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Acoustic characterization of antibubbles

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Introduction

Traditional contrast agents are gas bubbles encapsulated by a shell. Their nonlinear behavior is exploited by contrast-specific ultrasound imaging to enhance the contrast-to-tissue ratio for improved analysis of the vasculature. It has been shown that adding a sufficiently large inclusion inside the gas bubble increases its nonlinear behavior [1,2]. Such bubbles with inclusions are named antibubbles. This work investigates the harmonic response of antibubbles compared to corresponding reference bubbles without a inclusion and standard Sonovue contrast agent, when insonified at frequencies of 1 and 2.25 MHz. It also presents a dynamic measurement through a vascular phantom at 3.5 MHz. With this study we aim to evaluate to what extent the nonlinear behavior of antibubbles is enhanced compared to current contrast agents.

Methods

The studied antibubbles and reference bubbles have an average size of 10 microns. Filled with air, their core is composed of ZnO, and their shell is stabilized by silica particles. They were produced in a manner similar to that described in [3].

Static measurements were conducted by positioning a gelatin cuvette with the studied contrast agents in the focal region of a piezoelectric transducer source (Fig. 1. a., Table 1) . A 20-cycle pulse was transmitted to insonify the contrast agent, and a planar piston transducer was used as a receiver in a configuration perpendicular to the source's beam propagation direction. This allowed capturing the signal generated exclusively by the contrast agents, avoiding signals from the primary beam. Several insonifying pressures were used, corresponding to mechanical indexes in the range 0.1-0.3 inside the cuvette, measured by a hydrophone (Precision Acoustics) positioned in the center of the cuvette after the acquisition. Results of 5 experiments were averaged to derive the presented harmonic responses.

Table 1. Sources and receivers used for the harmonic response measurement.

Transmit frequency, MHz	Source (diameter, focal distance, central frequency)	Planar piston receiver (diameter central frequency)
1	V302-SU-F (2.54cm, 6.35cm, 1 MHz), Olympus	C304-SU (2.54cm, 2.25 MHz), Olympus
2.25	V304-SU (2.54cm, 6.55cm, 2.25 MHz), Olympus	V307-SU (2.54cm, 5 MHz), Olympus

The dynamic measurement was performed with a Vanatge system (Versonics) equipped with a linear probe L11-4. A frequency of 3.5 MHz was transmitted, and the signal was recorded in echo-mode utilizing a combination of pulse inversion and amplitude modulation. Water was pumped through a porous vascular phantom, made of tissue mimicking beads (Fig. 1 a). Indicator dilution curves were acquired and compared for their enhancement.

Results

Antibubbles generate stronger harmonic signal compared to the corresponding contrast agents when insonified at 1 MHz and 2.25 MHz. Figure 2 shows the acquired harmonic responses for a mechanical index of 0.23. The dynamic measurement shows that the indicator dilution curves produced by antibubbles are comparable to that of Sonovue, while the reference bubbles demonstrated much lower enhancement.

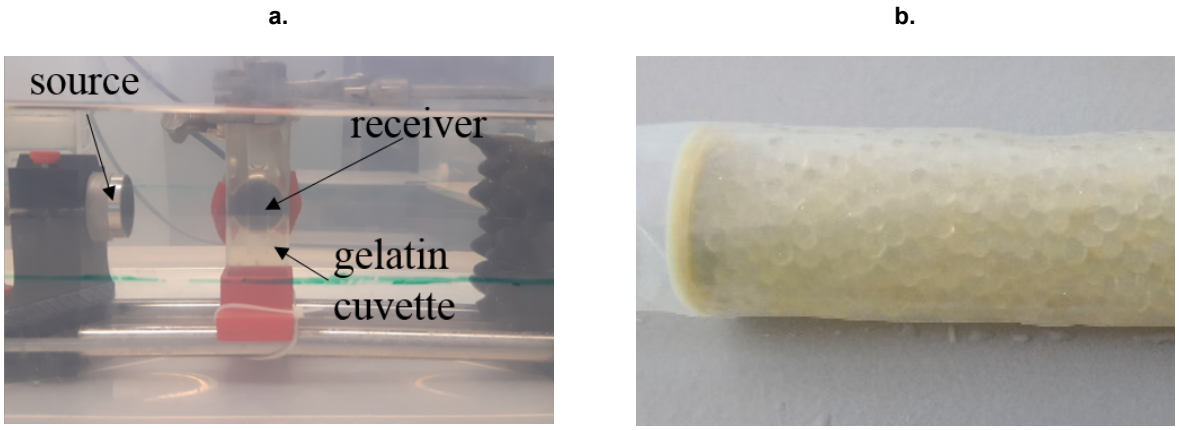

Figure 1. a, Illustration of the set up for the static measurement. b, Illustration of a part of the vascular phantom used for dynamic measurements.

Conclusions

This work demonstrates that antibubbles show strong nonlinear behavior and are therefore suitable contrast agents, especially at low frequencies. At higher frequencies, lower nonlinearity is observed. Further work involves additional experiments, adding more evidence to the current observations.

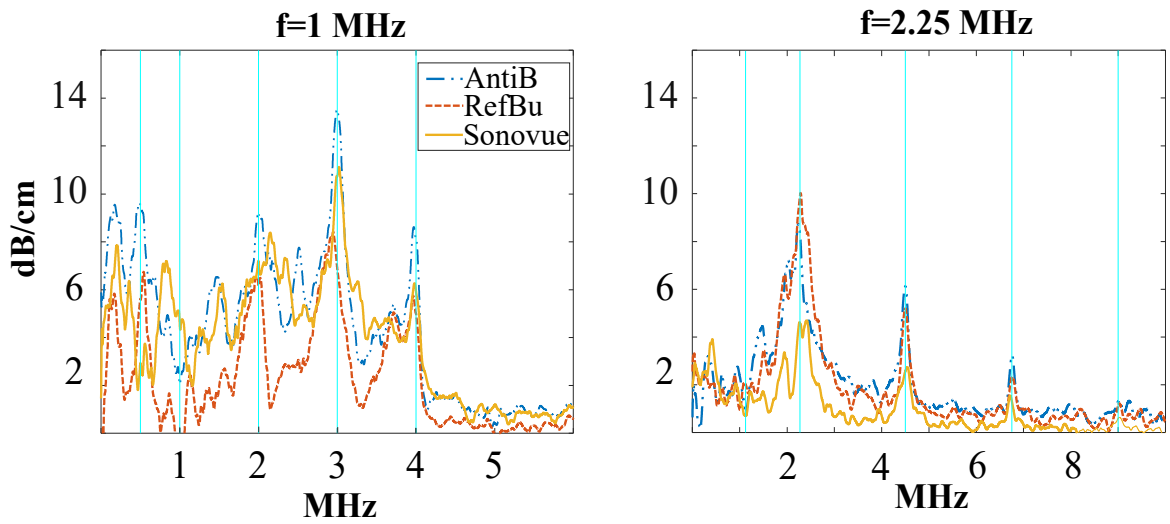

Figure 2. Acoustic response of antibubbles, reference bubbles and Sonovue when insonified at frequencies of 1 and 2.25 MHz, with mechanical index of 0.23.

References

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