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A NEW ACTIVE CAVITATION MAPPING TECHNIQUE FOR PULSED HIFU APPLICATIONS – BUBBLE DOPPLER

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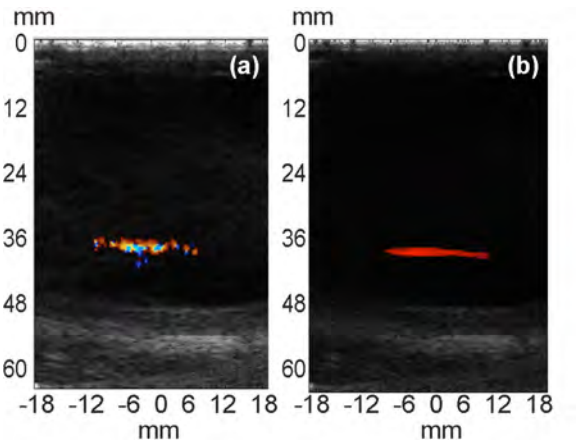
Pulsed high intensity focused ultrasound (pHIFU) therapy is a modality used in such clinical applications as drug and gene delivery, where mild mechanical disruption of tissue by bubbles is desired, and thermal effects are to be avoided. Therefore, pHIFU treatment protocols consist of short pulses, delivered at low pulse repetition frequency, to induce transient bubble activity. The current gold standard for detecting and monitoring that transient activity is passive cavitation detection (PCD), which provides minimal information on the spatial distribution of the bubbles. B-mode imaging can detect hyperecho formation, but has very limited sensitivity, especially to small-size, transient microbubbles. Here, we propose and evaluate the feasibility of a new method for pHIFU induced microbubble detection based on a fusion of two Doppler techniques, that were previously developed for imaging of ultrasound contrast agents – Doppler decorrelation and pulse inversion Doppler. This approach, that we term "bubble Doppler" can both spatially map the presence of transient bubbles and to estimate their sizes and the degree of nonlinearity. The pHIFU exposures of tissue mimicking gel phantoms, ex vivo tissues and small animals in vivo were performed using a 1 MHz focused transducer emitting 0.1-1 ms pulses at 1 – 3 kHz pulse repetition frequency with peak negative pressure amplitude within 1 – 12 MPa range. The cavitation activity was monitored using three high speed camera imaging (in the case of transparent gels), recording of the broadband emissions by a confocally aligned focused PCD transducer and the bubble Doppler method. An ultrasound imaging probe (ATL L7-4) controlled by Verasonics Ultrasound Engine (VUE) was operated in flash mode, and Doppler ensemble pulses with interchanging polarities were transmitted after each HIFU pulse. The raw signals received by the probe were post-processed to obtain maps of bubble presence from signal decorrelation between HIFU pulses, and the degree of bubble nonlinearity from pulse inversion processing across the received Doppler pulse ensemble. The bubble Doppler method proposed here was shown to provide accurate maps of pHIFU-induced bubbles, as verified by the high speed camera videos. The sensitivity of the bubble Doppler method to the mere presence of small, non-violently oscillating bubbles was found to be better than that of PCD. The degree of bubble nonlinearity estimated from pulse inversion algorithm corresponded to the level of broadband emissions recorded by the PCD. Figure 1(a) shows an image from conventional Doppler imaging and Figure 1(b) shows an example image reconstructed by the bubble Doppler method overlaid on a B-mode image in a gel phantom. The method produced maps of cavitation activity induced in the organs of small animals, in the presence of cardiac and breathing motion. A new ultrasound imaging protocol was developed to detect microbubbles induced by pHIFU using a modification of Doppler processing. This imaging modality was shown to provide the sensitivity superior to that of existing cavitation detection methods, and at the same time has high spatial resolution inherent to the conventional Doppler imaging. Work supported by RFBR and NIH (EB007643, 1K01EB015745, and R01CA154451).



(a) Conventional Color Doppler image of the distribution of bubbles induced by pHIFU in a gel phantom. (b) Bubble Doppler image reconstructed using the raw signals. Both images are overlaid on top of a Bmode image.