Why Stones Break Better at Slow Shockwave Rates Than at Fast Rates: *In Vitro* Study with a Research Electrohydraulic Lithotripter

YURI A. PISHCHALNIKOV, Ph.D., JAMES A. McATEER, Ph.D., JAMES C. WILLIAMS, JR., Ph.D., IRINA V. PISHCHALNIKOVA, M.S., and R. JASON VONDERHAAR, B.S.

**ABSTRACT**

**Background and Purpose:** Stones break better when the rate of shockwave (SW) delivery is slowed. It has been hypothesized that the greater cavitation accompanying a fast rate shields pulse propagation, thus interfering with the delivery of SW energy to the stone. We tested this idea by correlating waveforms measured at the SW focus with cavitation viewed using high-speed imaging.

**Materials and Methods:** A series of U30 gypsum stones held in a 2-mm mesh basket were exposed to 200 SWs at 30 or 120 SW/min from a research electrohydraulic lithotripter (HM3 clone). Waveforms were collected using a fiberoptic probe hydrophone. High-speed imaging was used to observe cavitation bubbles in the water and at the stone surface.

**Results:** Stone breakage was significantly better at 30 SW/min than at 120 SW/min. The rate had little effect on SW parameters in the water free field. In the presence of particulates released from stones, the positive pressure of the SW remained unaffected, but the trailing tensile phase of the pulse was significantly reduced at 120 SW/min.

**Conclusions:** Cavitation bubbles do not persist between SWs. Thus, mature bubbles from one pulse do not interfere with the next pulse, even at 120 SW/min. However, cavitation nuclei carried by fine particles released from stones can persist between pulses. These nuclei have little effect on the compressive wave but seed cavitation under the influence of the tensile wave. Bubble growth draws energy from the negative-pressure phase of the SW, reducing its amplitude. This likely affects the dynamics of cavitation bubble clusters at the stone surface, reducing the effectiveness of bubble action in stone comminution.

**INTRODUCTION**

The rate of shockwave (SW) delivery in lithotripsy can have a significant effect on the efficiency of stone fragmentation. Stone breakage is improved by slowing the SW rate, as has been demonstrated in a variety of *in vitro* test systems using model stones and an *in vivo* pig model in which artificial stones were implanted in the renal caliceal system via percutaneous access. Recently, several clinical studies have reported better outcomes when SWs are delivered at 60 SW/min than at 120 SW/min.

The mechanism responsible for this effect of SW rate likely involves the growth and collapse of cavitation bubbles. Shockwaves generate cavitation in fluid media such as the urine surrounding stones, and it has been suggested that the bubbles created by SWs delivered at a fast rate may shield subsequent SWs, blocking the transmission of SW energy to the stone. However, experimental studies of cavitation in lithotripsy using high-speed photography and a laser scattering bubble-detection method have shown that the lifetime of cavitation bubbles in lithotripsy is <1 msec. That is, the cavitation bubble growth–collapse cycle is about 1 thousandth of the interval between successive SWs delivered at the rate of 120 SW/min typically used in clinical lithotripsy. Thus, if cavitation bubbles disappear during the interval between SWs, what physical mechanism explains why stone breakage is better at slower rates? The current study examined this problem.
MATERIALS AND METHODS

The study was conducted using a laboratory electrohydraulic lithotripter patterned after the Dornier HM3 machine. The power supply to the shock source of this lithotripter charges the capacitor fully for operation at up to 5 Hz pulse-repetition frequency (300 SW/min). Filtered (5-μm) deionized water in the lithotripter test tank was degassed to about 20% saturation, and conductivity was adjusted to ~600 μS. Gypsum model stones held in a 2-mm mesh basket (Fig. 1) were used to test the effect of SW rate on the efficiency of stone breakage. Stones were treated with 200 pulses administered at 0.5 or 2 Hz (30 and 120 SW/min).

Shockwaves were recorded using an FOPH-500 fiberoptic probe hydrophone (RP Acoustics, Leutenbach, Germany) using a protocol for capture of SWs in a nonstop regimen. For these measurements, the optical fiber tip was positioned at the geometric F2 focal point of the lithotripter, perpendicular to the axis of SW propagation. Pressure waveforms were recorded either in the water free field or about 2 mm in front of the mesh basket (Fig. 1) and were post-processed using programs written in LabVIEW (National Instruments, Austin, TX).

An Imacon 468 (DRS Hadland, Inc., Cupertino, CA) ultra-high-speed digital imaging system was used to capture cavitation activity in the water free field and at the stone surface. This camera is capable of capturing 7 frames at rates as high as 100 million frames/sec, and inter-frame timing could be set to capture very rapid events (as short as 10 nsec between frames) or events over a longer time (microseconds to milliseconds).

RESULTS

Stones broke better at a slow SW rate than at a fast rate. An example of stone fragments retained in the mesh basket after 200 SWs is shown in Figure 2. The stone treated at 30 SW/min (left) was broken into numerous pieces, whereas the stone treated at 120 SW/min (right) remained largely intact.

We and others have hypothesized that the effect of the SW rate on stone breakage is a consequence of SW–bubble interactions. To test this idea, the high-speed camera was used to image the cavitation field, and in separate experiments, the FOPH was used to capture waveforms at different SW rates. Figure 3 shows bubbles generated in the water free field at rates of 30, 120, and 300 SW/min. It is clear that as the rate increased, more bubbles were produced. If bubbles generated along the SW axis pose a barrier to the transmission of SW energy, it should be possible to detect an effect of SW rate on the amplitude of the pressure pulse and possibly other characteristics of the waveform. Therefore, sets of 100 SWs were recorded at F2 in the water free field for pulses fired at 30 and 120 SW/min. Even with this large sample size (100 SW per condition), there was no difference in peak positive pressure (27.4 ± 5.1 MPa at 30 SW/min; 27.3 ± 4.4 MPa at 120 SW/min; P > 0.7) or peak negative pressure (−5.9 ± 1.3 MPa at 30 SW/min; −6.0 ± 1.3 MPa at 120 SW/min; P > 0.2) at these two rates.
MECHANISM OF RATE EFFECT IN SWL

Hydrophone measurements with the mesh basket and stone in place (Fig. 1) showed a different result. The mean peak positive pressures were about the same at both rates (26.8 ± 4.3 MPa at 30 SW/min; 26.1 ± 4 MPa at 120 SW/min; \( P > 0.13 \)), but there was a significant effect on the amplitude of the negative pressure at the two rates (−5.7 ± 1.6 MPa at 30 SW/min; −3.9 ± 1.6 MPa at 120 SW/min; \( P < 0.0001 \)). Figure 4 shows representative waveforms at the two rates and illustrates a reduction in the negative tail at 120 SW/min even though the positive pressure was virtually identical to that of the pulse at 30 SW/min.

The reason the leading positive-pressure phase of the SW remained the same at both rates can be understood from high-speed photography. Figure 5 presents a sequence of high-speed camera images capturing cavitation bubbles at the proximal surface of a stone treated at 120 SW/min. This series shows the entire cavitation cycle, from inception of bubble growth to bubble collapse. The bubble cycle is longer at the stone surface than in the surrounding water, such that at 600 \( \mu \)sec, the cloud at the stone is collapsing, but no bubbles are visible in the surrounding water. All visible bubbles—including those on the stone—disappear long before the arrival of the next lithotripter pulse (at 500,000 \( \mu \)sec). Cavitation clouds (see Figs. 3 and 5) are not present when the next SW arrives and thus do not interfere with the propagation of the leading positive-pressure phase of the pulse. Still, there was a measurable effect of SW rate on the amplitude of the negative pressure of the wave (see Fig. 4). Previous studies have shown that, whereas visible bubbles do not last between pulses, there are microscopic bubbles—bubbles visible by B-mode ultrasound— that can persist.17,19 These are too small to affect propagation of the positive-pressure phase of the SW, but the negative-pressure phase stimulates these microscopic bubbles to grow. Thus, energy from the negative-pressure phase remains with the growing bubbles and does not propagate with the SW.

DISCUSSION

Our observations suggest that cavitation along the path from the SW source to the focal zone of the lithotripter can interfere with the delivery of acoustic energy to the target. However, this does not appear to be a matter of crude shielding or blocking of the SW, as the SW rate had no effect on the leading positive-pressure phase of the pulses. This is understandable, because even at a rate of 120 SW/min, the delay between SWs (pulse interval) is vastly longer than the lifetime of cavitation bubbles in the water. That is, the cavitation bubbles generated by one SW do not last long enough to interfere with the next SW. Instead, the rate of SW delivery appears to affect the amplitude of the trailing negative-pressure phase of the SW, but only in the immediate vicinity of the target stone. That is, the negative pressure is reduced for SWs delivered at 120 SW/min, but only when a stone is present. It may be that particulates dislodged from the stone by SW impact or the action of cavitation bubbles at the stone surface serve as nuclei that seed cavitation in the vicinity of the stone. Thus, the rate effect may be dependent on the quality of the medium—the ability of the medium to support cavitation.

In previous studies,17 we observed that increasing the gas content of the water in the lithotripter tank can reduce the amplitude and duration of the negative-pressure phase of the SW, regardless of the rate of SW delivery. Those experiments showed that as bubbles grew under the influence of negative pressure, the energy for bubble growth came from the negative tail of the lithotripter pulse. That is, some of the energy of the negative phase of the SW was recruited into the growth of cavitation bubbles. Under conditions that favor cavitation, some of the energy of the SW does not continue to propagate with the pulse but is instead left behind in the water, in the form of the kinetic and potential energy of water surrounding the growing cavitation bubbles. Thus, during propagation through cavitation liquid, the lithotripter pulse loses some of the energy that would otherwise have been delivered to the stone.

The current study suggests an acoustic mechanism for the reduced negative pressure delivered to stones at a fast rate, but it does not explain how lowering the amplitude of the negative-pressure phase of the SW reduces the efficiency of stone comminution. One possible explanation involves the role of shear waves in stone breakage. During propagation through a stone, the negative tail of the SW contributes to local stress gradients that lead to fracture. For example, when the leading positive-pressure component of the pulse reflects off the back side of a stone, and its pressure is reversed in phase to negative, the maximum tensile force generated within the stone occurs at the point where this reflected wave (now negative pressure) is amplified.

FIG. 3. Cavitation bubbles in water free field at different firing rates (30, 120, and 300 SW/min). It is clear that number of bubbles increases as firing rate of lithotripter is increased.
Several clinical studies\(^6\)–\(^8\) have demonstrated that stone comminution is more efficient when SWs are delivered at slower rates, but the potential effect of rate on renal injury has not been addressed thoroughly. In a prospective study, Pace and colleagues\(^6\) assessed the efficacy and safety of treatment at 60 v 120 SW/min and observed a significant improvement in success rate (i.e., stone-free status or asymptomatic fragments at 3 months) at the slower rate. The occurrence of complications (emergency room visit, hospital admission, stent or nephrostomy, Steinstrasse, urinary infection) within 3 months of treatment was no different in the two groups of patients. Early in the history of lithotripsy, investigators exploited the ability of piezoelectric lithotripters to fire at exceptionally fast rates (e.g., 120 SW/sec). From this era, there is a report of the anecdotal observation of fewer subcapsular hematomas in patients treated at a rate of 75 v 7200 SW/min.\(^23\) A laboratory study of renal injury in rabbits treated with a piezoelectric lithotripter describes more vascular trauma in animals treated at 1200 SW/min than those treated at 150 SW/min,\(^24\) and a study performed using a research electrohydraulic lithotripter\(^25\) showed a substantial increase in renal injury in dogs treated at 600 SW/min compared with the more conventional rate of 60 SW/min. These reports suggest that SW rate is a factor in renal injury, but by current standards, the conditions of treatment were extreme. It is quite possible that the mechanisms of injury at the exceptionally fast rates used in these studies are different from those at the much slower rates used in current clinical practice. This is an area where additional investigation could be beneficial.

These in-vitro experiments, our past work using stones implanted in pig kidneys,\(^5\) and laboratory and clinical studies by others\(^1\)–\(^4\),\(^6\)–\(^8\) clearly demonstrate that stone breakage by SWs becomes less efficient as the firing rate is increased. Our findings point to the value of slowing the rate of delivery but do not suggest whether rates slower than 30 SW/min would be beneficial, nor do they show how rapidly SWs can be administered without compromising breakage efficiency. Three recent clinical studies that address the effect of rate on the clearance of renal stones\(^6\)–\(^8\) show that a rate of 60 SW/min is more effective than treatment at 120 SW/min. It is possible that rates slower than 60 SW/min would be even better. We know of only one study in which patients were treated at a rate slower than this (20 SW/min),\(^26\) but the effect of rate was not investigated in this work. Because treatment time is an important consideration at many centers,\(^5\) there may be value in finding ways to achieve the best comminution at faster rates. Our observations suggest that fine particles dislodged from stones enhance cavitation that, in turn, reduces the negative pressure of the SWs. Further study will be needed to establish the role of stone particles as cavitation nuclei and in the mechanism of rate. However, it is in-

by the negative pressure contributed by the original trailing negative phase of the SW.\(^20\) The magnitude of this constructive interference would be reduced by a lower amplitude of the negative tail of the pulse. Cavitation at the stone surface may also be affected by a reduction in negative pressure secondary to bubble growth along the path of the SW; cavitation cluster collapse can generate substantial forces that can cause fractures, widen fissures, and erode the stone surface. In addition, cluster collapse produces strong secondary SWs. Thus, the collapse of cavitation bubbles at the stone surface can contribute to comminution at more than one level—directly in the sense that cluster collapse causes pitting, and indirectly in that the force of impact sends SWs into the stone that contributes to the internal stresses involved in fracture failure. A reduction in the negative pressure of SWs would reduce the driving force for cavitation and possibly affect stone breakage.

Our findings show that treatment at a fast rate reduces the amplitude of the negative pressure of the SW. This does not mean that SWs delivered at fast rate are safer. The rate mechanism could be a local effect around the stone, as hydrophone measures in the free field of well-degassed water showed no reduction in negative pressure. Fluids in the body have few cavitation nuclei, and, thus, the system studied here imitates their state. Fast-rate SWs that are on target to hit the stone may show reduced negative pressure, but those that miss the stone because of incorrect targeting, patient movement, or ventilatory motion\(^21\) will be full-energy, full-impact pulses. Because it takes significantly more shots to break stones at a fast rate than at a slow rate, SWs delivered at fast rate have the potential to cause more vascular damage, not less.\(^22\)

**FIG. 4.** Representative waveforms (shot 32 of 200) recorded at 0.5 Hz (30 SW/min) and 2 Hz (120 SW/min) in front of basket with stone. Leading positive-pressure phase was virtually identical at both rates, but trailing negative pressure phase was reduced at 2 Hz.

**FIG. 5.** Cavitation bubbles generated at surface of model stone treated at 120 SW/min. These sequential images captured at 120-µsec steps show that cavitation cycle lasts only about 600 µsec. First frame (0 µsec) was recorded when SW had just arrived at stone and shows fine particles that were dislodged from stone by previous shot. Frame at 600 µsec shows implosion of cavitation cloud at stone surface. Bubbles are no longer visible in surrounding water.
interesting to speculate that if a means could be devised to clear cavitation nuclei from the vicinity of a stone during SW delivery, more efficient treatment might be possible at faster rates.

ACKNOWLEDGMENTS

The high-speed camera results presented here were obtained through efforts of Drs. Oleg A. Sapozhnikov and Michael R. Bailey, and authors sincerely appreciate their valuable contribution to this project. This research was funded by grants from the National Institutes of Health, DK43881 and DK55674.

REFERENCES


Address reprint requests to:
Yuri A. Sapozhnikov, Ph.D.
Dept. of Anatomy and Cell Biology
Indiana University School of Medicine
635 Barnhill Drive
Indianapolis, IN 46202-5120

E-mail: yura@anatomy.iupui.edu