

## Highly Efficient Cavitation-Enhanced Heating with Dual-Frequency Ultrasound Exposure in High-Intensity Focused Ultrasound Treatment

強力集束超音波治療における高調波重畳法による  
キャビテーションを用いた効率的加熱法

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### 1. Introduction

High-Intensity Focused Ultrasound (HIFU) treatment is a method of non-invasive cancer treatment,<sup>1)</sup> in which physical and mental stresses on the patient is minimal. A drawback of HIFU treatment is the need of a long treatment time for a large tumor due to a small therapeutic volume by a single exposure.

Enhancing the heating effect of ultrasound by cavitation bubbles may solve this problem. To maximize this possibility, we are developing a method to both generate cavitation bubbles and use them to enhance heating efficiently.

### 2. Materials and methods

#### 2.1 Triggered HIFU

The ultrasound sequence we called “Triggered HIFU” is a HIFU method employing cavitation bubbles.<sup>2)</sup> In this method, a high-intensity and short pulse, named as “Trigger Pulses”, generate and grow cavitation bubbles first. Then, a low-intensity and long-duration burst, named as “Heating Waves”, vibrate the cavitation bubbles to enhance the heating effect. As the result, a large region can be efficiently coagulated.<sup>3)</sup>

#### 2.2 Dual-Frequency ultrasound exposure

Negative pressure is significant to generate cavitation bubbles and positive pressure is important to make them expand to a cloud. However, obtaining highly negative pressure at the focal point is difficult because of the nonlinear propagation. By superimposing the second-harmonic onto the fundamental, one can emphasize either the positive-peak pressure (P-waves) or the negative-peak pressure (N-waves)<sup>4)</sup> as shown in Fig. 1.

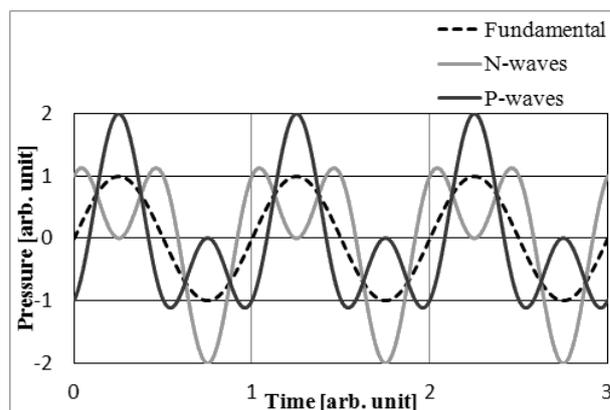


Fig.1. Schematic waveforms of dual-frequency ultrasound exposure

In this study, 0.8 and 1.6 MHz were chosen as the fundamental and second-harmonic frequency because the efficiency of the transducer was similar at these frequencies. The effect of this method was tested ex-vivo as Trigger Pulses in Triggered HIFU treatment in this study.

#### 2.3. HIFU sequences

Fig.2 shows the Triggered HIFU sequence. First, cavitation bubbles were generated and potentially grown by Trigger Pulses at an intensity of 12 kW/cm<sup>2</sup> with a duration of 150 μs. The PP, NN, PN and NP sequences and single frequency Trigger Pulses at 0.8 MHz were tested. After the Trigger Pulses, cavitation bubbles were oscillated by Heating Waves at 1 MHz with an intensity of 2 kW/cm<sup>2</sup> with a duration of 500 ms. In this method, the focal point of ultrasound was moved every 25 μs sequentially among six positions. This is to effectively utilize heating effect while maintaining cavitation bubbles. In PN and NP sequences, P-waves and N-waves were exposed for 12.5 μs sequentially. In PP and NN sequences, P-waves and N-waves were exposed 25 μs, respectively. In Heating Waves, 25 μs exposure was repeated 3334 times for each focal spots.

This cycle of ultrasound sequence was repeated 20

times for a total duration of 10 s.

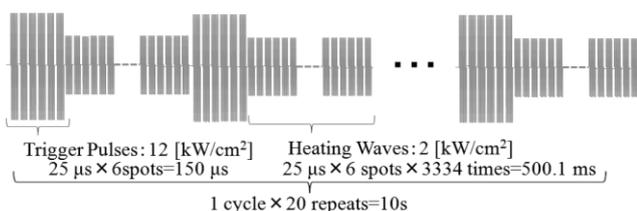


Fig.2. Irradiation sequence for Triggered HIFU

In order to verify of cavitation enhanced heating, a HIFU sequence with Heating Waves only, in which Trigger Pulses were changed to Heating Waves, was also tested.

#### 2.4. Experimental setup

Fig.3 shows the setup of the experiment in a water tank. The water was degassed (DO: 20-30%) and kept at 36 degrees. A 128-channel array transducer (Imasonic) connected to staircase voltage amplifiers (Microsonic) controlled by a PC. Degassed chicken breast muscle tissue was used as the object for ultrasound irradiation.

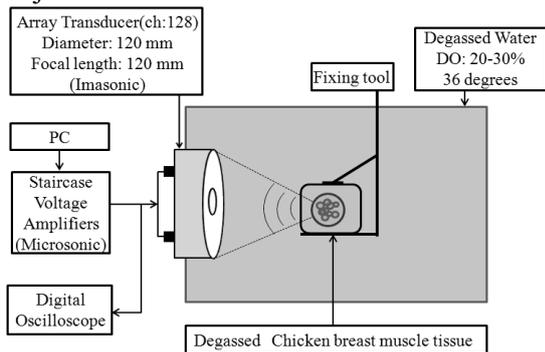


Fig.3. Schematic of experimental setup

### 3. Results and Discussion

Fig.4 shows the averaged coagulation volumes and the standard division in the tissue for each irradiation sequence.

The volume by NP sequence was larger than all the other sequences. The difference was significant except for Triggered HIFU at single frequency. This indicates that NP sequence is most effective to generate reactive cavitation bubbles among the second-harmonic superimposed sequences. This result agrees well with the previous report on high-speed camera observation that NP sequence is most effective to initiate cavitation bubbles and expand them to a cloud.<sup>5)</sup>

In contrast, the volumes by PP and PN sequence were just as large as Heating Waves only. This indicates that these sequences were not effective to generate reactive cavitation bubbles. The volume by NN sequence was significantly less than other sequences. This may be because

cavitation nuclei in chicken breast were decreased by N-waves.

It should be noted that the volume by Heating Wave only was much larger than a conventional HIFU sequence. It is because virtually simultaneous HIFU irradiation with properly packed multiple focal spots enhances the thermal efficiency.<sup>6)</sup>

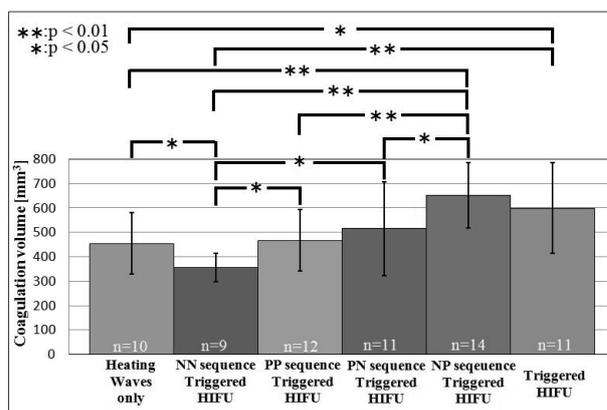


Fig.4. Averaged coagulation volumes in chicken breast tissue

### 4. Conclusion

NP sequence as Trigger Pulses was proven to be effective to coagulate a large volume. However, further study is needed to optimize the sequence to obtain significantly higher efficiency than the single frequency Triggered HIFU.

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