CAVITATION CLUSTER DYNAMICS IN SHOCK-WAVE LITHOTRIPSY: PART 1. FREE FIELD

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Abstract—The spatiotemporal dynamics of cavitation bubble growth and collapse in shock-wave lithotripsy in a free field was studied experimentally. The lithotripter was equipped with two independently triggerable layers of piezoceramics. The front and back layers generated positive pressure amplitudes of 30 MPa and 15 MPa, respectively, and −10 MPa negative amplitude. The time interval between the launch of the shock waves was varied from 0 and 0.1 s, covering the regimens of pulse-modification (regimen A, delay 0 to 4 µs), shock wave-cavitation cluster interaction (B, 4 µs to 64 µs) and shock wave-gas bubble interaction (C, 256 µs to 0.1 s). The time-integrated cavitation activity was most strongly influenced in regimen A and, in regimen B, the spatial distribution of bubbles was altered, whereas enhancement of cavitation activity was observed in regimen C. Quantitative measurements of the spatial- and time-integrated void fractions were obtained with a photographic and light-scattering technique. The preconditions for a reproducible experiment are explained, with the existence of two distinct types of cavitation nuclei, small particles suspended in the liquid and residuals of bubbles from prior cavitation clusters. (E-mail: c.d.ohl@tnw.utwente.nl) © 2005 World Federation for Ultrasound in Medicine & Biology.

Key Words: Shock-wave lithotripsy, Acoustic control, Cavitation, Cavitation nuclei, Particle image velocimetry.

INTRODUCTION

In extracorporeal shock-wave lithotripsy (SWL), a focused pressure wave is targeted on renal calculi from outside the patient’s body. The positive pressure wave arrives at the acoustic focus as a steepened shock front and is followed by a tensile stress wave. When the tensile part of the wave is strong enough to overcome the cavitation threshold of the liquid, vapor bubbles are nucleated and expand explosively (Leighton 1997). The bubble activity has been convincingly detected not only in vitro, but also in vivo (Huber et al. 1994; Coleman et al. 1996; Cleveland et al. 2000).

Although some researchers have addressed cavitation dynamics from lithotripters, a quantitative evaluation of the bubble distribution in space and time is seldom stated in the literature. This might be the result of the poor reproducibility of the bubble patterns. In the experiments reported in this paper, very reproducible cavitation clusters are observed when certain experimental modalities are applied. These are addressed in Appendix A.

This study is focused on the cavitation cluster dynamics in a so-called free field, where the effects of solid objects (e.g., renal stones) along the acoustic path acting as partial reflectors are not studied. They will be discussed in a second part (Arora et al. 2005). Although we limit this study to the free-field case, which is rather artificial in medical practice, the results are still valuable for comparison with new numerical modeling efforts of lithotripters, where bubble dynamics and nonlinear acoustics are solved simultaneously (Tanguay and Colomnius 2001, 2003). In addition, in shock-wave–induced drug-delivery experiments, cells in suspension are typically contained in acoustically transparent flasks. Here, we expect that the dynamics of the cavitation cluster resemble, to some extent, that of a free field.

To underline the importance of high-quality measurements of cavitation activity, it is noted that both cavitation bubble activity and the passage of the shock wave are considered to be responsible for the fragmentation of stones. However, the scientific community has not agreed on the exact contribution of the individual or the combination of both mechanisms. For a recent dis-
cussion and experimental results, see Eisenmenger (2001) and Zhu et al. (2002). Nevertheless, it is agreed that cavitation activity is causing unwanted side-effects. Cavitation bubbles might rupture a blood vessel during their explosive growth (Zhong et al. 2001). Therefore, current research in lithotripsy discusses the possibility of controlling the cavitation activity globally and locally to limit bubble expansion near the target.

A simple method to reduce cavitation activity globally uses an increased ambient pressure. Delius (1997) found that even a slightly increased static pressure greatly reduces the hemolysis of red blood cells. Sapozhnikov et al. (2002) demonstrated that this increased pressure causes a faster dissolution of gaseous remains. To prevent cavitation activity completely, the static pressures had to be raised to that of the negative pressure amplitude of the wave (Lokwandhalla et al. 2001).

A prospective local method for the in vivo control of bubble activity can be realized by using a second acoustic wave timed relative to the first wave. Research in this direction started with the demonstration of Delius and Brendel (1988) that two shocks administered in fast succession (a time interval of 67 ms between shocks) cause increased hemolysis of red blood cells. This observation was explained with a “tandem action,” so that the first pulse creates cavitation bubbles that have not dissolved when the second wave arrives. This work also emphasizes the importance of bubble-shock–wave interaction for cell damage. Shorter time-intervals between the waves are reported from Huber et al. (1999) and Loske et al. (2002), using an electromagnetic and a piezoelectric lithotripter, respectively. Huber et al. (1999) found that cavitation activity is enhanced when the second shock wave is triggered shortly after the collapse of the cavitation cluster generated from the first wave (1-ms delay between the shock waves). A second observation was the decrease of cavitation activity enhancement with increasing time intervals between the two waves. This work, again, indicates that nondissolved gaseous nuclei play an important role when shock waves are administered in rapid succession.

Xi and Zhong (2000) and Loske et al. (2002) succeeded in modifying the collapse of the cavitation cluster by applying the second wave during its growth and collapse. Interestingly, Xi and Zhong (2000) were able to increase the fragmentation efficiency of stone phantoms to 60% when the second wave was timed so that it impacted the cluster during collapse. Here, two separate shock generators were used. A modification of the reflector geometry of electrohydraulic shock-wave generators makes it possible to generate two separate waves from a single source (Zhong et al. 1997, 1999; Zhong and Zhou 2001).

The above-mentioned studies used a so-called “tandem shock wave” set-up, where the waves are traveling along the same acoustic path. In contrast, Bailey (1997) and Sokolov et al. (2001) focused two lithotripters from opposite sides into a common focal volume. With this set-up, they demonstrated enhanced cavitation activity in the focus, surrounded by bands of much decreased activity and the cavitation pattern shrunk to a smaller volume. In addition, this set-up can more efficiently fragment stones as compared with a single shock wave (Sokolov et al. 2003).

In this paper, we study the possibility of cavitation control with tandem shock waves. Therefore, we first document the experimental set-up to obtain reproducible cavitation patterns with two detection methods, stroboscopic photography and light scattering. Then, we report on experimental results of the temporal and the spatio-temporal bubble-cluster dynamics. Both were studied as a function of the time interval between the two shock waves. Our main findings are the alteration of cavitation activity and the spatial modification of the cluster pattern.

MATERIALS AND METHODS

Shock-wave generator

We took advantage of a piezoelectric transducer already equipped with two layers of piezoceramics. The design had been developed by Dreyer et al. (2000) to reduce the size of the aperture of former single-layered sources. Each of the layers consists of hundreds of hexagonal-patterned single piezoelectric elements wired in parallel. For clinical applications, the double-layer source is operated at a fixed delay that is set to match the travel-time from the back to the front layer, so that both waves superimpose at the surface of the front layer. In contrast to the clinical system, the device used in this study was furnished with circuitry that makes it possible to trigger both layers independently at an arbitrary time. The standard delay $\Delta t = 0$ refers to the clinically used setting. Unless otherwise stated, the shock-wave generator was operated at 1/60 Hz. The charging voltage was 5 kV for both front and back piezoelectric layers in all reported experiments.

Figure 1 sketches the experimental set-up viewed from the top (left) and from the side (right), with the acoustic source adapted from the commercial lithotripter (Piezolith 3000, Richard Wolf GmbH, Knittlingen, Germany). The acoustic source has an aperture of 251 mm in diameter and an opening angle of 94° with respect to its acoustic focus. The source was attached at an angle of 45° to a rectangular basin made of stainless steel. On three of the four circumferential sides, glass windows were attached. The basin was filled with approximately...
50 L of degassed (3 mg/L O₂ content, which corresponds to approximately 30% of the saturation concentration) and deionized water. During the course of the experiment, the gas saturation did not increase above 50%. The center of the curved piezoelectric transducer is equipped with an optical window through which a laser beam is aligned along the direction of the acoustic wave propagation. Two additional laser beams cross from the sides to mark the position of the acoustic focus (not shown in Fig. 1).

A glass fiber hydrophone (FOPH-500, RP Acoustics, Stuttgart, Germany) was used to measure the pressure-wave profile, especially the tensile stress waves, with high accuracy (Wurster et al. 1994). Figure 2 displays pressure recordings (average of 10 successive pulses) taken near the focus of the lithotripter. The two uppermost curves depict the pressure pulses from the back and front transducers, respectively. Below, three curves are presented for delay settings of £t = 0, £t = 2 µs and £t = 4 µs. Clearly, the profile and amplitude of pulses from front and back layers alone differ substantially, although they both have positive pressure levels of the same order (approximately 10 to 20 MPa). The pulse of the front transducer, see the second frame of Fig. 2, shows nonlinear steepening that becomes more prominent for the superimposed waves, £t = 0. The negative pressure was followed by some oscillations of substantial magnitude at the resonance frequency of the transducers. The delay setting of £t = 2 µs, as will be shown later, suppresses cavitation very effectively, whereas we see prominent cavitation activity for £t = 4 µs. For all experiments reported, the back layer of the lithotripter was triggered first.

Please consider that these measurements are only local measurements. The focal full width at half maximum (FWHM) of the positive amplitude is only about 1.5 mm and its length is around 15 mm; thus the shape of the acoustic pulse varies to a large extent within the volume investigated. A complete characterization of the pressure field (as a function of the delay setting) is hardly feasible because of the erosive nature of shock-excited cavitation bubbles and by secondary waves emitted from collapsing bubbles that obscure the main signal.

For reproducible measurements of the cavitation pattern, 60 s were waited before the experiment was repeated. This requirement is explained in Appendix A, with the time scale of dissolution of gaseous remains from the cavitation activity and the time needed to resuspend the focal volume with fresh cavitation nuclei.

To measure the spatial and the temporal evolution of the cavitation cluster, two techniques were used, stroboscopic photography and light scattering.

**Stroboscopic photography**

For the stroboscopic photography, a digital charge-coupled device (CCD) camera (Pulnix TM-6710, Alzenau, Germany) was exposed with a xenon flash (Flash-pack LS1130-1, Perkin Elmer, Freemont, CA, flash du-
ration 2 μs) at variable delays relative to the shock waves. A programmable delay generator (BNC 555, Nucleonics, Berkeley, CA, USA) controls the timing of the two shock wave generators, the frame-grabber (ME-Enable, Silicon Software, Mannheim, Germany) and the flash lamp. The delay between triggering the shock-wave generator and the flash lamp was varied in steps of 10 μs up to a maximum delay of 720 μs, to capture the cluster dynamics to their full extent. At each setting, 10 images were taken for averaging. In addition, an image taken just before the application of the shock wave served as a background image. By subtracting this background image from the image with the cavitation bubbles, most of the minor inhomogeneities in the illumination were removed. The scene was illuminated by diffuse back-illumination, which allowed for a good contrast: the bubbles were imaged as dark, filled circles. The size of the image was fixed to 51 mm × 78 mm, giving a spatial resolution of 106 μm per pixel.

The intensity distribution of the background-corrected images can be described to 0th order as a normal distributed noise process. The pixels belonging to bubbles were separated by seven standard deviations (SDs) from the maximum of the histogram and, thus, of the underlying noise process. This enables us robustly to segment the bubbles from the background. Before the segmentation with a simple threshold, a watershed transformation (Vincent and Soille 1991) was applied to separate partly overlapping bubbles. Then, the detected objects were labeled and their characteristics (e.g., their size, location, eccentricity, etc.) were measured with standard software tools from the image-processing toolbox of Matlab® (The Mathworks, Natick, MA, USA). Objects with too high eccentricity attributed as highly overlapping bubbles and areas of less than three pixels attributed as noise were rejected.

The above-stated image-processing routine will tend to underestimate the number of bubbles. To document the bias introduced, the summed areas of all detected bubbles are compared with the summed area of the thresholded picture. Typically, the former value is 30% lower than the latter.

Figure 3a displays the background-subtracted photograph for a delay of Δt = 64 μs taken at time t = 180 μs after the trigger of the lithotripter. The shock wave travels from the lower right to the upper left corner. At these delay settings, a nonuniform bubble distribution in the direction of the wave propagation is obtained. Figure 3b depicts the probability distribution of the bubble activity from 10 experimental runs with the same settings as in Fig. 3a. It was obtained after applying the aforementioned scheme of image-processing steps. The darker a spot is displayed in Fig. 3b, the higher is the averaged probability of bubble activity; for example, a maximum count of 10 (darkest value) is equivalent to the occurrence of a bubble every time the shock wave is triggered. The band of low probability is because of the compression of bubbles from the second pulse.

A second example of the cluster dynamics is presented in Fig. 4. Here, the images are rotated; thus, the direction of shock-wave propagation is from bottom to top. From the temporal sequence, see Fig. 4, the growth of the cluster starting at the bottom of the frame and its successive shrinkage become easily visible. The overall shape of the cavitation cluster is cigar-like; however, for special settings, the distribution of bubbles can greatly vary, as shown by the banded structure in Fig. 3.

Light scattering

For the light-scattering method, the intensity change of a laser beam was recorded, which was injected in the basin through the center of the piezoelectric transducer. The beam was aligned along the central axis of wave propagation and was sensed approximately 100 mm past the focus by a fast photodiode (FDS 100, Thorlabs, Newton, NJ, USA), see Fig. 1. A lens in front of the photodiode collected the beam. The lens and the photodiode were encased in a water-tight PVC holder and submerged into the basin. The collimated laser beam is 8 mm in diameter, but the aperture of the lens in front of the photodiode limited the probed volume to a cylinder of 5 mm in diameter and 300 mm in length. The advantage of the light-scattering method is its higher sensitivity to minute bubbles not being resolved within the optical resolution of the camera and its easier data analysis.

Void fraction

To quantify the bubble population, we made use of the concept of void fraction. Generally, the void fraction is defined as the percentage of volume occupied by the vapor or gas phase in a two-phase liquid. Here, the void fraction, $\beta(t)$, is calculated from the processed images as the sum over all volumes occupied by the cavitation bubbles at a given time:

$$\beta(t) = \frac{1}{NV_{\text{ref}}} \sum_{n=1}^{N} \sum_{v=1}^{V_b(t)} V_b(t),$$  \hspace{1cm} (1)

where $N$ is the number of repetitions of the experiment, $V_{\text{ref}}$ is a reference volume and $V_b$ is the volume of bubbles detected in the pictures. This method is limited to low void fractions, as long as the bubbles on the optical path of the camera (perpendicular to the major axis of the cavitation cluster) do not overlap. This condition was fulfilled in the experiments reported here, because only a few percent of the objects in the raw pictures overlapped. For absolute void fraction estimates, we took a reference volume $V_{\text{ref}} = 20 \times 20 \times 80 \text{ mm}^3$. 


The specific choice is arbitrary but was chosen here to present quantitative data. In addition, it is approximately the volume where bubble dynamics have been recorded.

In contrast, the light-scattering method does not allow for as simple an evaluation of the absolute void fraction. However, a relative void fraction can be approximated by assuming that each individual bubble acts as a geometrical light scatterer, decreasing the intensity of light by a factor proportional to its cross-sectional area, \( \pi R^2 \), where \( R \) is the bubble radius. With the additional assumption that all the light scatterers are of the same size, the signal sensed with the photodiode, \( U_{pd} \), can be related to the void fraction by:

\[
(U_0 - U_{pd}) \propto \beta(t)^{1/2},
\]

where \( U_0 \) is a constant offset voltage. Please note that the laser beam was aligned along the major axis of the cigar-shaped cavitation cluster, and the photographs were taken perpendicularly. Therefore, the light-scattering method saturates at lower overall void fractions as compared with the photographic method. To compare the effect of bubble growth for different delay settings, we introduced an integral void fraction:

\[
b = \int_{t=0}^{T} \beta(t) dt,
\]

where \( T \) is the time when bubble dynamics are observed. The integral void fraction, \( b \), can be considered as a measure of the overall bubble activity. However, it does not provide an insight on how “violent” the bubble collapse proceeds (or how much energy is stored in the bubbles), nor is it a measure of bioeffects. Yet, \( b \) is a convenient measure combining the duration and volume occupied with bubbles. It allows one to compare, with simple numerical values, the effects of different delays between the two shock waves on bubble growth/inhibition.

**EXPERIMENTAL RESULTS**

**Temporal cavitation cluster dynamics**

Figure 5 depicts the experimentally determined void fractions, \( \beta(t) \), for different delays as solid lines (photographic method) and dashed dotted lines (light-scattering method). For both data sets, 10 individual runs were averaged.

Fig. 4. Averaged and image-processed pictures of bubble cluster for superimposing waves from front and back shock-wave generators (\( \Delta t = 0 \)) at various instants of time. Acoustic focus is located at \( x = 19 \text{ mm} \) and \( y = 45 \text{ mm} \).
and the cluster collapses approximately around 320 μs thereafter, a few after-bounces are visible. After 420 s, the maximum void fraction decreases to 0.41% and the life-time drops by a factor of one half when compared to the maximum void fraction at 160 μs.

***Photographic method***

Let us first concentrate on the photographically-determined void fraction (solid lines in Fig. 5). In the upper graph of Fig. 5, both shock-wave generators are triggered at the standard setting so that both waves overlap at the surface of the front transducers, Δτ = 0. The void fraction reached a maximum of 0.58% at 160 μs and the cluster collapses approximately around 320 μs; thereafter, a few after-bounces are visible. After 420 μs, no bubble dynamics are observable in the photographs, indicating that the bubbles have shrunk to diameters less than the resolution of the photographic and image-processing system.

The strong influence on the cavitation cluster dynamics as a function of the delay becomes evident even for a relatively short delay of Δτ = 4 μs. For this delay, the maximum void fraction decreases to 0.41% and the life-time drops by a factor of one half when compared to Δτ = 0 μs. Because the delay of Δτ = 4 μs is comparable with the duration of the negative pressure cycle of the first pulse, we expect that, for this setting, the cavitation bubbles are only slightly expanded by the first pulses and are then collapsed by the compression phase of the second pulse. This expansion and collapse is not resolved in Fig. 5, because a spatial averaging was carried out. Because the tensile stress of the second pulse alone was smaller than the one of the perfectly superimposing waves, Δτ = 0, the overall cavitation activity is reduced.

It is interesting to note, that Zhong and Zhou (2001) used a delay of 4 μs to suppress bubble activity in order to decrease vascular damage.

The collapse times for delays of 16 μs and 64 μs are hardly influenced, whereas we find, for the longer delay, a reduction of the maximum void fraction from 0.25% to 0.19% for Δτ = 16 μs and Δτ = 64 μs, respectively.

This finding can be attributed to the forced collapse and/or inhibition of growth of the cavitation cluster by the compressive phase of the second wave. During its passage, expanding bubbles might be either hindered in growth or forced to collapse, depending on the velocity and size of the expanding bubbles. The reader might expect that a local minimum of the void fraction should be resolved for a delay of Δτ = 64 μs; here, we argue its absence by the fact that it takes around 50 μs for the pressure pulse to pass: during this time, the expanding cluster is progressively compressed and expanded in the subsequent tensile stress wave. This complex dynamic, which becomes revealed in detail later, cannot be resolved without looking at the spatially resolved void fraction.

For the longest delay time given in Fig. 5, Δτ = 256 μs, both pulses were separated in time for long enough that the cavitation cluster generated by the first pulse had already collapsed when the second pulse arrived. The cavitation pattern generated by the first pulse only is revealed in the time interval from 20 μs to 120 μs. During this time, a comparably low void fraction of 0.08% was found. Interestingly, the second wave caused a highly pronounced bubble activity, starting at 260 μs and lasting for 460 μs, being even higher than the void fractions of the superimposed pulse (Δτ = 0 μs) of β = 0.73%. Clearly, the bubbles generated by the first pulse had not dissolved and acted as very effective cavitation inception sites for the second acoustic wave.

***Light-scattering method***

The dashed-dotted lines in Fig. 5 present the results obtained with the light-scattering method, where again 10 consecutive experiments are averaged with a pause of 60 s between shots. Overall, the timing of the onset of growth and the collapse agree with the photographic method (solid lines). Still, differences in the shape of the two curves prevail. Most prominently, we find a saturation of the void fraction signal. This can be accounted for with the direction of sensing the bubble cluster; the laser beam shines along the major axis of the cavitation cluster where the strongest bubble activity is found. Therefore, even at relatively low bubble densities, full obstruction of the light beam can be reached, leading to a saturation of the voltage across the photodiode, $U_{ph}$.

A second difference between both signals is the
higher sensitivity at low void fractions (e.g., the photodiode detects a signal 70 μs longer than the camera for delays of Δt = 4 μs and Δt = 16 μs after the bubble cluster appears to have collapsed at a time of 210 μs). A simple explanation for this difference is the limited spatial resolution of the camera, as stated before.

The void fraction determined with the light-scattering method, as derived from eqn (2), is only known up to a constant factor. This factor is derived by demanding that the integral void fraction b is equal for both methods. Therefore, b is measured for a delay of Δt = 64 μs, where no saturation of the light-scattering method occurs. The good agreement of both methods is shown for the first expansion of the cluster for a delay of Δt = 256 μs in Fig. 5, validating this approach within the limits mentioned above.

In summary, both methods to determine the void fraction show similar results, although they probe the fluid volume from different directions. Differences are obtained when the saturation of the scattering method is reached (around η = 0.1%) and bubbles are present that are not resolved with the camera (bubbles with 200 μm and less in diameter). The light-scattering method has the advantage of measuring the overall cluster dynamics much faster, with greatly reduced data-processing time and is sensitive to much smaller bubbles. Still, the photographic method is important to account for the limitations of the light-scattering method.

Integral void fraction

Now, after discussing the drawbacks and benefits of the light-scattering method, we investigate the void fraction as a function of the delay Δt over a longer range. Figure 6 depicts the dependence of the integral void fraction b(Δt) normalized to the value of superposition, b₀ = b(Δt = 0). Here, the values obtained with the light-scattering method are attributed with solid lines and the SDs from 10 experimental runs are given as error bars. Three temporal intervals of Δt can be distinguished, and are indicated in Fig. 6 by letters A, B and C. The time scales of the individual regions correspond to those of the acoustic waves (A), the lifetime of the cluster from the back layer of the shock-wave generator (B) and the dissolution time of microscopic gaseous bubbles (C).

For delays in the order of a few microseconds, regimen A, both acoustic waves overlap so that the tensile stress causing the inception of the cavitation is modified. The bubble cluster expanded and collapsed, with no further interaction with the second acoustic wave. In regimen A, spanning a temporal interval of the duration of the individual pulse widths, we find the strongest decrease of integral void fraction. Here, b/bo dropped by two orders of magnitude from 100% for zero delay to less than 1% at a delay of Δt = 2 μs. This result can be qualitatively explained by the fact that, at these settings, the tensile stress is most effectively diminished by superposition of both the waves. For a delay of Δt = 4 μs, the integral void fraction increased back to 50% of b(Δt = 0). In region A, small changes in the delay led to considerable variation in the integral void fraction.

In contrast, in region B, the integral void fraction was only mildly affected by the delay. Even though the second wave caused a forced collapse of the cavitation cluster, its timing relative to the first wave did not change the temporal integrated bubble activity. A more detailed picture will be presented later.

Region C shows a clear tendency: the integral void fraction decreased with increasing delay. And, interestingly, for delay times between Δt = 512 μs and Δt = 10 ms, the void fraction b was even larger than b₀; thus, an increased cluster activity is observed compared with the case of perfectly superimposing waves. Most of the signal b/bo can be attributed to the growth of the second cavitation cluster; see the bottom row of Fig. 5. During the first cluster expansion, noncondensable gas was collected through the bubble walls. For an estimate of this amount of gas collected during the rapid bubble dynamics, a simplified model is presented in Appendix B. Inserting the maximum bubble radius Rmax = 0.5 mm and the bubble lifetime τ = 100 μs into this model, we obtained an equivalent bubble radius of R₀ = 12 μm. The bubbles then slowly dissolved under the action of the surface tension pressure. In our experiments, the tensile stress wave after the second shock wave expanded these gaseous bubbles. For longer delays, Δt > 512 μs, between the first and the second shock waves, more gaseous cavities have shrunk to sizes smaller than...
the critical radius, the so-called Blake threshold (Walton and Reynolds 1984), which is here approximately 20 nm.

To give an estimate of the dissolution time of the gaseous bubbles, the diffusion equation was numerically solved (see equation 16 in Sapozhnikov et al. 2002), and is plotted in Fig. 6 as a dashed line. For example, for the experimental level of gas content in the liquid, bubbles of 12 μm dissolved below the critical radius within a time interval of 1.7 s; smaller bubbles did so much earlier. As more and larger bubbles dissolved, fewer cavitation nuclei remained; thus, the integral void fraction dropped for longer delays (see solid line in Fig. 6 in regimen C).

For \( t = 250 \, \mu s \) and \( t = 500 \, \mu s \), the slight increase of \( b/b_0 \) can be considered as a transition regimen between regimen B and regimen C. In regimen B, the second wave was scattered by already present bubbles; hence, they affected shock-wave passage (shock-wave-bubble interaction). As the gap between the two pulses, \( \Delta t \), was increased, more and more bubbles had dissolved, their affect on the wave reduced. Presumably, the presence of bubbles reduced the geometrical focusing of the wave, thus reducing the positive and negative amplitudes of the wave.

Spatiotemporal dynamics

We now turn back to the evaluation of the images taken from the cavitation bubbles. Here, the cylindrical symmetry of the cavitation cluster, see Fig. 3, permits a visualization of the spatiotemporal bubble distribution in a single plot. To do so, the void fraction is now integrated along slices oriented perpendicular to the wave propagation. The temporal evolution of the spatial void fraction is plotted in grey-scales as a function of time. For quantifying the void fraction, we set a reference volume of 20 mm \( \times \) 20 mm \( \times \) 0.1 mm, similar to the reference volume used for overall void fraction, but now the integration is done in slices of one pixel, 0.1 mm thickness, along the direction of wave propagation.

Figure 7 depicts a plot of the spatiotemporal bubble distributions obtained thereby for different delays \( \Delta t \). In addition, the positions of the shock fronts are indicated with lines, assuming a sound speed of 1500 m/s. We start with a discussion of the standard case of \( \Delta t = 0 \, \mu s \) in Fig. 7. Here, cavitation bubbles are detected within 10 \( \mu s \) after the shock front passage. The highest bubble concentrations are found in the center of the cluster, where the bubbles persist for the longest time. The cluster collapses around \( t = 300 \, \mu s \) and reappears. At a time \( t = 420 \, \mu s \) cavitation activity is no longer detectable. Although we find the formation of bubbles immediately behind the shock front, the life-time of bubbles at positions below 10 mm is only a few microseconds.

The second frame in Fig. 7 depicts the void fraction dynamics for the short delay of \( \Delta t = 4 \, \mu s \), with greatly altered bubble dynamics: the center of the cluster shifts approximately 8 mm toward the transducer, the maximum void fractions are reduced and the cluster collapses at \( t = 200 \, \mu s \); thus, \( t = 100 \, \mu s \) earlier than with the standard case.

For a delay of \( \Delta t = 16 \, \mu s \), the maximum achievable void fraction reduces further and the center of the cluster moves closer to the transducer. Please note that hardly any cavitation bubbles are nucleated above a position of 60 mm. In contrast, for a longer delay of \( \Delta t = 64 \, \mu s \), bubble activity is found up to 75 mm. At this timing, the cluster generated by the first pulse is already shrinking. We find, after the passage of the second wave, a spatially-patterned cluster with three distinct regions separated by bands of lower bubble activity. Especially in-
triguing in this observation is the fact that cavitation activity is observed at farther distances from the transducer than in the standard case, Δt = 0 μs; see the small upper cluster between 160 μs and 200 μs and between position 65 mm and 75 mm. A possible explanation could be that the first pulse creates small cavitation bubbles that are below the optical resolution limit. Still, they have gained noncondensable gas by rectified diffusion during their growth; later, they are only dissolving slowly and are activated when the second wave passages. A second hypothesis could be that the pressure wave is altered by the presence of the cavitation cluster from the first pulse, possibly refocusing the tensile stress of the second wave.

The bottom frame in Fig. 7, Δt = 256 μs, illustrates again the important contribution of gaseous cavitation nuclei on the cluster dynamics. In addition, it shows the cluster dynamics generated with the first shock-wave generator only. Here, a relatively short-lived and sparse cavitation cluster is observed. Even though not resolved with the camera, small bubbles remain, because of a net gain caused by the radial bubble oscillation. At the instant the second wave interacts with these bubbles (presumably much below 100 μm in radius), a very pronounced cluster is observed, which lasts for approximately 420 μs. This cluster resembles in space and time the cluster in the standard case, although, for Δt = 0 μs, higher void fractions are found in the core. In addition, we find more homogeneous void fraction distribution for a delay of Δt = 256 μs.

Figure 8 displays the radius distributions vs. time for the five delays. Therefore, at each time step, a histogram of the bubble radius was computed and plotted vertically. The grey-scale bar on the right of each frame in Fig. 8 shows the corresponding number of bubbles. Again, 10 experiments have been evaluated for each time step. In general, we find bubbles in the size range from 0.1 mm to 1.1 mm; most bubbles possess a radius below 0.4 mm. For delays of 16 μs and 64 μs, the maximum achievable bubble sizes are greatly reduced to 0.8 mm and 0.65 mm, as compared with the standard case. The largest bubbles are found for Δt = 256 μs, with bubbles being even larger than for Δt = 0 μs.

It is interesting to compare the measured time of the first cluster collapse with twice the Rayleigh collapse time:

\[ T_{2c} = 1.83R_{\text{max}} \sqrt{\frac{\rho}{P_0}}, \]  

(4)

where \( R_{\text{max}} \) is the maximum bubble radius in the cluster, \( \rho \) is the liquid density and \( P_0 \) is the pressure far from the bubbles. This equation is only valid for a single bubble in an infinite medium. The duration to the first collapse for the standard case is 300 μs, which would correspond to a maximum bubble radius of \( R_{\text{max}} = 1.6 \) mm. The largest bubbles measured in the experiment possessed a radius of 1.1 mm (see Fig. 8, top). Thus, they are considerably smaller than predicted; or, in other words, the measured collapse time is 45% longer than that which would be predicted by eqn (4). A similar observation of the prolongation of the bubble life-time has been reported by Sokolov et al. (2001) and references cited within. Tanguay and Colonius (2003) attribute this prolongation in collapse time to bubble-bubble interaction. The argument of bubble-bubble interaction is supported for our delay setting of Δt = 256 μs. The first cluster expansion leads to seven times lower bubble densities than with the standard case; thus, bubble-bubble interaction is reduced. In this case, the double Rayleigh collapse time, eqn (4), and the bubble life-time (for the first expansion) agree very well, using the measured maximum bubble radii of 0.5 mm (\( T_{2c} = 100 \mu s \)). However, for the second expansion with much higher bubble densities, we find again a prolongation of bubble life-time similar to the above-mentioned standard case (Δt = 0 μs) of 45%.

Fig. 8. Histogram of bubble radius distribution in cavitation clusters as a function of time for indicated delays.
DISCUSSION AND CONCLUSIONS

In this paper, we have demonstrated an experimental method to study and analyze the bubble cluster dynamics after shock-wave passage in a free liquid, with specific interest in the modification of the cluster pattern by the passage of a second shock wave.

We found that three regimens of cavitation modification exist. For delays in the range of the pressure wave duration, $\Delta t$ between 0 $\mu$s and 4 $\mu$s, the influence of acoustic driving on the cluster pattern is revealed. Here, the formation of cavitation can be influenced in large ranges by relatively small changes of the delay. For longer delays, the second pulse interacts with already expanding cavitation bubbles. For this timing range, a modification of the spatial shape of the cavitation cluster is found. For even longer delays, the cavitation cluster generated by the first pulse has already collapsed. When the second pulse propagates, the slowly-dissolving remains of the cavitation bubbles cause enhanced cavitation inception, leading to longer-lasting and larger bubbles. The observation of these three accessible regimens can be considered as general features of all tandem shock-wave generators. Regimen A has been used to inhibit bubble growth (Zhong and Zhou 2001) and regimen B has been explored by Bailey (1997); Huber et al. (1999); Xi and Zhong (2000), and Loske et al. (2002). Huber et al. (1999) also studied regimen C; however, they used a rather high pulse-repetition frequency.

The observations show that high-quality void fraction measurements are feasible with the methods reported here. The next logical step would be to correlate the cluster dynamics with biologic and/or medical parameters in free-field applications. For example, one can obtain the yield of drug delivery to cells and correlate it with measurements of the void fraction. Here, the integral void fraction, $b$, might suffice, but probably a more careful evaluation of the spatiotemporal cavitation activity will be necessary. A study like this might support the importance of gas-bubble–shock-wave interaction, as proposed by Delius and Brendel (1988)

A second very active research field that might benefit from these investigations is lithotripsy. The results found in this study suggest that cavitation can be modified spatially and minimized by adjusting the relative delay of the shock waves. Although the presence of a stone that is acting as an acoustic impedance change affects the overall cavitation pattern, we expect, again, a strong influence of the delay on the cluster pattern. Investigations of its influence on fragmentation and a possible beneficial exploitation are currently underway.

A third topic of interest is numerical simulations on focused nonlinear wave propagations (e.g., Averkiou and Cleveland 1999; Ginter et al. 2002), where reasonable agreement between experimentally-measured pressure distributions have been obtained. Still, only very limited numerical work is found in the literature dealing with a combined modeling of finite-amplitude waves and bubble clusters in lithotripsy (Tanguay and Colonius 2001, 2003; Arora et al. 2004a). It is to be hoped that this paper might demonstrate unique features of the cluster dynamics that can be used as test cases.

The technique to quantify cavitation activity is limited to moderate values of the void fraction. At much higher bubble concentrations, the number of overlapping bubbles does not allow for automated bubble segmentation and only qualitative measurements seem feasible. In clinical practice, positive pressure levels of 50 MPa and above are used. This level was only reached in the present measurements for the $\Delta t = 0$ case.

Coming back to the inception of cavitation bubbles, the key to obtain reproducible bubble distributions is to account for the “history” of the liquid. On the one hand, prior shock waves diminish the number of cavitation sites of particles in the focal volume. On the other hand, the gaseous remains of the cavitation bubbles act as nucleation sides until they dissolve.

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REFERENCES


APPENDIX A

Reproducibility of the cavitation cluster shapes

In the experiments conducted, the cavitation bubbles nucleate in a statistical manner (Ohl 2002). The positions where cavitation bubbles emerge vary but, for fixed experimental settings, the overall shape of the cluster is similar from shot-to-shot. We found that this reproducibility of the cluster shape was only high when either a sufficient time interval was given between two experimental runs (e.g., for our experimental set-up we needed to wait for more than 30 s), or until some stirring fluid in the liquid was applied.

Particle-attributed cavitation nuclei

Figure 9 documents this observation: the three columns a) to c) display the cavitation activity for three different experimental conditions. In Fig. 9a, a weak flow is excited from a fully submerged pump of a thermostat (EC-basis, Julabo, Seelbach, Germany) and the shock-wave generator is operated at 1 Hz. The rows in column a) of Fig. 9 depict the cavitation cluster from the second, third, fourth and tenth shots taken at 170 μs after shock-wave excitation. By comparing the individual rows, we find similar number and size range of the bubbles for every shot. Hence, reproducible conditions are reached. In column b) of Fig. 9, the bubbles are nucleated again at 1 Hz but with the pump switched off. Although the second shot shows some similarities to that of column a), far fewer bubbles are nucleated in the fourth shot for these settings. When the experiment was operated at a lower repetition rate (e.g., with a time interval of 60 s between shots), as in Fig. 9c), we again observe a reproducible pattern of cavitation activity. The first shot is omitted in Fig. 9, because the pattern of cavitation depends on the waiting time between the experiments.

A plausible explanation for this observation is that particles in the liquid are serving as one-time triggerable cavitation nuclei (Arora et al. 2004a, 2004b); for a general discussion on denucleation and references, see, for example, Leighton (1997), pages 75 and following. The particles enable by some means cavitation inception; for example, by preventing the dissolution of attached/entrapped gas pockets. Thus, the individual inhomogeneity/particle can be considered to be “used up” after activation by the passage of the tensile stress wave, unless the amplitude of the subsequent tensile stress is not increased. To allow for inception of cavitation with the next wave, new nuclei have to be transported into the focal volume of the shock-wave generator. This transport can be initiated either with the flow induced during the collapse of the cavitation cluster (Junge et al. 2003), with the demonstrated additional stirring flow, column a) of Fig. 9, or with some background flow. In all cases, we supposed that the waiting time for a reproducible pattern is correlated with the time needed for the transport of fresh cavitation nuclei into the focal volume.

To underline the hypothesis that the cavitation bubbles induce a stirring flow, measurements of the flow pattern taken after the bubble collapse have been conducted. Particle image velocimetry (PIV) measurements were done in a cross-sectional plane through the focus of the...
shock-wave generator and perpendicular to the horizontal; for the
gallery, see the side view in Fig. 1. Details on the experimental
set-up and data analysis are covered in Arora and Ohl (2005). In short,
a sensitive camera (High Speed Star 3, 512 × 512 pixels², LaVision,
Göttingen, Germany) recorded the particle displacements (Sphericial
110P8 hollow glass spheres with 10²m mean diameter, Potters Indus-
tries, Valley Forge, PA, USA) in field of view of 21.7 × 21.7 mm²,
with up to 600 frames/s. The particles were illuminated with a light
sheet of approximately 1-mm thickness generated with a dual-cavity
frequency-doubled Nd:YAG laser (LaVision), for an exposure time of
10 ns. The particle displacements were cross-correlated (interrogation
window 8 × 8 pixels²) and analyzed with the software package DaVis
6 Pro (LaVision). All measurements were conducted shortly after the
first bubble cluster collapse (1.9 ms after triggering the lithotripter);
prior frames with bubbles present were overexposed because of spec-
ular reflections.

Figure 10a presents an overview of the temporal development of
the maximum velocity, \( u \), obtained in a square area of 21.4 × 21.4
mm² at the focus. At first, \( u \) increases within 0.2 s up to \( \approx 50 \) mm/s.
Then, it decreases on a slower time scale of approximately 1 s to 10
mm/s, approaching the background velocity measured in the absence of
cavitation activity of \( \approx 5 \) mm/s.

The maximum flow velocities are found near the cores of vorti-
ces. Figure 10b shows a vector-plot of the instantaneous flow field 150
ms after cavitation activity. The scale arrow in Fig. 10b, top, depicts a
value of 50 mm/s. In addition, the magnitude of the vorticity (\( \omega = \nabla \times \vec{u} \)) is shown in color, where red denotes clockwise and blue, anti-
clockwise, rotation.

Figure 10b demonstrates a flow pattern with counter-rotating vortexes, which support the hypothesis that a mixing flow introduces fresh cavitation nuclei into the focal area. The flow pattern spreads out slowly over time (not shown here). Arora and Ohl (2005) discuss this phenomenon in more detail. Here, we only briefly mention that the size of the bubble cluster and, thus, the energy setting of the shock-wave generator influences the flow field and, thus, its mixing properties to a large extent.

Gaseous cavitation nuclei

When the shock waves are applied in rapid succession, some
gaseous remains might not have dissolved and will act as nuclei for the
following tensile wave. In addition, they can attenuate and scatter the
acoustic wave; see, for example van Wijngaarden (1972); Mørch (1989);
Watanabe and Prosperetti (1994), thus influencing the shape of the new
cluster. The size of these microbubbles is determined by the bubble
dynamics leading to a net gain of gas and, in addition, from the fusion
and fission of the bubbles during expansion and collapse, respectively.
A modeling effort to calculate the gas uptake of lithotripter-generated
cavitation bubbles is given in Appendix B.

We want to emphasize that, for reproducibility of the cavitation
pattern, both time scales, the dissolution time scale of gaseous micro-
bubbles and the time scale for resuspension of the focal volume with
fresh particles have to be accounted for.

**APPENDIX B**

**Model for gas diffusion**

Numerical schemes to calculate the amount of gas uptake during
transient growth of a cavitation bubble have been presented by Church
(1989) and Sapozhnikov et al. (2002). There, the bubble dynamics is
solved with the Gilmore model and the gas uptake is simultaneously
calculated with a zero-order solution of the diffusion equation in a
spherical coordinate system (Eller and Flynn 1965). Yet, the Gilmore
model does not take into account the prolongation of the bubble
expansion phase because of bubble-bubble interaction. As pointed out
by Tanguay and Colonius (2003), the duration of the expansion phase
of the bubble is considerably underestimated with a single-bubble
model. This effect is also documented in our experiments.

With the elegant approximation of the gas flux into an expanding
bubble from Akhatov et al. (2001) we can estimate the gas flux from the
measured maximum bubble size and bubble lifetime. The model as-
sumes an exponential profile of the gas concentration in the diffusion
boundary layer with a variable thickness. They obtained the following
ordinary differential equation for the gas uptake:

\[
\frac{dC}{dt} = -kC
\]
\[ \frac{d}{dt}[m_g - m_g(t = 0)]^2 = 32\pi^2 D R(t) (c_a(t) - c(t))^2, \]  

(B1)

where \( m_g \) and \( m_g(t = 0) \) are the instantaneous and initial masses of gas in the bubble, respectively. The diffusion constant is \( D = 2.42 \times 10^{-9} \text{ m}^2/\text{s} \) for water, \( c_a \) is the gas concentration far from the bubble and \( c(t) \) is gas concentration in the bubble. Both are expressed in units of kg/m\(^3\) (e.g., air-saturated water has a concentration of \( c_{\text{sat}} = 0.024 \text{ kg/m}^3 \) at 293 K). For explosively expanding bubbles, the gas pressure in the bubble is very low; thus, \( c = c(t) \approx c_a \) and the initial mass \( m_g(t = 0) \) can be neglected.

Now, we approximate the radial bubble dynamics with a parabola:

\[ R(t) = 4R_{\text{max}} \left( 1 - \frac{t}{\tau} \right)^{1/2}, \]  

(B2)

with the measured maximum bubble radius \( R_{\text{max}} \) and measured bubble life-time till the first collapse \( \tau \). After inserting eqn (B2) into the gas uptake equation, eqn (B1), and integration, we obtain the expression for the mass of gas:

\[ m_g = \frac{64}{9} \sqrt{\frac{D\tau}{35} R_{\text{max}}^2 c_a}, \]  

(B3)

that diffuses into the bubble. The gas uptake derived from this expression has been compared with reported numerical solutions using the Eller-Flynn scheme (Church 1989; Sapozhnikov et al. 2002). For this comparison, the calculated maximum bubble radius and the duration of the first oscillation cycle is inserted into eqn (B3) and an equivalent equilibrium radius, \( R_0 \), is obtained from the solution of the gas law:

\[ \left( \frac{P_0 + 2\sigma}{R_0} \right) \cdot 4\pi R_0^2 = m_g R_{\text{max}} T_0. \]  

(B4)

Here, \( \sigma = 0.0725 \text{ N/m} \) is the surface tension of water, \( R_{\text{max}} = 287 \text{ mM}^3/\text{Pa K}^{-1} \text{kg}^{-1} \) is the specific gas constant for air and \( T_0 = 293 \text{ K} \) is the water temperature. Our comparison reveals differences in the equilibrium radius \( R_0 \) of less than 15% for bubble life times \( \tau \) from 40 \( \mu \text{s} \) to 260 \( \mu \text{s} \) and maximum bubble radii \( R_{\text{max}} \) from 0.2 mm to 1.2 mm. Thus, we are confident that the approximation of the gas uptake through eqn (B3) is very reasonable. The benefit of eqn (B3) is that no detailed knowledge of the bubble dynamics or of the driving pressure is necessary to predict the accumulated gas. This is important insofar as no simple model describes the radial bubble dynamics in cavitation clusters.