

## Highly sensitive ultrasound bubble imaging by triplet pulse sequence with interleaved HIFU pulses between imaging pulses

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### 1. Introduction

High-intensity focused ultrasound (HIFU) is a minimally invasive treatment. It can treat cancer by focusing ultrasound to a target tissue from outside the body. The throughput of a HIFU treatment can be improved by cavitation bubbles. To selectively imaging bubbles, an imaging method called triplet pulse (3P) sequence<sup>1)</sup> that extracts nonlinear echo signals from bubbles has been proposed.

However, the sensitivity of bubble detection by 3P method may not be sufficient under certain situations. For instance, when the stiffness of the tissue is high, the inertial bubble expansion is suppressed, and the cavitation initiation threshold is significantly increased<sup>2)</sup>, resulting in the weak echo signals from cavitation bubbles. We propose a method to extract cavitation bubbles with high sensitivity by interleaving HIFU pulses between imaging pulses in a 3P sequence and changing the state of bubbles during the 3P sequence.

### 2. Materials and Methods

#### 2.1 Triplet pulse sequence

In a 3P sequence, three pulses are transmitted with phase shifts of  $\pm 120^\circ$  and the three received echoes are added. In this method, the fundamental and second harmonic components of the tissue signal are canceled out when added because the phase shifts between the three received echoes from the tissue are maintained to be  $\pm 120^\circ$ . On the other hand, the phase shifts of the oscillation of bubbles may change from those in the three pulses. Therefore, the signals from cavitation bubbles are difficult to be canceled out the fundamental and second harmonic components. Furthermore, bubbles may generate a 1.5 harmonic component due to strong nonlinearities, a feature not found in tissue. The 3P sequence utilizes these differences in scattering characteristics between tissues and bubbles to extract only the bubbles.

#### 2.2 HIFU exposure and RF data acquisition sequence

**Fig. 1** shows a schematic of the experimental setup. Experiments were performed in a water tank with a 128-ch 2D-array transducer at the center of the side wall. A sector probe for ultrasound imaging was mounted in the central hole of the transducer. The focus of the HIFU was located at a depth of 70 mm in the imaging plane. The tank was filled with

degassed water (dissolved oxygen saturation of 20% at room temperature). A chicken breast as a target tissue was set and exposed to HIFU at 1.0 MHz. The center frequency of the transmitted waves for imaging was 2.45 MHz.

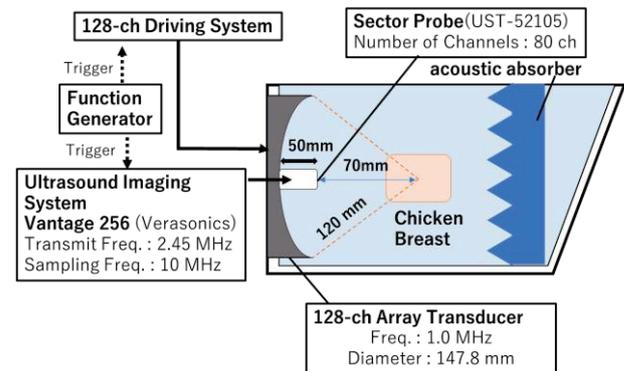


Fig. 1 schematic of the experimental setup

**Fig. 2** shows the sequence of the HIFU exposure and RF data acquisition. Trigger HIFU sequence was used, consisting of short pulses called “trigger pulses (TP)” to generate cavitation bubbles and bursts called “heating bursts (HB)” to oscillate the bubbles and heat tissue. The focal depth of trigger pulses was set at 77 mm in the imaging plane, and that of heating burst was set at 70 mm. The intensity of the trigger pulse was  $67 \text{ kW/cm}^2$ , and that of the heating burst was  $0.67 \text{ W/cm}^2$ . The intensity of the heating burst was determined with reference to HIFU exposure parameters when the contrast ratio of the bubbles in the 3P images was the worst in previous study<sup>3)</sup>. This sequence was repeated for 7 cycles. RF signal is acquired after the heating burst when the amount of bubbles is considered to be reduced and the detection sensitivity is decreased, compared to the detection after the trigger pulse<sup>3)</sup>. In the 3P sequence, three pulses are transmitted with phase shifts by  $120^\circ$ ,  $0^\circ$  and  $240^\circ$  and the received waves are added to construct 3P images. Single pulse (1P) image is constructed from the echoes of the  $0^\circ$  wave. As HIFU pulses interleaved in the 3P sequence, pulses at the same intensity of the trigger pulse with a duration of  $3 \mu\text{s}$  were used. The focus of the interleaved pulse was set to 70 mm in the imaging plane to match the position of cavitation bubbles generated. Then, a 2.5 MHz high-pass filter was

applied to 3P RF data to remove low-frequency components generated through nonlinear propagation of imaging pulses, which are not canceled by the addition of three echoes.

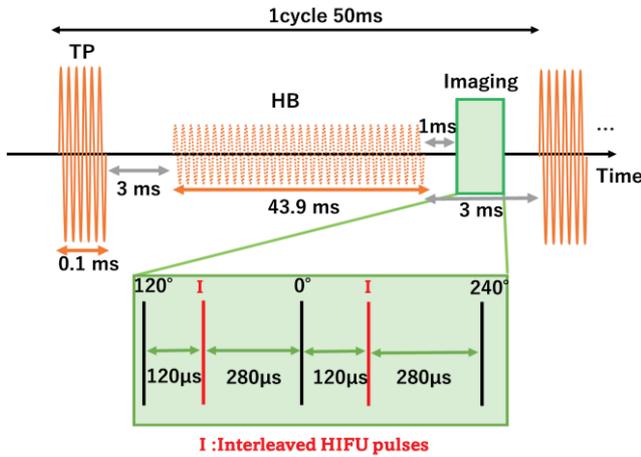


Fig. 2 HIFU and imaging sequence

### 3. Results and Discussion

Fig. 3 shows B-mode images created from 1P and 3P IQ data at 1st cycle without and with interleaving HIFU pulses. Each of the data was obtained at a different place of the same sample. Cavitation bubbles in both 1P images seem to have the similar brightness. However, in 3P image, the brightness of bubbles increased with interleaving HIFU pulses compared to without interleaving HIFU pulses.

Fig. 4 shows average contrast ratio of the bubble region to the tissue in the 3P image over all cycle. The bubble region was defined as a depth from 64 to 70 mm and width from -4 to -1 mm, and the tissue as a depth from 60 to 70 mm and width from 10 to 13 mm from the image. The average contrast ratios in the 3P image without and with interleaving HIFU pulses were  $10.5 \pm 1.71$  (N = 5) and  $19.1 \pm 0.91$  dB (N = 3), respectively. Interleaving HIFU pulses improved contrast ratio of the 3P image by about 8 dB. It is considered that the bubbles were imaged with higher sensitivity with the proposed method probably because the state of the bubbles changed between the consecutive imaging pulses, exposed to the interleaved HIFU pulse.

### 4. Conclusion

In this study, interleaving HIFU pulses between imaging pulses in the 3P sequence increased the brightness of bubbles and improved the contrast ratio of bubbles to tissue in the 3P images. These results suggest that this method allows imaging of bubbles with high sensitivity, even if they are difficult to visualize with conventional methods.

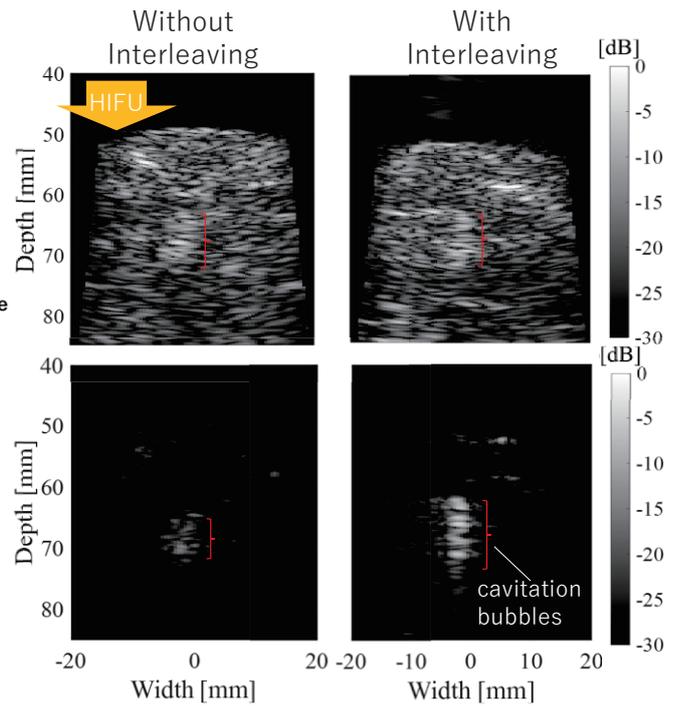


Fig. 3 3P and 1P B-mode images without and with interleaving HIFU pulses

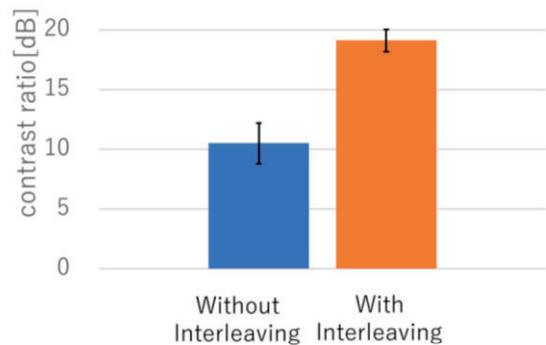


Fig. 4 Average contrast ratio of the bubble to the tissue in the 3P image

### References

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