Histotripsy Produced by Dual Frequency of Fundamental and Harmonic Superposition with Protocol of Millisecond Length Pulses and Three Stages

Mingzhu Lu[1], Dan Han[1], Yanshan Liu[1], Yujiao Li[1], Yizhe Geng[1], Xuan Wang[1], Quan Zhang[1],Yehui Liu[1], Ruixin Li[1] , Mingxi Wan[1]*

[1]Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, Xi' an, People's Republic of China

Background, Motivation and Objective

Histotripsy is a pulsed ultrasound technique that produces non-thermal mechanical homogenization of targeted tissue for tumor treatment. In this study, in order to improve histotripsy efficiency for large tumor treatment, we propose two schemes: first is based on millisecond length pulses and three stages for inducing main mechanism of high-efficiency boiling histotripsy; 2nd consists in achieving simultaneously two foci for increased lesion size. In addition, the dual frequency of fundamental and harmonic superposition can enhance cavitation activities, resulting accelerating boiling events.

Statement of Contribution/Methods

A custom-designed 4-element sector array (Fig.1 (a)) of 1.2 /2.4 MHz and 2-element annular array (Fig.1 (b)) of 1.1 /3.3 MHz were used. The sector array can generate simultaneously two or four foci in the focus plane for larger focal volume via phase shift. The annular array can generate single focus. The waveform (Fig.1 (c)) of millisecond length pulses and three stages was used: stage 1 and 2, pulses with same pulse duration (PD) of a few millisecond, much higher 5% duty factor (DC) and pulse repetition frequency (PRF) of approximate 10 Hz; stage 3, same PD and PRF as those in stage 2 and 1% DC. The peak negative pressure of each frequency exceeding -10 MPa. The experiments were implemented in gel-phantom with bovine-serum-albumin, ex vivo porcine kidneys, monitored via high-speed camera or B mode imaging.

Results/Discussion

As expected, the experiments achieved successful and complete disintegrated large lesions (Fig.1 (d)) using 1.2/2.4-MHz two foci (Fig.1 (e)) with typical lesion dimension of approximate 5 by 6.5 mm (lateral by axial length) that is three times larger than the single-focus lesion. The selected images from high speed imaging show the cavitation cloud structure at first pulse (Fig.1 (f)) and boiling event at 5 s (Fig.1 (g)). By using 1.1/3.3-MHz single focus, the disintegrated lesions (Fig.1 (h)) are generated with dimension of 2.5 by 8.8 mm (lateral by axial length) that is 2.5 times larger than the lesion of our previous hundred-microsecond-pulse scheme. Large lesion formed by single lesion scanning along a line with 1.1/3.3MHz with B-mode image monitoring (Fig.1 (k)). In this study, the large sized lesion with wider 5-mm lateral dimension generated in prefocal region. The main regimes can attribute to dual-frequency parallel boiling bubbles and beams with shock waves and strong cavitation-bubble-layer reflection effects.

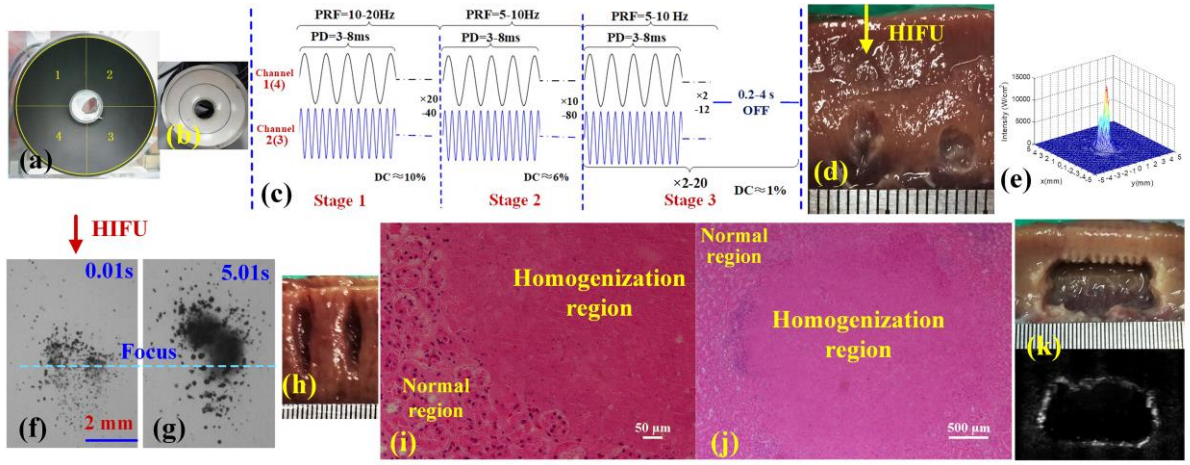

Fig.1 Histotripsy of millisecond length pulses and three stages using (a) 1.2/2.4 MHz array and (b) 1.1/3.3MHz transducer. (c) Protocol of millisecond length pulses and three stages. (d) Histotripsy lesion in pig kidney from (e) two focus pattern with 1.2/2.4 MHz arrays. Both (f) and (g) show images from high speed imaging. (h) Single focus lesion in pig kidney with 1.1/3.3 MHz. Both (i) and (j) show H&E stained slides. (j) Lesion formed by single lesion scanning along a line with 1.1/3.3MHz, above: lesion, below: B mode image of lesion.