A high-frequency phased array system for transcranial focused ultrasound therapy in small animal models

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Background, Motivation and Objective

Existing systems for applying focused ultrasound (FUS) to the brain in small animal models produce large focal volumes relative to the size of the anatomical structures available for interrogation [1]. Although the use of higher frequencies can improve targeting specificity, the aberrations induced by rodent calvaria at these frequencies severely distort the acoustic fields produced by single-element focused transducers [2]. Here we present the design, fabrication, and characterization of a high-frequency phased array system for transcranial FUS delivery in small animals.

Statement of Contribution/Methods

A transducer array was constructed by micromachining a spherically-curved PZT-5H bowl (25 mm diameter, 20 mm radius of curvature, 560 µm thickness, 3.3 MHz fundamental frequency) into 64 independent elements with equal surface area (7.25 mm^2) [Fig. 1A]. The acoustic fields generated from targeting various locations in water were measured by a calibrated fiber-optic hydrophone, and were used to estimate the array's effective electronic beam steering range. The array's transcranial focusing capabilities were investigated by measuring the acoustic fields generated from focusing through *ex-vivo* rodent skullcaps (male Sprague-Dawley rats, 190-350 g, n = 4) both with and without hydrophone-assisted phase aberration corrections [3].

Results/Discussion

The focal beam size obtained when targeting the array's natural focus was 0.4 mm x 0.4 mm x 2.6 mm in water (pressure full-widths at half-maxima). The array can electronically steer the FUS beam over cylindrical volumes of 5-mm in diameter and 10-mm in height. Insertion of rat skullcaps resulted in substantial distortion of the acoustic field ($\boldsymbol{p}_{\text{no corrs}}$ = 20±7% $\boldsymbol{p}_{\text{water}}$), however, skull-specific phase corrections restored partial focal quality ($\boldsymbol{p}_{\text{skull corrs}}$ = 39±5% $\boldsymbol{p}_{\text{water}}$) [Fig. 1B]. Using phase corrections the array can generate a trans-rat skull peak negative pressure of ~2.5 MPa (driven at 10V peak-to-peak), which is sufficient for performing microbubble-mediated blood-brain barrier permeabilization experiments at this frequency [4]. Future work will involve *in-vivo* testing of the phased array.

[1] Ellens *et al*, *Med Phys* 2015 [2] O'Reilly *et al*, *UMB* 2011 [3] Hynynen and Jolesz, *UMB* 1998
[4] McDannold *et al*, *UMB* 2006

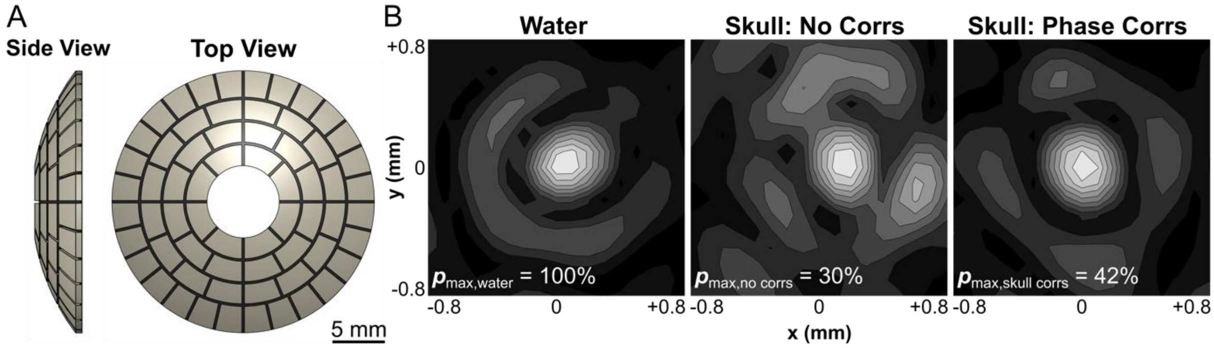

Fig.1 (A) Computer-aided design schematic of the phased array. (B) Normalized lateral acoustic field distributions at the array's natural focus in water, as well as through rat skull with and without hydrophone-assisted phase corrections. The phased array was driven at its fundamental frequency (3.3 MHz). Spatial-peak temporal-peak negative pressure values for each case are provided normalized to the water-path case. Linear countours are displayed at 10% intervals.