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Bubble size distribution in acoustic droplet vaporization via dissolution using an ultrasound wide-beam method

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ABSTRACT

Performance and efficiency of numerous cavitation enhanced applications in a wide range of areas depend on the cavitation bubble size distribution. Therefore, cavitation bubble size estimation would be beneficial for biological and industrial applications that rely on cavitation. In this study, an acoustic method using a wide beam with low pressure is proposed to acquire the time intensity curve of the dissolution process for the cavitation bubble population and then determine the bubble size distribution. Dissolution of the cavitation bubbles in saline and in phase-shift nanodroplet emulsion diluted with undegassed or degassed saline was obtained to quantify the effects of pulse duration (PD) and acoustic power (AP) or peak negative pressure (PNP) of focused ultrasound on the size distribution of induced cavitation bubbles. It was found that an increase of PD will induce large bubbles while AP had only a little effect on the mean bubble size in saline. It was also recognized that longer PD and higher PNP increases the proportions of large and small bubbles, respectively, in suspensions of phase-shift nanodroplet emulsions. Moreover, degassing of the suspension tended to bring about smaller mean bubble size than the undegassed suspension. In addition, condensation of cavitation bubble produced in diluted suspension of phase-shift nanodroplet emulsion was involved in the calculation to discuss the effect of bubble condensation in the bubble size estimation in acoustic droplet vaporization. It was shown that calculation without considering the condensation might underestimate the mean bubble size and the calculation with considering the condensation might have more influence over the size distribution of small bubbles, but less effect on that of large bubbles. Without or with considering bubble condensation, the accessible minimum bubble radius was 0.4 or 1.7 μm and the step size was 0.3 μm. This acoustic technique provides an approach to estimate the size distribution of cavitation bubble population in opaque media and might be a promising tool for applications where it is desirable to tune the ultrasound parameters to control the size distribution of cavitation bubbles.

1. Introduction

Besides nucleation, bubble growth and collapse, temperature and sonoluminescence (SL) [1], bubble size distribution is also an important area of cavitation research. The performance and efficiency of numerous cavitation enhanced applications in a wide range of areas of science, including both fundamental and applied ultrasonic and interfacial science [2,3], depend on the cavitation bubble size distribution. Predicting and controlling the ambient radii of the majority bubbles in the sonicated media within active size range, spanning from Blake-threshold to radii in the order of magnitude of the linear resonance radius as theoretically proposed by Yasui [4], is crucial to improve efficiency of the cavitation enhanced applications, since active bubbles oscillate strongly as a response to the applied acoustic field [5] and further undergo inertial collapse to produce SL or sonochemistry [6]. In other words, cavitation can be obtained at a low pressure or enhanced over time for a given acoustic pressure provided that the ambient radii of the oscillating bubbles are within the active bubble size interval. Therefore, knowing the size distribution of the bubbles that are present in the sonicated media is important.

Differing from tensile cavitation, which is driven by peak negative pressure (PNP) of a sufficient magnitude on endogenous dust or entrapped gas in crevices [7], energetic dominated cavitation [8], such as acoustic droplet vaporization (ADV) where nano or micro-droplets were activated and then vaporized to gaseous bubbles upon ultrasound irradiation even at a diagnostic ultrasound scale, has recently been applied to a variety of biomedical applications [9]. Diagnostically, the droplets have the potential to leak out of the blood vessels such as those found in tumors into the interstitial tissue [10]. Immediately after vaporization, the newly induced

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microbubbles scatter diagnostic US nonlinearly, allowing their detection with contrast specific imaging techniques, such as pulse-inversion [11]. For the therapeutic purpose, ADV have been investigated for a wide range of applications such as embolotherapy [12], therapeutic drug delivery [13] and HIFU thermal ablation [14]. It is obvious that the performance and efficiency of the subsequent imaging techniques in diagnostic application and the vascular occlusion in therapeutic application related to size distribution of the induced gas bubbles which are often much less soluble than air bubbles. Therefore, have knowledge of the produced bubble size distribution in ADV is significant for, but not limited to, aforementioned applications.

Optical techniques such as photography [15] only give information on one or a few bubbles. Lee et al. deduced the time intensity curve (TIC) by measuring average SL intensities while varying the off time between pulses for a constant pulse duration (PD) to characterize the "active" bubble size distribution [16], whereas at low power SL might not be detected. Also, optical techniques cannot be applied in opaque media [17,18]. Labouret and Frohly determined the bubble size distribution via the void rate dissipation curve in gas saturated liquid by gauging changes in electromagnetic resonant frequency of the cavity [19]. Unfortunately, the measured smallest bubble radius and the step size were limited to 19 and 4 μm due to the heavy measurement noise in the resonant electromagnetic cavity. Chen et al. estimated the size distribution of bubbles released from encapsulated ultrasound contrast agents using a tightly focused ultrasound transducer [20], but they had difficulty in tracing the octofluoropentane (OFP) bubble dissolution process due to a limited sensing region and movement of OFP during long dissolution time and could not resolve the size distribution of released OFP bubbles.

During ADV process, the nano or micro-droplets, size distribution of which can be measured prior to vaporization [11], are expected to increase approximately fivefold in diameter according to the ideal gas law [21]. Nevertheless, not all of the present droplets would be vaporized. Therefore, the produced bubble size distribution could not be simply obtained with a droplet size distribution with a fivefold increase in diameter. The majority of studies investigating the produced ADV bubble and its further growth concentrated on optical observations, which provided information on one or a few droplets/bubbles [11,21–25]. Seldom method was developed to achieve size distribution of the ADV bubble population.

In this study, we propose an acoustic method using a wide beam with low pressure to acquire the TIC of the dissolution process for the cavitation bubble population and then determine the bubble size distribution. Dissolution of the cavitation bubbles in saline and phase-shift nanodroplet emulsion diluted with undegassed (PNE-S) or degassed (PNE-DS) saline was obtained to quantify the effects of PD and PNP of focused ultrasound (FUS) on the size distribution of cavitation bubbles in both strict tensile cavitation and energetic dominated cavitation, such as ADV. In addition, condensation of cavitation bubble produced in diluted suspension of phase-shift nanodroplet emulsion was involved in the calculation to discuss the effect of vapor bubble condensation in the bubble size estimation in ADV.

2. Methods and materials

2.1. Experimental set-up

2.1.1. FUS systems

The concave and spherically focused single-element transducer A (1.2 MHz, focal width 1.6 mm, focal length 8 mm and aperture diameter 15 cm, Imasonic, Besancon, France) driven by a power amplifier (AG1017, T&G Power Conversion Inc., Rochester, NY, USA) and a double channel arbitrary waveform generator (AWG 420, Tectronix, Beaverton, OR, USA) as indicated in Fig. 1(a) or transducer B (5 MHz, focal width 1 mm, focal length 2 mm and aperture diameter 28.575 mm, Olympus NDT Inc., Waltham, MA, USA) driven by a toneburst pulser-receiver system (RPR-4000, Ritec Inc., Warwick, RI, USA) was respectively used to initiate cavitation, axis symmetrically, in undegassed saline (tensile cavitation) or PNE-S/PNE-DS (energetic dominated cavitation). Acoustic power (AP), calculated from the transmission efficiency (65%) and the electrical load power [26], was applied in experiments using transducer A instead of PNP in those using transducer B. The FUS transmission parameters were carefully selected to induce a cavitation bubble cloud of relatively low density to minimize the multiple scattering effects.

2.1.2. Wide beam ultrasound detection

A 5-MHz linear array (L14-5/38, Ultrasonix, Richmond, Canada) aligned parallel to the axis of transducer A or B, as illustrated in Fig. 1(a), depending on the sample involved was used to detect the dissolution of the cavitation bubble population in plane wave transmitting and receiving mode (Sonix DAQ, Ultrasonix, Richmond, Canada) at around 90 kPa (Fig. 1(b)), which was sufficiently weak to not yield acoustic driven diffusion yet strong enough to maintain a reasonable signal to noise ratio. Comparing with the conventional B-mode imaging, the detection of the bubble cloud in the whole field of view using a wide-beam ultrasound not only reduced delivered acoustic energy upon bubbles from multi-shots to one-shot here but also avoided non-synchronized signal acquisition due to the time-interval between sequentially scanned A-lines, which was especially important for detection of rapidly dissolving cavitation bubbles. Quadrature arrangement of the linear array to the FUS transducer was assumed to suppress the acoustic shadowing effect in the detection of the bubble cloud, which often showed the cone-shape geometry along the FUS axis due to radiation force [27]. The acoustic pressure distribution of the interrogating wide beam was measured in a degassed water tank with a needle hydrophone (0.5 mm diameter, Precision Acoustics Ltd., Dorchester, UK) when the excitation voltage of the ultrasound scanner (Sonix RP, Ultrasonix, Richmond, Canada) was 18 V, which was also applied through all the experiments in this study. The linear array was synchronized with a pulser-receiver (5800 PR, Panametrics Inc., Waltham, MA, USA) and the hydrophone output was connected to the input of the pulser-receiver, amplified and digitized at 100 MS/s with the resolution of 8 bits [26].

2.1.3. Synchronization sequence

Wide-beam detection was started 2 ms after the FUS was turned off at a PRF of 100 Hz (time synchronization illustrated in Fig. 1(c)), to ensure reverberations from the FUS would not interfere with wide-beam detection until after 2 ms, and 100 Hz was deemed to be optimal for tracking rapidly dissolving cavitation bubbles of low density (Fig. 2(a)) and not introducing acoustic driven diffusion (Fig. 2(b)).

It should be noted that the bubble dissolution in this work refers to the static dissolution of a bubble [28]. In theory, the higher the PRF of the wide beam detection was employed, the more detailed dissolution information could be obtained. Nevertheless, it is known that as for the dissolution of microbubbles in the sound field, besides the static dissolution, acoustic driven diffusion that produces a more rapid decrease in bubble diameter compared with that predicted by static dissolution also exists [29]. From Fig. 2(b), it was obvious that the dissolution rate of the microbubbles from the TIC obtained at 500 Hz was more rapidly than that obtained at 100 Hz. However, decreasing the PRF of wide beam detection to 10 Hz will leave out some dissolution information of the low