Characterization of microbubble cavitation in transcranial theranostic ultrasound-mediated blood-brain barrier opening

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Objectives

Characterizing the microbubble cavitation induced by theranostic ultrasound (ThUS) during transcranial blood-brain barrier opening using the harmonic frequency components from a frequency-domain beamformer.

Methods

We utilized the ThUS system comprised of a P4-1 phased array (ATL, Philips) driven at 1.5 MHz to transmit bursts of 100 focused, 10-cycle pulses, to the brain of 8-week-old male C57BL/6 mice, with pulse and burst repetition frequencies of 1000 Hz and 0.5 Hz, respectively. Signals passively received after each pulse at 10 MHz sampling frequency were Fourier transformed before delay-and-sum beamforming for passive acoustic mapping.

Results

Cavitation doses were calculated within a ROI (Fig. **a**) for the entire frequency spectrum and within 200 kHz bands around the second and third harmonic and ultraharmonic frequencies. The full-spectrum and ultraharmonic cavitation doses were lowest at the beginning of each burst (total cavitation shown in Fig. **b**), whereas the harmonic cavitation dose peaked at the first pulse (Fig. **c**). Baseline cavitation measurements revealed no significant fluctuations throughout the burst. Total, ultraharmonic, and harmonic cavitation doses remained at near-baseline levels for the remainder of each burst and only peaked at the beginning of each burst after microbubble injection.

Conclusions

These results demonstrate that most cavitation events occur within the first pulses of each ThUS burst. Additionally, harmonic frequency components best reflect the microbubble depletion within the focus throughout the burst, while the trends observed for total and ultraharmonic cavitation are due to broadband noise from spectral leakage (Fig. **d**).

Acknowledgements

This study was supported by the National Institutes of Health under grants R01AG038961 and R01EB009041, the Focused Ultrasound Foundation and the Onassis Foundation.