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Antibubbles in an ultrasound field

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Introduction

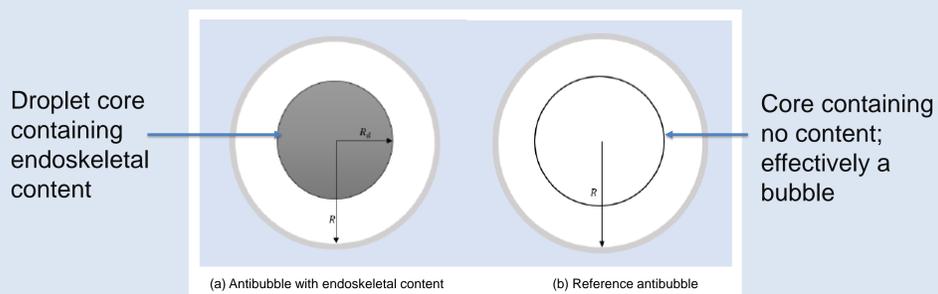
Antibubbles are gas bubbles with liquid cores. Their specific acoustic properties allow for clinical imaging of blood flow and localised drug delivery. This study investigates these properties with particular focus on their predictability and stability, with more controlled drug delivery in mind.

Objectives

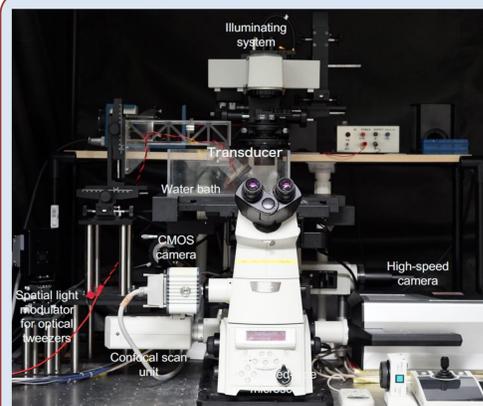
To investigate the acoustic properties of micron sized antibubbles for application in drug delivery:

- Determine whether the endoskeletal content of the droplet core of an antibubble results in predictable and stable oscillation whilst under sonication.
- Determine whether antibubbles can still be made to rupture and release their contents at a medically safe amplitude.

Antibubble structures studied



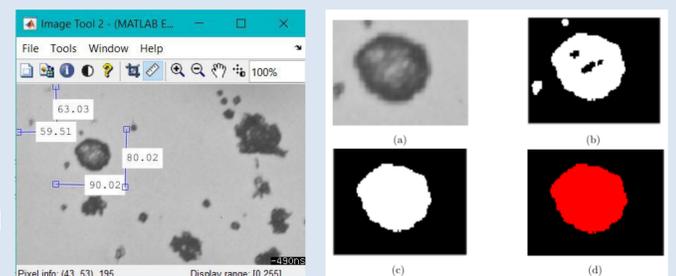
Data acquisition and processing



Optical footage of antibubbles under the influence of a single pulse, consisting of 3 cycles, of ultrasound was recorded with a high-speed camera at the University of Hokkaido. Medically safe conditions were maintained with an ultrasonic frequency of 1MHz used in all experiments, and either a peak negative pressure of 200kHz (1V amplitude) or of 1MHz (5V amplitude). The setup used to record the experiments is pictured on the left.

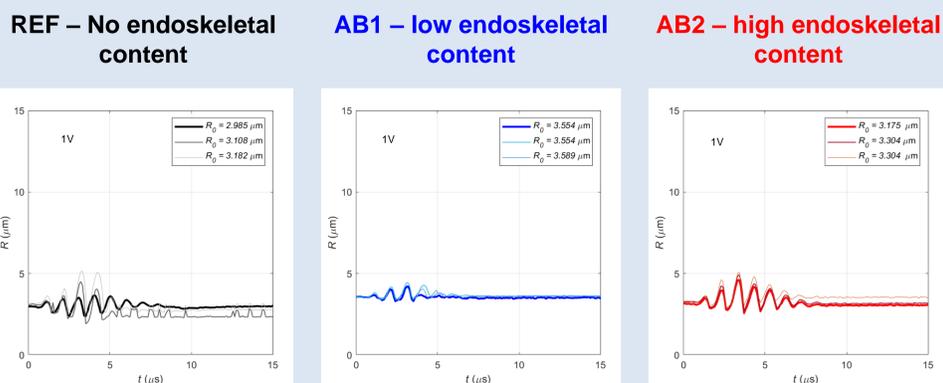
Antibubbles (AB1 & AB2) containing varying amounts of endoskeletal content as well as reference antibubbles (REF) containing no endoskeletal content were selected for analysis based on criteria such as visibility throughout sonication.

Image segmentation and processing in MATLAB was used to analyse the footage and quantify the contraction and expansion in individual antibubble radius size throughout sonication.

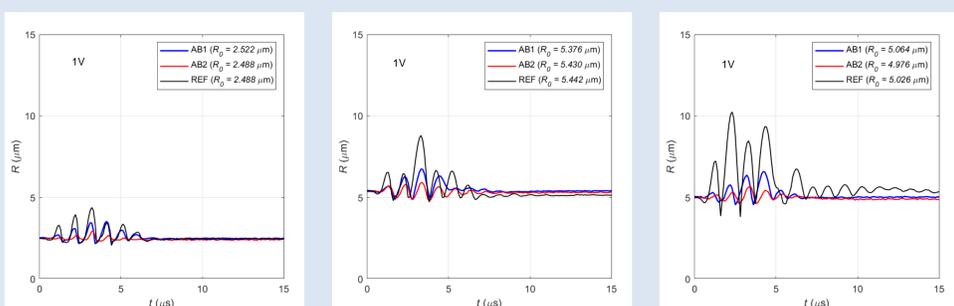


Results

Predictability (1V analysis)

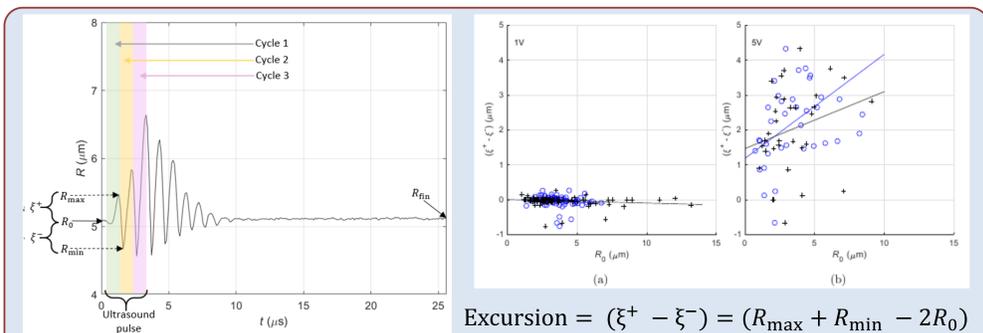


The radius(time) curves of three different antibubbles of the same type and of similar size, under sonication at an amplitude of 1V, are compared against one another for each antibubble type. It is clear that REF antibubbles are the least predictable, whilst AB2 are the most predictable.



A comparison of antibubbles of each type of similar size was done for three different initial radius size values. In each of the above cases the reference bubbles showed the highest amount of oscillation whilst AB2 showed the least, most probably owing to its greater endoskeleton content.

Stability (1V & 5V analysis)

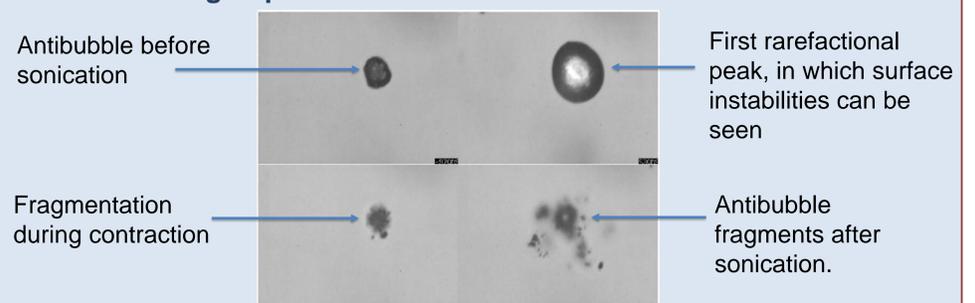


$$\text{Excursion} = (\xi^+ - \xi^-) = (R_{\max} + R_{\min} - 2R_0)$$

Excursion as a function of initial radius size is investigated in the two plots on the right. At an amplitude of 1V the REF antibubbles displayed slightly higher contraction and expansion than their AB1 counterparts. At an amplitude of 5V the REF antibubbles displayed a significantly higher contraction, but lower expansion than AB1. AB1 also displayed a far more asymmetric oscillatory response at the higher acoustic amplitude.

Fragmentation (5V)

Four high-speed frames of a sonicated AB1 antibubble.



It was found that at an amplitude of 5V all antibubbles were disrupted within three cycles.

Conclusion

At low acoustic amplitudes micron-sized antibubbles are more stable and predictable than their bubble counterparts. This is probably owing to the endoskeleton content of an antibubble. It was also found that only a single pulse of ultrasound at a higher, but still clinically safe, amplitude was enough to cause an antibubble to rupture. This indicates that at lower acoustic amplitudes antibubbles can be carefully controlled and used in diagnostics, and at higher acoustic amplitudes they can be made to rupture and release their therapeutic contents.