Innovations in Lithotripsy Technology

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Abstract. The introduction of shock wave lithotripsy (SWL) in the early 1980’s revolutionized the surgical management for kidney stone disease. Since then, although numerous 2nd- and 3rd-generation lithotripters have been developed using various means for shock wave generation, focusing, patient coupling and stone localization, the technical improvements in these devices were largely made based on practical concerns for user convenience and multifunctionality of the system rather than a clear understanding of the working principles of SWL. In this paper, the fundamental mechanisms of stone comminution and tissue injury in SWL revealed by basic studies in the past two decades are first reviewed. This is followed by a summary of the innovations in SWL technology developed in recent years that have been demonstrated to provide improved stone comminution with concomitantly reduced tissue injury both in vitro using phantom systems and in vivo in animal models. Furthermore, the role of treatment strategy in determining the overall outcome of clinical lithotripsy is emphasized, and future prospects for lithotripsy research and technological innovations are discussed.

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HISTORY AND EVOLUTION OF SWL TECHNOLOGY

Dornier Medical Systems in Germany invented shock wave lithotripsy in the early 1980’s. The first lithotripter, the Dornier HM-3, was built based on electrohydraulic (EH) principles using an underwater spark discharge for shockwave generation and a truncated ellipsoidal reflector for wave focusing. The patient was immersed in a large water tub filled with degassed and deinoized water for acoustic coupling, and stone location was realized with bi-planar fluoroscopy. The FDA approved the clinical use of the HM-3 in the United States in 1984, and since then SWL has become the treatment of choice for upper urinary stone disease with widespread clinical applications [1].

The initial success of SWL prompted several manufacturers to introduce in the late 1980’s the 2nd-generation lithotripters, using different techniques for shock wave generation, wave focusing and patient coupling. Representative 2nd-generation lithotripters include the Siemens Lithostar, which uses an electromagnetic (EM) generator with an acoustic lens, both enclosed in a water cushion (“dry” lithotripter), and the Richard Wolf Piezolith-2300 that utilizes a self-focusing piezoelectric (PE) generator placed at the bottom of a small water basin. The primary changes in the design of the 2nd-generation lithotripters were the increased aperture angle of the shock

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wave source and reduced acoustic output energy [2] so that SWL could be performed under intravenous sedation rather than regional or general anesthesia as for the HM-3 [3]. Continued evolution in lithotripter design in the 1990’s led to the introduction of the 3rd-generation lithotripters, which are characterized by their multifunctional use for SWL, ureteroscopic and percutaneous procedures [4]. Up to now, more than 30 different models of commercial lithotripters have been designed and marketed. However, it should be noted that the technical improvements in the 2nd- and 3rd-generation lithotripters were largely made based on practical concerns for user convenience and multifunctionality of the system rather than a rigorous understanding of the underlying mechanisms in SWL [3,5].

Limitations of Current SWL Technology

Although the means for shock wave generation, focusing, patient coupling, and stone localization in lithotripter design have evolved significantly in the past two decades, the fundamental principle of SWL remains unchanged. Independent of the technologies used, almost all commercial lithotripters produce a similar pressure waveform at the focus, which can be characterized by a leading shock front with a compressive wave followed by a trailing tensile wave. The acoustic fields produced by different lithotripters differ from each other in peak amplitude and pulse profile of the pressure waveform, beam size, pulse energy, and therefore, their overall performance [2]. Moreover, the evolution of lithotripter design thus far has overwhelmingly, and perhaps mistakenly, relied on the importance of the compressive component of the lithotripter shock wave (LSW) with almost total neglect of the contribution of the tensile component of the waveform [5]. Further, a growing number of clinical studies have demonstrated that the 2nd- and 3rd-generation lithotripters are often less effective in stone comminution yet with increased propensity for tissue injury and higher stone recurrence rate, compared to the original Dornier HM-3 lithotripter [3,6,7]. Although multiple factors (e.g., beam size, total acoustic energy, and coupling condition, etc.) may contribute to the reduced effectiveness of the newer generation lithotripters, it is critical to gain a fundamental understanding of the mechanisms of stone comminution and tissue injury before better and improved SWL technologies can be developed.

MECHANISMS OF STONE COMMINUTION IN SWL

In the past two decades, significant progress has been made in understanding how SWL works. At the fundamental level, several mechanisms have been proposed as contributory factors for stone comminution in SWL. These include stress gradients built up in the target stone near wave entry and exit sites [8], spalling at the posterior surface due to acoustic impedance mismatch and geometric focusing [8-10], cavitation [11-13], shear stress [10,14], squeezing [15], and dynamic fatigue [16]. In general, these multiple mechanisms can be divided into two categories: stress waves that act inside the stone and cavitation that acts in the surrounding fluid, as revealed by high-speed photoelastic imaging (Fig. 1). Since most kidney stones are brittle materials
[17,18], they fail easily under tension and shear stress or by separation of crystalline-matrix boundaries [19], leading to the formation of relatively large fragments. Cavitation bubbles induced by LSW, in contrast, first expand several hundred times their original size, and then collapse violently, generating strong secondary shock waves and/or high-speed liquid jets impinging toward the stone surface [20-22]. Cavitation damage is characterized by minute pittings as a result of localized stress concentration [12,23].

FIGURE 1. High-speed photoelastic imaging sequence demonstrating the transient shock wave-stone interaction with resultant stress wave generation inside an epoxy stone phantom (10 mm in diameter), and the expansion, coalescence, and violent collapse of cavitation bubbles in the fluid surrounding the stone phantom. The incident shock wave propagates from the bottom to the top, and the number in each frame indicates the time delay in microseconds after the spark discharge of the HM-3 lithotripter. DSW: direct shock wave, FSW: focused shock wave.

At the practical level, the contributions of stress waves and cavitation to the overall success of stone comminution in SWL have been investigated [24]. It was found that stress wave-induced fracture dominates the initial disintegration of kidney stones while cavitation is necessary to produce fine, passable fragments that are most critical for the success of clinical SWL. The action of lithotripter-induced stress waves alone was found to be much less effective in comminuting small residual fragments, presumably due to destructive wave superposition. It was suggested that stress waves and cavitation work synergistically, rather than independently, to produce effective stone fragmentation in SWL [24]. Further, cavitation induced pittings could weaken the structure of residual stone fragments, making them much more susceptible under the impact of subsequent lithotripter pulses. This speculation is confirmed by the failure of stone phantoms with geometric configuration that are refractive to spalling and shear-induced damage in castor oil, with damage occurring only when pittings generated by the collapse of laser-induced single bubbles are present on the surface of the phantom before the treatment (Fig. 2).
MECHANISMS OF TISSUE INJURY IN SWL

Tissue injury in SWL is characterized primarily by vascular lesions (damage of endothelial cells and rupture of small blood vessels), which extend along the shock wave propagation path throughout the thickness of the kidney [25,26]. Animal studies have identified several risk factors, including lithotripter parameters (shock number, output energy, pulse repetition rate) and kidney status (solitary or pediatric kidneys, renal infection, elderly patients with pre-existing hypertension) [27,28]. Over the years, two primary mechanisms have been postulated for SWL-induced vascular injury: cavitation [29,30] and shear stress [31,32]. However, other than anecdotal evidence, there is no direct proof to substantiate these theories because of the difficulties in measuring cavitation and LSW-induced shear stresses in vivo. Using vessel phantoms made of 200 μm cellulose hollow fibers, we have shown via high-speed imaging in vitro that LSW-induced bubble dynamics in small vessels are distinctly different from that induced in free field. Specifically, the initial expansion of the bubble is significantly constrained by the vessel wall. The bubble deforms asymmetrically, leading to substantially weakened collapse. Conversely, the vessel wall could be dilated substantially by the rapid, large intraluminal expansion of the bubble, which could lead to the rupture of small blood vessels [33]. This hypothesis is supported by animal experiments using inverted lithotripter pulses, which significantly suppress intraluminal bubble expansion and lead to minimal tissue damage even after a clinical dose of shock wave exposure [32]. In addition to the direct mechanical damage caused by LSW, there is also evidence of a secondary injury caused by ischemia/reperfusion [34,35].

**FIGURE 2.** Thin slabs of BegoStone phantoms (10x10x3.5 mm, LxWxH), which are refractive to stress wave-induced fracture in castor oil after 200 shocks in an HM-3 at 20 kV, can be damaged (i.e., with new fracture line formation) if cavitation pittings are present on the surface of the phantom before the shock wave treatment. To mimic cavitation damage, the surfaces of the stone samples were treated by laser-induced single bubbles to create 3x3 mm pitting arrays with average pitting size ranging from 100 to 250 μm. The propensity of fracture line formation was found to increase with pitting size.
INNOVATIONS IN SWL TECHNOLOGY

In the past decade, several methods have been proposed to improve the effectiveness and safety of SWL. Most of the improvements have been focused on control of LSW-induced cavitation. Michael Delius first proposed the concept of tandem pulse lithotripsy [36]. Bailey and colleagues have developed a dual head lithotripter design that was intended to concentrate cavitation towards the lithotripter focus while suppressing bubble activities outside the focal volume [37,38]. In Bailey’s design, two EH generators, aligned coaxially facing each other, are fired simultaneously and they produce comparable shock waves. We have employed a different approach to achieve cavitation control in SWL. We have designed and fabricated a piezoelectric annular array (PEAA) generator that can be retrofitted around the outer surface of an HM-3 reflector. The PEAA generator is aligned coaxially and confocally with the HM-3, making it convenient for patient coupling. In addition, the PEAA generator is used to produce a time-delayed, much weaker shock wave (~10 MPa) with longer compressive pulse duration (~3 μs). This unique feature of the PEAA generator can be used to selectively intensify the primary collapse of LSW-induced cavitation bubbles near the stone surface for improved stone comminution [5,39]. Microsecond tandem-pulse lithotripsy has also been tested in a piezoelectric shock wave lithotripter with improved stone fragmentation in vitro [40]. A second significant development in SWL technology is the in situ pulse superposition concept, which can be easily implemented in an EH lithotripter via a reflector insert to reduce large intraluminal bubble expansion and thus the propensity of LSW-induced vascular injury [41,42].

Figure 3. In vivo animal experiments comparing stone comminution after 2,000 shocks produced by the original HM-3 at 20 kV, HM-3 with upgraded reflector at 22 kV, and combined system of HM-3 with upgraded reflector at 22 kV and PEAA generator at 4 kV. No stone fragmentation could be produced by using the PEAA generator at 4 kV alone. At least 4 pigs were used in each group.

By upgrading the original HM-3 lithotripter with a reflector insert and a PEAA generator, we have shown in a swine model that in vivo stone comminution could be
significantly improved (Fig. 3) while collateral tissue injury was substantially reduced following a clinical dose of shock wave treatment. These preliminary results support the hypothesis that optimization of lithotripter pulse profile and sequence may improve the overall stone comminution with reduced tissue injury.

Another interesting development in SWL technology is the introduction of the self-focusing electromagnetic shock wave lithotripter, characterized by wide-focus and low-pressure, which has been shown to be very effective in clinical studies [43].

**IMPACT OF TREATMENT STRATEGY ON SWL OUTCOME**

An important factor that may influence significantly the outcome of clinical SWL is treatment strategy. For a given total amount of shock waves and acoustic energy, it has been shown that a progressive increase of lithotripter output will produce better stone comminution, compared to other strategies (i.e., progressive decrease or constant output) [44-46]. This result is presumably caused by the impact of treatment strategy on the relative contributions of stress waves and cavitation to the overall stone comminution process in SWL [45]. In addition, it has been shown that a slow pulse repetition rate (i.e., 0.5 Hz) produces better stone fragmentation than a fast rate (i.e., 2.0 Hz). This result has been attributed to the attenuation effect of residual micro-bubbles in the fluid surrounding the stone on the transmission of the tensile component of the ensuing LSW’s to the target stone [47,48]. An added benefit of the progressive increase of output energy strategy is that it may also reduce tissue injury. This speculation is supported by recent animal experiments which demonstrate that pre-treatment of the kidney with a few hundreds of low energy shocks can protect the same region of the kidney from a subsequent clinical dose of high-energy shocks, presumably due to SWL-induced vasoconstriction [49].

**FUTURE PROSPECTS**

The evolution of lithotripsy technology depends critically on our improved understanding of the fundamental mechanisms of stone comminution and tissue injury, as well as on a better appreciation of the critical factors that influence the outcome of clinical lithotripsy procedures. Although much progress has been made in basic research of SWL in the past ten years, new questions have also emerged regarding the interaction of various mechanisms in determining the overall treatment outcome. Specifically, there is a need to better understand the role of various mechanisms in the progressive comminution of residual stones of different size and irregular geometry to fine particles (less than 2 mm) that can be discharged spontaneously following SWL. The interaction between stress waves and cavitation, and how to maximize their synergy to produce more effective stone comminution in SWL needs to be further investigated. Moreover, the influence of the profile of LSW, pressure and energy distribution (i.e., beam size), as well as cavitation activities on lithotripsy outcome should be further examined using more realistic phantoms of the kidney and collecting system, as well as animal models. Furthermore, there is a need for the development of
relevant and efficient 3-D numerical models of shock wave generation, propagation, focusing and interaction with kidney stones and renal tissues.

For the practical application of SWL, there are concerns regarding maintaining adequate coupling of the shock wave into the patient, especially for “dry coupling” lithotripters [50]. Therefore, development of techniques to monitor the coupling condition during SWL and/or better coupling methods for shock wave delivery to the patient should directly impact the success of clinical lithotripsy. Further, monitoring of stone comminution progress in vivo with concomitant adjustment of lithotripter focusing is another area that needs more thorough investigations. Finally, optimization of treatment strategy to maximize stone comminution and minimize tissue injury should be systematically investigated. Recent studies have already demonstrated the benefit of “priming” with low-energy shock waves on the success of stone comminution and in protecting renal tissues from the treatment of an ensuing clinical dose of high-energy shock waves. Development of better treatment strategies should directly benefit the clinical success of lithotripsy procedures.

Although the feasibility of several novel SWL technologies have already been demonstrated in in vitro phantoms and in animal models, these technologies must be further optimized in terms of engineering design (for example, optimization of transducer design, pressure waveform, and reflector insert geometry), system integration, and combination with improved treatment protocols so that their potential can be fully utilized to provide better and safer SWL. As demonstrated clearly by the introduction of SWL technology in the early 1980’s, the success of translating novel lithotripsy technologies from academic laboratories to clinical practice in the near future will ultimately depend on multidisciplinary collaborations between academic researchers, urologists, and lithotripter manufacturers.

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