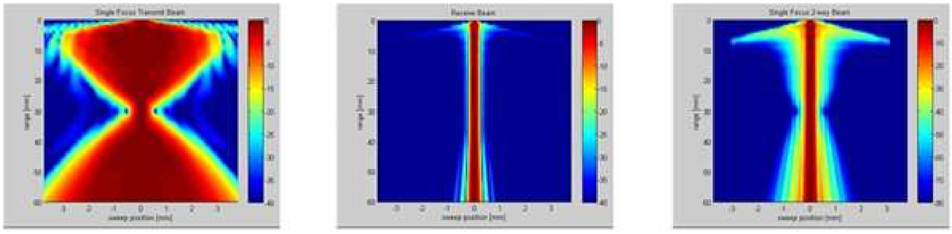


Figure 3 Principle of the ZST^+ technology

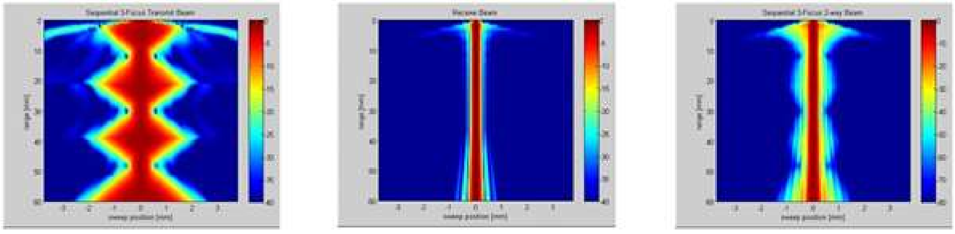
However, wide-beam transmission results in poor lateral resolution and penetration. Achieving high frame rate without compromising image quality is an issue to be addressed by the ZST^+ technology at the receive end. Figure 4 shows the transmission, receiving, and synthetic sound fields of the focused ultrasound imaging in the single-focus, multi-focus, and ideal continuous focused transmission scenarios. For focused imaging, the lateral resolution and signal-to-noise ratio (SNR) of the sound field at the focus are the best, but the performance is gradually degraded away from the focus. The lateral resolution of the entire field can be improved by increasing the number of transmission focuses or adopting continuous focused transmission at the cost of an inevitably decreased frame rate. This is infeasible for the focused imaging with a low upper limit of the frame rate.

Transmission sound field Receiving sound field Synthetic sound field



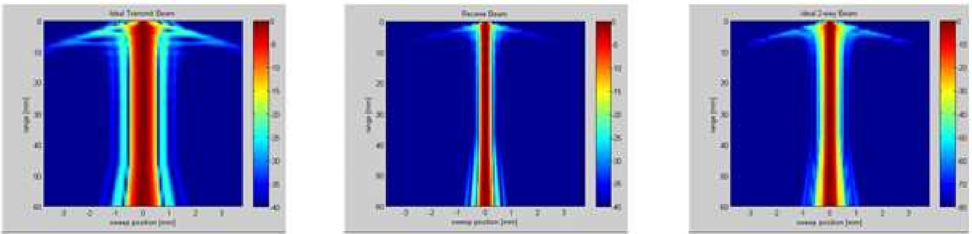
(a) Single-focus

Transmission sound field Receiving sound field Synthetic sound field



(b) Multi-focus

Transmission sound field Receiving sound field Synthetic sound field



(c) Continuous focused transmission

Figure 4 Transmission, receiving, and synthetic sound fields of the traditional focused imaging technology

Transmission sound field Receiving sound field Synthetic sound field

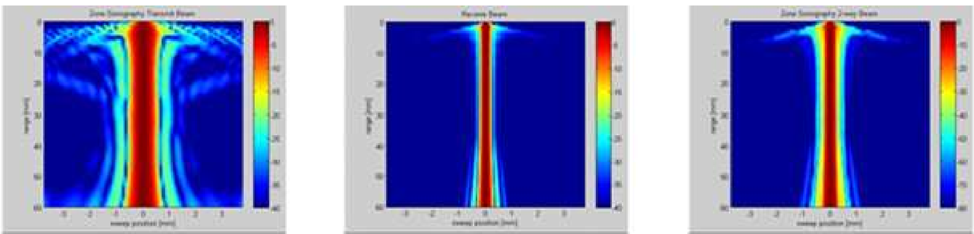


Figure 5 Transmission, receiving, and synthetic sound fields of the ZST^+ technology

The ZST^+ technology adopts weak focused transmission at the front end. Although the overall lateral resolution is poorer than that at the focus of the focused transmission, the sound field is more uniform. With the reconstruction of the receiving sound field, the continuous transmission focused synthetic sound field could be achieved. In addition, with the coherent transmission synthesis technology, the number of transmissions is significantly reduced. Furthermore, in order to tackle the problem of line artifact and SNR loss caused by decreased transmissions, each receiving line is generated through optimized compounding of echoes from adjacent multiple transmissions.

To sum up, the ZST^{+} technology is the key to HiFR CEUS by increasing the frame rate of CEUS without compromising image quality.

2.2.2. Plane Wave Technology

The plane wave technology can be regarded as the ultimate form of zone transmission. Spherical waves are emitted simultaneously by all the elements from a linear probe, and a plane is formed at the wave-front of each spherical wave, as shown in Figure 6. It can be learned that only linear arrays are physically capable of transmitting plane waves. So, the ultrasound plane wave technology can only be applied to contrast imaging of small parts, such as thyroid, breast, and vein.

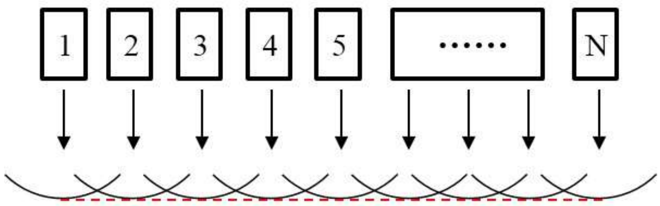
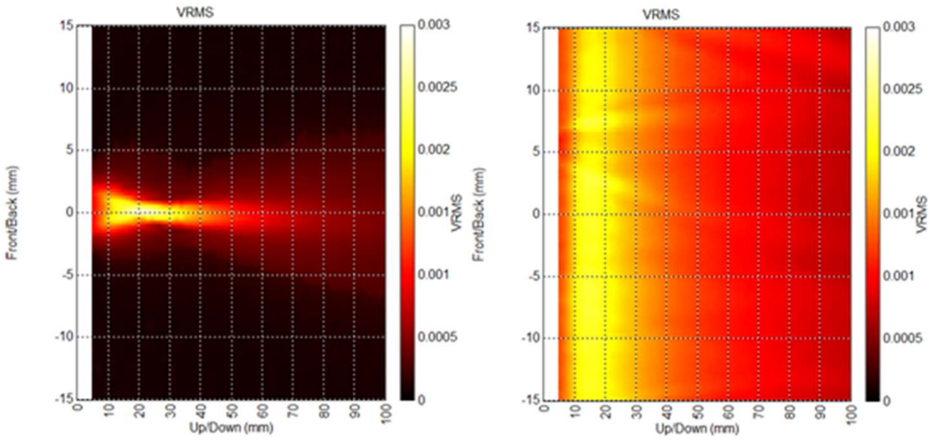


Figure 6 Transmission of a plane wave (red dashed line indicating the final wave-front of the plane wave)

Figure 7 compares the transmission sound fields of a focused wave and a plane wave of a linear array. Within the typical depth range of 5 cm for contrast imaging of superficial tissue, the signal intensity of the transmission sound field of plane wave can reach that of a focused wave only in the range of 1–2 cm, but is poorer than the focused wave when deeper than 3cm. It can be concluded that, under the frame-by-frame imaging mode of plane wave technology, an ultra-high frame rate is achieved inherently, while poorer penetration and lateral resolution issue remains. The coherent angle compounding technology is the key to improving the penetration and lateral resolution of plane-wave images. Specifically speaking, multiple angle-deflected plane waves are emitted in the front-end, and then the coherent compounding is carried out at the receive-end. An example with three-angle plane wave transmission is given in Figure 8. With an increased number of coherent angle compounding, a higher image quality is accomplished at the cost of a decreased frame rate.

Mindray's technical white paper for the ultrasound plane wave contrast imaging describes the advantages of plane wave contrast imaging in terms of SNR and duration of microbubble detection as compared with the traditional focused wave contrast imaging and specifies a strategy for image optimization: In clinical scenarios with high priority in signal intensity than image frame rate, angle compounding should be applied as much as possible without the microbubble destructions, to achieve a higher SNR.



(a) Transmission sound field of a focused wave (b) Transmission sound field of a plane wave

Figure 7 Transmission sound fields of a focused wave and a plane wave of a linear array

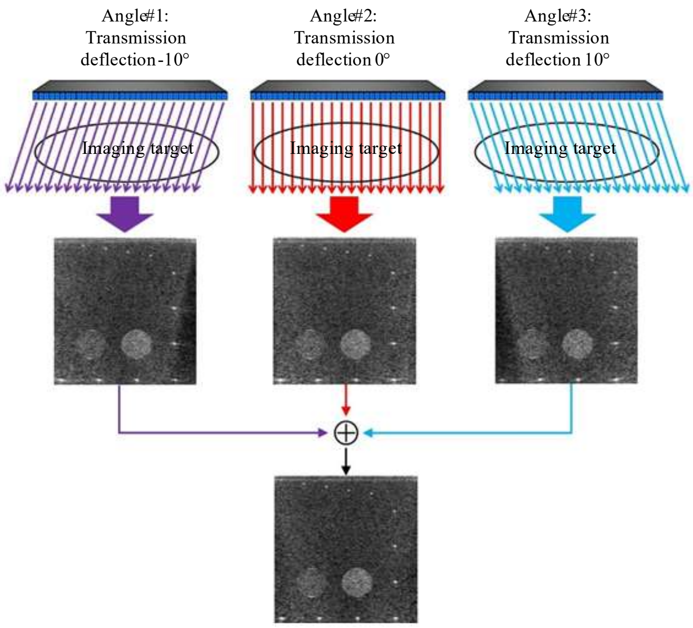


Figure 8 Coherent angle compounding technology for plane waves

However, in specific scenarios requiring a higher frame rate, the strategy has to be modified: The number of coherent angle compounding should be reduced to make a trade-off between a higher frame rate and intensity of contrast signal that meet clinical requirement.

In summary, the plane wave technology is an alternative method enabling HiFR CEUS based on

Resona 7 platform, and is of practical significance in the case of contrast imaging in superficial tissue.

3. Clinical Applications of the HiFR CEUS Based on the Resona 7 Platform

The development of HiFR CEUS has been completed with the Resona 7 platform and will be officially released in the next product generation. As shown in Figure 9, after entering the conventional contrast mode, users can enter or exit the HiFR CEUS mode by tapping the "HiFR CEUS" button on the touchscreen.

Figure 9 HiFR CEUS function on the Mindray Resona 7 platform

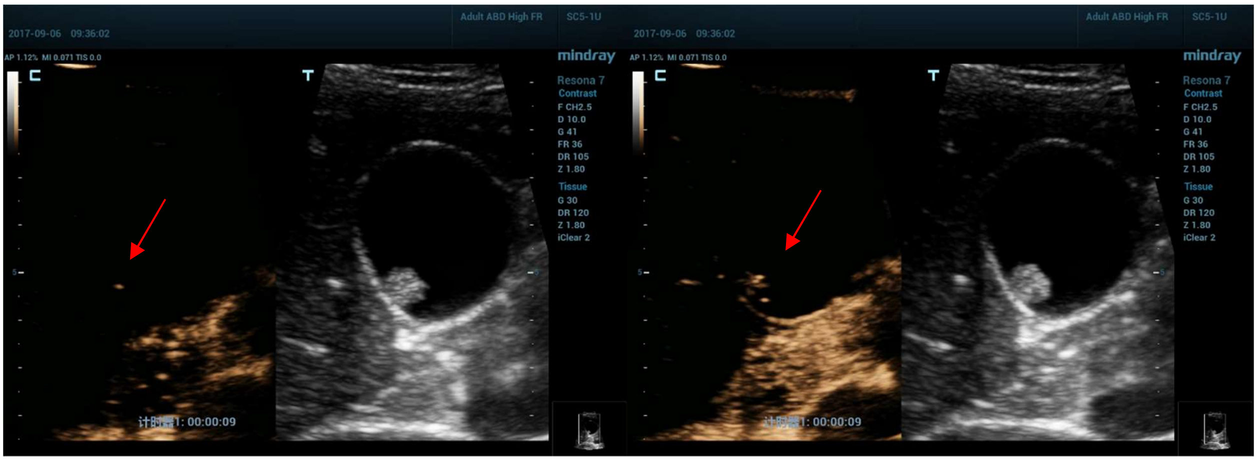
The increased frame rate of contrast imaging provides more information for clinical diagnosis and enhances clinicians' confidence in making conclusions.

The Ultrasonic Diagnosis Department of Chinese PLA General Hospital has applied the HiFR CEUS to the diagnosis of benign and malignant gallbladder polyps and focal liver lesions (FLLs). The Ultrasonic Diagnosis Department of the Second Affiliated Hospital of Zhejiang University School of Medicine has applied the HiFR CEUS to the diagnosis of benign and malignant nodules of superficial organs. The above two examples verify the clinical significance of HiFR CEUS in the diagnosis of minor lesions (≤ 1 cm). Typical cases are described below.

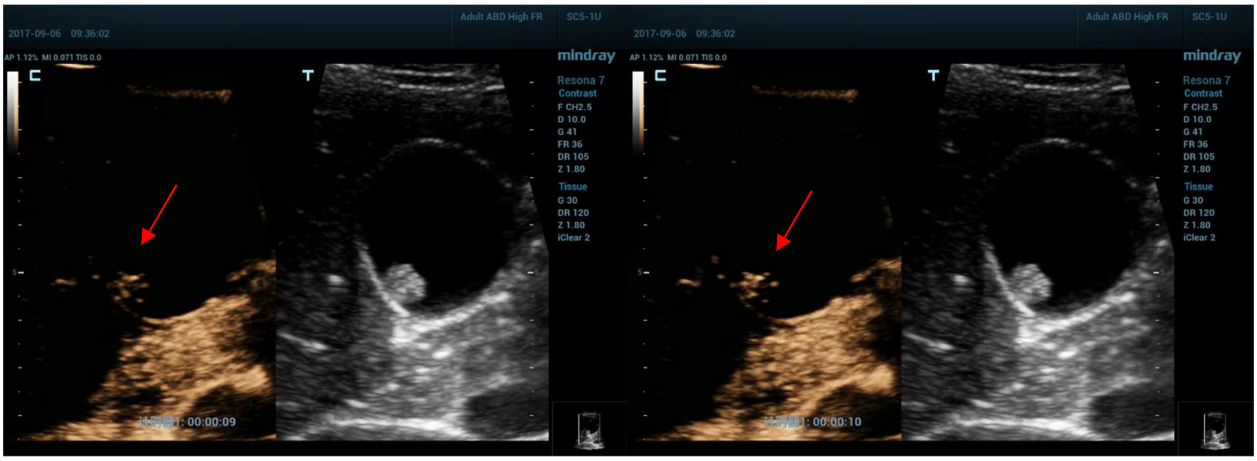
- **Polypoid lesions of gallbladder, contrast agent volume of 1.2 mL, SC5-1U probe, and frame rate of 36 FPS**

Polypoid lesions of gallbladder include cholesterol polyps and adenomas, which are typical minor lesions (≤ 1 cm) and are filled rapidly upon arrival of the contrast agent. If the frame rate is not high enough, the perfusion procedure of polyps cannot be completely observed and cannot be compared with the perfusion of the gallbladder wall, increasing the difficulty of diagnosis between cholesterol polyp (benign) and adenoma (potentially malignant).

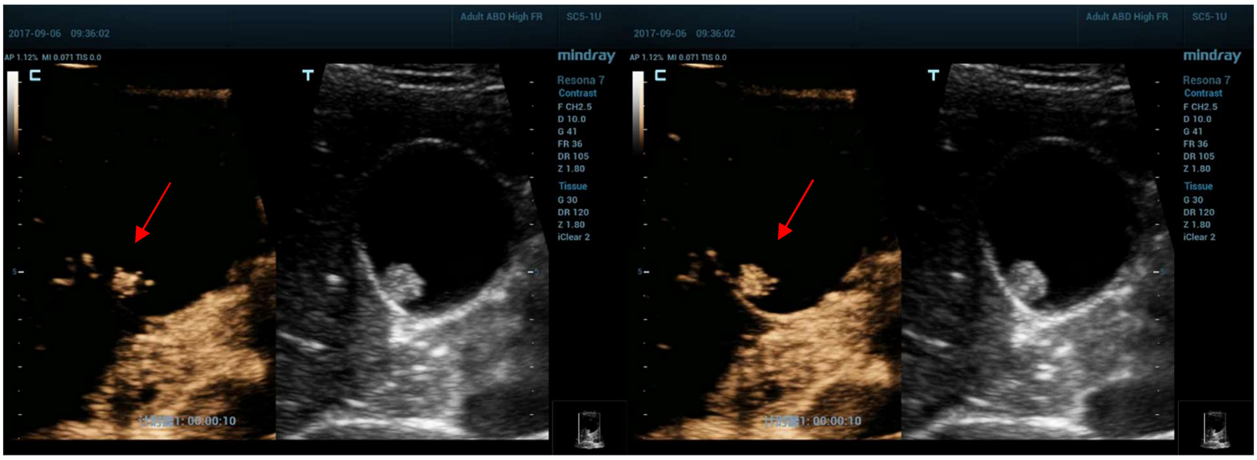
Figure 10 shows HiFR CEUS images, which capture the complete perfusion procedure of the polyp. Iso-enhancing is found in the polyp and gallbladder wall. Therefore, the polyp is identified as a cholesterol polyp (non-tumorous polyp, benign lesion).



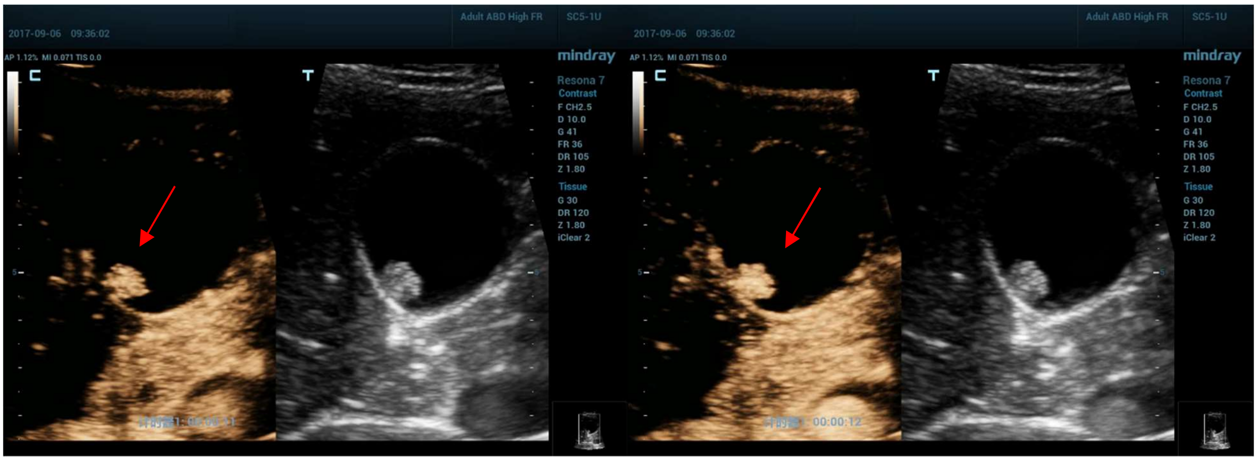
(a) Moment 1　　(b) Moment 2



(c) Moment 3　　(d) Moment 4



(e) Moment 5 (f) Moment 6

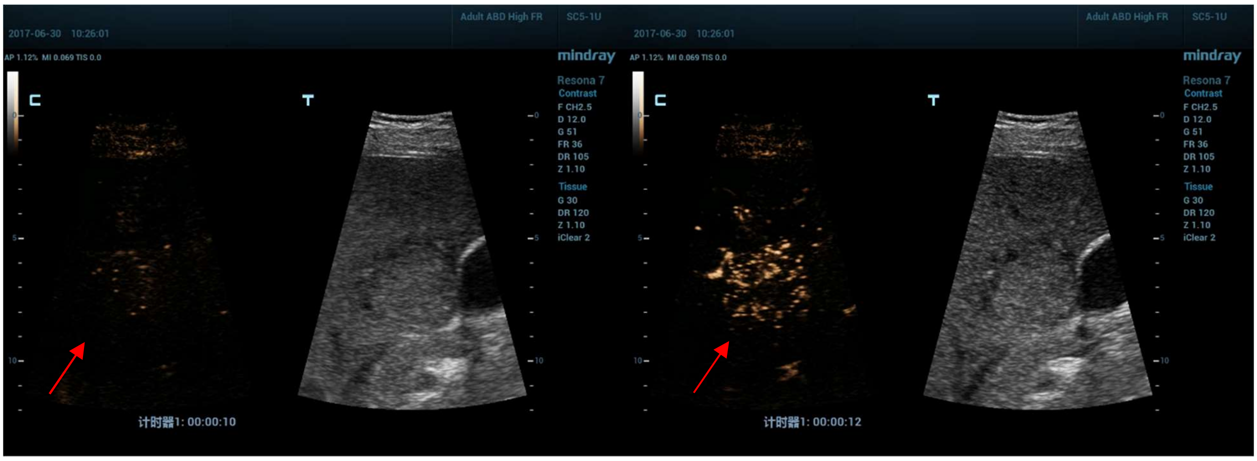


(g) Moment 7 (h) Moment 8

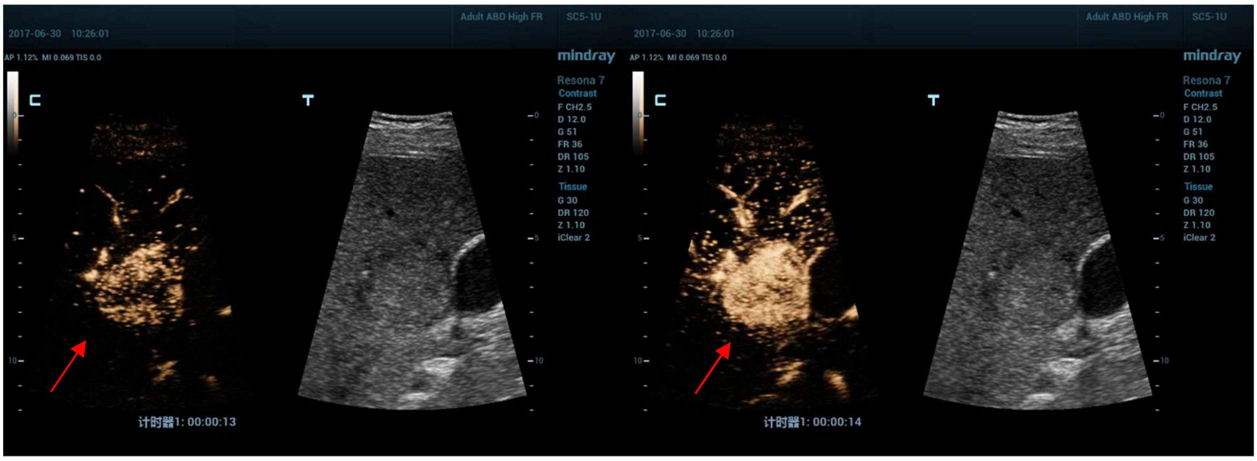
Figure 10 HiFR CEUS of a cholesterol polyp (SC5-1U, contrast frame rate of 36 FPS)

- **Hepatocellular carcinoma (HCC), contrast agent volume of 1.8 mL, SC5-1U probe, and frame rate of 36 FPS**

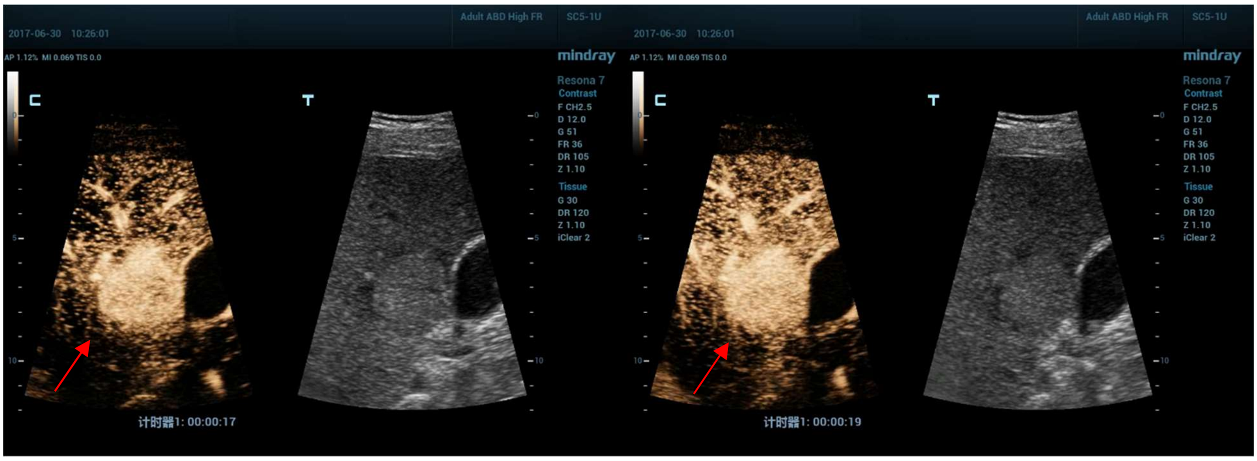
The HCC is one of most common malignant hepatic tumors. Its typical manifestations in ultrasound contrast imaging are hyper-enhancing in the arterial phase and hypo-enhancing in the portal and late phases. Some lesions show the enhancement of capsules and the new blood vessels infused into the lesions in a globular way.



(a) Arrival moment of the contrast agent (b) Moment 1 in the arterial phase



(c) Moment 2 in the arterial phase (d) Moment 3 in the arterial phase



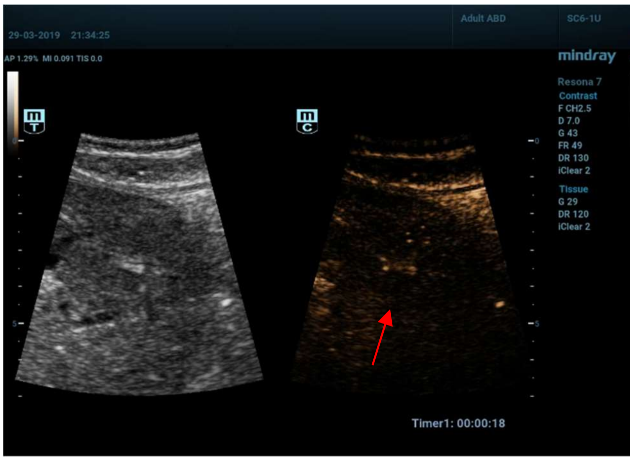
(e) Moment 4 in the arterial phase (f) Moment 5 in the arterial phase

Figure 11 HiFR CEUS of the HCC (SC5-1U, contrast frame rate of 36 FPS)

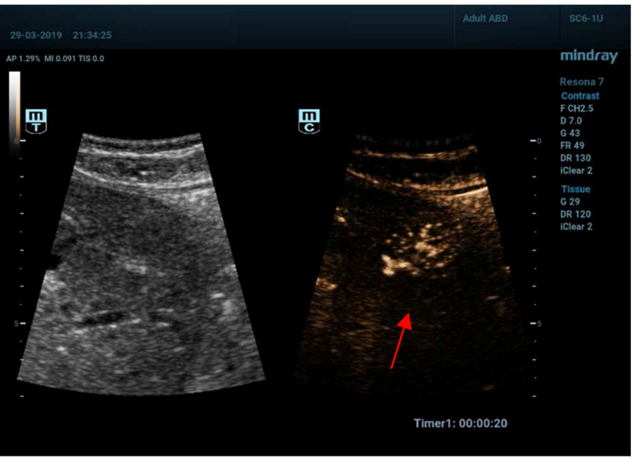
Figure 11 shows HiFR CEUS images of the liver, which present the hyper-enhancing of the lesion in the arterial phase and show the globular perfusion of new blood vessels in the lesion in a more detailed way. It is very helpful when performing ultrasound-guided interventional planning.

- **Focal nodular hyperplasia (FNH), contrast agent volume of 1.0 mL, SC6-1U probe, and frame rate of 49 FPS**

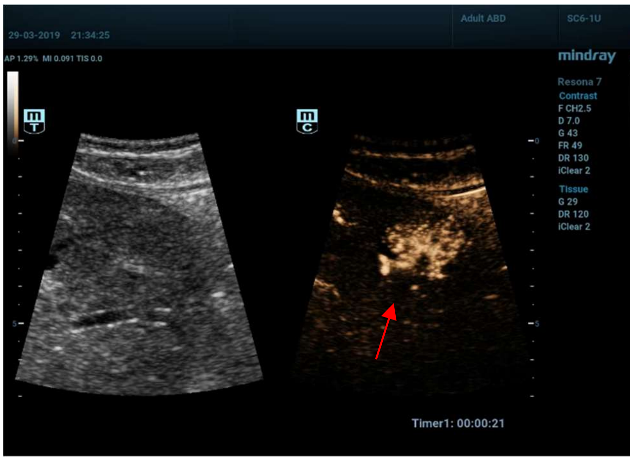
The FNH is a common benign lesion of the liver. Its typical manifestations in ultrasound contrast imaging are centrifugal hyper-enhancing in the arterial and portal phases and hypo-enhancing or iso-enhancing in the late phase.



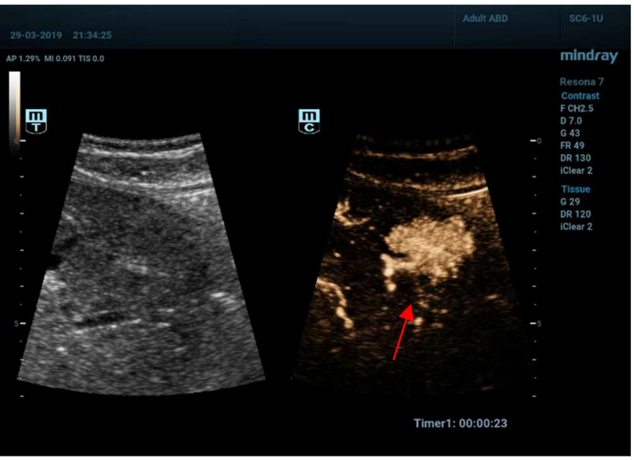
(a) Arrival moment of the contrast agent



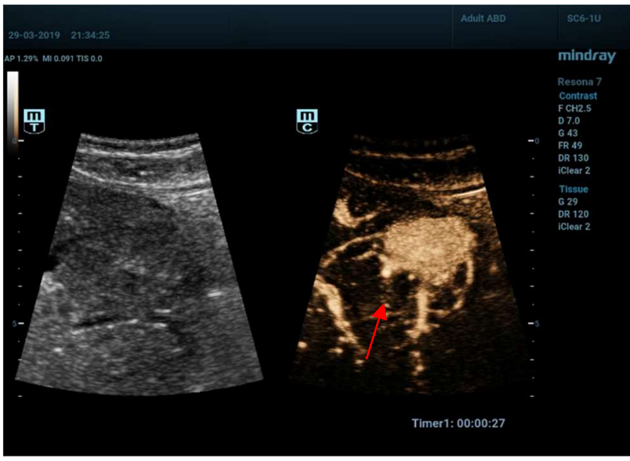
(b) Moment 1 in the arterial phase



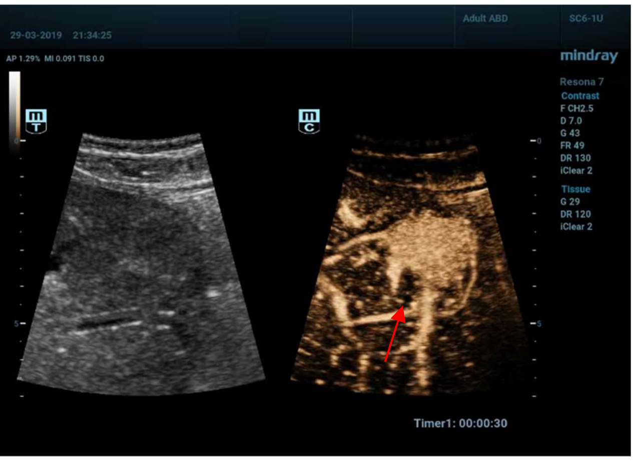
(c) Moment 2 in the arterial phase



(d) Moment 3 in the arterial phase



(e) Moment 4 in the arterial phase



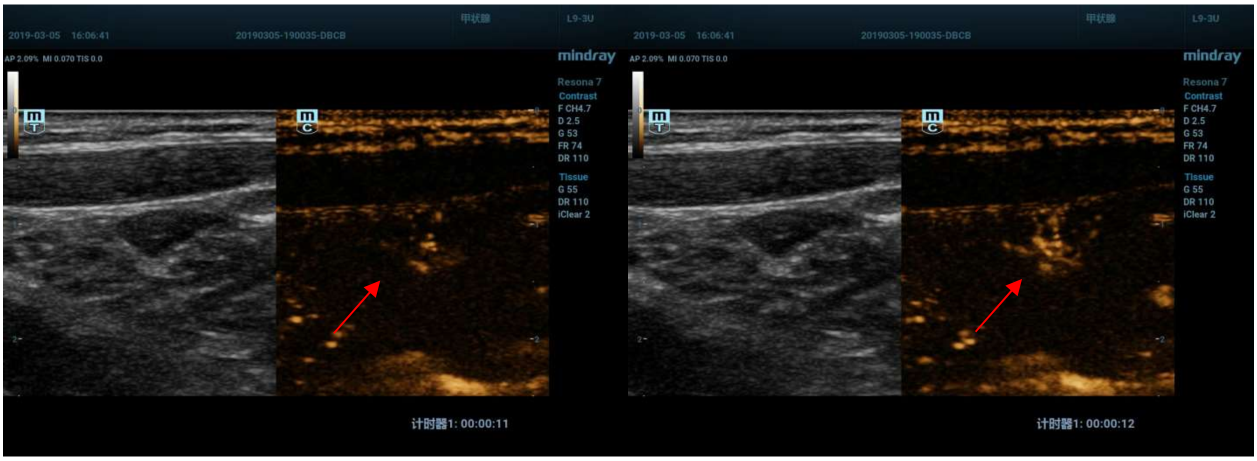
(f) Moment 5 in the arterial phase

Figure 12 HiFR CEUS of the FNH (SC6-1U, contrast frame rate of 49 FPS)

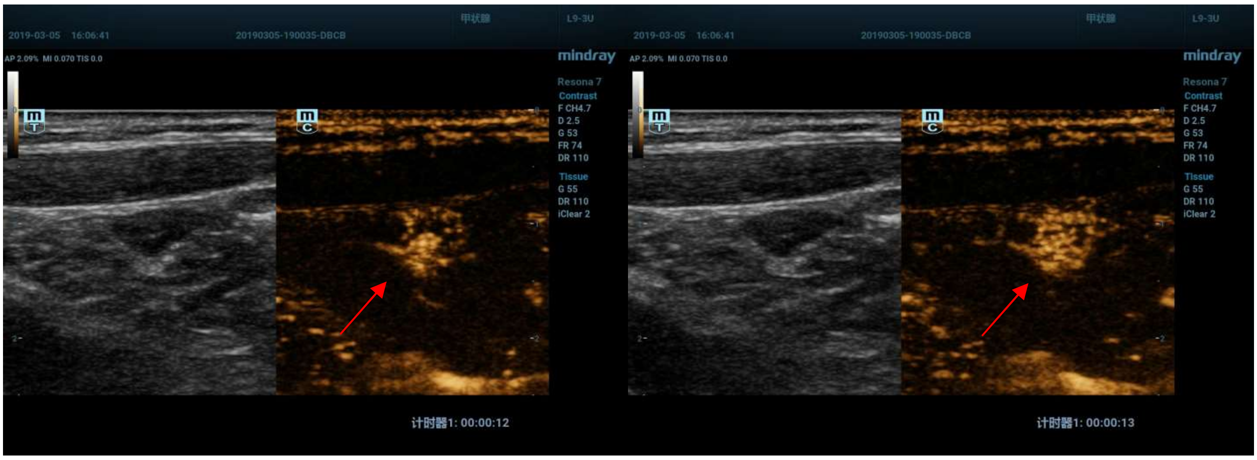
The key for its diagnosis is the wheel-shaped perfusion in the early arterial phase and a centrifugal enhancing pattern afterwards.

The HiFR CEUS images given in Figure 12 shows that the lesion is first hyper-enhancing in the center for the early phase and then spreads outwards in a wheel shape, with a centrifugal enhancing pattern afterwards. The lesion is therefore identified as a FNH.

- **Reactive hyperplasia of the cervical lymph node, contrast agent volume of 2.0 mL, L9-3U probe, and frame rate of 74 FPS**



(a) Arrival moment of the contrast agent (b) Moment 1 of centrifugal high enhancement



(c) Moment 2 of centrifugal hyper-enhancing (d) Moment 3 of centrifugal high enhancement

Figure 13 HiFR CEUS of the cervical lymph node (L9-3U, contrast frame rate of 74 FPS)

Ultrasound contrast description: After 2.0 mL SonoVue is injected through the anterior cubital vein, followed by 5.0 mL 0.9% normal saline, the contrast image of the lymph node in the left neck area III radially shows significant and uniform hyper-enhancing from the lymph node hilum, in which a typical centrifugal enhancing pattern can be observed.

CEUS indicates: Reactive hyperplasia of the cervical lymph node may occur in the left neck area III.

It can be learned that the centrifugal enhancing pattern of the lesions is manifested in a more detailed way when the contrast frame rate reaches 74 FPS.

4. Conclusion

Based on the ZST$^+$ and plane wave technologies, Mindray has developed the HiFR CEUS with Resona 7 platform. The increased frame rate of contrast imaging is capable of providing more diagnostic information. The typical applications given in this technical white paper indicate that HiFR CEUS is of clinical significance, especially for the diagnosis of minor lesions with abundant blood supply.

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