Contrast-Enhanced Ultrasound Imaging of Perfluorocarbon Nanodroplets Using Analysis of Echogenicity Decay from Multiple Laser Activations

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Background, Motivation and Objective

Under laser irradiation, perfluorohexane nanodroplets (PFHnDs), a theranostic ultrasound and photoacoustic (US/PA) agent, can repeatedly vaporize into gaseous bubbles and stochastically recondense to liquid droplets, creating "blinking" US signals. The repeatable activation and random recondensation of PFHnDs enables contrast-enhanced ultrasound (CEUS) imaging. However, the milliseconds-long transient echogenicity generated by optically-activated PFHnDs makes it difficult to capture their "blinking" signals, even with ultrafast US imaging. Here we exploited the US imaging schemes to manipulate the echogenicity dynamics associated with laser-activated PFHnDs to improve CEUS imaging.

Statement of Contribution/Methods

The PFHnDs consisted of a PFH core (56°C boiling point), a stabilizing lipid shell (DSPE-PEG2k and DSPC), and a dye (peak absorption near 1064 nm) to enable optical triggering. The PFHnDs were distributed in viscous gel, which filled a cylindrical inclusion within a tissue-mimicking phantom made of polyacrylamide mixed with silica particles acting as US scatters (Fig. 1a). The phantom was irradiated with 5 ns laser pulses (10 Hz PRF, 1064 nm wavelength) and visualized using ultrafast pulse-inversion imaging (CL15-7 US array transducer, Verasonics Vantage 256 system, 10 kHz pulse repetition rate). Two pulse sequences were used: traditional ultrafast US imaging with thousands of US images after a single laser pulse and burst-mode imaging, where sets of only 2 post-laser-pulse US images were used. Each burst-mode set had various delay between the laser pulse and first US frame.

Results/Discussion

After one optical activation (Fig. 1b), PFHnD-induced echogenicity in traditional ultrafast US imaging lasted for about 1 ms. In contrast, US imaging of PFHnDs using only the first US frame from each burst-mode set showed up to a two order-of-magnitude slower decay of US echogenicity (Fig. 1c). The discovery that the US imaging transmit pulse affects the decay of PFHnD-induced echogenicity has direct implications for PFHnD-based molecular CEUS imaging. An imaging sequence emphasizing slow echogenicity decay alone can identify PFHnDs if ultrafast US imaging is unavailable. Further, the combination of single laser activation and multiple laser activations can be used to enhance PFHnD detection.

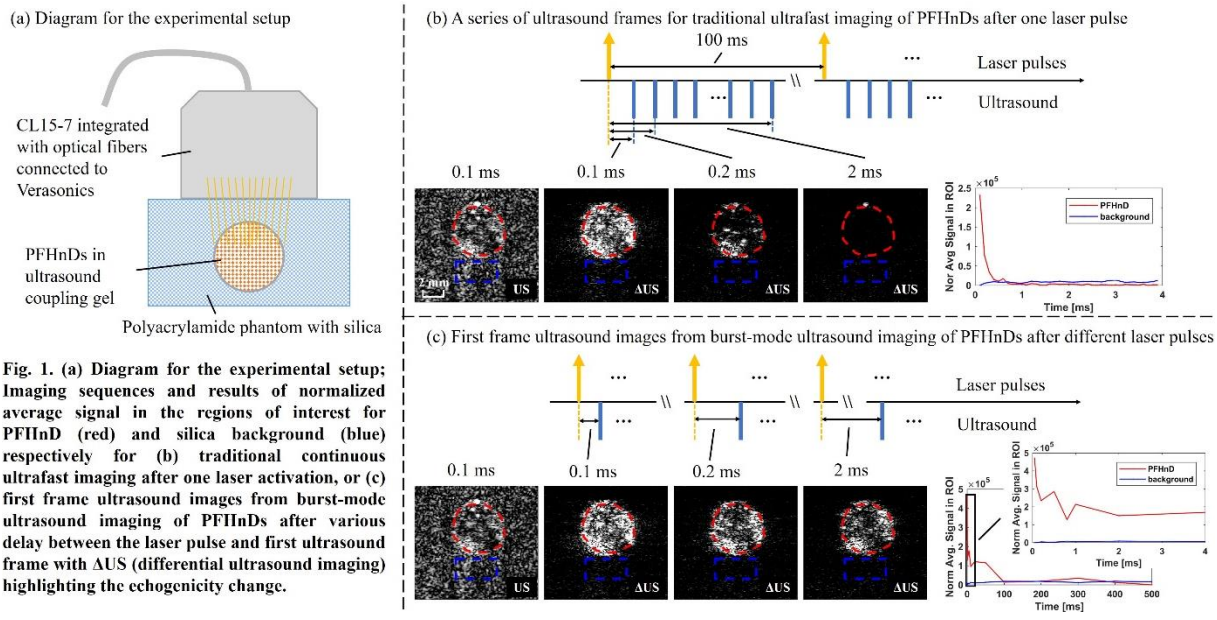

Fig. 1. (a) Diagram for the experimental setup; Imaging sequences and results of normalized average signal in the regions of interest for PFHnD (red) and silica background (blue) respectively for (b) traditional continuous ultrafast imaging after one laser activation, or (c) first frame ultrasound images from burst-mode ultrasound imaging of PFHnDs after various delay between the laser pulse and first ultrasound frame with ΔUS (differential ultrasound imaging) highlighting the echogenicity change.