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LETTER TO THE EDITOR

High Frame-Rate Contrast Echocardiography: In-Human Demonstration

Contrast Echocardiography (CE) using microbubble contrast agents enables sensitive imaging of chamber flow dynamics and myocardial perfusion (1). However, the clinical value of CE is affected by the image quality achievable by the existing systems. Recent advances in ultrasound engineering, by transmitting nonfocused waves and digital beamforming, have made it possible to achieve thousands of frames per second (2) and offered new opportunities for imaging the dynamics of the heart. Although high frame-rate (HFR) echocardiography has recently been shown, challenges exist in noncontrast applications due to the difficulty of generating sufficient tissue harmonic signals in deep tissue using nonfocused waves, reducing image quality (3). In CE, such challenges disappear because the nonfocused waves can generate significant harmonics from microbubbles. HFR acquisition has the potential to enhance the imaging of both intraventricular flow and myocardial perfusion, although the mechanism of impacts is different. For imaging flow, HFR enables tracking of fast flow/vortex in the chamber. During perfusion imaging, in either triggered or continuous mode, HFR can acquire up to ~100 frames within the same time as that required by the existing technique to acquire just a single frame. This can potentially reduce noise and minimize heart movement artifacts through temporal filtering or averaging a significant number of frames acquired within milliseconds. In this work we present, as far as we are aware, the first in human demonstration of HFR-CE.

Contrast specific images at 5,500 frames per second were acquired on healthy human volunteers with infusion of Sonovue (Bracco Imaging SpA, Milan, Italy, 1.2 ml/min) (approved by the Imperial College Research Ethics Committee). Low mechanical index (0.08 to 0.12) diverging waves and pulse inversion sequences were transmitted using an ultrasound research platform (Verasonics, Kirkland, Washington) and a phased array probe (ATL P4-1, Phillips, Seattle, Washington). To improve the spatial resolution and the signal-to-noise ratio, the diverging waves were steered with 11 steering angles ranging between −15° and 15°, and the corresponding echoes were coherently compounded. A destruction-reperfusion sequence was implemented to observe myocardium perfusion replenishment. In addition, conventional line-by-line scanning was also implemented on the same system for comparison.

To evaluate the image quality and contrast-to-noise ratio, a measure of the image contrast between the chamber and myocardium relative to noise was calculated on the compounded images and the results were averaged. Image speckle size at the top, middle, and bottom part of the images was also calculated and averaged as a measure of spatial resolution. To quantify the chamber flow dynamics, ultrasound imaging velocimetry (UIV) (also known as echo-particle image velocimetry) processing (4) was used to track the microbubbles and generate a time-resolved flow velocity map. Finally, the myocardium was segmented and the time-intensity curves (TICs) of the myocardium contrast enhancement were calculated. Results are shown in **Figure 1**.

For image quality, HFR-CE improves image contrast-to-noise ratio by an average of 151% over conventional CE after motion compensation. The speckle size in the image is also improved by an average of 30% for the same mechanical index. Furthermore, the flow velocity map within the cardiac chambers based on HFR-CE and UIV are successfully obtained while the tracking failed in the conventional CE control study (**Figure 1**). Finally, we are able to quantify the replenishment of contrast signal after destruction and generate the TIC as displayed in **Figure 1**. Some individual microbubble events are also observed in the myocardium.

In conclusion, we have shown the feasibility of HFR-CE in humans. Initial results show significant improvement in image quality, and quantification of both chamber flow and myocardium perfusion is demonstrated. These are new, experimental techniques demonstrated on a research ultrasound platform and optimization of the imaging parameters and data processing algorithms is required for them to be used for clinical application.

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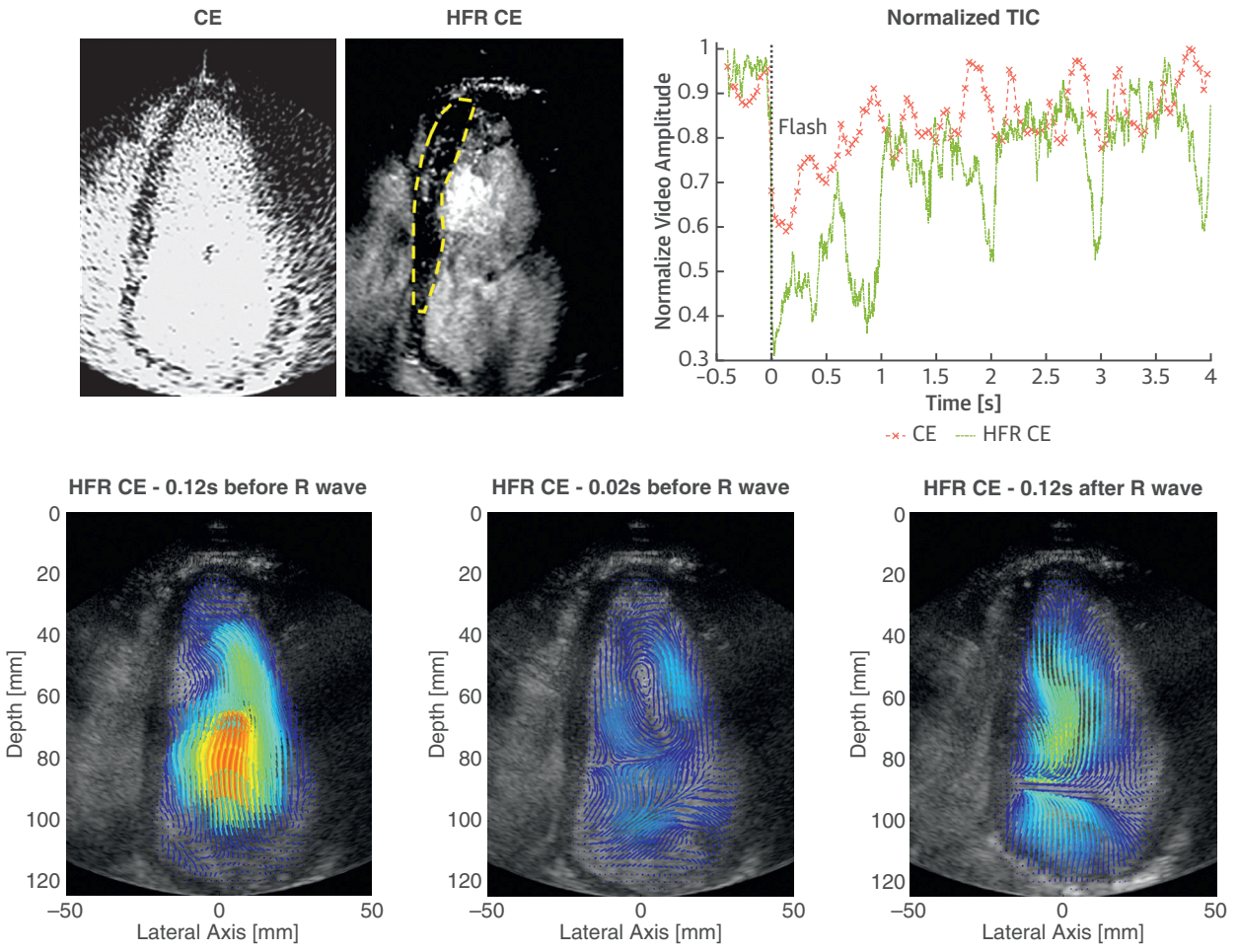
FIGURE 1 **Human High Frame Rate Contrast Echocardiography**



(Top) Conventional CE **(left)** versus HFR-CE **(middle)** frames, and the TIC **(right)** over the ROI **(yellow dashed line)** of a human heart. Time 0 corresponds to the bubble destruction/flash pulse. **(Bottom)** Chamber flow dynamics visualized by HFR-CE and UIV at different cardiac phases before and after R-wave (R −0.12 s, R −0.02 s, and R +0.12 s, respectively). CE = contrast echocardiography; HFR = high frame-rate; ROI = region of interest; TIC = time intensity curve; UIV = ultrasound imaging velocimetry.

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