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PHASE ABERRATION CORRECTION IN NONLINEAR HIGH INTENSITY FOCUSED ULTRASOUND FIELDS CONTAINING SHOCK FRONTS

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OBJECTIVES High intensity focused ultrasound (HIFU) therapies are often affected by aberrations induced by soft tissue heterogeneities. This effect is especially detrimental for treatment regimes that rely on shock front formation of certain amplitude at the focus, e.g. rapid thermal ablation, shock-scattering histotripsy, and boiling histotripsy. Due to the extremely short duration of the shock front, irregular changes in the speed of sound on the way from the transducer to the focus may cause incoherence in wave front arrival time, splitting the shock front and reducing its amplitude. If the HIFU transducer is a multi-element array, introducing phase corrections at different elements of the array could mitigate the effect of aberration if a feedback mechanism is provided. In this work, an aberration correction method based on backscattering of strongly nonlinear HIFU waves at the focus is proposed, validated through hydrophone measurements, and tested in tissue-mimicking phantoms, and *ex vivo* tissue.

METHODS The HIFU transducer was a spherically focused 12-element sector array (aperture and radius of curvature 75 mm) operating at 1.5 MHz, with a central opening (Fig.1). It was integrated with either a coaxially aligned imaging probe (ATL P7-4, connected to Verasonics Ultrasound Engine) or a single-element focused high-frequency transducer (Olympus Panametrics V309). In the first series of experiments, a point scatterer – the tip of a fiber-optic probe hydrophone (FOPH-2000) - was placed at the focus of the HIFU transducer, and an aberrating layer (a flat polyvinyl alcohol phantom or a freshly harvested porcine body wall) was placed in front of the transducer. Each element of the HIFU array emitted a short (3-4 cycles), high-amplitude pulse that was detected at the focus by the hydrophone. The signal backscattered from the hydrophone tip was recorded by the imaging probe or the single-element detector. The transmit time delay for each element required to restore the shock amplitude at the focus for all-element excitation was calculated based on cross-correlation between the backscattered signals corresponding to different sector elements. In the second series of experiments, the point scatterer, i.e., the fiber tip, was replaced by a random distribution of scatterers present in an gellan gum-based tissue mimicking phantom (FDA TMM) or bovine liver tissue.

RESULTS Figure 2 shows examples of the focal waveforms recorded by the FOPH from different HIFU array elements with an aberrating layer in place. Each sector element created a highly nonlinear waveform at the focus at output levels relevant to boiling histotripsy exposures. The aberrating layer introduced time shifts between the shock fronts of the waveforms corresponding to different sector elements, ranging over 40-250 ns. This led to the decrease of the shock front amplitude when the elements were activated simultaneously. Introduction of proper time delays at the array elements resulted in restoration of the shock front to its unaberrated amplitude. The necessary time delays yielded by cross-correlation of the backscattered signals recorded by the imaging probe coincided with those yielded by direct measurements with FOPH. When the FOPH tip was replaced by tissue or TMP, the presence of higher harmonics generated by separate elements only at the focus created a local “beacon” for phase correction feedback (Figure 3) even in the absence of a single-point scatterer.

CONCLUSIONS The results of hydrophone measurements and *ex vivo* tissue experiments of this study demonstrate the feasibility of the proposed approach for aberration correction in highly nonlinear HIFU fields. This approach can be implemented using an arbitrary multi-element HIFU array, provided that its elements can be grouped in a fashion that preserves circular symmetry and sufficient focal gain of each group to produce a localized shock wave at the focus. Work supported by NIH R01GM122859, R01EB007643, and RFBR 16- 02-00653.

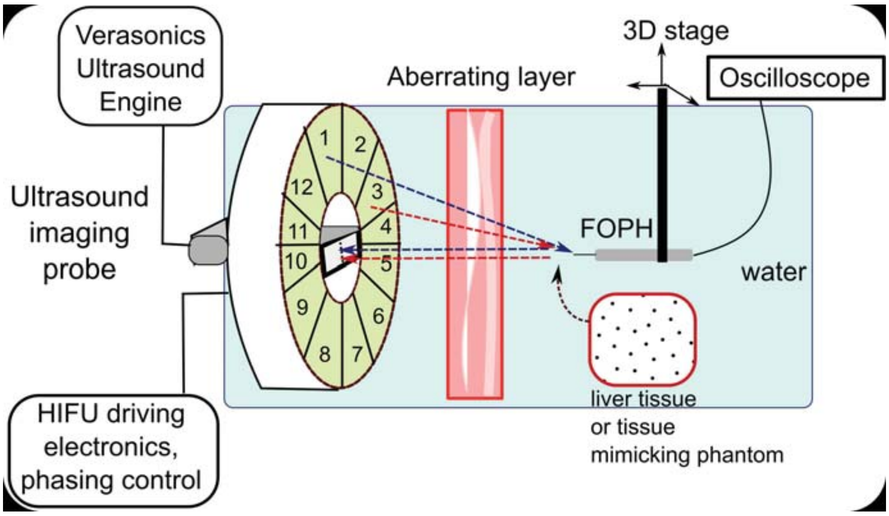

Figure 1. Schematic of the experimental setup and the idea of the method for phase aberration correction. Short, high amplitude pulses are emitted by each of the HIFU array sector elements, and shock waves are formed only at the focal area. The higher harmonics of the HIFU wave, backscattered from the focus, are detected by an imaging probe focused on receive or by a single-element focused transducer. These signals serve as feedback for phase correction approach.

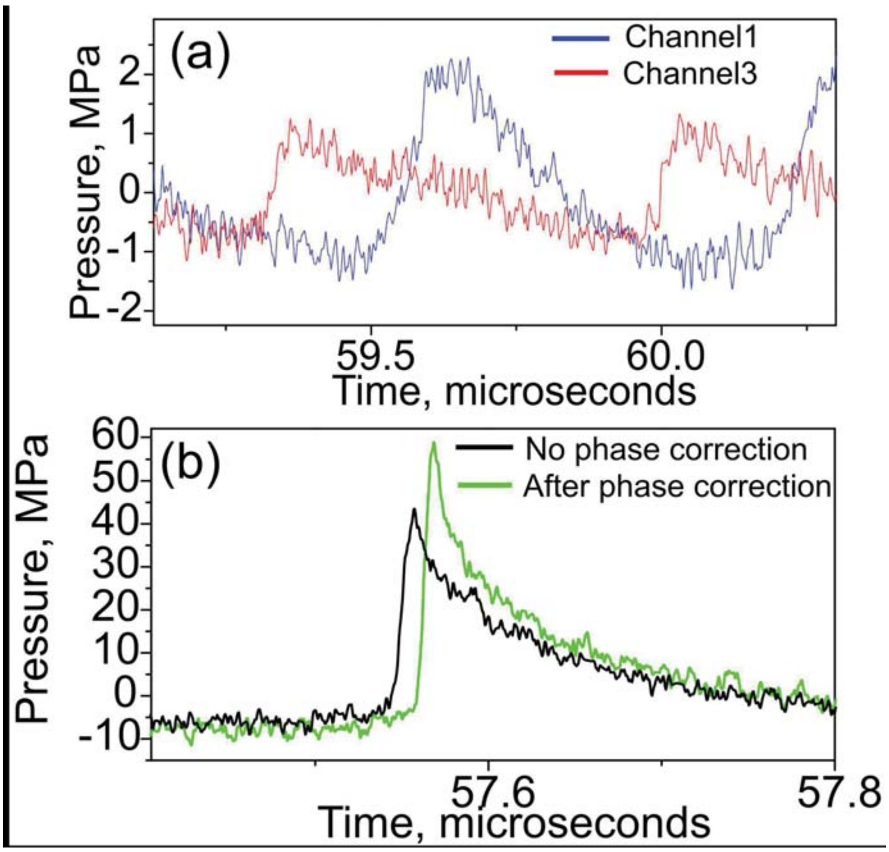

Figure 2. **(a)** Focal waveforms from two separate array elements measured by FOPH behind porcine body wall and **(b)** from all elements activated simultaneously with and without phase correction.

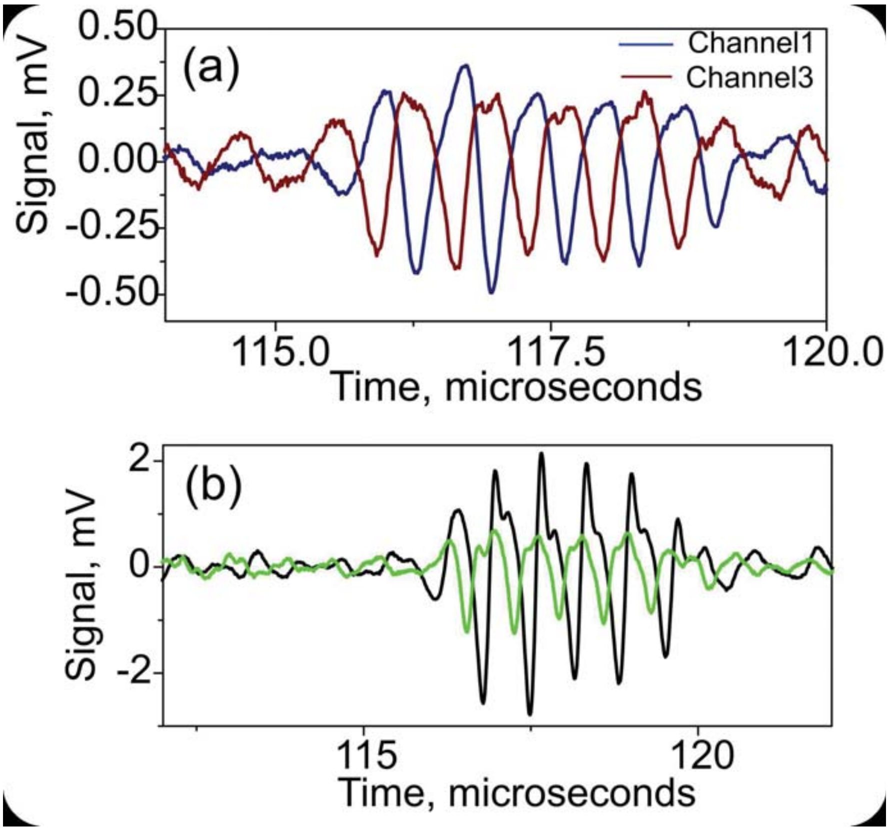

Figure 3. (a) Short HIFU pulses from individual array elements backscattered from porcine liver sample and recorded by the central element of the ultrasound imaging probe. **(b)** Recorded signals corresponding to all elements turned on simultaneously, with (black line) and without (green line) phase correction.