Characterization and modification of cavitation pattern in shock wave lithotripsy

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Abstract: The temporal and spatial dynamics of cavitation bubble cloud growth and collapse in extracorporeal shock wave lithotripsy (ESWL) is studied experimentally. The first objective is obtaining reproducible cloud patterns experimentally and comparing them with FDTD-calculations. Second, we describe a method to modify the cavitation pattern by timing two consecutive pressure waves at variable delays. It is found that the spatial and temporal dynamics of the cavitation bubble can be varied in large ranges. The ability to control cavitation dynamics allows discussing strategies for improvement of medical and biological applications of shock waves such as cell membrane poration and stone fragmentation.

1. Introduction and motivation
In extracorporeal shock wave lithotripsy a focused pressure wave is targeted on renal calculi from outside the patients body. In generally, the finite amplitude wave consists of a shock front followed by a tensile stress wave strong enough to expand nuclei within the liquid into cavitation bubbles.

Both, the passage of the shock front and the cavitation bubble activity, are considered to be responsible for the fragmentation of stones [1,2]. However, the scientific community has not yet agreed on the exact contribution of one of the two or a combination of both mechanisms. Nevertheless, it is agreed that cavitation activity is causing unwanted side effects. Cavitation bubbles can rupture blood vessels during their explosive growth [3]. This is one of the reasons why current research in lithotripsy investigates methods to control the cavitation activity globally and locally to limit bubble expansion near the target. To do this task the first step is to measure and define the cavitation cloud dynamics. Here, we report on optical observations of the cloud activity, which allows analyzing the spatial void fraction and comparing some results with numerical calculations. Further, we present experiments where applying two successive acoustic waves controls the cloud dynamics. Similar strategies have been described in literature:

Huber et al. [4] used an electromagnetic lithotripter with a two capacitor systems to allow for the application of two successive shock waves at variable delays ranging between 200µs and 1.5s. They operated the device at a constant repetition rate from 0.3 Hz to 1Hz and found that for short delays (still larger than 1ms) between the two pulses the cavitation activity is strongly enhanced when compared to that of a single pulse and decreases for longer delays. This type of cavitation control has

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convincingly been interpreted with the dissolution of cavitation bubble residuals serving as nuclei for the succeeding pulse. For delays below 1ms they observed a strongly varying cloud pattern. In contrast, Bailey [5] and Sokolov et al. [6] focused two lithotripters from opposite sides onto the same focal area. With this setup they demonstrated enhanced cavitation activity in the focal area surrounded by bands of much decreased activity and the cavitation pattern shrunk to a smaller volume. Additionally, this setup can move efficiently fragment stones as compared to a single shock wave [7]. Loske et al. [8] use the term "tandem shock wave" for the application of two shock waves from the same acoustic transducer. They modified a commercial piezoelectric source by adding a second capacitor system to test the influence of the inter-pulse delay on the fragmentation efficiency. This tandem shock wave setup would have the benefit for possible therapeutic applications as only a single acoustic path to the stone has to be found and the convenience in aligning a single source.

The optical observation relies on reproducible experiments because a stroboscopic illumination is used to capture the cloud dynamics. In short we found only a good reproducibility of the cloud shape when either long enough time is waited between two experiments or the liquid is stirred. With no stirring more than 30s were necessary to obtain similar shaped clouds. This behavior can be explained with the presence of inhomogeneities acting as cavitation nuclei. After their activation by the tensile wave, new nuclei have to be resuspended into the volume of observation. This is achieved by the flow being set up during the collapse of the cavitation bubbles. Additionally, during cavitation activity non-condensable gas diffuses into the bubbles. These gas bubbles will act as a cavitation site for the following acoustic wave. Therefore, the lower bound for reproducible experiments is given by the dissolution time of the created gas bubbles [9] and the strength of the flow set up by the bubbles leading to homogeneous mixing of the observation area with nuclei.

First, the experimental set-up is described then a comparison of the experiment with numerical simulations for a single wave application is presented in section 3, and in section 4 we demonstrate experimentally the modification of the cloud pattern for two waves applied under a variable delay.

2. Experimental set-up

2.1 Shock wave generator

For the acoustic modification of cavitation pattern we take advantage of a piezoelectric transducer already equipped with two layers of piezo-ceramics. In contrast to the clinical system the device used in this study is furnished with two independent high voltage circuits which can be triggered independently at arbitrary time. Figure 1 sketches the experimental setup viewed from the top with the acoustic source adapted from the commercial lithotripter (Piezolith 3000, Richard Wolf GmbH, Germany) possessing an aperture of 25.1 mm in diameter and an opening angle of 94°. The source is attached at an angle of 45° horizontally to a rectangular basin made of stainless steel. On three of the four circumferential sides glass windows are attached. The basin is filled with approximately 50 l of degassed (3 mg/l O2 content) and de-ionized water.

A fiber optic hydrophone (FOPH-500, University of Stuttgart, Germany) is used to measure the pressure wave profile. Figure 2 displays pressure recordings taken near the focus of the lithotripter. The two uppermost curves depict the pressure pulses from the back and front transducer layer, respectively. Below, three curves are presented for delay settings of Δt =0µs, Δt =2µs, and Δt =4µs. Clearly, the shapes of the front and back recordings differ substantially in amplitude of the positive and negative pressure. Still, the positive pressure levels are of the same order (approximately 10 to 20 MPa). The curve of the front transducer, see the second frame of figure 2 shows nonlinear steepening which becomes more prominent for the superimposed waves, Δt =0µs. The negative pressure is followed by some pressure oscillations of substantial magnitude at the resonance frequency of the transducers. In section 4 we will show that the delay setting of Δt =4µs suppresses cavitation; strongest suppression occurs at a delay of Δt =2µs (not shown here). For all experiments reported the back layer of the lithotripter is triggered first. Stroboscopic photography is employed to measure the cavitation cloud dynamics.
Therefore, a digital CCD camera (Pulnix TM-6710, Alzenau, Germany) is exposed with a xenon flash (Flashpack LS1130-1, Perkin Elmer, flash duration 2µs) at variable delays relative to the shock waves. A programmable delay generator (BNC 555, Nucleonics, Berkeley, 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 shock wave generator and the flash lamp is varied in steps of 10µs up to a maximum delay of 600µs to capture the cloud dynamics to full extent. At each setting 10 images are taken for averaging with diffuse back illumination. Additionally, an image taken just prior to the application of the shock wave serves as a background image, which is subtracted before image processing routines to determine the size of the individual objects are applied. Now, by subtracting this background image from the image with the cavitation bubbles most of the minor inhomogeneities in the illumination are removed. Objects with two high eccentricity attributed as highly overlapping bubbles and areas of less than three pixels attributed as noise are rejected. The spatial resolution for the zero delay case is 80µm/pixel (Fig. 3a) and 106µm/pixel for the tandem shock application (Fig.4).

3. Cloud dynamics and comparison with simulation for zero delay
An example of the cloud dynamics is presented in figure 3a. The direction of shock wave propagation is from bottom to top. The shock wave arrives at the focus at about 135µs. From the temporal sequence the growth of the cloud starting at the bottom of the frame, and its successive shrinkage becomes easily visible. The overall shape of the cavitation cloud is cigar like, however for special settings the distribution of bubbles can greatly vary.

A continuum model based on effective equations for the propagation of nonlinear pressure waves in a bubbly liquid [10, 11] is used for simulations. For the two-phase medium of gas bubbles in a liquid a dilute mixture is assumed, which means that direct bubble-bubble interactions are neglected. In this approach the bubble radius $R(x,t)$ is treated as a field variable that specifies some average radius for bubbles in the neighborhood of a point $x$. To account for the effects of relative motion between bubbles and liquid, the conservation equations for mass and momentum are solved for both phases, the gas and the liquid. The dynamics of the radial bubble motion is calculated by the Gilmore equation. Further basic assumptions for modeling the bubble behavior are that the bubbles retain their spherical shape, a fixed amount of non-condensable gas is inside the bubble, which is compressed or expanded isothermally and effects of mass or heat diffusion are neglected. For the numerical implementation of nonlinear ultrasound propagation in the bubbly mixture, a two-dimensional explicit FDTD-algorithm in cylindrical coordinates is chosen. A detailed description of the numerical treatment is given in [12]. The Gilmore equation is solved numerically using an explicit fifth-order Runge-Kutta scheme with adaptive time steps. For the calculations presented in figure 3b the following parameters were used: uniformly distributed bubbles with an equilibrium radius of $R_0 = 3µm$ and an initial bubble number.
density of $n_0 = 5$/cm$^3$. Figure 3b shows the temporal development of the calculated two-dimensional bubble radius distribution. A qualitative good agreement for the spatio-temporal evolution and localization of the bubble cloud can be observed between experimental and numerical results.

4. Modification of the spatio-temporal cloud dynamics
The cylindrical symmetry of the cavitation cloud, see figure 3a, permits a visualization of the spatio-temporal bubble distribution in a single plot. To do so, the void fraction is integrated now along slices oriented perpendicular to the wave propagation. The temporal evolution of the spatial void fraction is plotted in gray scales as a function of time. For quantifying the void fraction we make use of a reference volume of 20mm x 20mm x 0.1mm, with the integration done in steps of one pixel 0.1 mm, along the direction of wave propagation. Figure 4 depicts a plot of the thereby obtained spatiotemporal bubble distributions for different delays $\Delta t$. Additionally, the position of the shock fronts is indicated with lines assuming a speed of sound of 1500m/s. We start with a discussion of the standard case of $\Delta t=0$ $\mu$s. Here, cavitation bubbles are detected within 10 $\mu$s following the shock front passage. The highest bubble concentrations are found in the center of the cloud. There the bubbles persist for the longest time. The cloud collapses around $t=300$ $\mu$s and reappears. At a time $t=420$ $\mu$s cavitation activity is no longer detectable. Although we find immediately behind the shock front the formation of bubbles, the lifetime of bubbles at positions below 10 mm is only a few microseconds.
The second frame in figure 4 depicts the void fraction dynamics for the short delay of $\Delta t = 4 \mu s$, with greatly altered bubble dynamics: the center of the cloud shifts approximately 8 mm towards the transducer, the maximum void fractions are reduced, and the cloud collapses at $t = 200 \mu s$, thus 100$\mu$s earlier as compared for the standard case.

For a delay of $\Delta t = 16 \mu s$ the maximum achievable void fraction reduces further and the center of cloud moves nearer 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 cloud generated with the first pulse is already shrinking. The cloud dynamics generated with the first shock wave generator and being unaffected by the second wave is revealed in the last frame of figure 4. Here, the second wave passages long time after the first cloud has ceased. We find after the passage of the second wave a spatially patterned cloud with three distinct regions separated by bands of lower bubble activity. Especially intriguing in this observation is the fact that cavitation activity is observed at further distances from the transducer than for the standard case, $\Delta t = 0 \mu s$, see the small upper cloud between 160$\mu$s and 200$\mu$s and between position 65 mm and 75 mm. One of the two possible explanations could be that the first pulse creates small cavitation bubbles, which are below the optical resolution limit. Still, they have gained non-condensable gas by rectified diffusion during their growth; later they are only slowly dissolving 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 cloud from the first pulse, possibly refocusing the tensile stress of the second wave.

The last frame in figure 4, $\Delta t = 256 \mu s$, illustrates again the important contribution of gaseous cavitation nuclei on the cloud dynamics. Here, the first wave causes only a relatively mild cavitation cloud. Even though not resolved with the camera, small bubbles remain due to a net gain caused by the

![Figure 4](image-url)

**Figure 4.** Temporal evolution of the void fraction in direction of the major axis of the bubble cloud. The void fraction was integrated over the minor axis. The delay, $\Delta t$, of the lithotripter shock waves increases from the left to right and top to bottom. The dashed-dotted lines indicate the position of the front of the pressure pulses traveling at 1500 m/s.
radial bubble oscillation. At the instant the second wave interacts with the cluster of bubbles below 100µm in radius a very pronounced cloud is observed, which lasts for approximately 420µs. This cloud resembles in space and time the cloud in the standard case, although for ∆t = 0µs higher void fractions are found in the core. Additionally, we find more homogenous void fraction distribution for a delay of ∆t=256µs.

5. Summary
The experimental results on the tandem shock wave passage can be summarized as following: For delays in the range of the pressure wave duration, ∆t between 0µs and 4µs, the influence of the acoustic driving on the cloud pattern becomes 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 cloud is found. For even longer delays the cavitation cloud 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 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, which is acting as an acoustic impedance change, effects the overall cavitation pattern we expect a strong influence of the delay on the cloud pattern. Investigations on its influence on fragmentation and a possible beneficial exploitation of are currently underway. A second topic of interest are numerical simulations on focused nonlinear wave propagations [12,13] where reasonable agreement between experimentally measured pressure distributions have been obtained. Still, only very limited numerical work is found in literature dealing [14] with the cloud dynamics from lithotripter shock waves.

Acknowledgments
The funding of the experimental work by FOM (The Netherlands) under projects 00PMT04 and 99MS07 is greatly acknowledged. We further appreciated the discussions with Thomas Dreyer (Univ. of Karlsruhe) on the details of the shock wave source and Knud Aage Mørch (Univ. of Lyngby) for the inspiring discussion on the mysteries of cavitation inception. We also thank Lutz Junge, Detlef Lohse and Andrea Prosperetti for their valuable support.

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