

PROGRESS IN LITHOTRIPSY RESEARCH

Michael R. Bailey

*Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington
Seattle, Washington 98105*

James A. McAteer

*Department of Anatomy and Cell Biology, Indiana University School of Medicine
Indianapolis, Indiana 46202*

Yuri A. Pishchalnikov

*Department of Anatomy and Cell Biology, Indiana University School of Medicine
Indianapolis, Indiana 46202*

Mark F. Hamilton

*Department of Mechanical Engineering and Applied Research Laboratories, The University of Texas at Austin
Austin, Texas 78713-8029*

Tim Colonius

*Department of Mechanical Engineering, California Institute of Technology
Pasadena, California 91125*

Introduction

Shock wave lithotripsy (SWL) for the non-invasive treatment of kidney stones was introduced in the United States in 1984. SWL virtually eliminated the need for open surgery to remove kidney stones, and it did not take long for physicians and patients to endorse this revolutionary technology. Early reports told of the efficient removal of even the most troublesome stones without apparent complications, and SWL quickly became the “treatment modality of choice.” It was not long, however, before concerned physicians began to report the occurrence of adverse effects in SWL,¹ particularly involving vascular trauma and including cases of severe hemorrhage in the kidney and acute renal failure—significant side effects of serious consequence. Researchers quickly recognized the challenge and opportunity to determine the mechanisms of shock wave action in lithotripsy, and in 1988, the Acoustical Society of America held the first in a series of popular sessions devoted to the topic of shock waves in medicine. The goal of the inaugural session was to improve the fundamental understanding of lithotripsy—to bring better devices and treatments to patients. The goal of this paper is to report on progress in this effort.

Background

Roughly 10% of all people suffer from kidney stones.² Historically, stone disease (urolithiasis) has accounted for seven to ten of every 1000 hospital admissions in the United States,³ and currently, treatment approaches \$2 billion annually.⁴ The introduction of SWL revolutionized the treatment of symptomatic stones. In SWL, shock waves are focused through the body wall, to target stones in the kidney or other sites within the urinary tract, Fig. 1(a). Generally, 2000–4000 shock waves are administered at a rate between 0.5 and 2 Hz. Lithotripters produce shock pulses such as those shown in Fig. 2. A roughly 1 μ s duration, positive pressure spike is followed by a \sim 5 μ s duration, negative pressure trough. Peak amplitudes range from 15–150 MPa. Even with a recent surge

in the popularity of more invasive surgical methods such as using tools built into catheters that can be threaded up the urinary tract (ureteroscopy), or gaining access to the interior of the kidney through a narrow (\sim 1 cm diameter) channel established through the body wall (percutaneous nephrostolithotomy)—and acousticians’ intuition that applying a sequence of high-pressure shock waves is an extreme therapy—SWL remains the most common treatment for symptomatic kidney stones.⁵

Lithotripters have three main components, a shock wave source, a method of acoustically coupling shock waves to the patient, and an imaging system for targeting. In the first lithotripter the patient (under anesthesia) reclined in a water bath, which acoustically coupled the shock waves to the body. In subsequent systems—dry-head lithotripters—the shock

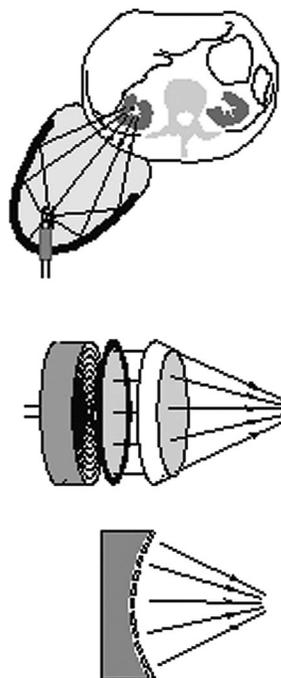


Fig. 1. Three technologies for shock wave sources. Electrohydraulic (spark source and reflector) is shown at top with the shock wave focused in a cross-sectional view of a patient's abdomen. The drawing, also, illustrates the concept of a dry treatment head in which the shock source is enclosed in a water-filled cushion that must be wetted to the patient with a coupling gel or fluid. The electromagnetic lithotripter (center) utilizes a high electrical current through a coil to displace a metal plate to generate the acoustic wave that is then focused. The piezoelectric lithotripter (bottom) uses a focused arrangement of piezoceramic elements. (Reprinted with permission from *Acoustical Physics*.⁴⁹)

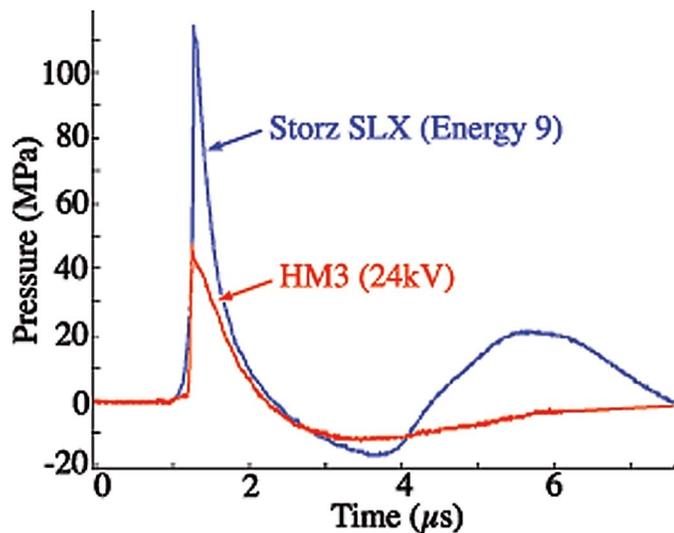


Fig. 2. Lithotripter waveforms generated by electrohydraulic and electromagnetic shock sources. Pressure waveforms measured in water were generated by the original electrohydraulic clinical lithotripter (red: Dornier HM3) and by a recent popular electromagnetic lithotripter (blue: Storz SLX). All lithotripters produce a shock pulse consisting of a positive spike followed by a negative trough. The pulse of the electromagnetic lithotripters (EML) includes a trailing positive pressure oscillation.

source has been enclosed within a water-filled cushion, and the enclosing, acoustically-matched membrane (latex or silastic rubber) is coupled to the patient's skin with gel or oil. Fluoroscopy remains the standard for targeting, especially in the United States, although many lithotripters have B-mode ultrasound as well. Shock wave sources have been engineered from three technologies (Fig. 1), which is evidence in itself that there is no consensus on correlation between source technology and performance. Electrohydraulic lithotripters (EHL) are the least complicated to manufacture, and use a spark source to generate the shock wave that is focused by an ellipsoidal reflector. Disadvantages are that shock strength tends to be variable, especially as the electrodes wear, and electrodes must be periodically replaced. In electromagnetic lithotripters (EML), a high current in a coil abruptly displaces a plate to create an acoustic wave that is focused by the curvature of the plate, a lens, or a reflector. EML devices produce stable and reproducible shock waves, and a well-built shock source has a lifetime of a million or more pulses. Currently, the three largest manufacturers of lithotripters provide only electromagnetic devices. In piezoelectric lithotripters (PEL), piezoceramic elements excited by a voltage spike rapidly distend to produce an acoustic pulse that is focused by the curvature of the element or the scaffold supporting the elements. Like electromagnetic lithotripters, PELs rely on nonlinear acoustic propagation (see Anthony Atchley's article in the first issue of *Acoustics Today*) to develop a shock wave, while the spark-generated pulse in EHL is shocked from inception. A potential advantage of PEL is the possibility of tailoring the pulse, altering the standard lithotripter waveform by changing the excitation of the elements. Waveform shaping is just one of many areas where basic research has the potential to deliver significant improvements.

Progress in research on tissue injury in SWL: Making good use of acoustic principles

Most anyone with a background in acoustics would not be surprised to learn that lithotripter shock waves can cause tissue injury. That is, it seems reasonable to expect that a shock front moving through the urine space and the surrounding renal tissue and blood vessels could generate significant acoustic cavitation and focal shear stress, and that shock pulses capable of shattering stones might also have the potential to damage living cells. However, at the time that shock wave lithotripsy was introduced and, indeed, throughout much of the history of clinical lithotripsy, the medical community has been somewhat reluctant to accept that such adverse effects occur. In recent years, however, researchers have made considerable progress in characterizing shock wave injury, including the mechanisms of shock wave action involved. Thus there has been a change in awareness of the potential for shock waves to cause trauma, and a new appreciation for the role that acoustics plays in understanding how shock waves break stones, the origins of tissue trauma, and what needs to be done to make lithotripsy safer and more effective. This work has generated practical recommendations, specific steps aimed at improving clinical outcomes.

Tissue is responsive to shock waves, and shock wave dose can be excessive: Shock waves may be intended to break stones but, unfortunately, can cause collateral tissue damage as well. Indeed, all SWL patients suffer some level of tissue injury, and some patient groups, such as children and the elderly, are at greater risk that this damage can be significant.⁶ Studies have shown that the lesion produced in lithotripsy is acute vascular trauma in which the hemorrhage can be mild to severe.⁷ The lesion volume is dose-dependent: more shock waves or higher amplitude pulses cause greater injury. Also, hemorrhage leads to scarring that in turn can lead to a permanent loss of functional tissue.⁸ In addition, the long-term effects of SWL trauma can include hypertension, diabetes, and with multiple treatment sessions, a progression in stone disease to a type (brushite disease) that is significantly less responsive to SWL.⁹ This is compelling evidence to minimize shock wave exposure, and to find treatment strategies that improve the efficiency of stone comminution.

Ed.—The authors point out that a recent *New York Times* article ("Blasting of Kidney Stones Has Risks, Study Reports" by Lawrence K. Altman, 10 April 2006) cites a report* that, after nineteen years of follow-up study, shows that patients who received lithotripsy developed diabetes at almost four times the rate of those whose kidney treatment was other than lithotripsy. There was also a positive relationship between lithotripsy treatment and an increase in high blood pressure.

* A.E.Krambeck, et al., "Diabetes Mellitus and Hypertension Associated with Shock Wave Lithotripsy of Renal and Proximal Ureteral Stones at Nineteen Years of Follow-up." *J. Urology* 175, 1742–1747 (2006).

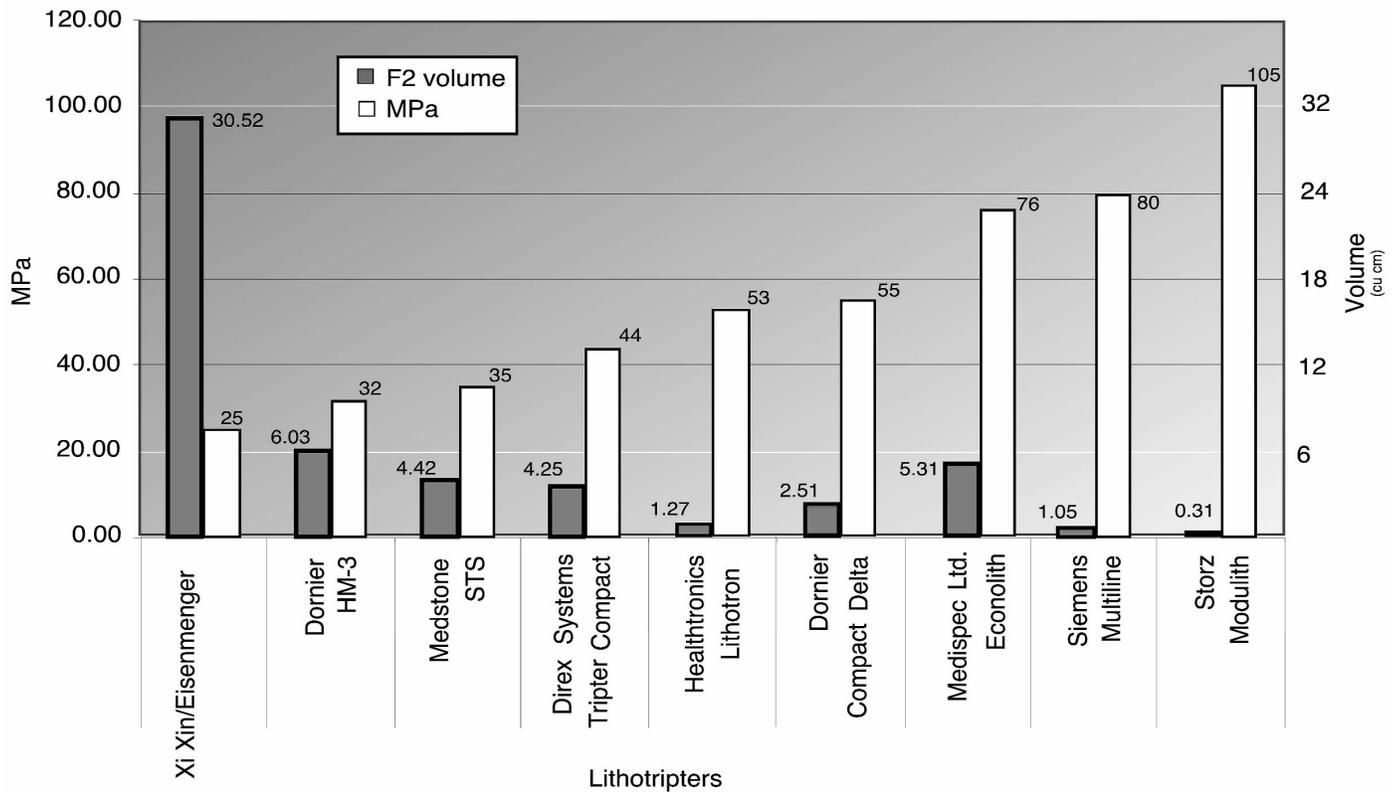


Fig. 3. Acoustic output of representative clinical lithotripters. This table charts the focal volume (F2 volume) and peak positive pressure (MPa) of a sampling of the greater than 50 models of lithotripters that have been used in the United States. Values are for power settings (or kV) used for a typical patient treatment. Since focal volume and pressure are dependent on power or charging potential at the shock source, there is no metric for equivalence that allows the direct comparison of the absolute values of these data. Still, it can be seen that as used in the clinical setting, most lithotripters developed since the HM3 generate greater pressures focused to a smaller focal zone. Clinical outcomes with these machines have not been as good as with the HM3. The Xi Xin/Eisenmenger lithotripter has the largest focal volume and is used at the lowest pressure (and lowest rate). (Reprinted with permission from Martin Dunitz Limited, London.¹⁰)

Side effects are increased with narrow focus, high amplitude lithotripters: Most current lithotripters are EMLs that generate high amplitude (upwards of 100 MPa) shock pulses delivered to a relatively narrow (4-8 mm) focal volume—defined by the half maximum of the pressure field (Fig. 3).¹⁰ These devices have proven to be less effective than lithotripters with broader focal volumes. Stone-free rates are lower, and re-treatment rates are higher.⁹ A significant con-

cern is the frequency and severity of adverse effects seen with narrow focus lithotripters. Kidney hematoma rates as high as 12% have been reported for narrow focus machines, compared to an occurrence of less than 1% observed with the original clinical lithotripter [10 and references within]. Perforation of the colon and rupture of the spleen have occurred.^{7,10} Reports voicing concern for the higher occurrence of side effects with these machines have caught the attention of urologists and the lithotripsy community, and there is now an increased awareness of the potential for injury with such narrow focus lithotripters.

Shock wave-induced cavitation can occur in tissue, and cavitation is the likely mechanism of vascular trauma: Cavitation—in short, bubble action—is capable of generating impressive force (Fig. 4)¹¹ and is understood to play a critical role in stone comminution. It has been shown that cavitation occurs in the kidney of patients during lithotripsy.¹² Other studies have demonstrated that cavitation occurs within the urine in the kidney in fewer than 100 shock waves and in the tissue itself after many more shock waves (preliminary evidence indicates approximately 1000 shock waves).¹³ A variety of studies have shown that cavitation is involved in vessel rupture in SWL. For example, fitting the ellipsoidal reflector of a Dornier HM3 lithotripter with an acoustically pressure-release material produced effectively time-inverted waveforms (due to amplitude inversion on reflection, focusing, and nonlinear wave propagation) in which the amplitude of the positive pressure (compression) phase was not affected,

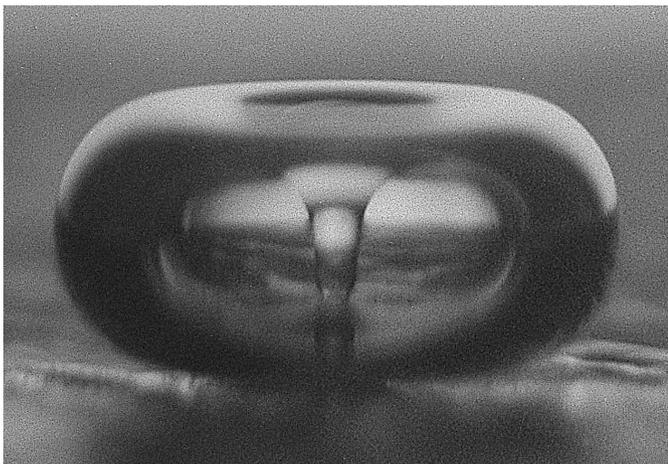


Fig. 4. High-speed photograph of a 1-mm diameter bubble collapsing in response to acoustic excitation.¹¹ The surface on the lower side leads to a water jet through the bubble that damages the metal surface. The process has been responsible for erosion of the tip of ship propellers. Photograph reprinted with permission from L. Crum and IEEE. (© IEEE)

but the negative pressure (rarefaction) phase preceded the positive phase of the wave.¹⁴ Thus, bubble expansion initiated by the negative phase was suppressed by the positive spike.¹⁵ Kidneys treated with conventional waveforms suffered a substantial lesion, while kidneys treated with pulses produced by the pressure-release reflector (pulses that suppressed cavitation) showed no measurable lesion.¹⁶ Delivery of staggered dual pulses can be used to manipulate cavitation, and when the trailing pulse is timed to interrupt the cavitation cycle initiated by the first pulse, renal injury is reduced.^{17,18}

Shear has the potential to damage cells: *In vitro* studies have shown that in the absence of cavitation, shock waves still generate differential forces (shear) and accelerations capable of tearing cell membranes.¹⁹ Shear is amplified by narrowing the beam or decreasing the shock rise time by increasing the shock strength. Shear damage to tissue by lithotripter shock waves has not been demonstrated *in vivo*, but it has been hypothesized that the structural inhomogeneities of organized tissues should act as foci to disrupt shock wave propagation, creating local stress gradients sufficient to cause mechanical failure.²⁰ It may be that shear stress tears vessels, causing blood to pool, and then cavitation takes hold, causing further damage.

The kidney vasculature shows a vasoconstrictive response to shock wave treatment: One of the most fascinating observations to come from studies of SWL trauma is the finding that shock waves stimulate blood vessels in the kidney to constrict.²¹ The induction of vasoconstriction proves to be a physiologic response of considerable importance. Researchers have shown that treatment of kidneys with a minimal dose (~100 pulses) of low energy shock waves acts to protect the kidney from injury when a complete dose of 2000 pulses is delivered at high energy.²² That is, a priming dose of shock waves capable of inducing vasoconstriction will protect the kidney from subsequent damage. In this way, strategically delivered shock waves can be used to minimize the adverse effects of a full clinical dose of pulses. As a first step, this suggests a protective strategy,

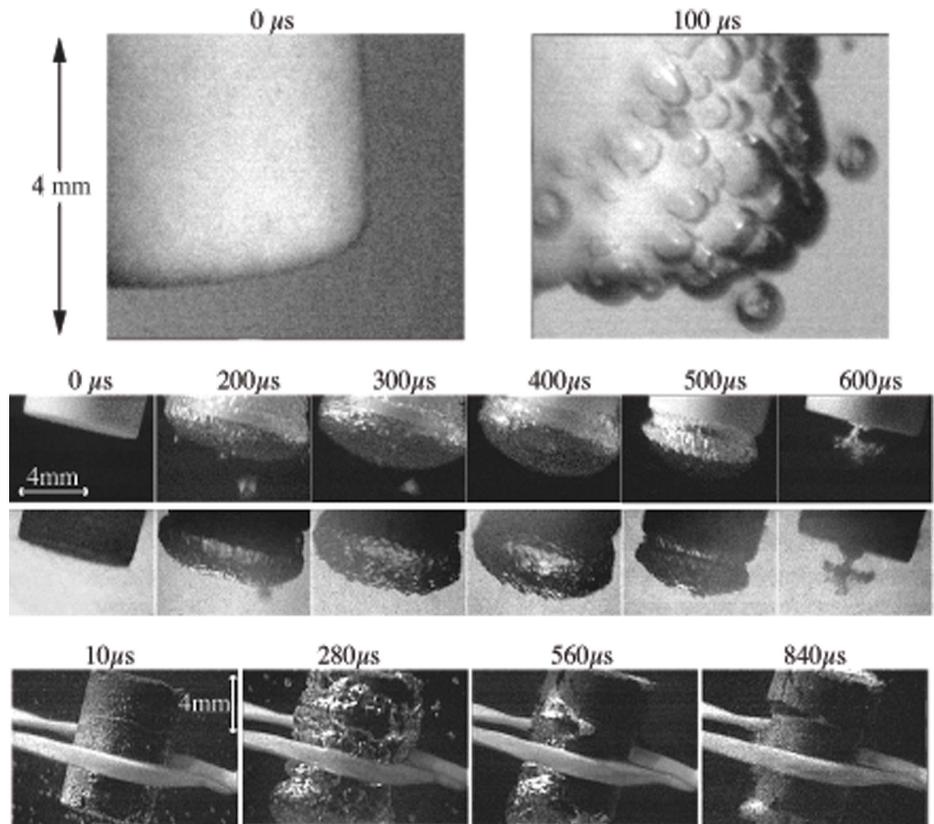


Fig. 5. Cavitation bubble clouds contribute to stone breakage in SWL. Top plate shows a cluster of bubbles that have formed at the leading edge of a gypsum model stone 100 μ s after the passage of the shock wave. Middle plate illustrates the bubble cloud cycle caught in 100 μ s steps, as shown using backlighting (top row) and incident lighting (bottom row). The bubble cloud grows to fully engulf the end of the stone then collapses to a narrow spot. Cluster collapse can generate secondary shock waves (not shown) equal in amplitude to that of the incident pulse. Bottom plate shows several steps of the cloud cycle in which bubble activity appears to have forced open a crack in the stone. (Reprinted with permission from *Journal of Endourology*.²⁶)

a recommendation that urologists start at a low power setting before increasing the power in order to give the kidney a chance to develop a self-protective response.

Progress in understanding stone comminution

Stone-free rates (a clinical metric for relative success of treatment) for current lithotripters are as much as 2-3 times lower than values reported with the first lithotripter (Dornier HM3) used widely in clinical practice.^{9,10} Roughly half of current treatments do not leave the patient stone-free, and as reported above no lithotripsy is without risk of side-effects. The original lithotripter is still considered the “gold standard” because of its low re-treatment rates, high stone-free rates, and low occurrence of side effects.²³ There has been considerable effort, therefore, to understand how stones break in order to improve these success levels, and

research to determine how shock waves break stones has yielded a num-

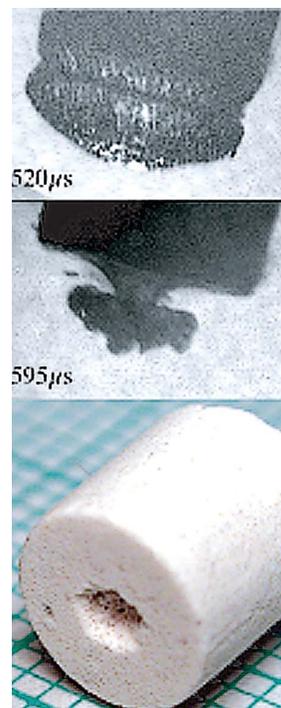


Fig. 6. High speed images of the cavitation cloud collapse and damage induced by SWL on the proximal face of a model stone. (Reprinted with permission from *Journal of Endourology*.²⁶)

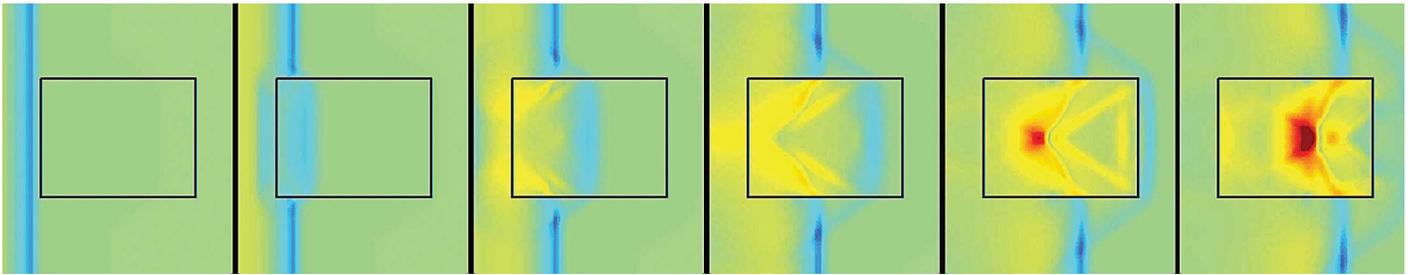


Fig. 7. Sequence of simulations of the stress induced by a lithotripter shock wave (Fig. 2) in a cylindrical stone as shown in Fig. 6. The wave, modeled as a plane wave, propagates to the right. The linear elastic model shows compression as blue and tension as yellow and higher tension as red. The shock wave in water encircling the stone reinforces the shear wave generated at the proximal corner of the stone and yields the highest maximum tensile stress in the stone.³⁷ The location of the maximum agrees well with the location where these stones fracture. The model, together with an understanding of cavitation, offers useful insight into the mechanisms of stone comminution and has enabled progress in improving the complex, evolving process on fragmentation.

ber of findings of practical value to clinical lithotripsy.

Cavitation clouds play a critical role in stone comminution: *In vitro* experiments (we mention only a few here) have shown that stones are difficult to break when cavitation is suppressed. Stones do not break well in glycerol, the viscosity of which softens bubble collapse,²⁴ and fragmentation is prevented when stones are held under static pressure greater than the negative pressure of the shock wave.²⁵ High speed photography of stones in water (Fig. 5) shows a densely populated bubble cloud that can surround the stone. Figure 6 shows the violent collapse of the cloud and the resulting crater in the stone surface.²⁶ The force of the fluid or shock wave impact following cloud collapse creates surface cracks that then grow under the stress of subsequent lithotripter shock waves or cloud collapses. Therefore, cavitation appears to be important in initiating the fragmentation (comminution) process. Cavitation also appears to be important in the final stages of stone comminution. As the stone breaks into pieces smaller than the shock pulse length, constructive interference and focusing of waves within the fragments is suppressed, and internal stresses are reduced relative to the surface impact of cavitation. Cavitation is therefore believed to be responsible for grinding stone fragments to a size that can be passed through the urinary tract.²⁷

Rate of shock wave treatment can be too fast: In clinical lithotripsy, patients are typically treated at a pulse repetition frequency of 2 Hz. Faster treatment rates have been attempted, but there is concern that shock waves at fast rate can induce cardiac arrhythmias in some patients, and earlier research showed severe damage to kidneys at extreme rates.²⁸ Until recently, physicians rarely treated at rates slower than 2 Hz. This is largely because using slower rate would lengthen the time of treatment, and there was no obvious benefit of slowing down. However, both *in vitro* and *in vivo* experiments have shown that shock waves break stones better at slow rate (0.5 or 1 Hz) than at fast rate (2 Hz).²⁹⁻³¹ These studies include model stones implanted in kidneys and a prospective clinical trial. Cavitation appears to be involved in the observed rate effect. At faster rates, bubbles generated by one shock wave have less time to dissolve before the next shock wave and act as nuclei that lead to a large cavitation cloud.³² Both experiments^{13,33} and numerical simulations³⁴ show that such clouds attenuate the low-frequency negative phase of the shock wave and may reflect the shock wave altogether. The result is to shield the stone. Calculations of 2-Hz pulse

repetition rates show that clouds can grow sufficiently in number to collapse less energetically as well. Thus, reducing the rate of shock wave administration is a simple step that clinicians can take to improve treatment.

A broad focus promotes stone breakage: Most lithotripters generate a narrow focal width smaller than 8 mm. Such narrow spot sizes deliver substantial energy to a small volume, but a narrow beam is difficult to keep on target.³⁵ Recent studies suggest that a wider focal zone may break stones better. A beam larger than the stone creates a

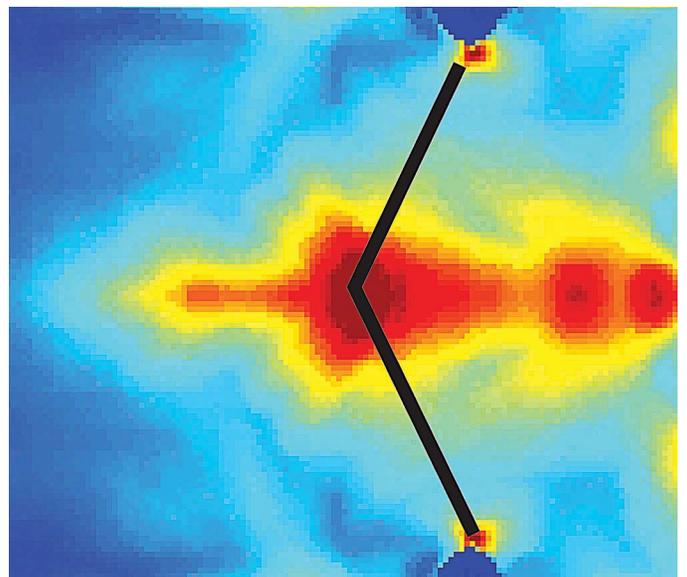
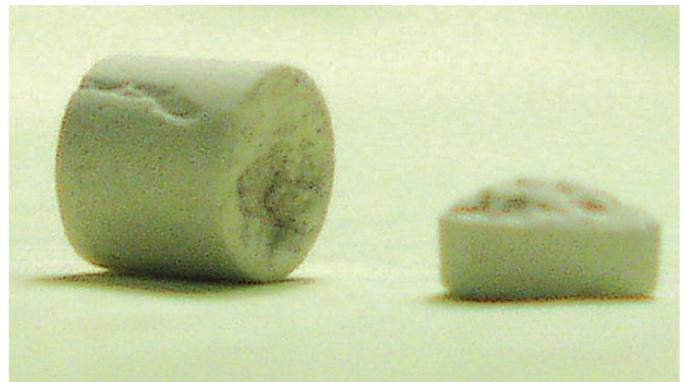


Fig. 8. The fracture grows from surface cracks as may be generated by cavitation to the point of maximum stress. Cracks in this figure were etched 2 mm from the distal end and yielded a conical break. Collapsing bubble clouds have been seen in high-speed movies to ring the stone near the distal end where fracture first occurs.

hoop stress, dubbed “squeezing,” around the stone that helps break the stone.³⁶ Squeezing has since been captured innately in a linear elastic model of stress within a stone³⁷ and tested with the model and experiment.³⁸ Figure 7 includes a sequence of images showing the shock-wave-induced stress within a cylindrical stone (a common shape used for industry and research stone phantoms). First, a longitudinal wave enters the stone. Eventually this reaches the back end of the stone and reflects and inverts from the “acoustically soft” stone-water interface. The inverted wave adds to the trailing negative trough of the incident wave and creates a locally maximum tensile stress and transverse fracture. This fracture mechanism is termed spallation. Following the longitudinal wave is a wake that is generated at the surface of the stone where the wave travels faster than the sound speed of water. Traveling at the sound speed in water along the stone surface and encircling the stone is the shock wave, and it creates squeezing. In addition, the shock wave incident on the corners of the stone generates shear waves that focus in the distal half of the stone. Because the shear wave speed in the stone is close to the sound speed in water, the squeezing wave reinforces the shear wave and together they create the highest tensile stress within the stone.³⁸ The location agrees with the location of the fracture of the stone. These mechanisms—shear, squeezing, spallation, and cavitation (described above)—all participate to varying degrees in the breakage of stones of different shapes. Cracks in the surface (as may be produced by cavitation) lead to stress concentrations at the crack tip that, when connected linearly to the site of maximum stress in the stone, trace the conical fracture pattern seen in stone experiments (Fig. 8). The model predicts a decrease in stress in the stone with decreasing beam width and with decreasing stone size.³⁷

This mechanistic understanding of how shock waves break stones supports the concept of a broad focus lithotripter. This may be an important positive trend for the future, one in line with the national concern for constructive regulatory oversight, as beam width and peak pressure are the two primary parameters used to characterize and differentiate devices for approval by the US Food and Drug Administration (FDA).

When improvements take a step backward

Sometimes even well intentioned improvements in technology do not work out for the better, and the evolution of the lithotripter may be a good example. Currently SWL is attempting to recover from an industry-wide miscalculation in which modifications to lithotripter design reduced both the efficacy and the safety of SWL. As mentioned above, in the original clinical lithotripter (Dornier HM3), the anesthetized patient lay in a water bath. The Dornier HM3 was an electrohydraulic lithotripter that produced shock waves of moderate peak positive pressure (~35 MPa) delivered to a relatively wide focal zone (~15 mm). The HM3 was a great success, yielding stone-free rates of nearly

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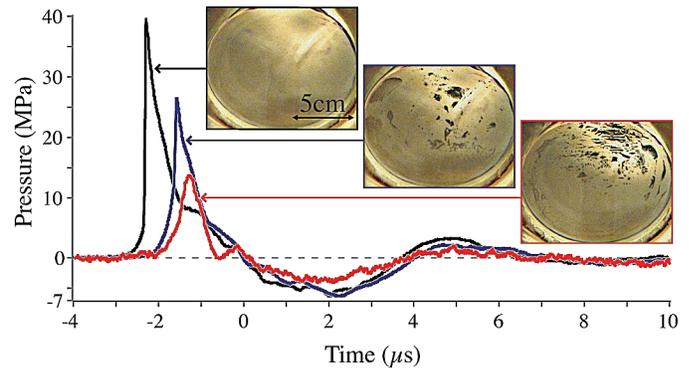


Fig. 9. Poor coupling in dry-head lithotripters blocks the acoustic transmission of the shock pulse. An *in vitro* experiment was performed in which the water cushion of the treatment head of an EML was wetted to the acoustic window of a test tank with coupling gel. Waveforms show mean values for pulses when air pockets were trapped at the coupling interface (blue and red), or when all air pockets were removed manually (black). Photographs show air pockets (dark shadows) at the interface. The quality of coupling was highly variable and reduced pulse amplitude in some cases by more than 50%.

90%. To improve convenience and ease of use, effort was made in subsequent lithotripters to forego the water bath and anesthesia.

Early-on, lithotripters were so large that they occupied a dedicated suite in the hospital, and lithotripsy units operated as referral centers serving a substantial geographic area. Urologists wanted to bring SWL to their patients and make lithotripsy more accessible. The principal change needed to make lithotripters transportable was to eliminate the water bath, so dry head lithotripters were created. Indeed, all lithotripters currently in production use dry-head technology. However, recent *in vitro* studies³⁹ have shown that routine coupling with a dry treatment head is decidedly inefficient, and can pose a substantial barrier to transmission of shock waves. Air pockets get trapped at the coupling interface, and this can reduce the breakage of model stones by 20-40%. Breaking and re-establishing contact, as when a patient is repositioned during treatment can reduce the focal pressure by 50% (Fig. 9). It is not known if the acoustic energy is focused elsewhere in the tissue. The quality of coupling is highly variable, and it seems quite feasible that this variability could contribute to variability in clinical outcomes, and that poor coupling could lead to treatment with an excessive number of shock waves, increasing the potential for adverse effects.

There was also great interest in making lithotripsy an anesthesia-free procedure, so that SWL could be performed on an outpatient basis. The effort to reduce pain sensed in the patient’s skin resulted in refinement of electromagnetic shock sources in which the aperture was large and highly focused. The design produced low pressure over a broad skin surface and still produced high peak pressures in the kidney. Such focusing yielded small focal volumes. As discussed above, the stone drifts in and out of the focal zone during respiratory motion. Thus, by narrowing the focus, fewer shock waves hit

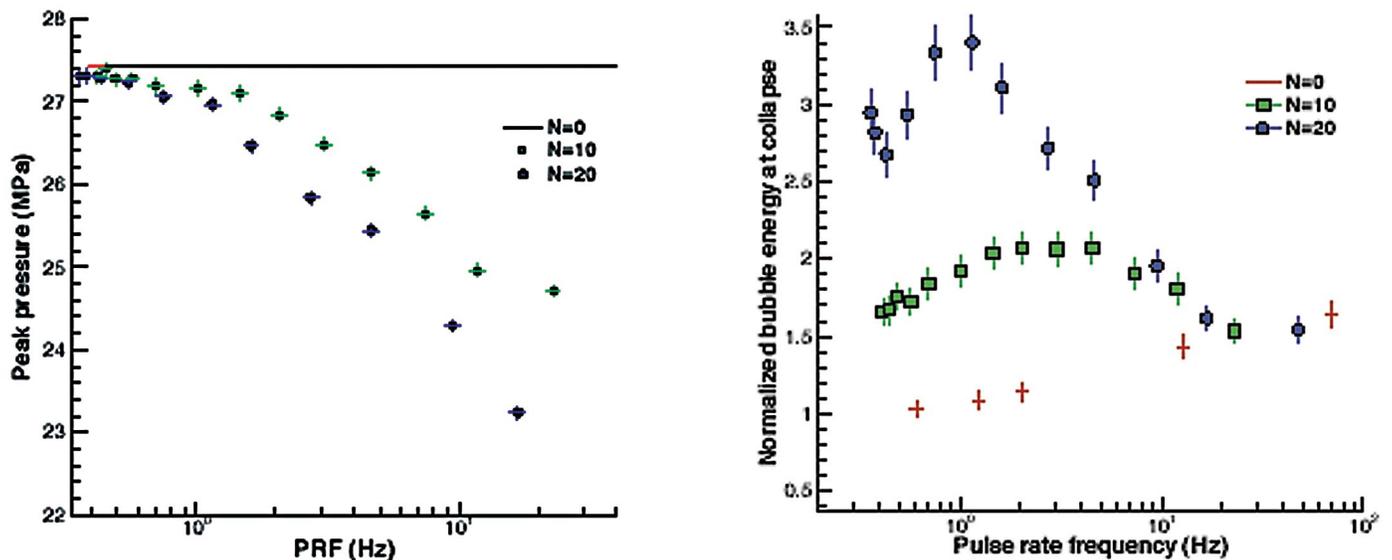


Fig. 10. Numerical simulations³⁴ were used to predict shock focusing and bubble cloud dynamics in an electrohydraulic (Dornier HM3) lithotripter. The simulations revealed that at high pulse rate frequency (PRF) and bubble numbers (N , bubbles/cm³), there is a strong shielding effect—a decrease in peak pressures obtained at the focus (left)—and an associated decrease of energy released by collapsing cavitation bubbles (right). Bars indicate an estimate of the uncertainty in the numerical results.

their target. It takes more pulses to break the stone, and this increases exposure of the kidney to shock waves, increasing the potential for tissue trauma. Interestingly, the attempt to make lithotripsy totally anesthesia-free never caught on with physicians. Urologists prefer to treat patients who are under conscious sedation, as they are less likely to move in reaction to pain and, thereby, affect targeting—and outcomes with patients under sedation are significantly better than with patients who are not sedated.⁴⁰

Thus, the evolution of the modern lithotripter has seen its ups and downs. Research reminded the SWL community of the importance of fundamental acoustics and led to a new understanding of stone-comminution mechanisms, such as squeezing and shear. The knowledge gained has led to significant changes in the lithotripter industry.

Innovations in technology

Basic research has inspired the introduction of two new clinical lithotripters. One is the wide-focus lithotripter, and the other is the dual-pulse machine. Both employ novel designs that show a dramatic departure from the more incremental changes that have characterized the lithotripter industry in previous years.

The theoretical merits of a broader focus were recognized by W. Eisenmenger and form the foundation of his theory of “quasi-static squeezing.” The Eisenmenger broad-focus, low-pressure lithotripter also operates at the slowest rate of any clinical devices (0.3 Hz). This machine was developed and introduced for clinical use in China. Preliminary data and reported clinical data on safety and efficacy are encouraging.⁴¹ The concept of a broad focal zone appears to be gaining acceptance, and two of the three lithotripter manufacturers with the largest world-wide market share have since offered modified machines that allow the urologist to broaden the focus of their machines.

Two dual-pulse, or two-source lithotripters have been approved by FDA. Both consist of dual confocal shock sources arranged at roughly 90 degrees. In one machine, the pulses are triggered non-simultaneously at a proprietary

short delay. In the other machine, the pulses may be triggered simultaneously or alternated at rates up to 4 Hz. There are many potential advantages of a dual pulse lithotripter, but we contend that the most persuasive relates to the rate effect discussed previously. When dual sources are triggered alternately, the rate of each source can be halved without increasing the length of treatment. One manufacturer suggests running both sources at the standard rate in order to complete a treatment session in half the time. Improvement relies on the assumption that the two shock wave paths are sufficiently different that bubbles generated by one source are not affected by the shock waves from the other source. In addition, if the confocal sources are triggered non-simultaneously then only half the total number of shock waves will be triggered along either one of the tissue paths. Lastly, an optimal interpulse delay could intensify cavitation¹⁷ or enhance internal waves within the stone. Timing a second shock wave to accelerate the collapse of cavitation bubbles excited by the first shock wave was the goal of the first dual pulse lithotripter, introduced at a meeting of the Acoustical Society of America in 1996.⁴² Additional benefits result from simultaneous triggering of the sources.⁴³ The additive effect of the simultaneous pulses meeting at the stone means the peak pressure of each source could be halved, sparing tissue damage along each path. Also, the additive pressure field is broader along the center line of the sources than the transverse field of either single source, perhaps yielding the benefit of additional squeezing.

Thus a scientific basis exists for the dual-pulse design, but some technical hurdles to clinical implementation remain. Challenges include timing variability (between the two sources or by different travel paths) that can lead to a change in the location of peak pressure within the body, and greater potential for tissue injury due to larger volumes of exposed tissue. Finally, coupling is doubly difficult with a dual-source dry-head lithotripter. All these effects could offset the potential benefits of dual-pulse lithotripsy, but are problems that should be reasonable to solve.

Looking to the future

Considerable progress is being made in understanding the mechanisms of shock wave action, and in finding ways to improve how lithotripsy is performed. Still, it is clear that the problem of adverse effects has not been solved, and ironic that the first lithotripter design is still the “gold standard.” Several areas of investigation promise to yield further advances, and refinement of protocols is ongoing in order to reduce the dose of shock waves needed to break stones, to improve coupling between the shock source and the patient, to explore the use of dual pulses to enhance stone breakage (and perhaps cancel out the adverse effects of cavitation on tissue), and to improve on imaging, targeting and real-time monitoring of stone breakage and tissue injury. These challenges leave open many avenues for future basic and translational research. Here we highlight several areas of active research in the field: computational modeling to optimize lithotripter design, image guidance to improve targeting and real-time monitoring, and the use of shock waves for orthopedic therapy.

SWL stands to gain from numerical modeling and simulation: Numerical modeling and simulation can help explain mechanisms of shock wave action, investigate parameter spaces, and predict outcomes. Shock-capturing numerical simulations of the Euler equations, for example, have led to new insights into the mechanisms by which tensile pressures are generated in the focal region.³⁴ Combined with models for the nucleation and dynamics of bubble clouds, these Euler simulations have also been used to confirm the “bubble shielding” hypothesis that is the basis of the rate effect discussed previously (Fig. 10). Models are also being developed to calculate the forces

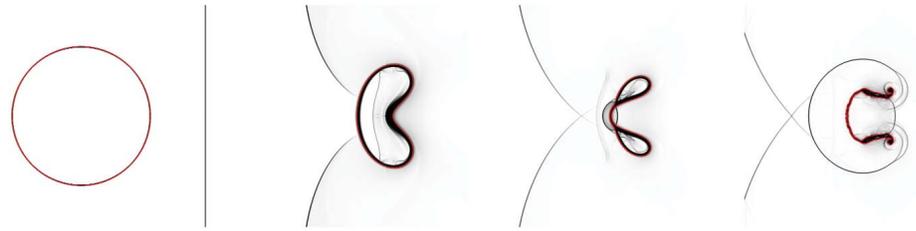


Fig. 12. Computed interaction of a shock wave with a cylindrical air bubble in water. Time progresses from left to right as a Mach 1.02 shock wave propagates from right to left. The shock initiates bubble collapse and a reentrant jet forms. When the reentrant jet collides with the distal side of the bubble, a secondary shock wave is formed.

generated from the collapse of a bubble cloud and to track the growth of cracks in model stones. A key benefit of simulations (especially when used in conjunction with experiments and clinical trials) is that it can be easier to isolate and control different physical effects (e.g. number of cavitation nuclei). An ultimate goal of modeling and simulation is in the design of more effective (and less injurious) lithotripters. For example, dual-head and piezoelectric-array based devices have more degrees of freedom than classical lithotripters; simulations provide a means by which different designs can be rapidly assessed. Simulations may determine optimal shock wave shape and delivery rate to maximize the force of impact of the bubble cloud (Fig. 11)⁴⁴ and individual bubbles (Fig. 12) to create the highest stresses within the stone. One might speculate on ways in which mature numerical tools may be integrated with imaging feedback to aid in treatment planning, perhaps even in real-time. For example, based on initial images of the stone, the beam width could be calculated and set. Then based on feedback that the stone has broken, a new beam width might be selected.

Imaging feedback could improve treatment: Imaging feedback coupled with the knowledge of how to adapt treatment has great potential. Researchers are currently probing x-ray computerized tomography (CT)

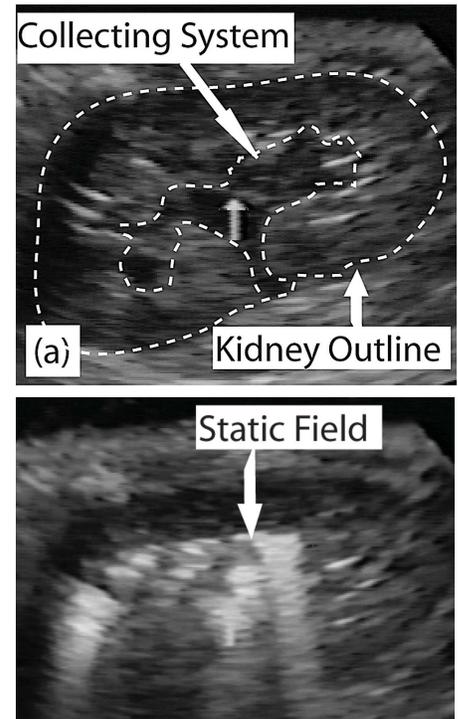


Fig. 13. B-mode ultrasound image of a pig kidney before (top) and during (bottom) SWL. The fluid collecting system in the center of the kidney lights up on the image with what appear to be bubbles. Transmission loss through the bubble cloud may effect treatment and the image provides the urologist feedback on the cloud. (Reprinted with permission from World Federation of Ultrasound in Medicine and Biology.¹³)

images used to diagnose stones for information on stone fragility.⁴⁵⁻⁴⁶ Stones with little chance of breaking might be screened from SWL treatment. Such images could also be input to one of the models described above to

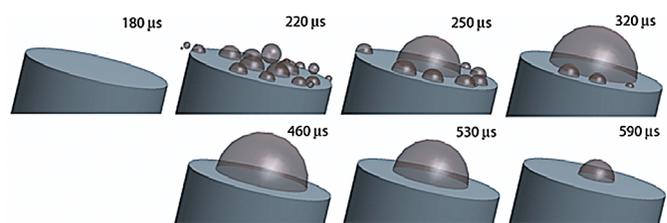
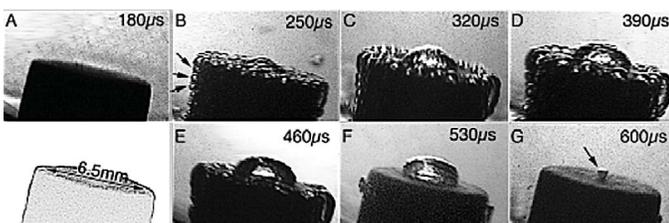


Fig. 11. Comparison of measured³⁶ and simulated bubble cluster collapse⁴⁴ at the distal face of a cylindrical model stone. The model can capture the complex cloud behavior around a stone, and potentially be used to test parameters, for example to maximize the pressure generated in the stone at collapse. Reprinted with permission from Journal of Endourology and IEEE. (© IEEE)

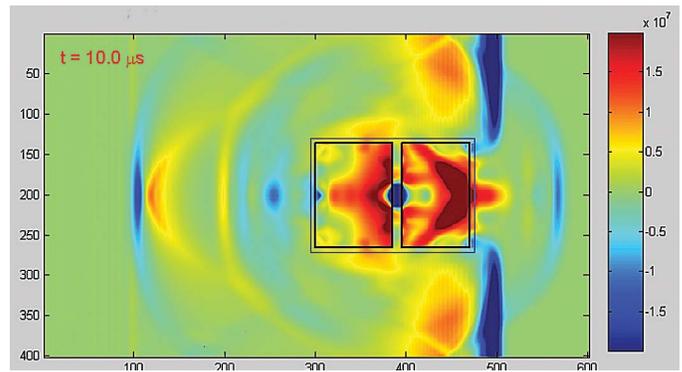
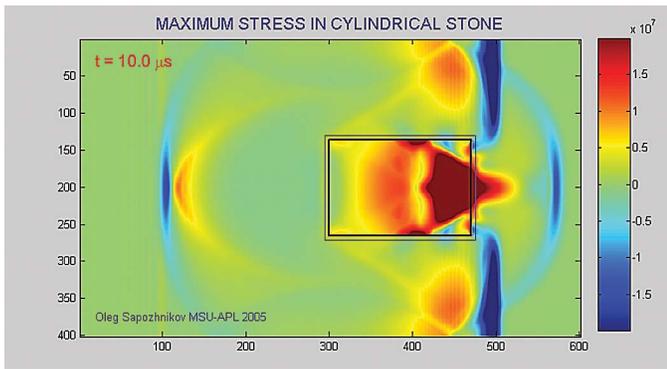


Fig. 14. Predicted acoustic scatter of a lithotripter shock wave from an intact cylindrical stone (left) and a cylindrical stone fractured vertically through its center (right). The differences can be detected by passive broadband remote hydrophones, and would give indication of whether the stone is fragmenting.⁴⁸

determine which angle of shock wave incidence will yield the highest internal stress. Fluoroscopy is the standard targeting modality for SWL in the U.S., in part because early ultrasound systems provided on lithotripters were poor compared to today's state-of-the-art radiology machines. However, fluoroscopy can only be used a handful of times throughout treatment to correct for significant changes in alignment, and it is difficult to discern whether the stone is even breaking. Imaging is only used to grossly align the stone in the focus. Portability, cost, real-time feedback, and avoidance of ionizing radiation have pushed an increasing number of manufacturers to provide ultrasound on shock wave devices. Ultrasound is already available, and largely untapped. There is an obvious need and opportunity for research to bring new imaging capabilities to this field. A reader of the second issue of *Acoustics Today* article on diagnostic ultrasound by E. Carr Everbach appreciates that ultrasound is well suited to detecting a solid stone within soft tissue and has the potential to provide other useful information.

In general, there is little feedback available to the clinician during SWL. Research on feedback includes monitoring cavitation (Fig. 13),¹³ identifying injury, tracking stone movement,⁴⁷ determining stone comminution, and detecting blood flow changes. Research *in vivo* indicates that the shielding by bubble clouds responsible for the rate effect appears as a highly reflective region in an ultrasound image. Thus, the clinician may choose to stop until the echogenicity dissipates in the image. Similarly, hematomas are identifiable in ultrasound images during lithotripsy. Research continues to attempt to correlate cavitation and injury. There is merit to the idea of tracking the stone during treatment, aiming or directing shock waves to hit the stone as it moves. Researchers have developed image processing techniques to determine stone location and mechanical and electronic beam steering techniques to place the lithotripter focus on the stone. This long-established research work may gain new influence now that the injuries associated with missing the stone with high-amplitude shock waves are appreciated and a new value is given each shock wave when attempting to slow rate but speed treatment. Surprisingly little has been done in determining whether a stone is breaking. It is not known if existing high-end ultrasound imagers can resolve stone fragments. Figure 14 shows one technique currently in development, the use of resonant

scattering of the shock wave off the stone to detect a change in stone size. The same linear elastic model from Fig. 7 shows different backscatter between the stone and the stone with a fracture.⁴⁸

Shock waves are not just for lithotripsy anymore: Currently in the U.S., shock wave therapy (SWT) is used in orthopedics to reduce pain in soft tissues around joints—plantar fasciitis (inflamed connective tissue in the heel), lateral epicondylitis (tennis elbow), and shoulder tendonitis. It is used more broadly in other parts of the world, for example to mend broken bones that will not heal, and to regenerating new blood vessels following a heart attack. SWT devices are shock wave generators that are patterned closely after, and in some cases duplicate, shock wave lithotripters. SWT would do well to learn from the wealth of experience developed in lithotripsy research. The first step would logically be to determine (numerically or experimentally) the acoustic fields created around reflective bony tissue targets. Hydrophones and methods to calibrate these high amplitude sources continue to be developed and refined. Two standards currently exist: a polyvinylidene fluoride (PVDF) piezoelectric film sensor and a fiber optic hydrophone which detects the change in refractive index due to the shock wave. From the acoustic fields, mechanisms of action and biological response can be determined by leveraging the understanding gained in SWL. Progress in understanding shock wave-tissue interactions will be essential before SWT can be refined much beyond its current state.

However, the SWT community appears to be receptive to research findings. Many SWT practitioners and manufacturers are attending and helping organize ASA special sessions on shock waves in medicine. Also, a decrease in pressure amplitudes and pulse repetition rates can be seen in the SWT literature. SWT was born at the pinnacle of the high peak pressure machines, and early SWT publications reported use of higher numbers, amplitudes, and rates of shock waves than used in SWL. Recently developed “ballistic” sources operate by launching an internal mass against the mass at the tip of the device in contact with the skin. Ballistic sources generate low peak positive pressures (~5 MPa) and do not generate a true shock front. Thus, early clinical SWT is responding to research findings, and reciprocally, SWL may benefit. For example, diagnostic ultrasound is more common for ortho-

pedics than urology, which may lead to increased use of ultrasound for guidance of shock wave delivery.**AT**

Conclusions

The acoustics community has played an important role in lithotripsy research, and this effort has had a major effect on how lithotripters are now being designed and how lithotripsy is being performed. Today the field of shock waves in medicine is open, with many opportunities for research and involvement in the continued development of novel therapies to treat important health problems. Progress seems inevitable, and with continued involvement and contribution from the acoustics community, we can look forward to significant advances in the future.

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References for further reading:

1. P.M. Knapp, T.B. Kulb, J.E. Lingeman, D.M. Newman, J.H. Mertz, P.G. Mosbaugh, and R.E. Steele, "Extracorporeal shock wave lithotripsy induced perirenal hematomas," *J. Urology* **139**, 700-703 (1988).
2. Consensus conference, "Prevention and treatment of kidney stones," *J. Am. Med. Assn.* **260**, 977 (1988).
3. F.L. Levy, B. Adams-Huet, and C.Y.C. Pak, "Ambulatory evaluation of nephrolithiasis: An update of a 1980 protocol," *Am. J. Med.* **98**, 51 (1995).
4. M.S. Pearle, E.A. Calhoun, and G.C. Curhan, "Urologic diseases in America Project: Urolithiasis," *J. Urology* **173**, 848-857 (2005).
5. D. Gravenstein, "Extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy," *Anesthesiology Clinics of North America* **18**, 953-971 (2000).
6. J. Lingeman, M. Delius, A. Evan, M. Gupta, K. Sarica, W. Strohmaier, J. McAteer, and J. Williams, "Bioeffects and physical mechanisms of SW effects in SWL," in *Stone Disease: First International Consultation on Stone Disease*, edited by J. Segura, P. Conort, S. Khoury, C. Pak, G.M. Preminger, and D. Tolley (Heath Publications, Paris, 2003), pp. 251-286.
7. A.P. Evan and J.A. McAteer, "Q-Effects of shock wave lithotripsy," in *Kidney Stones: Medical and Surgical Management*, edited by F.L. Coe, M.J. Favus, C.Y.C. Pak, J.H. Parks, and G.M. Preminger, (Lippincott Raven Publishers, Philadelphia, 1996), pp. 549-570.
8. A.P. Evan, L.R. Willis, J.E. Lingeman, and J.A. McAteer, "Renal trauma and the risk of long-term complications in shock wave lithotripsy," *Nephron* **78**, 1-8 (1998).
9. J.A. McAteer, M.R. Bailey, J.C. Williams, Jr., and R.O. Cleveland, and A.P. Evan, "Strategies for Improved Shock Wave Lithotripsy," *Minerva Urologica* **57**, 271 (2005).
10. A.P. Evan, J.A. McAteer, J.C. Williams, Jr., L.R. Willis, M.R. Bailey, L.A. Crum, J.E. Lingeman, and R.O. Cleveland, "Shock Wave Physics of Lithotripsy: Mechanisms of shock wave action and progress toward improved SWL," in *Textbook of Minimally Invasive Urology* edited by R. Moore, J.T. Bishoff, S. Loening, and S.G. Docimo (Martin Dunitz Limited, London, 2004), Chap. 28, pp. 425-438.
11. L.A. Crum, "Acoustic cavitation," *Proceedings of the IEEE Ultrasonics Symposium* **1**, 1-11 (1982).
12. A.J. Coleman, M.J. Choi, and J.E. Saunders, "Detection of acoustic emission from cavitation in tissue during extracorporeal lithotripsy," *Ultrasound in Med. and Biol.* **22**, 1079-1087 (1996).
13. M.R. Bailey, Y.A. Pishchalnikov, O.A. Sapozhnikov, R.O. Cleveland, J.A. McAteer, N.A. Miller, I.V. Pishchalnikova, B.A. Connors, L.A. Crum, and A.P. Evan, "Cavitation detection during shock wave lithotripsy," *Ultrasound in Med. and Biol.* **31**(9), 1245-1256 (2005).
14. M.R. Bailey, D.T. Blackstock, R.O. Cleveland, and L.A. Crum, "Comparison of electrohydraulic lithotripters with rigid and pressure-release ellipsoidal reflectors: I. Acoustic fields," *J. Acoust. Soc. Am.* **104**, 2517-2524 (1998).
15. M.R. Bailey, D.T. Blackstock, R.O. Cleveland, and L.A. Crum, "Comparison of electrohydraulic lithotripters with rigid and pressure-release ellipsoidal reflectors: II. Cavitation fields," *J. Acoust. Soc. Am.* **106**, 1149-1160 (1999).
16. A.P. Evan, L.R. Willis, B.A. Connors, Y. Shao, J.E. Lingeman, J.C. Williams, Jr., J.A. McAteer, N.S. Fineberg, M.R. Bailey, and L.A. Crum, "Kidney damage and renal functional changes are minimized by waveform control that suppresses cavitation in SWL," *J. Urology* **168**(4, Pt. 1), 1556-1562 (2002).
17. M.R. Bailey, R.O. Cleveland, D.T. Blackstock, and L.A. Crum, "Use of two pulses to control cavitation in lithotripsy," *Proceedings of the 16th International Congress on Acoustics* (Seattle, Washington, USA, 1998), pp. 2807-2808 and M.R. Bailey, "Control of acoustic cavitation with application to lithotripsy," Technical Report ARL-TR-97-1, Applied Research Laboratories, The University of Texas at Austin, Austin, Texas and Defense Technical Information Center, Belvoir, Virginia (1997).
18. Y. Zhou and P. Zhong, "Suppression of large intraluminal bubble expansion in shock wave lithotripsy without compromising stone comminution: Refinement of reflector geometry," *J. Acoust. Soc. Am.* **113**, 586-597 (2003).
19. J.C. Williams, J.F. Woodward, M.A. Stonehill, A.P. Evan, and J.A. McAteer, "Cell damage by lithotripter shock waves at high pressure to preclude cavitation," *Ultrasound in Med. and Biol.* **25**(9), 1445-1449 (1999).
20. D. Howard and B. Sturtevant, "In vitro study of the mechanical effects of shock-wave lithotripsy," *Ultrasound in Med. and Biol.* **23**, 1107-1122 (1997).
21. L.R. Willis, A.P. Evan, B.A. Connors, P.M. Blomgren, R.K. Handa, and J.E. Lingeman, "Same-pole application of low- and high-energy shock waves protects kidney from SWL-induced tissue injury," *J. Urology* **171**(4 suppl. S), 294 (abstr) (2004).
22. L.R. Willis, A.P. Evan, B.A. Connors, R.K. Handa, P.M. Blomgren, and J.E. Lingeman, "Prevention of lithotripsy-

- induced renal injury by pretreating kidneys with low-energy shock waves," *J. Am. Soc. Nephrol.* (in press) (2006).
23. J.E. Lingeman, "Extracorporeal shock wave lithotripsy devices: Are we making progress?" in *Topics in Clinical Urology*, edited by J.E. Lingeman and G.M. Preminger (Igaku-Shoin Medical Publishers, New York, 1996), pp. 79-96.
 24. N. Vakil, S.M. Gracewski, and E.C. Everbach, "Relationship of model stone properties to fragmentation mechanisms during lithotripsy," *J. Lithotripsy and Stone Disease* **3**(4), 304-310 (1991).
 25. M. Delius, F. Ueberle, and W. Eisenmenger, "Extracorporeal shock waves act by shock wave-gas bubble interaction," *Ultrasound in Med. and Biol.* **24**, 1055-9 (1998).
 26. Y.A. Pishchalnikov, O.A. Sapozhnikov, M.R. Bailey, J.C. Williams, Jr., R.O. Cleveland, T. Colonius, L.A. Crum, A.P. Evan, and J.A. McAteer, "Cavitation bubble cluster activity in the breakage of kidney stones by lithotripter shock waves," *J. Endourol.* **17**(7), 435-446 (2003).
 27. S.L. Zhu, F.H. Cocks, G.M. Preminger, P. Zhong, "The role of stress waves and cavitation in stone comminution in shock wave lithotripsy," *Ultrasound in Med. and Biol.* **28**, 661-671 (2002).
 28. M. Delius, M. Jordan, H. Eizenhoefer, E. Marlinghaus, G. Heine, H.G. Liebich, and W. Brendel, "Biological effects of shock waves: kidney haemorrhage by shock waves in dogs--administration rate dependence." *Ultrasound in Med. and Biol.* **14**(8), 689-94 (1988).
 29. R.F. Paterson, D.A. Lifshitz, J.E. Lingeman, A.P. Evan, B.A. Connors, J.C. Williams, Jr., and J.A. McAteer, "Stone fragmentation during shock wave lithotripsy is improved by slowing the shock wave rate: Studies with a new animal model." *J. Urol.* **168**, 2211-2215 (2002).
 30. K.T. Pace, D. Ghiculete, M. Harju, and R.J.D'A. Honey, "Shock wave lithotripsy at 60 or 120 shocks per minute: a randomized, double-blind trial," *J. Urol.* **174**, 595-599 (2005).
 31. K. Madbouly, A.M. El-Tiraifi, M. Seida, S.R. El-Faqih, R. Atassi, and R.F. Talic, "Slow versus fast shock wave lithotripsy rate for urolithiasis: a prospective randomized study," *J. Urol.* **173**, 127-130 (2005).
 32. O.A. Sapozhnikov, V.A. Khokhlova, M.R. Bailey, J.C. Williams, Jr., J.A. McAteer, R.O. Cleveland, and L.A. Crum, "Effect of overpressure and pulse repetition frequency on shock wave lithotripsy," *J. Acoust. Soc. Am.* **112**(3), 1183-1195 (2002).
 33. Y.A. Pishchalnikov, O.A. Sapozhnikov, M.R. Bailey, I.V. Pishchalnikova, J.C. Williams, Jr., and J.A. McAteer, "Cavitation selectively reduces the negative-pressure phase of lithotripter shock pulses," *Acoust. Res. Lett. Online* **6**(4), 280-286 (2005).
 34. M. Tanguay and T. Colonius, "Progress in modeling and simulation of shock wave lithotripsy (SWL)," *Proceedings of the 5th International Symposium on Cavitation* (Osaka, Japan 2003) <http://cav2003.me.es.osaka-u.ac.jp/Cav2003/Papers/Cav03-OS-2-1-010.pdf>. See also M. Tanguay, Ph.D. Thesis, California Institute of Technology.
 35. R.O. Cleveland, R. Anglade, and R.K. Babayan, "Effect of stone motion on in vitro comminution efficiency of a Storz Modulith SLX," *J. Endourol.* **18**(7), 629-33 (2004).
 36. W. Eisenmenger, "The mechanisms of stone fragmentation in ESWL," *Ultrasound in Med. and Biol.* **27**, 683-693 (2001).
 37. R.O. Cleveland and O.A. Sapozhnikov, "Modeling elastic waves in kidney stones with application to shock wave lithotripsy," *J. Acoust. Soc. Am.* **118**(4), 2667-76 (2005).
 38. O.A. Sapozhnikov, M.R. Bailey, A.D. Maxwell, B. MacConaghy, R.O. Cleveland, and L.A. Crum, "Assessing the mechanism of kidney stone comminution by a lithotripter shock pulse," *Proceedings of the 4th International Symposium on Therapeutic Ultrasound*, (Kyoto, Japan, 2005), 164-166.
 39. Y.A. Pishchalnikov, J.A. McAteer, I.V. Pishchalnikova, S. Beard, J.C. Williams, Jr., and M.R. Bailey, "Bubbles trapped at the coupling surface of the treatment head significantly reduce acoustic energy delivered in shock wave lithotripsy," *Proceedings of the 5th International Symposium on Therapeutic Ultrasound* (Boston, MA, October 2005) (in press).
 40. L. Eichel, P. Batzold, and E. Erturk, "Operator experience and adequate anesthesia improve treatment outcome with third-generation lithotripters," *J. Endourol.* **15**, 671-673 (2001).
 41. W. Eisenmenger, X.X. Du, C. Tang, S. Zhao, Y. Wang, F. Rong, D. Dai, M. Guan, and A. Qi, "The first clinical results of 'wide focus and low pressure' ESWL." *Ultrasound in Med. and Biol.* **28**(6), 769-774 (2002).
 42. M.R. Bailey and D.T. Blackstock, "Intensified cavitation produced with pressure release and rigid ellipsoidal reflectors," *J. Acoust. Soc. Am.* **99**(4, pt. 2), 2560 (1996).
 43. D.L. Sokolov, M.R. Bailey, and L.A. Crum, "Dual-pulse lithotripter accelerates stone fragmentation and reduces cell lysis in vitro," *Ultrasound in Med. and Biol.* **29**(7), 1045-1052 (2003).
 44. E.A. Zabolotskaya, Yu.A. Ilinskii, G.D. Meegan, and M.F. Hamilton, "Bubble interactions in clouds produced during shock wave lithotripsy," *Proceedings of the IEEE Ultrasonics Symposium* (IEEE 2004), 890-893.
 45. J.C. Williams, Jr., S.C. Kim, C.A. Zarse, J.A. McAteer, and J.E. Lingeman, "Progress in the use of helical CT for imaging urinary calculi," *J. Endourol.* **18**, 937-941 (2004).
 46. L-J. Wang, Y-C. Wong, C-K. Chuang, S-H. Chu, C-S. Chen, L-C. See, and Y-J. Chiang, "Predictions of outcomes of renal stones after extracorporeal shock wave lithotripsy from stone characteristics determined by unenhanced helical computed tomography: a multivariate analysis," *European Radiol.* **15**, 2238-2243 (2005).
 47. C. Bohris, T. Bayer, and C. Lechner, "Hit/miss monitoring of ESWL by spectral Doppler ultrasound," *Ultrasound in Med. and Biol.* **29**, 705-712 (2003).
 48. O.A. Sapozhnikov, L. Trusov, N.R. Owen, M.R. Bailey, and R.O. Cleveland, "Detecting fragmentation of kidney stones in lithotripsy by means of shock wave scattering," *Proceedings of the 5th International Symposium on Therapeutic Ultrasound* (Boston, MA October 2005) (in press).
 49. M.R. Bailey, V.A. Khokhlova, O.A. Sapozhnikov, S.G. Kargl, and L.A. Crum, "Physical mechanisms of the therapeutic effect of ultrasound," *Acoust. Phys.* **49**(4), 369-388 (2003).



Tim Colonius, Mark F. Hamilton, James A. McAteer, Michael R. Bailey, and Yuri A. Pishchalnikov

Michael R. Bailey worked with Robert Apfel, Glynn Holt, and Christy Holland as an undergraduate at Yale University. He received his Ph.D. from The University of Texas at Austin (1997) with David Blackstock as his advisor. Bailey moved to Lawrence Crum's group, now the Center for Industrial and Medical Ultrasound at Applied Physics Laboratory (APL), University of Washington. Bailey is currently a Senior Research Engineer at APL and PI of the APL portion of the lithotripsy program project (NIH DK43881) with Indiana University Medical School and Caltech. Bailey is chair of the ASA Technical Committee on Biomedical Ultrasound/Bioresponse to Vibration, an R. Bruce Lindsay Award winner (2004), an organizer of ASA special sessions, and a member of the AIUM Bio-effects Committee.

James A. McAteer is Professor of Anatomy and Cell Biology at the Indiana University School of Medicine, Indianapolis, and has worked in lithotripsy research for 20 years. Dr. McAteer is a member of the Acoustical Society of America, serving on the ASA Biomedical Ultrasound/Bioresponse to Vibration technical committee, and has contributed to several ASA special sessions on shock waves in medicine including Seattle (1998), Chicago (2001), Austin (2004), and Vancouver (2005).

Yuri A. Pishchalnikov received his M.S. degree in physics and Ph.D. degree in acoustics from M.V. Lomonosov Moscow State University, Moscow, Russia, in 1994 and 1997, respectively. He was a faculty member in the Department of Acoustics, Physics Faculty at Moscow State University from 1997 until 2003, where he worked in the nonlinear acoustics laboratory of Drs. Oleg V. Rudenko and Oleg A. Sapozhnikov. In 2003 Dr. Pishchalnikov joined the Department of Anatomy and Cell Biology at Indiana University, Indianapolis, Indiana. His primary research interests are in nonlinear acoustics and its application to medicine, focusing on research in shock wave lithotripsy. Dr. Pishchalnikov received a Joint Stipend award from the Acoustical Society of America and the Russian Acoustical Society in 1995. He is a member of the Biomedical Ultra-sound/Bioresponse to

Vibration technical committee of the Acoustical Society of America.

Mark F. Hamilton is the Harry L. Kent, Jr. Professor in Mechanical Engineering at the University of Texas at Austin, and he is Research Professor at Applied Research Laboratories, UT Austin. He earned his B.S. in Electrical Engineering at Columbia University, and his M.S. and Ph.D. in Acoustics at the Pennsylvania State University. He is actively involved in the Acoustical Society of America, having served most recently as its Vice President. He is a Fellow of the Society and was a recipient of the ASA F. V. Hunt Postdoctoral Research Fellowship and the R. Bruce Lindsay Award. He was also a recipient of the Fellowship for Science and Engineering from the David and Lucile Packard Foundation. He conducts research in physical acoustics, mainly nonlinear acoustics. His research currently focuses on biomedical applications, such as acoustic cavitation in lithotripsy in collaboration with Michael Bailey at Applied Physics Laboratory, University of Washington.

Tim Colonius received his B.S. degree from the University of Michigan and his M.S. and Ph.D. degrees from Stanford University (1994). He subsequently joined the faculty at the California Institute of Technology where he is now Professor of Mechanical Engineering. He and his group develop and use numerical simulation to study complex unsteady flow phenomena including turbulence, instability, aeroacoustics, shock waves, cavitation, and flow control. He was introduced to lithotripsy by the late Prof. Brad Sturtevant and joined the lithotripsy program project (NIH DK43881) with Indiana University in 1999. Colonius also leads a group of researchers working on closed-loop flow control for small unmanned air vehicles through a Multidisciplinary University Research Initiative (MURI). He received an NSF Career Award and serves on committees for the AIAA and the editorial board of *Theoretical and Computational Fluid Dynamics*.