DYNAMICS OF BUBBLE OSCILLATION IN CONSTRAINED MEDIA AND MECHANISMS OF VESSEL RUPTURE IN SWL

PEI ZHONG, YUFENG ZHOU andSONGLIN ZHU
Department of Mechanical Engineering and Materials Science, Duke University, Durham, NC, USA

Abstract—Rupture of small blood vessels is a primary feature of the vascular injury associated with shock-wave lithotripsy (SWL) and cavitation has been implicated as a potential mechanism. To understand more precisely the underlying mechanical cause of the injury, the dynamics of SWL-induced bubble dynamics in constrained media were investigated. Silicone tubing and regenerated cellulose hollow fibers of various inner diameters (0.2 to 1.5 mm) were used to fabricate vessel phantoms, which were placed in a test chamber filled with castor oil so that cavitation outside the phantom could be suppressed. Degassed water seeded with 0.2% Albunex® contrast agent was circulated inside the vessel phantom, and intraluminal bubble dynamics during SWL were examined by high-speed shadowgraph imaging and passive cavitation detection via a 20-MHz focused transducer. It was observed that, in contrast to the typical large and prolonged expansion and violent inertial collapse of SWL-induced bubbles in a free field, the expansion of the bubbles inside the vessel phantom was significantly constrained, leading to asymmetric elongation of the bubbles along the vessel axis and, presumably, much weakened collapse. The severity of the constraint is vessel-size dependent, and increases dramatically when the inner diameter of the vessel becomes smaller than 300 μm. Conversely, the rapid, large intraluminal expansion of the bubbles causes a significant dilation of the vessel wall, leading to consistent rupture of the hollow fibers (i.d. = 200 μm) after less than 20 pulses of shock wave exposure in a XL-1 lithotripter. The rupture is dose-dependent, and varies with the spatial location of the vessel phantom in the lithotripter field. Further, when the large intraluminal bubble expansion was suppressed by inversion of the lithotripter pressure waveform, rupture of the hollow fiber could be avoided even after 100 shocks. Theoretical calculation of SWL-induced bubble dynamics in blood confirms that the propensity of vascular injury due to intraluminal bubble expansion increases with the tensile pressure of the lithotripter shock wave, and with the reduction of the inner diameter of the vessel. It is suggested that selective truncation of the tensile pressure of the shock wave may reduce tissue injury without compromising the fragmentation capability of the lithotripter pulse. (E-mail: pzhong@acpub.duke.edu) © 2001 World Federation for Ultrasound in Medicine & Biology.

Key Words: Cavitation, Shock-wave lithotripsy, Tissue constraint, Tissue injury, Vessel phantoms, High-speed imaging, Passive cavitation detection.

INTRODUCTION

Although shock-wave lithotripsy (SWL) has been used routinely for the treatment of urolithiasis in the past two decades (Chaussy et al. 1980; Chaussy and Fuchs 1989; Renner and Rassweiler 1999), it also causes acute renal injury, such as hemorrhage, hematoma and edema (Knapp et al. 1988; Delius et al. 1988; Jaeger et al. 1988; Karlson et al. 1991). The primary features of the injury are vascular lesions, characterized by extensive damage of the endothelial cells and rupture of blood vessels, with capillary and small blood vessels much more susceptible to SWL injury than large vessels (Delius et al. 1988; Weber et al. 1992). Although most patients with normal renal function recover well following SWL, there are subgroups of patients who are at much higher risk for chronic injury (Evan and McAteer 1996). These include patients with solitary kidneys, preexisting hypertension and, in particular, pediatric and elderly patients (Lifshitz et al. 1998; Knapp et al. 1996). In fact, the long-term clinical consequences of SWL on renal function of high-risk patients are still under investigation (Evan et al. 1998b). To reduce the adverse effects of SWL, it is essential to understand the mechanisms whereby lithotripter shock waves cause tissue injury, so that appropriate counteractive strategies may be developed.
Two different mechanisms have been implicated for tissue injury in SWL: cavitation and shear stress. Evidence supporting a cavitation mechanism includes the spatial correlation between hyperechogenicity in B-scan ultrasound (US) imaging (scattered from SWL-induced bubbles and/or their remnants) and intrarenal hemorrhage (Kuwahara et al. 1989), increased tissue injury at high pulse-repetition rate (Delius et al. 1990b), and with the injection of US contrast agents, even at pressure levels ineffective for stone fragmentation (Dalecki et al. 1997). Alternatively, it has been suggested that shear stresses can be generated at a shock front propagating in a heterogeneous medium, such as kidney, due to wave scattering (Howard and Sturtevant 1997). In vitro experiments have demonstrated that such a mechanism can cause damage to nitrocellulose membranes (Howard and Sturtevant 1997). However, whether such a mechanism could lead to vascular injury in vivo is still uncertain and requires further investigation. One way to separate the effect of cavitation from that due to shear stress is the use of inverted lithotripter pulses, which can be generated by a pressure-release reflector (Bailey et al. 1998). Although comparable in pressure amplitude, pulse duration and acoustic energy with the standard lithotripter shock wave (LSW), the inverted LSW has a leading tensile wave, followed immediately by a much stronger compressive wave, which significantly suppresses cavitation (Bailey et al. 1998, 1999). Yet, in principle, shock front distortion and shear stress generation would still be produced by an inverted LSW propagating through inhomogeneous tissues. Animal studies using inverted LSWs revealed minimal tissue damage after shock-wave exposure at a clinical dose of 2000 shocks between 16 and 24 kV (Evan et al. 1998a). This finding seems to favor cavitation over shear stress as the primary mechanism of tissue injury in SWL.

The dynamics of LSW-induced cavitation in a free field are characterized by an initial large and prolonged expansion (a few hundred \( \mu s \)), followed by subsequent violent collapses of the bubbles (Church 1989; Coleman et al. 1992; Zhong et al. 1997, 1999a). The mechanical stresses generated either by the symmetrical collapse of the bubbles with strong secondary shock-wave emission or asymmetrical collapse with microjet formation are important contributory factors to stone comminution (Coleman et al. 1987; Crum 1988; Sass et al. 1991; Zhong and Chuong 1993; Zhong et al. 1993; Philipp and Lauterborn 1998; Xi and Zhong 2000). The violent collapse of cavitation bubbles and associated shock-wave emission and shear stresses generated by the rapid fluid movement are also believed to contribute to the cellular damage observed in in vitro studies (Carstensen et al. 1993; Delius 1994) However, because of the limited fluid-filled space in tissue, LSW-induced cavitation bubbles in vivo cannot expand freely to the maximum size achievable in vitro; instead, their expansion is significantly constrained (Zhong et al. 1997, 1998). Recent study using EHL-generated single bubbles has clearly demonstrated that, due to constrained expansion, the collapse of a cavitation bubble in a silicone tube is substantially weakened compared to the collapse of an unconstrained bubble in a free field (Zhong et al. 1999b). These observations suggest that a mechanism different from the classic theory of cavitation damage in vitro in an unconstrained medium (i.e., strong secondary shock emission or jet formation due to violent bubble collapse) may be responsible for cavitation-produced vascular injury, especially in small blood vessels where tissue constraining effect on bubble expansion is most pronounced. Based on theoretical calculations, we have postulated that LSW-induced intraluminal bubble expansion could cause significant dilation of the blood vessel, which may lead to rupture of capillary and small blood vessels, provided that cavitation nuclei larger than 10 nm in radius exist in blood (Zhong et al. 1998).

To ascertain the mechanism of cavitation-induced vascular injury in SWL, it is imperative to understand the dynamics of bubble oscillation in vessels. This information is currently lacking, due to either insufficient temporal and spatial resolution of the B-scan US imaging that has been used to assess cavitation in tissue during SWL (Kuwahara et al. 1989; Delius et al. 1990a; Coleman et al. 1995) or difficulties in observing LSW-induced inertial cavitation in vivo directly. Although various alternative techniques such as passive cavitation detection (PCD) via a focused hydrophone (Coleman et al. 1996; Zhong et al. 1997, 1998) and optical cavitation detection (OCD) via laser fiberoptic device (Huber et al. 1994) have been used to assess cavitation in vivo, these methods provide little information about the mechanical interaction between the oscillating bubbles and surrounding tissue structure. Therefore, their implication on the mechanism of vascular damage is limited. To elucidate bubble-tissue interaction, high-speed photography would be the most appropriate technique. Yet, so far, it has been used primarily to study LSW-induced bubble oscillation in vitro in unconstrained media (Sass et al. 1991; Philipp et al. 1993; Jochle et al. 1996; Zhong et al. 1997, 1999a).

In this work, we first investigated LSW-induced bubble oscillation in silicone tubing and cellulose hollow fibers, which were used to mimic blood vessels of various sizes. These vessel phantoms were immersed in an optically and acoustically transparent chamber filled with castor oil, so that cavitation outside the phantom could be suppressed. Degassed water containing 0.2% Albunex® US contrast agent serving as cavitation nuclei was circulated inside the tube. With this arrangement, bubble dynamics inside the phantom could be visualized by
high-speed imaging while the associated acoustic emission recorded by PCD technique. Using such an approach, a clear size-dependent constraining effect of the vessel phantom on SWL-induced intraluminal bubble expansion was observed, on the other hand. The intraluminal expansion of the bubbles, on the other hand, was found to cause significant dilation of the phantom wall, leading to consistent rupture of the hollow fibers (i.d. = 200 μm) after less than 20 pulses of shock-wave exposure. The rupture is dose-dependent, and varies with the spatial location of the vessel phantom in the lithotripter field. Furthermore, it was found that, when the large intraluminal bubble expansion was suppressed by inversion of the LSW, rupture of the hollow fiber could be avoided even after 100 shocks. All together, these results provide the first experimental evidence that supports the hypothesis that rapid, large intraluminal bubble expansion could cause rupture of small blood vessels in SWL, if appropriate cavitation nuclei exist in the blood. In the second part of this study, we evaluated the potential of vascular injury due to intraluminal bubble expansion and the size-dependency of the injury based on theoretical calculations of LSW-induced bubble dynamics in blood.

EXPERIMENTAL DESIGN AND METHODS

Lithotripter

The experiments in this study were carried out in a Dornier XL-1 experimental electrohydraulic shock-wave lithotripter, which employs a hemi-ellipsoidal reflector with semimajor axis \( a = 110.3 \) mm, semiminor axis \( b = 78 \) mm, and half-focal length \( c = 78 \) mm. At the beam focus (F2), the XL-1 generated LSW at 25 kV has a peak positive/negative pressure of \( 68/\pm 17.6 \) MPa, with a 6-dB beam size of 22 × 5 mm, along and transverse to the lithotripter axis, respectively (Zhong et al. 1999a). In the experiments where waveform inversion of the LSW was needed, a pressure-release hemi-ellipsoidal reflector insert (\( a = 98.3 \) mm, \( b = 60 \) mm, and \( c = 78 \) mm) made of polyurethane foam (Last-a-Foam, General Plastics, Tacoma, WA) was placed snugly inside the original XL-1 reflector. The insert reflector shared the same foci with the original XL-1, despite that the aperture angle of the reflector was reduced from 90° to 75°. Pressure-release reflector has been used previously to produce inverted LSWs that significantly suppress cavitation (Bailey et al. 1998, 1999).

Vessel phantoms

Silicone tubing of various i.d. (0.3, 0.5, 1.0, and 1.5 mm, 62,999–850, –852, –858, and –860, VWR S/P, Atlanta, GA) and thin-walled, regenerated cellulose (RC) hollow fibers of 200-μm i.d. were used to construct vessel phantoms. The RC hollow fibers were taken from commercially available fiber bundles (132290, Spectrum, Gardena, CA) developed for dialysis and ultrafiltration. The silicone tubing and hollow fibers were cut into ~70-mm long segments, and then embedded in straight connectors (E-31801–00, Cole-Parmer, Vernon Hills, IL) at both ends using fast curing epoxy. The free space between the connectors is about 34 mm, sufficiently wider than the beam diameter of the lithotripter field. In the experiment, each tubing or fiber assembly was connected to a circulation system driven by a peristaltic pump (Model 7619–50, Cole-Parmer) operating at its lowest speed, which yields a mean flow rate ranging from 4.0 to 241 mm/s inside the tube, depending on its size. To allow a clear observation of LSW-induced bubble dynamics inside the tube, degassed water (O2 concentration: < 4 mg/L) containing 0.2% Albunex® serving as cavitation nuclei was used as the test fluid. Further, the assembly was immersed in a 100-mm cubic test chamber made of Lucite® (with a 115-μm thick polyester membrane bottom) filled with freshly poured, highly viscous castor oil that significantly suppressed cavitation outside the tube. The test chamber was placed on top of the XL-1 reflector, and the chamber has optical and acoustic windows (D = 50 mm) built-in on its lateral walls to facilitate high-speed imaging and PCD. The tube assembly was attached to an inverted U-shape holder fixed on a three-axis translation stage for positioning and scanning the vessel phantom in the lithotripter field (Fig. 1). To minimize the influence of reflected wave from the oil surface on bubble dynamics at F2, an independently positioned conical pointer (cone angle = 30°) was placed downward along the lithotripter axis 15 mm into the
castor oil. In a typical setup, the distance between oil surface and F2 was 30 mm, and from F2 to the bottom of the test chamber was 50 mm. The conical pointer was used to diverge (or reflect) the incident LSW to the lateral sides, away from F2. Table 1 summarizes the physical dimensions, properties and flow condition of the vessel phantoms.

Limited data are available on the mechanical properties of the silicone tubing and RC hollow fibers for a thorough comparison with blood vessels. Based on manufacturer-supplied information, the elastic modulus of the silicone tubing is 2 MPa, which is within the range of 0.5 to 5.0 MPa reported for human arteries (Learoyd and Taylor, 1986). Yet, the tensile failure strength of the silicone tubing ($\sigma_f = 8.4$ MPa) is much higher than that ($\sigma_f = 1.47$ to 5.07 MPa) reported for human thoracic aorta (Mohan and Melvin, 1982). All these values were obtained under static or low strain-rate conditions. For the RC hollow fiber, the static tensile failure occurs at 15% elongation, with a corresponding $\sigma_f = 1.35$ MPa (Product information, Spectrum, Gardena, CA) similar to that of the human thoracic aorta.

**Physical characterization**

Several techniques (detailed in the following) were used to characterize the dynamics of LSW-induced bubble oscillation in the vessel phantoms. To provide a baseline comparison, similar measurements were also carried out in free field (test chamber filled with degassed water).

**High-speed imaging.** Bubble dynamics in the free field were characterized by using a high-speed shadowgraph imaging system (low magnification) set up inside a modified XL-1 lithotripter tank (Fig. 2). A pulsed Nd:YAG laser (MiniLaseI, New Wave Research, Sunnyvale, CA, $\lambda = 512$ nm and $t_p = 6$ ns) was expanded by a concave lens and collimated using a Schlieren mirror to form a parallel light beam through the test chamber. In the experiment, the spark discharge of the lithotripter was picked up by a fast photodetector (PDA50, Thorlabs, Newton, NJ) and fed into a digital storage oscilloscope (Model 9314, LeCroy, Chestnut Ridge, NY), which established a reference time ($t = 0$ s) for the whole event. The synchronized output of the scope was relayed to a multichannel digital delay generator (DS535, Stanford Research Systems, Sunnyvale, CA) to control the trigger of the pulsed laser, a CCD camera (GP-MF 552, Panasonic, Secaucus, NJ) and a frame grabber (DT3155, Data Translation, Marlboro, MA), respectively. By adjusting the delay time of the trigger signals, a series of high-speed shadowgraph images can be recorded at various stages of the bubble oscillation. In general, triplicate of images was recorded at each selected time instant, from which a representative sequence of the whole event was then composed.

To examine bubble dynamics in the vessel phantom, a high-magnification optical imaging system consisting of a reading telescope (450100, Spinder & Hoyer, Milford, MA) with an auxiliary close-up lens (449006, Spinder & Hoyer; working distance = 165 to 200 mm) was established. Both the low- and high-magnification imaging systems were mounted on an optical breadboard (30.5 × 45.7 × 1.9 cm) that can be slid horizontally, allowing an easy exchange between the two systems. Magnification of each optical system was calibrated by imaging a transparent scale (0.1-mm resolution) placed

---

**Table 1. Physical dimensions, properties and flow rate of the vessel phantoms**

<table>
<thead>
<tr>
<th>Materials</th>
<th>Cat. no.</th>
<th>i.d. (mm)</th>
<th>o.d. (mm)</th>
<th>$\sigma_f$ (MPa)</th>
<th>$v$ (mm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RC hollow fiber</td>
<td>132290</td>
<td>0.200</td>
<td>0.216</td>
<td>1.35</td>
<td>241</td>
</tr>
<tr>
<td>Silicone tubing</td>
<td>62999-850</td>
<td>0.305</td>
<td>0.635</td>
<td>8.40</td>
<td>93.7</td>
</tr>
<tr>
<td>Silicone tubing</td>
<td>62999-852</td>
<td>0.508</td>
<td>0.940</td>
<td>8.40</td>
<td>33.8</td>
</tr>
<tr>
<td>Silicone tubing</td>
<td>62999-858</td>
<td>1.016</td>
<td>2.159</td>
<td>8.40</td>
<td>8.44</td>
</tr>
<tr>
<td>Silicone tubing</td>
<td>62999-860</td>
<td>1.473</td>
<td>1.956</td>
<td>8.40</td>
<td>4.02</td>
</tr>
</tbody>
</table>

*Supplied by SPECTRUM, Gardena, CA. RC = regenerated cellulose; † Supplied by VWR Scientific Products, Atlanta, GA; $\sigma_f$ = static tensile failure strength; $v$ = mean flow rate of the test fluid inside the vessel phantom.
either in water or in castor oil at F2 inside the test chamber.

**PCD.** Acoustic emission (AE) associated with LSW-induced bubble oscillation in the free field was detected using a PCD system with 1-MHz focused transducer (V392-SU, Panametrics, Waltham, MA) with a focal length \( F = 101.6 \text{ mm} \) and a nominal element diameter \( D = 38 \text{ mm} \) (Zhong et al. 1997). AE emanating from the vessel phantom was measured using a 20-MHz focused transducer (V317-SU, Panametrics) with \( F = 25.4 \text{ mm} \) and \( D = 6 \text{ mm} \). Based on manufacturer-supplied information (Technical Notes, Panametrics), the \( -6 \text{-dB} \) reception zone of the transducer was calculated using the following formulas:

\[
BD_{-6\text{-dB}} = \frac{1.028F\lambda}{D}, \tag{1}
\]

\[
F_{z-6\text{-dB}} = NS_{F}^{2}\left[\frac{2}{1 + 0.5NS_{F}}\right], \tag{2}
\]

with

\[
N = \frac{D^{2}}{4\lambda}\left[1 - \left(\frac{\lambda}{D}\right)^{2}\right], \tag{3}
\]

and

\[
S_{F} = \frac{F}{N}, \tag{4}
\]

where \( BD \) and \( F_{z} \) are the beam diameter (transverse) and focal zone length (longitudinal) of the focused transducer, \( \lambda \) the wavelength in water, \( N \) the near field of corresponding flat transducer in water, and \( S_{F} \) the normalized focal length, respectively. The calculations show a \( -6\text{-dB} \) reception zone \( (BD \times F_{z}) \) of \( 0.33 \times 9.72 \text{ mm} \) for the 20-MHz and \( 4.12 \times 71 \text{ mm} \) for the 1-MHz focused transducer, respectively. For the AE measurements, the transducers were aligned orthogonal to the lithotripter and the vessel axes, and confocally with F2. It was found that the small beam diameter of the 20-MHz transducer is essential for detecting AE emanating from inside the vessel phantoms, and avoiding picking up background noise generated in the test chamber during the shock-wave exposure.

**Rupture tests**

Previously, we have shown that exposure of the hollow fiber in the acoustic field of the XL-1 lithotripter leads to consistent rupture (Zhong et al. 1999b). To ascertain that the rupture was caused by intraluminal cavitation, rather than by other mechanisms such as shear stress (Howard and Sturtevant 1997), the hollow fiber phantom was immersed in freshly poured, homogenous castor oil and exposed to LSWs at a low pulse-repetition rate (< 0.1 Hz). Before the release of each shock pulse, any visible bubbles outside the hollow fiber were carefully removed using a syringe. This approach was used to minimize the effect of shear stress that may be generated by the scattering of LSW from bubbles trapped in castor oil or by simultaneous bubble expansion both inside and outside the hollow fiber (Zhong et al. 1999b). During the course of the experiment, high-speed imaging was used to monitor the presence of intraluminal bubbles inside the fiber. Rupture of the hollow fiber can be easily identified because the circulating fluid will leak out from the hollow fiber, forming a liquid droplet at the rupture site in the castor oil. At this point, the experiment was stopped, and the number of shocks delivered and the orientation of the rupture site in the fiber were documented. Before the next experiment, the portion of the castor oil mixed with the liquid droplet was removed and replaced with fresh castor oil. If no rupture was observed after 100 shocks, the experiment was also terminated. A total of at least six samples were used under each test condition, from which the mean value and standard deviation of the number of shock waves needed to produce rupture were determined.

**EXPERIMENTAL RESULTS**

**Bubble dynamics**

*In free field.* The general features of LSW-induced cavitation in a free field (test chamber filled with degassed water), as shown in Fig. 3a and b, are the initial rapid growth of cavitation bubbles in the wake of the incident shock front, bubble coalescence near their maximum expansion, and the subsequent violent collapse of the bubbles toward the lithotripter axis, followed by a few rebounds. During the initial growth period, individual bubbles were almost spherical in geometry and the density and size of the bubble cluster increased with the output voltage of the lithotripter. For individual, nonaggregated bubbles, the maximum size was found to increase from \( \sim 2.4 \text{ mm} \) at 16 kV to \( \sim 3.3 \text{ mm} \) at 24 kV, respectively. As observed previously (Zhong et al. 1999a), significant bubble aggregation occurs near the lithotripter axis that leads to substantially increased maximum size and collapse time of the bubble cluster. The inertial collapse of the bubble cluster in a free field is violent, generating strong secondary shock-wave emission, which can be visualized as circular rings expanding outward from the collapse sites (see \( t = 493 \mu s \) in Fig. 3a and \( t = 693 \mu s \) in Fig. 3b). Subsequently, a few rebound bubbles with irregular geometry were observed, but their
ensuing collapse was very weak. It is often believed that the violent collapse of cavitation bubbles and associated shock-wave emission and shear stresses generated by the rapid fluid movement may contribute to the cellular damage observed in in vitro studies (Carstensen et al. 1993; Delius 1994).

In contrast to the typical large expansion of cavitation bubbles produced by a LSW, bubble expansion generated by an inverted LSW is much smaller (Fig. 3c). Because of the shorter major axis of the pressure-release reflector insert, the inverted LSW arrived at F2 at about 133 µs, instead of at 144 µs for the original XL-1 reflector. Although cavitation bubbles were induced by the leading tensile wave of the inverted LSW, their expansion was quickly suppressed by the ensuing compressive wave, resulting in a substantially decreased maximum bubble size (≈0.75 mm) and collapse time (≈120 µs) of the bubble cluster. These observations are in reasonable agreement with the theoretical predictions of bubble dynamics in response to an inverted LSW (Bailey et al. 1999; Zhu and Zhong 1999). Because of the significantly suppressed bubble activity, inverted LSW (in contrast to the standard LSW) provides an experimental option to differentiate the contribution of cavitation from other potential mechanisms of tissue injury in SWL (Bailey et al. 1999).

In constrained media. Although, if unconstrained, a LSW-induced cavitation bubble has the potential to grow to a maximum diameter of ~2 mm, the expansion of such a bubble in a constrained medium such as renal vasculature will be limited. Using EHL-generated single bubble and LSW-induced bubbles in a silicone tube, it has been shown that the constraining effect of the silicone tube (i.d. = 0.3 ~ 3.5 mm) on bubble expansion increases as the tube size becomes smaller (Zhong et al. 1999b). Alternatively, in this work, we evaluated the constraining effect of the RC hollow fiber (i.d. = 200 µm) on LSW-induced bubble dynamics at different lithotripter voltage settings (which corresponds to different maximum bubble expansion potential in a free field). As shown in Fig. 4a and b, high-speed shadowgraph imaging revealed that the expansion of intraluminal bubbles induced by a LSW quickly established contact with the fiber wall in less than 6 µs after the passage of the shock front, nearly independent of the lithotripter output.

Fig. 3. Representative sequences of high-speed shadowgraphs of bubble dynamics in free field produced by (a) the standard lithotripter shock wave (LSW) at 16 kV, (b) LSW at 24 kV, and (c) the inverted LSW (ILSW) at 24 kV. The number above each image frame indicates the time delay in µs after the spike discharge. SW = shock wave.
voltage. After the interaction occurred, the expansion of the bubble was rapidly stopped within 2–3 μs due to the constraint of the fiber with, presumably, most of the remaining kinetic energy of the expanding bubble being absorbed by the elastic deformation of the fiber wall. At this moment, the bubble reached the maximum expansion inside the hollow fiber; and, conversely, the fiber wall was maximally dilated (t = 151 μs in Fig. 4a and b). Although the period of expansion was similar, the maximum dilation of the fiber wall by the intraluminal bubble was observed to be much greater at 24 kV than at 16 kV. After reaching the maximum expansion, the bubble collapsed in about 12 μs, partially due to hydrostatic pressure outside the bubble and partially due to the pressure applied to the bubble by the elastic recovery of the dilated fiber wall. Although the bubbles initially appeared in spherical geometry, they elongated substantially along the fiber axis (where the resistance against the expansion is minimal) during the course of the constrained expansion inside the hollow fiber. Consequently, the substantially reduced maximum expansion and asymmetric deformation, the collapse of the bubbles inside the hollow fiber was greatly diminished compared to the inertial collapse of the unconstrained bubbles in a free field (Fig. 3a and b). As expected, the inversion of the LSW was found to greatly reduce the intraluminal bubble expansion and minimize the dilation of the fiber wall, with an apparent expansion-to-collapse period of the bubbles inside the fiber to be about 10 μs (Fig. 4c).

**Acoustic Emission**

*In free field.* Both theoretical (Church 1989) and experimental studies (Coleman et al. 1992, 1996; Zhong et al. 1997, 1999a; Bailey et al. 1999) have shown that acoustic emission (AE) produced by the rapid oscillation of cavitation bubbles in a lithotripter field has a characteristic double burst structure. Figure 5 shows the typical

![Fig. 4. Representative sequences of high-speed shadowgraphs of bubble dynamics in the 200-μm hollow fiber, (a) standard lithotripter shock wave (LSW) at 16 kV, (b) LSW at 24 kV, and (c) the inverted LSW (ILSW) at 24 kV. The number above each image frame indicates the time delay in μs after the spike discharge.](Image)

![Fig. 5. Typical acoustic emission (AE) signals produced in free field by (a) standard lithotripter shock wave (LSW) at 16 kV, (b) LSW at 24 kV, and (c) the inverted LSW (ILSW) at 24 kV. The collapse time of the bubble cluster was determined by the time delay between the pressure peaks of the two distinct AE bursts.](Image)
AE signals produced in water at various voltage settings and reflector configurations. The characteristic double burst structure can be observed in each trace, with the first burst corresponding to the initial compression and ensuing expansion of cavitation nuclei by the incident LSW and the second burst corresponding to the subsequent inertial collapse of the bubbles. The collapse time of the bubble cluster \( (t_c) \), conveniently defined as the time delay between the pressure peaks of the two distinct AE bursts, increases from about 350 \( \mu s \) at 16 kV to about 525 \( \mu s \) at 24 kV. For the standard LSW, the peak pressure of the second AE burst is generally stronger than the first one. However, when the LSW was inverted, the collapse time of the bubble cluster was significantly shortened \( (t_c = 140 \mu s \text{ at } 24 \text{ kV}) \) and the second burst became much weaker. Overall, the temporal characteristics of the AE signals are in agreement with the bubble dynamics revealed by high-speed imaging (Fig. 3).

In constrained media. In contrast to the bubble oscillation in a free field, the collapse time of LSW-induced bubbles inside the hollow fiber was found to be greatly reduced \( (t_c \approx 25 \mu s) \), independent of the lithotripter output voltage (Fig. 6). Because of the small beam diameter of the 20-MHz transducer, the amplitude of the AE signals could vary significantly if the location of the bubble shifted slightly inside the hollow fiber (measurement of \( t_c \), however, would not be affected significantly). Therefore, a quantitative comparison of the collapse pressure of the intraluminal bubbles could not be made. Furthermore, when the LSW was inverted, the collapse time of the bubbles inside the hollow fiber became even shorter \( (\sim 12 \mu s) \). All these results are in good agreement with the high-speed imaging observation of the constrained oscillation of intraluminal bubbles inside the hollow fiber (Fig. 4). It is worth noting that, when castor oil was circulated inside the hollow fiber, the characteristic AE could not be detected and no intraluminal bubbles could be observed by high-speed imaging during the standard LSW exposure.

Comparison. Figure 7 summarizes the measurement results of \( t_c \) for LSW-induced bubbles both in a free field and in constrained media. Ten samples were recorded under each test condition. In water, the value of \( t_c \) (mean \( \pm \) SD) was observed to increase with the lithotripter output voltage, from 386 \( \pm \) 24 \( \mu s \) at 16 kV to 583 \( \pm \) 23 \( \mu s \) at 24 kV. For the standard LSW, the peak pressure of the second AE burst is generally stronger than the first one. However, when the LSW was inverted, the collapse time of the bubble cluster was significantly shortened \( (t_c = 140 \mu s \text{ at } 24 \text{ kV}) \) and the second burst became much weaker. Overall, the temporal characteristics of the AE signals are in agreement with the bubble dynamics revealed by high-speed imaging (Fig. 3).

In constrained media. In contrast to the bubble oscillation in a free field, the collapse time of LSW-induced bubbles inside the hollow fiber was found to be greatly reduced \( (t_c \approx 25 \mu s) \), independent of the lithotripter output voltage (Fig. 6). Because of the small beam diameter of the 20-MHz transducer, the amplitude of the AE signals could vary significantly if the location of the bubble shifted slightly inside the hollow fiber (measurement of \( t_c \), however, would not be affected significantly). Therefore, a quantitative comparison of the collapse pressure of the intraluminal bubbles could not be made. Furthermore, when the LSW was inverted, the collapse time of the bubbles inside the hollow fiber became even shorter \( (\sim 12 \mu s) \). All these results are in good agreement with the high-speed imaging observation of the constrained oscillation of intraluminal bubbles inside the hollow fiber (Fig. 4). It is worth noting that, when castor oil was circulated inside the hollow fiber, the characteristic AE could not be detected and no intraluminal bubbles could be observed by high-speed imaging during the standard LSW exposure.
Rupture of the RC hollow fibers

Using the standard reflector, rupture of the hollow fibers placed at F2 was observed consistently within 20 shocks at various output voltage settings (Fig. 8a). The rupture site could be easily identified because the circulating fluid inside the hollow fiber leaked out, forming a liquid droplet in the surrounding castor oil. No strong directional preference in the orientation of the rupture was observed, even though the percentage of the rupture was found to be slightly higher along (N and S) than transverse (E and W) to the shock-wave propagation direction (Fig. 8b). Optical microscopy revealed that the rupture was mainly in the form of a cleft along the axial direction of the hollow fiber (Fig. 9), which is typical for failure of a hollow tube due to circumferential stretching, such as that produced by internal pressurization. The length of the cleft increased significantly from \( \sim 100 \, \mu m \) to \( \sim 600 \, \mu m \) as the output voltage of the XL-1 lithotripter increases from 16 to 24 kV.

The rupture of the hollow fiber is dose-dependent (Fig. 10), and the number of shocks needed to produce a rupture \( (N_r) \) was found to decrease from 19 \( \pm 2 \) at 16 kV to 11 \( \pm 6 \) at 20 kV to 8 \( \pm 3 \) at 24 kV, respectively. The difference between 16 kV and 24 kV is statistically significant \( (p < 0.05, \text{paired } t\text{-test}) \). Further, the rupture of the hollow fiber was found to vary with its spatial location in the lithotripter field (Fig. 11). At 16 kV, although rupture of the hollow fiber could be produced in a large range along the shock wave axis from \( z = -10 \)
mm to \( z = 2.5 \) mm, the propensity of the rupture was found to be higher prefocally than postfocally. This finding is consistent with the observation that the peak negative pressure of the LSW tends to shift toward the shock-wave source, due to nonlinear wave propagation (Coleman and Saunders 1989; Averkiou and Cleveland 1999).

To confirm the correlation between the rupture and dilation of the fiber wall, the initial (\( OD_i \)) and maximum outer diameters (\( OD_M \)) of the fiber were measured from high-speed images recorded during the rupture experiments. The maximum circumferential strain, \( \varepsilon_M \), imposed on the fiber wall by the intraluminal bubble expansion was then calculated using the following equation:

\[
\varepsilon_M = \frac{OD_M - OD_i}{OD_i}.
\]

Assuming that the fiber wall was elastically deformed before the rupture, the circumferential stress component would be proportional to \( \varepsilon_M \). The results, shown in Fig. 12 in the form of \( \varepsilon_M \) vs. \( N_r \), revealed that the maximum circumferential strain increases significantly from 40 ± 10% at 16 kV to 64 ± 13% at 20 kV to 69 ± 17% at 24 kV, respectively. Similar measurements along the fiber axis revealed a maximum axial strain less than 1% at 24 kV, much smaller than the corresponding circumferential strain. These results are consistent with the damage pattern of the hollow fiber (see Fig. 9), that could be generated by the predominant circumferential stretching of the fiber wall due to intraluminal bubble expansion. It is interesting to note that the general trend in the \( \varepsilon_M \) vs. \( N_r \) curve is typical for material failure under cyclic loading (Dowling 1998), although the stress distribution in the fiber wall could vary significantly from one shock to another, depending on where the bubbles were formed inside the fiber. At higher kV, the dilation of the fiber wall was large and, therefore, fewer shocks were needed to cause the rupture. On the other hand, at lower kV, the fiber wall was less dilated and more shocks were needed to produce the rupture. For the inverted LSW, the dilation was so small that a much higher number of shocks are required to cause a rupture, as our experiment results have indicated. Overall, we conclude that the rupture of the hollow fiber depends on the shock wave dosage, spatial location, and pressure waveform of the lithotripter field, and the rupture is most likely caused by the intraluminal expansion of cavitation bubbles.

**THEORETICAL ASSESSMENT OF BUBBLE DYNAMICS IN BLOOD**

**Rationale**

If appropriate cavitation nuclei (initial radius \( R_0 > 10 \) nm) exist in the blood, theoretical calculations have shown that inertial cavitation can be induced in blood vessels near the beam focus of a clinical HM-3 lithotripter (Zhong et al. 1998). Without tissue constraint, the shock wave-excited bubbles in blood could reach a maximum diameter between 1.3 mm and 2.3 mm, depending on the tensile pressure of the LSW. Above the inertial cavitation threshold, the maximum bubble expansion in blood is insensitive to the initial radius of the nucleus (Zhong et al. 1998). Because this potential bubble ex-

---

**Fig. 11.** Spatial-dependence of the rupture of the hollow fibers. The number of shocks needed to cause a rupture (\( N_r \)) is significantly higher prefocally than postfocally. Outside the beam focus (\( z < -15 \) mm or \( z > 5 \) mm) no rupture could be produced even after 100 shocks.

**Fig. 12.** Relationship between the maximum circumferential strain \( \varepsilon_M \) imposed on the fiber wall by the intraluminal bubble expansion and the number of shocks needed to cause a rupture (\( N_r \)). The plot is in linear-log format.
pansion greatly exceeds the size of typical small blood vessels in the kidney, it has been postulated that significant dilation of the vessel would occur, which may lead to the rupture of the vessel (Zhong et al. 1998). This hypothesis is confirmed in this study using the hollow fiber vessel phantom. To gain further theoretical insights on the damage mechanism, it is important to understand the mechanical interaction between an intraluminal bubble and the surrounding tissue structure. A model for such an interaction, however, has not been developed because of the complex mathematical treatment needed to describe the dynamics of asymmetric bubble oscillation inside an elastic or viscoelastic tubular structure. This, however, should not in any way undermine the importance and the need for the development of such a model, which would not only be a theoretical advance, but also critical for a thorough understanding of the mechanisms of vascular injury in SWL.

In light of the current theoretical limitation, we attempt to search for features predicted by theoretical models of spherical bubble oscillation in a free field that may be useful in gauging qualitatively the potential of vascular injury due to intraluminal bubble expansion. This strategy is based on two important observations from the hollow fiber experiment (see Fig. 4). First, initially the LSW-induced intraluminal bubbles are approximately in spherical geometry before establishing contact with the fiber wall. Second, after the interaction occurs, the rapid expansion of the bubble is abruptly terminated due to the constraint of the fiber. In other words, the initial bubble expansion can be modeled as if it is produced in a free field, and the energy associated with the expanding bubble at the moment of the contact is largely absorbed by the elastic deformation of the fiber. We, therefore, assume that it is reasonable to use a spherical bubble model to simulate the bubble expansion up to the point of contact and to assess qualitatively the potential of the ensuing bubble-vessel interaction on vascular injury based on the remaining energy of the expanding bubble. The clinically relevant goal of such an investigation is to assess the effect of vessel size on SWL-induced injury. Specifically, we wonder when LSW-induced bubbles that have the same maximum expansion potential in a free field are constrained by blood vessels of different sizes, which vessel will have a higher propensity for rupture. Results from previous animal studies have demonstrated that vascular injury in SWL is vessel size-dependent, with capillary and small veins much more susceptible to SWL injury than large blood vessels; in particular, arteries (Delius et al. 1988; Weber et al. 1992; Delius 1994; Evan and McAteer 1996). The intraluminal bubble expansion mechanism for vessel rupture, if valid, should be able to explain this fundamental feature of the vascular injury in SWL.

Approaches

To simulate the radial oscillation of a spherical bubble in blood (without tissue constraint) in a lithotripter field, the original Gilmore formation for bubble dynamics was used:

$$R\left(1 - \frac{U}{C} \right) \frac{dU}{dt} + \frac{3}{2} \left(1 - \frac{U}{C} \right) U^2 = \left(1 + \frac{U}{C} \right) H$$

$$+ \frac{1}{C} \left(1 - \frac{U}{C} \right) R \frac{dH}{dt}.$$  \hspace{1cm} (6)

where $R$ is the bubble radius, $U$ ($= dR/dt$) is the velocity of the bubble wall, $C$ and $H$ are the speed of sound in the liquid at the bubble wall and the enthalpy difference between the liquid at pressure at the bubble wall $P(R)$ and pressure at infinity $P_\infty$, respectively, which are determined by $C = [C_\sigma^2 = (m - 1)H]^{1/2}$ and

$$H = \int_{P_\infty}^{P(R)} \frac{dP}{\rho}$$ \hspace{1cm} (7)

where $C_\sigma$ is the infinitesimal speed of sound in the liquid, $m$ is a constant, $P$ and $\rho$ are the time-varying pressure and density of the liquid, respectively. To determine $P$, the Tait equation of state for a compressible fluid, $P = A(\rho/\rho_0)^m - B$, was used where $\rho_0$ is the equilibrium liquid density, $A = C^2/\rho_0 P_0$ with $m = 7$ and $B = A - 1$. Further, the relation between $P(R)$ and the gas pressure inside the bubble ($P_g$), liquid viscosity ($\mu$), and surface tension ($\sigma$) in the liquid is given by:

$$P(R) = P_g - \frac{2\sigma}{R} - \frac{4\mu}{R^2} U,$$ \hspace{1cm} (8)

where

$$P_g = \left( P_0 + \frac{2\sigma}{R_0} \left( \frac{R_0}{R} \right)^{3\eta} \right.$$ \hspace{1cm} (9)

in which $R_0$ is the initial equilibrium radius of the bubble and $\eta$ ($= 1.4$) is the polytropic exponent of the gas. When a lithotripter shock wave $P_g$ is produced in the liquid far away from the bubble, we have $P_\infty = P_0 + P_g$ where $P_0$ is the ambient pressure of the surrounding liquid. Because we are interested in the expansion phase of the bubble dynamics, gas diffusion across the bubble wall, which has been shown to affect only significantly the collapse of the bubble (Church 1989), is not considered.

The Gilmore model (Eqn. 6) was nondimensionalized and solved using the fifth-order Runge–Kutta–Fehl-
berg method with a step-size control algorithm (Zhu and Zhong 1999). For the numerical calculation, the following parameters of the blood were used: \( \rho_0 = 1059 \text{ kg/m}^3 \), \( \mu = 5 \times 10^{-3} \text{ kg/m/s} \), \( \sigma = 56 \times 10^{-3} \text{ N/m} \), and \( C_0 = 1584 \text{ m/s} \). After the bubble dynamics in a free field were determined, the work done by the bubble during the expansion phase from the bubble radius at contact \( (R_c) \) to the maximum radius \( (R_{\text{max}}) \) against ambient pressure \( (E_{p0}) \), surface tension \( (E_\sigma) \), and viscous force \( (E_\mu) \) were calculated using the following equations:

\[
E_{p0} = \int_{R_c}^{R_{\text{max}}} P_0 4\pi R^2 dR = \frac{4}{3} \pi (R_{\text{max}}^3 - R_c^3) P_0
\]  
(10)

\[
E_{\sigma} = \int_{R_c}^{R_{\text{max}}} \left( \frac{2\sigma}{R} \right) 4\pi R^2 dR = 4\pi (R_{\text{max}}^2 - R_c^2) \sigma
\]  
(11)

\[
E_\mu = \int_{R_c}^{R_{\text{max}}} \left( \frac{4\mu}{R} U \right) 4\pi R^2 dR.
\]  
(12)

In addition, the kinetic energy of the mass of fluid surrounding the expanding bubble can be calculated by (Apfel 1981):

\[
E_k = \frac{1}{2} M_{\text{eff}} U^2,
\]  
(13)

where \( M_{\text{eff}} = 3 \rho_0 (4\pi/3) R^3 \) is the effective mass “felt” by the bubble (given by 3 times the mass of the liquid to fill the bubble), when the acoustic wavelength is large compared to \( R \). Because the gas pressure inside the bubble drops quickly during bubble expansion and becomes much smaller than \( P_0 \), the internal energy of the gas in the expansion phase of the bubble is negligible compared to \( E_{p0} \).

**Calculation results**

Unconstrained bubble dynamics in a lithotripter field is determined predominantly by the tensile pressure of the LSW (Church 1989; Choi et al. 1993). Figure 13 shows the typical response of a cavitation nucleus \( (R_0 = 3 \text{ \mu m}) \) in blood (assuming without tissue constraint) to different pressure waveforms in a HM-3 lithotripter field.

To account for tissue attenuation, the peak positive pressure \( (P^+) \) was reduced by 25% from typical values measured in water \( (40 \text{ MPa at } 20 \text{ kV}; Coleman and Saunders 1989) \). The peak negative pressure \( (P^-) \) was varied from \(-4 \text{ MPa to } -10 \text{ MPa} \), similar to the values measured in water because the effect of tissue attenuation on the tensile pressure is small (Coleman et al. 1995). The computed bubble dynamics are characterized by an initial rapid, large expansion of the bubble following the tensile pressure of the incident LSW, with the bubble size increasing by about 2 orders of magnitude within the first 10 \( \mu \text{s} \). This feature is in accordance with the experimental observation of the LSW-induced bubble expansion in the hollow fiber (see Fig. 4). In general, both the maximum radius and collapse time of the bubble in blood were found to increase as the tensile pressure of the LSW becomes stronger, similar to the trend predicted in water (Church 1989; Choi et al. 1993). These results suggest that the propensity for vessel rupture due to intraluminal bubble expansion will be higher in regions of the kidney where the peak tensile pressure of the LSW is produced. This prediction is consistent with the extensive hemorrhage in perirenal fat and large subcapsular hematoma in SWL (Delius 1994; Evan and McAteer 1996), which is in the proximity of the peak tensile pressure (Cleveland 1999) where the strongest cavitation activity was detected by B-scan US imaging in patients undergoing SWL (Coleman et al. 1995).

Another interesting feature of the bubble dynamics can be observed from the trajectory of bubble wall velocity \( U \) vs. \( R \), as shown in Fig. 14 for the initial expansion and a portion of the subsequent collapse of the bubble. The response of the cavitation nucleus to the leading compressive pressure \( (P^+ = 30 \text{ MPa, } t^+ = 1 \text{ \mu s}) \)
of the LSW is shown in the insert of Fig. 14. It consists of a rapid implosion, an immediate rebound, followed by a series of oscillations before both $U$ and $R$ increase monotonically. Subsequently, the tensile pressure ($P^- = -10$ MPa, $t^- = 5 \mu s$) of the LSW causes the bubble to expand significantly, in a time scale much longer than the pulse duration of the LSW. It is interesting to note, however, that the bubble wall is accelerating outward only in the initial short period, but decelerates in the remaining prolonged period of the bubble expansion. The maximum expanding velocity of the bubble wall was calculated to be 50, 66, and 81 m/s, as the magnitude of $P^-$ increases from $-4$, to $-7$, to $-10$ MPa, respectively. The corresponding bubble radii for the maximum $U$ were 44, 100, and 130 μm, respectively, which are quite small compared to the corresponding bubble radii (398, 766, and 1141 μm) at the maximum expansion. Because $U$ is smaller than $C_0$, the fluid surrounding the bubble can be considered incompressible during the expansion phase of the bubble.

During expansion, the work done by the bubble against ambient pressure ($E_{p_0}$), surface tension ($E_s$), and viscous force ($E_\mu$) drop monotonically with $R_c$, although initially $E_\mu$ may increase slightly if $R_c$ is smaller than 300 μm (Fig. 15, $P^+/P^- = 30/-10$ MPa for the LSW). Similarly, the kinetic energy of the fluid surrounding the bubble, $E_k$, will increase initially reaching a maximum at $R_c = 400 \mu m$ and then decrease monotonically with $R_c$. In comparison, $E_{p_0}$ and $E_k$ are at least 2 orders of magnitude greater than $E_s$ and $E_\mu$, so that most of the energy provided by the tensile pressure of the LSW are converted into the kinetic and potential energy ($E_k$ and $E_{p_0}$) of the expanding bubble. The close match between $E_k$ and $E_{p_0}$, when $R_c$ is greater than 500 μm indicates that, in the later stage of the expansion, the kinetic energy of the bubble was converted into the potential energy (i.e., the bubble expansion was slowed down primarily by the ambient pressure). Qualitatively, the implication of these results to vascular injury in SWL is that, if a cavitation bubble is produced in a blood vessel, the energy carried by the expanding bubble at the moment of contact (i.e., $R_c$) would be higher in a small vessel than in a large one. As the vessel size increases, the energy associated with the potential bubble expansion (as measured by $E_{p_0}$) will be reduced in proportion to $R_c^3$ (see Eqn. 10 and Fig. 16). Furthermore, when the tensile pressure of the LSW is reduced, the energy associated with the potential bubble expansion will drop significantly, indicating that the propensity of vessel rupture depends on both the output...
voltage of the lithotripter and the spatial location of the vessel in the lithotripter field. These predictions are verified by the experimental results shown in Figs. 10–12. In general, the theoretical predictions are consistent with the characteristics of vascular injury in SWL (Delius 1994; Evan and McAteer 1996).

**DISCUSSION**

Tissue injuries in SWL are primarily vascular lesions, characterized by extensive damage of the endothelial cells and mechanical rupture of small blood vessels (Delius et al. 1988; Weber et al. 1992; Delius 1994; Evan and McAteer 1996). Although cavitation is often considered as an important contributory factor for tissue injury in SWL (Delius 1994), the underlying mechanism has not been well understood. This is primarily due to the technical difficulties in assessing the mechanical interaction between LSW-induced cavitation bubbles and the surrounding tissue structure in vivo. In this work, we developed vessel phantoms made of silicone tubing and RC hollow fibers immersed in castor oil so that LSW-induced intraluminal bubble activity and bubble-vessel interaction could be quantified by high-speed imaging and PCD techniques, and the resultant damage readily determined. Using this approach, we have demonstrated a size-dependent vessel-constraining effect on LSW-induced bubble expansion, which leads to significantly reduced maximum expansion and collapse time of the bubbles compared to that produced in a free field. This finding is consistent with results from our previous animal studies, in which the collapse time of LSW-induced cavitation bubbles was found to decrease from in water, to renal pelvis, and to the low pole of the swine kidney, presumably due to increased tissue constraint on bubble expansion (Zhong et al. 1998). Furthermore, in small vessels (modeled by the hollow fibers), the large expansion of the intraluminal bubbles was found to cause significant dilatation and consistent rupture of the vessel wall within 20 pulses of shock-wave exposure. When either the pressure amplitude of LSW increases or the vessel size becomes smaller, the propensity for vessel rupture due to intraluminal bubble expansion will increase substantially. In contrast, when the large expansion of the intraluminal bubbles was suppressed by inverted LSW, the dilation of the hollow fiber was significantly reduced and no rupture could be produced even after 100 shocks. All together, these results confirm the hypothesis that the rupture of small blood vessels in SWL is caused primarily by the rapid, large expansion of intraluminal bubbles. This mechanism of vascular injury is distinctly different from the classic theory of cavitation damage in unconstrained media where damage is often attributed to the strong shock-wave emission or microjet impact due to the violent collapse of inertial bubbles (Tomita and Shima 1986; Philipp and Lauterborn 1998).

Under normal physiologic conditions, cavitation nuclei in blood are presumably scarce or small in size (Williams et al. 1989). Therefore, inertial cavitation is difficult to induce in mammals exposed to low-amplitude LSWs and, consequently, little damage can be observed in vivo except in organs with preexisting gas pockets, such as lung and intestine (Dalecki et al. 1997). On the other hand, theoretical calculation has suggested that the high-amplitude LSWs typically used for stone treatment can induce inertial cavitation in blood, provided that cavitation nuclei larger than 10 nm in radius are present (Zhong et al. 1998). Although the size and distribution of cavitation nuclei in the vasculature is currently unknown, inertial cavitation induced by LSWs in the intrahepatic branches of the portal vein and tributaries of hepatic veins has been observed (Delius et al. 1990a). Once a bubble is induced, it may generate multiple smaller bubbles upon collapse (Church 1989) and, therefore, provides more cavitation nuclei in the blood for the ensuing LSWs if the interpulse delay is not too long. Another important feature of the tissue response during SWL that may promote cavitation damage is vasoconstriction (Brendel et al. 1987), which significantly reduces the blood flow in the treated kidney (Knapp et al. 1996). It is conceivable that, after a single cavitation bubble is induced in small blood vessels or capillary beds, some residual microbubbles could be trapped in the beam focus of the lithotripter after each exposure due to vasoconstriction and become available nuclei for ensuing shock-wave pulses. As our experimental data and theoretical calculations have suggested, if adequate cavitation nuclei exist in the blood, the propensity of vessel rupture is particularly high for capillaries and small blood vessels. In fact, using a transparent window adapted to the dorsal skin fold of male Syrian golden hamsters, Brendel and associates have observed rupture of capillaries after only a single shock (Brendel et al. 1987). In large blood vessels, when the size of the residual bubbles becomes larger than 0.5 mm in diameter, shock wave-bubble interaction with resultant high-speed microjet impingement may also lead to the perforation of the vessel (Philipp et al. 1993).

Current thinking on SWL-induced tissue injury postulates that the mechanical stresses produced by cavitation and/or shear stress cause rupture of small blood vessels that initiates extensive hemorrhage, cellular damage and inflammatory response, which eventually leads to fibrosis and loss of functional renal mass (Evan et al. 1998b). Therefore, logically, the most effective and efficient way to minimize tissue injury in SWL would be to prevent or significantly restrain the mechanical events that initiate the vascular injury. One method that has
been demonstrated to minimize tissue injury is the inversion of LSW pressure waveform (Evan et al. 1998a). Unfortunately, the inverted LSW does not produce stone comminution either and, thus, it cannot be used for SWL. Based on theoretical calculation, it appears that a feasible approach to reduce tissue injury without compromising the fragmentation capability of the LSWs is the selective reduction or truncation of the tensile pressure of the LSW (Zhu and Zhong 1999). Although, with this approach, cavitation near the stone surface may also be weakened, the reduced bubble activity could be compensated by forcing the collapse of LSW-induced bubbles using an auxiliary shock wave (Xi and Zhong 2000). The other possibility for reducing tissue injury in SWL is to use overpressure to minimize the size and density of bubble nuclei available in the blood so that cavitation would not be induced even under the strong tensile pressure of a lithotripter pulse (Delius 1997).

In summary, using vessel phantoms made of silicone tubing and RC hollow fibers, we have demonstrated a size-dependent vessel-constraining effect on LSW-induced bubble expansion. Conversely, the rapid, large expansion of intraluminal bubbles was found to cause substantial dilation of the vessel wall, leading to consistent rupture of the vessel after a low dose of shock-wave exposure. Finally, suppression of the large bubble expansion prevents vessel rupture, indicating potential remedy to minimize tissue injury in SWL.

Acknowledgements—This work was supported in part by NIH grants RO1-DK52985, PO1-DK20543, and R21-CA83760. The authors also acknowledge the support of Dornier MedTech Inc. for providing the RO1-DK52985, PO1-DK20543, and R21-CA83760. The authors also acknowledge the support of Dornier MedTech Inc. for providing the XL-1 experimental lithotripter.

REFERENCES


Karlsen SJ, Smevik B, Hovig T. Acute morphological changes in