

The subharmonic amplitude of SonoVue increases with hydrostatic pressure at low incident acoustic pressures

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Background, Motivation and Objective

Physiologically important pressures in the heart and aorta are currently assessed with invasive pressure catheters. The subharmonic signal from ultrasound contrast agents, however, may be exploited to estimate pressures non-invasively. The objective of this work was (i) to develop a static phantom from commercially-available components for easy replication across different laboratories, and (ii) to investigate the subharmonic response of the ultrasound contrast agent SonoVue (Bracco, Milan, Italy) at physiological pressures within the phantom.

Statement of Contribution/Methods

A phantom capable of maintaining 0–200 mmHg static pressures (PRESS-S-000 sensor, PendoTech, USA; INFCS-112B meter, Newport Electronics, Inc., USA) was developed using a cell culture cassette with Luer connections (CLINicell 25, 175 μ m membrane, Mabio International, France). SonoVue was added (0.4 μ L/mL degassed water at room temperature) and radiofrequency data were recorded on the ULtrasound Advanced Open Platform (ULA-OP; transmit frequency 5 MHz, 16-cycle pulses, pulse-inversion; LA332E Marzo 2014, bandwidth 3–7 MHz). The mean subharmonic amplitude in a 1 MHz bandwidth (2–3 MHz) was extracted at: (i) 40 scanner acoustic output levels from 1–100% at ambient pressure (0 mmHg), and (ii) 20 levels from 3.5–23.5% at 0–200 mmHg pressures.

Results/Discussion

A single growth phase between 50–250 kPa peak-to-peak acoustic pressures was observed at 0 mmHg (>1 MPa at 100%; measured in a water bath). The subharmonic amplitude of SonoVue increased with hydrostatic pressures of 50 and 100 mmHg (Figure 1)—in line with the buckling effect of microbubbles predicted by the Marmottant model. The strongest direct relationship between subharmonic amplitude and hydrostatic pressure was observed at 10.5% acoustic output (\approx 130 kPa), with 0.06 dB/mmHg sensitivity. The dampened subharmonic amplitude at 150 and 200 mmHg was accompanied with visual evidence of bubble destruction. Interestingly, the growth phase previously associated with microbubble oscillations at moderate acoustic pressures (300–700 kPa)—within which subharmonic amplitude has been shown to vary inversely with hydrostatic pressure—was not observed in this study. In conclusion, a novel operation window for assessing hydrostatic pressure non-invasively with SonoVue was identified and associated with microbubble buckling.