Fast Liquefaction of Blood Clots Using histotripsy with Fundamental and Second Harmonic Superposition in an ex vivo Intracerebral Hemorrhage Model

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

Intracerebral hemorrhage (ICH) is a life-threatening acute cerebrovascular disease affecting millions of patients worldwide. Current treatment methods mainly include craniotomy surgery and minimally invasive stereotactic clot evacuation. Recently, histotripsy, a noninvasive ultrasound therapy that fractionates clots via cavitation or boiling, has been proved to be an alternative ICH treatment approach. In this study, we propose a strategy of using two-element annular array with small aperture size, combined fundamental and second harmonic superposition, with waveform of millisecond length. We sought that this approach would be able of achieving rapidly and efficiently liquefying of large volume clots for ICH treatment.

Statement of Contribution/Methods

Histotripsy pulses were delivered using a 1.1MHz/2.2 MHz annular array with a 94 mm aperture size and 65 mm geometric focal length. The histotripsy pulsing sequence consisted of 8 periods, each consisting of 10 pulses with pulse duration of 6-ms and pulse repetition frequency of 10 Hz, with 1.4-s off-time between periods. The duty cycle was 2.5%. The experiments were performed on ex vivo blood clots and BSA gel phantom embedded with a thin red blood cell (RBC) layer. Discrete liquefied lesions were first generated to demonstrate the feasibility of the proposed strategy. Large volume lesion was then created by performing a series of individual sonications (90 points) spaced by 2 mm, followed by repeated treatment performed in a second layer spaced by 10 mm axially. The liquefied lysates were drained with a syringe for post analysis using a Coulter Counter particle sizing system.

Results/Discussion

Using the designed pulses, histotripsy was able to generate long-ellipsoid-shaped lesions with dimensions of approximately 11.8 × 4.6 mm (axial × lateral) in blood clot successfully. The large-sized liquefied lesion (20 × 18 × 18 mm) was generated in clot and the hypoechoic regions indicated the liquefaction of fibrin matrix. The size of lysate debris mainly ranged from 2 to 10 μm, with over 99% smaller than 10 μm. The selected images showed the cavitation cloud structure and the resulting lesion after enhanced cavitation activities in RBC phantom. This study demonstrates the feasibility of using the described histotripsy protocol for rapid and safe treatment of ICH.

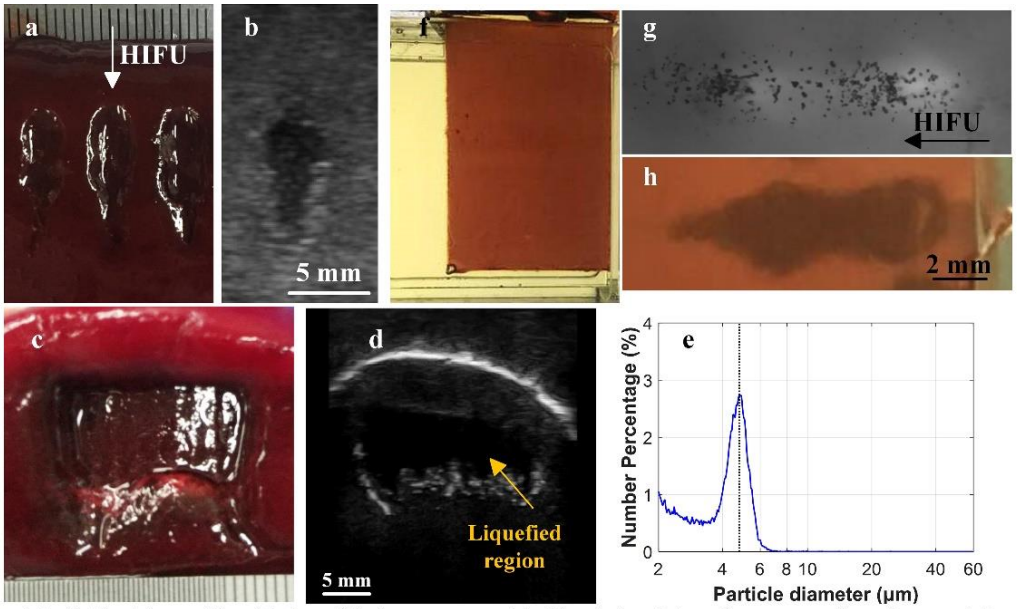

Fig. 1 Individual long-ellipsoid-shaped lesions generated in blood clot (a) and corresponding ultrasound B-mode image(b). Large volume liquefied void generated in clot (c) and corresponding ultrasound image (d), exhibited complete liquefaction of fibrin matrix in the clot. (e) Size distribution of liquefied debris. (f) Photograph of BSA gel phantom with thin red blood cell layer. Images of cavitation cloud structure (g) and final lesion in gel phantom (h).