A single linear array for simultaneous blood-brain barrier opening and cavitation mapping in non-human primates

Background, Motivation and Objective

Theranostic ultrasound (ThUS) uses a single linear array transducer and rapid short pulses to simultaneously open the blood-brain barrier (BBB) and perform cavitation mapping. ThUS BBB opening feasibility has been demonstrated in rodents, and a recently published pulse sequence called rapid alternating steering angle (RASTA) has performed bilateral BBB openings during a single by using electronic beam steering. This abstract aims to demonstrate the ability of a custom-built low-frequency linear area to perform ThUS BBB opening and RASTA in non-human primates.

Statement of Contribution/Methods

A low-frequency linear array (L500, fc = 500 kHz, 32 elements, Vermon) was fabricated and characterized using a capsule hydrophone. The L500 was used for both BBB opening and Power Cavitation imaging (PCI) in a non-human primate (NHP), with bursts of 100, 3-cycle pulses transmitted at a pulse repetition frequency of 1 kHz every 2 seconds. RASTA was applied within each burst, steering each pulse 5 mm alternately to the left and right of the central axis. With the L500 aperture placed in the sagittal plane of the NHP, the focused was steered anterior and posterior. A single PCI frame was generated for each burst by taking the total power across the ensemble of spatiotemporal clutter filtered frames. ThUS sonications with the L500 and systemically administered microbubbles were performed in an NHP using a real-time neuronavigation system and evaluated using contrast-enhanced T1-weighted MRI.

Results/Discussion

The hydrophone measurement of the L500 focused at an axial depth of 55 mm has an estimated full-width half max of 40.2 mm axially, 4.2 mm laterally, and 16.6 mm elevatioanlly. Before microbubble injections, a B-mode was acquired to ensure coupling and incidence angle is satisfactory (Fig 1A). Definity microbubbles were administered and ThUS was performed using the RASTA sequence for 4 minutes. Fig 1B shows the respective cumulative PCI maps generated during the whole treatment for the focused transmit steered posterior (left) and anterior (right), demonstrating localized cavitation signal only within the brain and in the respective steered locations. Contrast-enhanced T1-weighted MRI (Fig. 1C) revealed distinct regions of contrast enhancement in both the sagittal (left) and coronal (right) planes, indicating successful ThUS BBB opening using RASTA (Fig. 1C). In conclusion, this study demonstrated the capability of ThUS to simultaneously open two different regions in the NHP brain using RASTA and to generate cavitation maps that correlate with the underlying bioeffects. Ongoing studies continue to investigate the parametric space for ThUS BBB opening with the L500 array and the correlation of PCI maps with opening volume.