A heuristic model of stone comminution in shock wave lithotripsy

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A heuristic model is presented to describe the overall progression of stone comminution in shock wave lithotripsy (SWL), accounting for the effects of shock wave dose and the average peak pressure, $P_{+(avg)}$, incident on the stone during the treatment. The model is developed through adaptation of the Weibull theory for brittle fracture, incorporating threshold values in dose and $P_{+(avg)}$ that are required to initiate fragmentation. The model is validated against experimental data of stone comminution from two stone types (hard and soft BegoStone) obtained at various positions in lithotripter fields produced by two shock wave sources of different beam width and pulse profile both in water and in 1,3-butanediol (which suppresses cavitation). Subsequently, the model is used to assess the performance of a newly developed acoustic lens for electromagnetic lithotripters in comparison with its original counterpart both under static and simulated respiratory motion. The results have demonstrated the predictive value of this heuristic model in elucidating the physical basis for improved performance of the new lens. The model also provides a rationale for the selection of SWL treatment protocols to achieve effective stone comminution without elevating the risk of tissue injury. © 2013 Acoustical Society of America. [http://dx.doi.org/10.1121/1.4812876]

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I. INTRODUCTION

Since its introduction in the early 1980s, the first-generation Dornier HM3 electrohydraulic lithotripter has exemplified the pinnacle of efficacy in stone comminution despite several generations of lithotripters developed in its wake (Graber *et al.*, 2003; Gerber *et al.*, 2005; Lingeman *et al.*, 2009). This fact has presented a primary challenge and also motivated the investigators in the field of shock wave lithotripsy (SWL) to better understand the fundamental mechanisms that contribute to the success of this non-invasive technology in kidney stone treatment (Lingeman *et al.*, 2009; Rassweiler *et al.*, 2011). Specifically, numerous studies have been conducted to dissect the role of stress waves and cavitation in stone fracture (Zhu *et al.*, 2002; Sapozhnikov *et al.*, 2007). Many proposed mechanisms, such as spallation (Lubock, 1989), geometric superfocusing (Gracewski *et al.*, 1993; Xi and Zhong, 2001), circumferential squeezing (Eisenmenger, 2001), and shear-induced failure (Xi and Zhong, 2001; Cleveland and Sapozhnikov, 2005; Sapozhnikov *et al.*, 2007) were demonstrated during the fragmentation process in the early stage of SWL, when the stones are of sufficient size to favor the development of large stress concentrations. Other proposed mechanisms, such as dynamic fatigue (Lokhandwalla and Sturtevant, 2000) and cavitation (Coleman *et al.*, 1987; Sass *et al.*, 1991; Philipp and Lauterborn, 1998), describe processes that influence stone fragmentation throughout the entire course of SWL. Despite previous efforts, a disconnection still exists between the proposed mechanisms and the lithotripter shock wave

(LSW) parameters that drive the stone fracture processes in SWL (Cleveland and McAteer, 2007; Sapozhnikov *et al.*, 2007). Understanding of these relationships will be critical for the improvement of SWL technologies.

Early studies on the correlation between stone comminution and various parameters of the LSW have demonstrated that acoustic pulse energy correlates linearly to comminution efficiency (Granz and Kohler, 1992; Eisenmenger, 2001). However, acoustic energy is an integrated parameter that encompasses all aspects of the LSW and cannot be readily manipulated as a lithotripter design feature for the improvement of treatment efficacy. More recently, we have discovered that the average peak pressure incident on the target stone (i.e., $P_{+(avg)}$) is logarithmically correlated to stone comminution based on *in vitro* experiments using two different types of artificial stones and fluid media (Smith and Zhong, 2012). The correlation curve for each stone type was further found to converge distinctively to a minimal pressure threshold necessary to initiate fragmentation, independent of LSW dosage or surrounding fluid. While this observation is potentially important, it needs to be confirmed using shock wave sources of dissimilar acoustic focusing characteristics and pulse profiles.

In general, multiple shock waves are required to initiate first fracture (Xi and Zhong, 2001; Sapozhnikov *et al.*, 2007), and a few thousand pulses are often used to disintegrate kidney stones to fine fragments for spontaneous discharge (Bierkens *et al.*, 1992). Therefore, the overall process of stone fragmentation in SWL is best described by the concept of dynamic fatigue (Lokhandwalla and Sturtevant, 2000). Briefly, under transient loading produced by LSW-generated stress waves and/or cavitation bubble collapse, fracture is facilitated by the opening of pre-existing microcracks (or flaws) and their

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coalescence with adjacent microcracks within the context of a cohesive zone model (Ortiz, 1988). Although conceptually feasible, a quantitative prediction of the stone fracture based on model calculation of stress waves and fracture mechanics criterion has been limited to simple geometry and initial fractures (Mota *et al.*, 2006). Extension of such model analyses to predict the fracture of a stone or fragments with irregular geometries or random microstructures of crystalline-matrix interfaces over the entire fragmentation process in SWL remains a challenge (Zohdi and Szeri, 2005).

From a fracture mechanics point of view, two critical factors that dictate stone fragmentation in SWL are peak tensile and/or shear stresses built up by the LSW-stone interaction and the size of critical flaw distribution in the stone material. While the exact fracture pattern of a kidney stone during SWL is difficult to predict, it is plausible that the overall fragmentation process can be described by a phenomenological or probabilistic damage model based on Weibull statistics for strength analysis (Forquin and Hild, 2010). The fundamental concept of the Weibull theory is based on the “weakest link” hypothesis that failure in brittle materials is associated with the largest flaw under sufficient tension. The distribution of the critical flaws in a brittle material is an example of the extreme value distribution, although the general population of the flaws in the material may follow a normal or Gaussian distribution. In other words, the largest flaw within the highly stressed regions of the material will precipitate failure if uniform tension is applied (Quinn and Quinn, 2010).

In this work, we have developed a heuristic model of stone comminution in SWL based on the Weibull theory for brittle fracture. The model is constructed from relevant LSW parameters (i.e., $P_{+(\text{avg})}$ and dose) and stone comminution results of two stone types (soft and hard BegoStone) produced both in water and a cavitation-suppressing fluid (i.e., 1,3-butanediol) using two electromagnetic (EM) shock wave sources with different focusing characteristics and pulse profiles. Subsequently, the model is used to assess the performance of a newly developed acoustic lens for EM lithotripters in comparison with its original counterpart. Moreover, the model is applied to analyze the stone comminution outcome generated by both the original and new lenses under simulated respiratory motion. The implication of this heuristic model to the selection of rational treatment protocol for effective and safe SWL and for design improvement of lithotripter sources will be discussed.

II. MATERIALS AND METHODS

A. Weibull theory for brittle fracture

In 1933, Rosin, Rammler, and Sperling analyzed the fragmentation process of coal particles sieved through a mesh of size l and developed an empirical relationship for stone comminution (SC) as follows:

$$\text{SC} = 1 - \frac{m(>l)_{\text{def}}}{m_T} \stackrel{\text{def}}{=} 1 - \exp \left[- \left(\frac{l}{b} \right)^c \right], \quad (1)$$

where the mass (m) of residual particles with diameter greater than l normalized by the mass of the original sample (m_T) is equivalent to an exponential function of l (Rosin and Rammler, 1933). In Eq. (1), b is a normalization parameter related to the average size of fragments in the distribution, and c describes the uniformity of fragmentation. This relationship bears similarities to the heuristic “weakest link” model later described by Weibull in 1939 (Weibull, 1939), where the probability of a failure event (P_f) in a brittle material subjected to a tensile stress (σ) is defined by

$$P_f(\sigma) = 1 - \exp \left[- \left(\frac{\sigma - a}{b} \right)^c \right]. \quad (2)$$

This three-parameter Weibull function represents the cumulative distribution of stone failures over a range of σ -values, with a , b , and c representing statistical location, scale, and shape parameters, respectively (Weibull, 1951). Physically, a is a threshold value, or the minimum stress to initiate failure; b is functionally related to a characteristic value, typically stress, to result in $\sim 63.2\%$ probability of failure; c is commonly referred to as the Weibull modulus, a property of the brittle material related to flaw (or defect) distribution (Rinne, 2009). To demonstrate a standard process for estimation of these parameters, Fig. 1(a) shows the ranked failure stresses of various hard and soft (5:1 and 5:2 powder to water mixing ratios, respectively) BegoStone Plus (BEGO USA, Lincoln, RI) phantoms from quasi-static diametral compression [see inset Fig. 1(b)], which has been used to determine the tensile failure strength (σ_f) of renal calculi and stone phantoms (Esch *et al.*, 2010; Simmons *et al.*, 2010). Details of the stone preparation and diametral compression test have been described previously (Esch *et al.*, 2010). Using a least square parameter estimation technique (i.e., median rank regression) with (a) set to 0 MPa, hard and soft BegoStones are found to have normalization stresses (b) of 7.4 and 3.3 MPa, respectively, and Weibull moduli (c) of 9.4 and 7.5, respectively, with coefficients of determination (R^2) greater than or equal to 0.95. The application of Weibull

FIG. 1. (Color online) (a) Median rank regression of the tensile failure strengths of hard (dark) and soft (light) cylindrical BegoStone phantoms (5:1 and 5:2 powder to water mixing ratios, respectively, with $t = 1.76 \pm 0.32$ mm and $D = 6.12 \pm 0.03$ mm) determined by diametral compression. (b) Schematic of the diametral compression test.

theory to describe single fragmentation events of brittle materials under dynamic loading is common in many disciplines (Forquin and Hild, 2010); however, this approach has not been applied to analyzing stone fragmentation process in SWL.

B. Stone comminution setup and protocol

For all stone comminution experiments in this study, an axisymmetric EM shock wave generator was mounted at the bottom of a Lucite tank ($L \times W \times H = 40 \times 40 \times 30$ cm) filled with $0.2 \mu\text{m}$ -filtered and degassed water ($<3 \text{ mg/L O}_2$ concentration, 23°C). A 3-D positioning system (VXM-2 step motors with BiSlide-M02 lead screws, Velmex, Bloomfield, NY) placed above the water tank was used for precise alignment of a flat-base tube holder (inner diameter = 14 mm) containing a spherical stone phantom (diameter = 10 mm) to the geometric focus of the shock wave source [see Figs. 2(a) and 2(b)] or other positions in the lithotripter field as needed. The stone phantoms were made of BegoStone material with 5:1 and 5:2 powder to water mixing ratios (i.e. “hard” and “soft” BegoStone, respectively). They were weighed before treatment and soaked in water for at least 2 h prior to SWL. Lithotripter shock waves were administered at a pulse repetition frequency (PRF) of 1.0 Hz. After

the treatment, stone fragments were collected and thoroughly rinsed in water, dried overnight, and sequentially sieved. Stone comminution efficiency was determined according to Eq. (1) using a mesh size of $l = 2.0 \text{ mm}$. The results are shown as mean $\pm$ standard deviation, and statistical analysis was performed using the student's t -test.

The protocol for static stone comminution has been described previously (Smith and Zhong, 2012). Briefly, fragmentation tests were carried out at discrete positions both along the z axis ($r = 0 \text{ mm}$; $z = 0, -20, -40 \text{ mm}$) and in the focal plane ($z = 0 \text{ mm}$; $r = 0, 4, 8, 12 \text{ mm}$) to cover a broad range of pressure and cavitation activities in the lithotripter field. The effect of cavitation during stone comminution was further evaluated by varying the fluid within the stone holder (either water or 1,3-butanediol). 1,3-butanediol has similar acoustic properties to water (Granz, 1994) (and thus similar characteristics in LSW propagation), but is ~ 100 times more viscous, and therefore suppresses cavitation activities relative to water. Additionally, a varying number of lithotripter shock waves were administered (0–2000 shocks) in order to assess the role of dose in stone comminution. At least four stone samples were tested at each field position, and for positions off the central (z -) axis, stones were treated at the same radial distance in all four quadrants to reduce potential bias from holder misalignments.

For the investigation of respiratory motion experiments, the movement of the stone holder was controlled via the positioning system along a single horizontal axis using a custom program written in MATLAB (Mathworks, Natick, MA). Holder motion during 2000 shock treatments proceeded away from the focus (inspiration) and backed toward the focal region (expiration) to simulate inferior–superior respiration [see Fig. 2(b)]. As illustrated in Fig. 2(c), a basic four-phase translational scheme was adapted from Davies *et al.* where the respective phase durations for inspiration (I), inspiration pause (IP), expiration (E), and expiration pause (EP) were scaled from mean organ motion times in patients (Davies *et al.*, 1994). Excursion distances were selected from the aggregate data on kidney displacement as representative of normal respiration ($D = 15 \text{ mm}$) and forced respiration ($D = 30 \text{ mm}$) (Bromage *et al.*, 1989; Davies *et al.*, 1994; Moerland *et al.*, 1994). Three different breathing rates (measured by breath per minute or bpm) were chosen, representing relatively slow (12 bpm), fast (18 bpm), and abnormally fast (24 bpm) human respiratory rates (Bromage *et al.*, 1989; Coloma *et al.*, 2000). Additionally, randomizations for drifting from mean position and duration of each breath are built into the model. Breath duration was stochastically increased or decreased by $\leq 5\%$ each cycle to avoid discrete translation patterns. “Drift” was similarly randomized to simulate variability in kidney excursion or small patient movements. Low and high drift were specified as absolute variation in D of $\leq 0.2 \text{ mm/breath cycle}$ and $\leq 1.0 \text{ mm/breath cycle}$, respectively.

FIG. 2. (Color online) (a) Schematic of the lithotripter focus with static stone comminution positions marked in the focal plane and along the acoustic propagation axis (b) An illustration of the simulated superior–inferior respiratory motion. (c) A plot of the basic respiratory motion scheme adapted from Davies *et al.* (1994). T_{TOT} is the summation of four motion phases (T_I , T_{IP} , T_E , T_{EP}) shown with representative excursion distance ($D = 15 \text{ mm}$) and breath rate (=12 bpm). Black dots indicate LSW arrival to the focal plane at a PRF = 1.0 Hz.

C. Shock wave sources

In both the static and simulated respiratory motion stone comminution experiments, two different EM shock wave

FIG. 3. (Color online) (a) Photographs of the acoustic focusing lenses investigated in this study (inner spherical surface pointed upwards) (b). A schematic of the EM shock source with new lens, which demonstrates the enhanced focal width resulting from *in situ* pulse superposition.

sources were used for comparison. Each source was fitted with a unique focusing lens [see Fig. 3(a)], which determines both the pulse profile and acoustic field characteristics of the source. A cross-sectional schematic of the new lens source is presented in Fig. 3(b), illustrating the design principle based on *in situ* pulse superposition that simultaneously reduces the aperture of the primary LSW (relative to the original lens) and produces a delayed wave section for pulse profile manipulation. The reduced aperture enhances the focal volume of the source, while the delayed wave is primarily used to destructively cancel the secondary compression phase typical in EM lithotripter pulse profiles. Due to destructive interference, the new lens was operated at a higher source voltage ($=16.8\text{ kV}$) than the original lens ($=13.8\text{ kV}$) in order to produce equivalent effective acoustic pulse energies. In all stone comminution experiments, an effective acoustic energy of $\sim 50\text{ mJ}$ (calculated based on the IEC 61846 lithotripter field characterization protocol) is matched in a circular area of 12 mm in diameter, which encompasses most stones treated by SWL.

D. Hydrophone characterization and data processing protocol

All pressure measurements for this study were conducted using a fiber optic probe hydrophone (FOPH 500, RP

Acoustics, Leutenbach, Germany). The pressure waveforms and distributions in the geometric focal plane ($z = 0\text{ mm}$) and two pre-focal planes ($z = -20$ and -40 mm) of the shock wave source were characterized using radial step sizes of 1 mm ($0 < r < 6\text{ mm}$), 2 mm ($6 < r < 14\text{ mm}$), and 5 mm ($r > 14\text{ mm}$). Due to acoustic field asymmetry off the central (z -) axis, derived lithotripter field parameters such as effective acoustic energy (E_{eff}) and average peak pressure ($P_{+(avg)}$) within the stone holder were determined at all field positions through middle Riemann summation as described previously (Smith and Zhong, 2012). The Riemann sum approximations were validated along the z axis where exact solutions of the integration can be obtained due to axisymmetry. The approximations were found to be within 5% – 10% of the integration values. Additional error contributions from hydrophone laser instability and uncertainty are estimated to be $\sim 5\%$ in pressure and $\sim 10\%$ in energy (Smith *et al.*, 2012). FOPH calibrations and regression analyses of hydrophone and stone comminution results were conducted in MATLAB. For all fitting results, a nonlinear least square method with trust-region algorithm was implemented.

III. RESULTS

A. Characterization of lithotripter shock waves and static stone comminution

Representative pressure waveforms produced by the original and new lenses are plotted in Fig. 4. The FOPH measurements were conducted at stone holder centroid positions used during static stone comminution experiments. Compared to the original lens, it is evident that the

FIG. 4. (Color online) Averaged ($n = 4$) pressure waveforms as measured at six holder positions used during stone comminution experiments for (a) the original lens and (b) the new lens, where legend entries indicate (z, r) relative to the geometric focus.

secondary pressures from the new lens have been substantially suppressed along the central (z -) axis due to destructive wave interference. In the focal plane, the energy contribution from the second compressive wave has been reduced by nearly 100% by the new lens design. Peak positive pressure (P_+) of the original lens at the focus is 9% higher than that of the new lens; however, at positions pre-focally (in z) and off-axis in the focal plane (in r), the new lens generally has higher P_+ , which leads to a 47% enhancement in full-width half-maximum beam width. Similarly, average peak pressure ($P_{+(avg)}$) inside the stone holder of the new lens is 16%–37% higher than that of the original lens at positions used for stone comminution experiments. In a previous study, a dose- and holder fluid-independent threshold of fragmentation was estimated to be at a $P_{+(avg)}$ of approximately 7.6 and 5.3 MPa for hard and soft BegoStones, respectively (Smith and Zhong, 2012). For hard stones, the $P_{+(avg)}$ threshold corresponds to a fragmentation threshold radius ($r_{threshold}$) of 13.3 and 9.6 mm for the new and original lenses, respectively. In other words, the new lens is capable of breaking the hard BegoStone phantoms used in this study in an area within the focal plane that is 92% larger than the original lens. The corresponding area for fragmenting soft BegoStone is estimated to be 71% larger for the new lens compared to the original lens, with $r_{threshold}$ values of 22.1 and 16.9 mm, respectively.

Table I presents a comparison of the peak pressures and static stone comminution results at 500 and 1000 shocks from the original and new lenses. Generally, results of stone comminution from both lenses exhibit spatial dependence paralleling the changes in peak pressure, independent of dose, stone type, or holder fluid used. At the field position ($z=0$, $r=12$ mm) corresponding to the lowest overall $P_{+(avg)}$ (=6.2 MPa) tested with the original lens, no fracture

was seen in all four hard BegoStone samples treated in water after 1000 shocks. No hard BegoStone comminution experiments in 1,3-butanediol or at 500 LSW dose were subsequently pursued with the original lens at this field position. In contrast, fragmentation occurred in numerous samples treated at the same position using the new lens ($P_{+(avg)}=8.4$ MPa) in both water and 1,3-butanediol and for both 500 and 1000 shocks. In 12 out of 15 stone comminution experiments using 1000 shock wave dose at positions far from the geometric focus ($z \leq -20$ mm, $r \geq 8$ mm) where $P_{+(avg)}$ of the new lens was >25% higher than that of the original lens, stone comminution efficiencies were statistically higher for the new lens ($p \leq 0.05$). At the geometric focus, hard stone comminution efficiencies were statistically similar between the new and original lenses, whereas soft stone comminution efficiencies were statistically higher for the original lens ($p \leq 0.05$). The differences in these cases may be related to contributions from secondary compression to fragmentation using the original lens, as $P_{+(avg)}$ of secondary compression (=5.3 MPa) is equivalent to the estimated threshold of fragmentation of soft stone (Smith and Zhong, 2012). In other test conditions, and in general where the aggregate damage from cavitation and stress wave mechanisms was lower, it was found that the stone comminution results between lenses were typically either statistically similar or higher for the new lens ($p \leq 0.05$). Furthermore, in nearly all groups (independent of lens, stone type, or holder fluid used), a dependence of stone comminution on LSW dose is evident, indicating a progressive accumulation of fragmentation in SWL. Additionally, lower stone comminution efficiencies were obtained in 1,3-butanediol compared to water under otherwise comparable exposure conditions. This observation confirms the general consensus that cavitation is an important mechanism of stone fragmentation in addition

TABLE I. A comparison of peak pressure and stone comminution results at different field positions and doses using the original and new lenses. “-” indicates no stone comminution test conducted. Indicated p -values are for statistical comparison of original and new lens stone comminution results under comparable experimental settings.

Position (mm)		LSW pressure (MPa)			Stone comminution (%)							
					Soft BegoStones				Hard BegoStones			
					500 shocks		1000 shocks		500 shocks		1000 shocks	
Lens	(z)	(r)	P_+	$P_{+(avg)}$	1,3-but.	H ₂ O	1,3-but.	H ₂ O	1,3-but.	H ₂ O	1,3-but.	H ₂ O
Orig.	0	0	45.0	21.2	32.0 ^a	48.5 ^a	50.0 ^a	81.2 ^a	19.3	42.3	30.0	64.7
		4	20.7	16.2	25.8	41.6	40.4	69.5	10.3	32.6	20.9	44.8
		8	9.4	9.2	13.5	18.4	18.6	35.3	5.0	8.3	7.4	14.7
		12	6.4	6.2	4.1	6.0	6.8	11.4	-	-	-	0.7
	-20	0	31.2	17.9	36.2	56.4 ^a	48.0	78.3	18.2	36.1	28.8	55.2
	-40		19.5	15.3	31.9	36.0	34.6	57.6	10.1	21.9	15.6	31.9
New	0	0	41.2	24.5	26.6	41.9	42.5	72.5	20.0	37.0	26.4	65.6
		4	24.0	19.7	22.7	40.7	38.1	68.8	16.9 ^a	29.3	20.9	53.0 ^b
		8	13.7	12.6	16.9	24.8 ^a	28.1 ^a	40.5 ^a	8.9	16.5	11.8	27.9 ^b
		12	8.9	8.4	9.0	15.3	12.0 ^a	22.0 ^b	1.6	2.8	1.5	1.5 ^b
	-20	0	44.4	23.0	34.6	45.8	52.5	86.2 ^a	25.9	43.8	30.6	70.9 ^b
	-40		30.3	19.5	37.8 ^a	57.0 ^b	49.7 ^b	85.0 ^b	20.9	40.0 ^b	27.8 ^b	61.7 ^b

^a $p \leq 0.05$.

^b $p \leq 0.01$.

to stress waves (Zhu *et al.*, 2002; Cleveland and McAteer, 2007; Rassweiler *et al.*, 2011).

B. Dose- and average peak pressure-dependence in stone comminution

To better understand the effects of dose, $P_{+(avg)}$, and cavitation in stone fragmentation, the Weibull distribution was adapted to describe the multi-fracture processes of SWL. For heuristic regression analyses of the data sets presented in this section, the threshold values (a) from the 3-parameter Weibull function [Eq. (2)] were considered to be nonzero, in accordance with experimental observations. In Figs. 5(a) and 5(b), stone comminution at the lithotripter focus is plotted for the two lenses using four different LSW doses (250, 500, 1000, and 2000 shocks) and fitted using Eq. (2), where the probability of failure (P_f) and stress parameter (σ) are replaced by SC and dose, respectively. The Weibull functions were found to correlate well with their respective data sets (all $R^2 \geq 0.98$). Moreover, the extrapolated values on the horizontal axis from these fitted curves indicate that there are dose thresholds (a -values) for initiation of fragmentation, which are higher in 1,3-butanediol (~ 230 shocks) than in water (0–130 shocks) for both stone types. In other words, the presence of strong cavitation influences the minimal number of shocks required to initiate first fracture at a given lithotripter field position where the $P_{+(avg)}$ is above the pressure threshold for fragmentation. In Figs. 5(c) and 5(d), stone comminution efficiencies from two LSW doses (500 and 1000) and holder fluids (water and 1,3-butanediol) are compared against variations in $P_{+(avg)}$ for the two lenses combined. The results are fitted according to Eq. (2), where P_f and σ are replaced with SC and $P_{+(avg)}$, respectively. The coefficients of determination (R^2) for the four combinations of dose and holder fluid are between 0.76 and 0.92 for soft BegoStone and between 0.89 and 0.96 for hard BegoStone, similar to observed correlations for stone comminution efficiency and effective acoustic energy (Smith and Zhong, 2012). $P_{+(avg)}$ thresholds for the combined stone comminution results of the original and new lenses are in the range of 4.5–6.0 MPa for soft BegoStone and 6.9–8.2 MPa for hard BegoStone, which are also in good agreement with previous threshold values determined through logarithmic curve fits (Smith and Zhong, 2012).

In order to include both dose and $P_{+(avg)}$ in a heuristic 3-D representation of stone comminution efficiency using a Weibull-style model, it is assumed that the functions of dose and $P_{+(avg)}$ are separable and scale one another in the overall SC ($P_{+(avg)}$, dose) function. Adapting Eq. (2) to a six-parameter function,

$$SC(P_{+(avg)}, \text{dose}) \stackrel{\text{def}}{=} \left\{ 1 - \exp \left[- \left(\frac{P_{+(avg)} - a}{b} \right)^c \right] \right\} \cdot \left\{ 1 - \exp \left[- \left(\frac{\text{dose} - d}{f} \right)^g \right] \right\}, \quad (3)$$

FIG. 5. (Color online) Dose-dependent stone comminution in the shared geometric focus of the original (dark) and new (light) lenses for (a) hard and (b) soft BegoStones. Curve fits for the combined data sets in water (solid) and 1,3-butanediol (dashed) are three-parameter Weibull functions (all $R^2 \geq 0.98$). (c) Hard and (d) soft stone comminution results of the combined original and new lens data sets plotted against corresponding $P_{+(avg)}$ values for doses of 500 (circle) and 1000 (square) shocks (color online). Curve fits for water (solid) and 1,3-butanediol (dashed) and shock wave doses of 500 (light) and 1000 (dark) are three-parameter Weibull functions (all $R^2 \geq 0.76$).

where a , b , c , d , f , and g are coefficients. In this context, coefficients a and d represent location parameters, or the minimum $P_{+(avg)}$ and dose to produce fragmentation, respectively. The six-parameter heuristic model for stone comminution can be reduced to four coefficients using the previously determined $P_{+(avg)}$ fragmentation thresholds ($=7.6$ MPa and 5.3 MPa for hard and soft BegoStone, respectively) in place of a and experimental estimations of minimum dose for first fracture in place of d . Using the original lens shock source at 13.8 kV and stones placed at the focus, first fracture doses were determined to be ~ 45 shocks and ~ 100 shocks for hard BegoStones in water and in 1,3-butanediol, respectively, and ~ 15 shocks and ~ 60 shocks for soft BegoStones in water and in 1,3-butanediol, respectively. Strictly speaking, d is a function of $P_{+(avg)}$, and should affect the rate of fragmentation [i.e., the partial derivative of Eq. (3) with respect to dose], though for the purposes of this initial validation, it is assumed to be a constant.

Contour plots of the four-parameter heuristic model of stone comminution for the combined results of the original and new lenses are shown in Fig. 6. The models are constructed using data from Table I, with supplemental data at 250 and 2000 shocks at the lithotripter focus. For the purposes of improving prediction capabilities, stone comminution results at greater than or equal to four additional field positions and 2000 shock dose are used in developing the heuristic models in water. The validity of the heuristic model fit for hard BegoStones in water was further verified by comparing stone comminution results and heuristic model predictions at 3 arbitrarily chosen field positions and doses >1000 shocks [see data points in Fig. 6(a)]. Corresponding stone comminution efficiencies from the heuristic fit are (from left to right) 68.5% , 71.4% , and 81.1% . Overall, the correlations in Fig. 6 are strong, with R^2 values between 0.91 and 0.93 . The models (particularly in water) indicate that for both $P_{+(avg)}$ and dose, there are comminution lines resembling asymptotes along which one should not expect to dramatically increase comminution efficiency. In the case of $P_{+(avg)}$, the asymptotic feature is a reflection of variability of stone comminution for $P_{+(avg)} > 15$ MPa (see Table I), which may be influenced by differences in local cavitation activities. Since each heuristic model fit in Fig. 6 is a reflection of the mean cavitation activity within the data set used for its construction, the implication is that increasing $P_{+(avg)}$ while maintaining a similar cavitation environment to the affiliated data set will not substantially improve stone comminution efficiency. In the case of dose, the asymptotic feature is a reflection of the slowing rate of fragmentation as dose increases [see Figs. 5(a) and 5(b)]. The implication is that for a constant $P_{+(avg)}$, the benefits to using more shock waves diminish gradually beyond the first ~ 500 shocks.

Details of the heuristic model coefficients are provided in Table II. Generally, the shape coefficients (c and g) for the heuristic model are dependent on fluid medium, decreasing by 15% – 37% in 1,3-butanediol compared to water. A dependence on stone type is also apparent in both shape and scale (b and f) parameters, as shape coefficients vary from -4% to $+34\%$, while scale coefficients decrease by 10% – 42% for soft BegoStones compared to hard

FIG. 6. (Color online) Contour plots of the four-parameter heuristic model of stone comminution for (a) hard BegoStones in water, (b) hard BegoStones in 1,3-butanediol, (c) soft BegoStones in water, and (d) soft BegoStones in 1,3-butanediol. The coefficient of determination (R^2) and number (n) of data points used in each fit are indicated on each subplot. Stone comminution results of three arbitrarily chosen field positions and doses are shown next to corresponding “+” marks in (a) for the original lens (dark) and new lens (light).

TABLE II. Fit coefficients and R^2 values for the four-parameter heuristic model of stone comminution. Coefficients a and d are fixed values determined through experimentation.

Coefficients	H ₂ O		1,3- but.	
	Hard	Soft	Hard	Soft
a (MPa)	7.6	5.3	7.6	5.3
b (MPa)	4.83 ± 0.79	4.34 ± 0.52	18.9 ± 14.0	14.6 ± 4.2
c	1.07 ± 0.18	1.15 ± 0.21	0.910 ± 0.171	0.871 ± 0.124
d	45	15	100	60
f	900 ± 99	743 ± 53	$1,250 \pm 1200$	726 ± 204
g	1.25 ± 0.16	1.32 ± 0.17	0.784 ± 0.214	1.05 ± 0.22
R^2	0.93	0.92	0.92	0.91

BegoStones. In the heuristic models, the influences of stone (and fluid) type on coefficients are divided among the respective functions of $P_{+(avg)}$ and dose; thus, these results are typically lower in comparison to the trends in derived Weibull parameters from Fig. 1, which indicate a 25% increase in Weibull modulus and 55% decrease in normalization stress for soft BegoStones when compared to hard BegoStones.

C. Effect of respiratory motion on stone comminution

Previously, it was demonstrated that the $P_{+(avg)}$ value at which hard BegoStone phantoms begin to fracture can be used to determine effective fragmentation areas of the original and new lenses (defined by $r_{threshold} = 9.6$ and 13.3 mm, respectively). During simulated respiratory motion stone comminution experiments detailed in this section, the selected excursion distances ($D = 15$ and 30 mm) exceeded $r_{threshold}$ values of both lenses. A comparison of 2000 shock stone comminution results for static ($n = 4$ stones) and simulated motions ($n = 44$ stones) is shown for both lenses in Table III. Notably, the various simulated respiratory motions produce a reduction in stone comminution efficiencies for both lenses, similar to the observation of a previous *in vitro* study (Cleveland *et al.*, 2004). However, the influence of stone motion on the efficacy of the new lens is substantially less than on the original lens, resulting in a statistically higher stone comminution efficiency overall ($p < 0.0001$) for the new lens. During simulated motions, when the stone holder centroid position exceeds $r_{threshold}$ of the lithotripter in use, incident shock waves can be considered to have negligible contribution to stone comminution. Removing the

TABLE III. Comparison of 2000 shock stone comminution efficiencies of the original and new lenses during static experimentation at the focus and various simulated respiratory motion patterns. Parameters determined by the $P_{+(avg)}$ threshold of fragmentation are also presented for comparison of the two lenses.

Lens	Stone comminution efficiency (%)				Missed shock waves (%)
	Static ($n = 4$)	Resp. motion ($n = 44$)	$r_{threshold}$ (mm)	dose _{eff}	
Orig.	93.4 ± 2.3	62.8 ± 11.4	9.6	1227	39
New	90.4 ± 3.7	76.6 ± 15.1	13.3	1428	29

ineffectual pulses from the total LSW dose (i.e., 2000 shocks) gives a representation of effective dose (dose_{eff}), from which it was determined that $39\% \pm 11\%$ of shock waves missed the target stone during the motion simulations for the original lens compared to $29\% \pm 18\%$ for the new lens ($p < 0.01$). These values are consistent with clinical observations of percentages of missed shock waves during SWL (Leighton *et al.*, 2008; Sorensen *et al.*, 2012).

The simulated respiratory motion experiments are comprised of 6 subsets for each lens representing unique motion types detailed in Sec. II B. In order to assess the similarity of motion histograms for the original and new lenses, an average static radius of treatment, i.e.,

$$r_{avg} = \sum_{r=0}^{r_{max}} r \cdot \frac{\text{dose}(r)}{\text{dose}_{tot}}, \quad (4)$$

was calculated for each of the six motion pattern groups through a summation of the histogram of stone holder positions weighted by percentage of total dose (dose_{tot}) at those positions, where r_{max} is the maximum radius of motion from the lithotripter focus. In all but one motion group, r_{avg} values were statistically similar ($p > 0.09$) between the two lenses. The exceptional group is represented by $D = 30$ mm, breath rate = 12 bpm, and “low” drift, in which $r_{avg} = 12.2 \pm 0.3$ mm was obtained for the original lens compared to 12.8 ± 0.6 mm for the new lens ($p = 0.04$). Although statistically significant, this small difference (< 1 mm) in r_{avg} is likely of little consequence in comparison of stone comminution efficiencies.

Equation (4) may be adapted from its estimation of the average holder position during respiratory motion to an estimation of equivalent static radius for effective treatment, i.e.,

$$r_{eq} = \sum_{r=0}^{r_{threshold}} r \cdot \frac{\text{dose}(r)}{\text{dose}_{eff}}. \quad (5)$$

This is accomplished through summation of only the effective shock waves during treatment, or the respiratory motion histogram from $0 \leq r \leq r_{threshold}$. In Fig. 7, sample respiratory motion histograms for the original and new lenses are plotted with both $r_{threshold}$ and r_{eq} values indicated. Generally, r_{eq} (as

FIG. 7. (Color online) Average ($n = 6$) histograms of $D = 15$ mm, 12 bpm, “low” drift simulated respiratory motions for the original (dark) and new (light) lenses. Fragmentation thresholds ($r_{threshold}$) and effective static radii (r_{eq}) are indicated for each lens on the plot.

FIG. 8. (Color online) Two thousand shock stone comminution of the original (solid dark fill) and new (solid light fill) lenses and their corresponding predicted stone comminution results using the heuristic model (dark outline with light fill and light outline with very light fill, respectively). Indicated p -values from paired t -tests are for comparison of heuristic model predictions and results from respiratory motion.

well as dose_{eff} values for the new lens are higher than for the original lens because its $r_{\text{threshold}}$ is larger.

Using r_{eq} values, equivalent static $P_{+(\text{avg})}$ may be determined for each simulated respiratory motion using characterization results of the respective lenses. In combination with dose_{eff} , equivalent $P_{+(\text{avg})}$ can subsequently be used to “predict” stone comminution efficiency using the heuristic model of stone comminution [see Eq. (3)] for comparison with actual fragmentation results from respiratory motion. The combined results for actual and predicted stone comminution efficiencies are shown in Fig. 8 for each of the six aforementioned respiratory motion groups and both lenses. In 5 out of 6 motion groups, the new lens produced statistically higher stone comminution efficiency than the original lens, whereas the heuristic model predicts statistically higher stone comminution efficiency for new lens in 4 out of 6 motion groups using an unpaired t -test. The exceptional motion group (i.e., $D = 30$ mm, 12 bpm, and “high” drift) resulted in higher stone comminution efficiency for the new lens in both the heuristic model predictions and experimental comminution results, with $p = 0.38$ and 0.05 , respectively. Overall stone comminution efficiency predictions from the heuristic model are statistically similar ($p > 0.07$) to the experimental results of respiratory motion in four out of six motion groups for both the original and new lenses. Predominantly, these results indicate the heuristic model can be effective in predicting outcomes from more complex SWL experiments than the static stone comminution from which it was developed.

The following are general observations pertaining to the parameters of simulated respiratory motion that influence the stone comminution efficiencies of both lenses (see Fig. 8): An increase in excursion distance (D) from 15 mm to 30 mm resulted in statistically lower comminution efficiency ($p < 0.01$), with the exception of “high” drift motion using the new lens ($p = 0.21$). Similarly, low drift motion patterns produced higher comminution efficiencies than their high

drift counterparts ($p \leq 0.06$) with the exception of $D = 15$ mm using the new lens ($p = 0.26$). These results are mirrored by the predictions from the heuristic model, and generally agree with the consensus that reduced motion, whether by shallower breathing or reduced patient movements, is beneficial to SWL (Ng *et al.*, 2007). Furthermore, a breath rate effect is evident in Fig. 8. With all other variables held constant, increasing breath rate from 12 to 24 bpm resulted in statistically lower comminution efficiencies ($p < 0.05$). This effect may be partly artificial and related to Brownian motion, where an increase in total number of mimicked breath cycles during treatment increases the likelihood of stone drift away from the focus. However, the predicted results from the heuristic model indicate that differences in histograms between varying breath rates may be inconsequential, as stone comminution changes insignificantly as breath rate increases from 12 to 24 bpm. Potentially, the reduction in stone comminution during simulated respiratory motion may be compounded by changes in cavitation activities induced inside the holder, as the increased motion can alter the duty cycle of the incident lithotripter shock waves. It should be noted that as with all predicted outcomes in Fig. 8, the unique fracture histories of stones moving in and out of the focal region and their effects cannot be entirely simulated in a static model.

IV. DISCUSSION

In this study, a heuristic model of stone comminution during SWL has been developed through adaptation of the Weibull theory for brittle fracture. The model accounts for shock wave dose and the average peak pressure, $P_{+(\text{avg})}$, incident on the stone during the treatment. Furthermore, the model also incorporates the distinctive threshold values in dose and $P_{+(\text{avg})}$ that are required to initiate fragmentation under the particular lithotripter field conditions used in the experiments. The results show that stone comminution in SWL correlates with the dose and $P_{+(\text{avg})}$ through an exponential relationship [see Eq. (3)] that has been substantiated by the experimental data obtained using two shock wave sources of different beam width and pulse profile both in water and in 1,3-butanediol. This work represents a significant departure from most of the previous studies that were mainly focused on specific mechanisms of stone fragmentation during the early stage of SWL [see reviews in (Cleveland and McAteer, 2007; Rassweiler *et al.*, 2011)] while largely ignoring their contribution or effectiveness in the later stage of the treatment. In contrast, the heuristic model developed in this work, although unable to describe the exact mechanisms that drive the stone comminution process, captures the fundamental contribution of two important parameters in SWL (i.e., dose and $P_{+(\text{avg})}$) to the overall treatment outcome. Therefore, this model provides a critical relationship that can directly benefit the design and implementation of effective treatment protocols in SWL. For example, the asymptotic lines in Fig. 6 suggests that, depending on stone type, effective SWL can be achieved by using moderate average peak pressure in the range of 15 to 20 MPa within 2000 shocks. The model also indicates that

prolonged treatment to high doses may only gain marginal improvement in stone comminution while elevating the risk for tissue injury.

The significant difference in stone comminution produced in water vs 1,3-butanediol (see Fig. 6) confirms again the importance of cavitation in stone fragmentation (Zhu *et al.*, 2002; Sapozhnikov *et al.*, 2007). As shown in Fig. 5, this discrepancy increases with shock wave dose and $P_{+(avg)}$, indicating an accumulated contribution of cavitation damage and potential synergy with stress waves in producing effective stone comminution. The closer fit of the data in water compared to 1,3-butanediol, despite larger data sets in water, also suggests that cavitation-induced pitting on the surface (Sass *et al.*, 1991; Zhu *et al.*, 2002) may constitute a more uniform, extrinsically induced flaw population than the pre-existing, intrinsic flaws distributed inside the stone material. As the treatment progresses, the extrinsic flaw population increases significantly and may become the dominant weakest links whereby the incident LSWs drive the fracture of residual fragments (Zhong, 2013). This speculation is supported by previous observations that stone comminution in SWL can be augmented substantially by tandem pulses that selectively enhance cavitation damage (Xi and Zhong, 2000).

The performance of the new acoustic lens, designed specifically to broaden the beam width while suppressing the secondary compressive wave has been compared with the original lens. Overall, it was found that the new lens produces better fragmentation than the original lens at positions far from the lithotripter focus ($z \leq -20$ mm, $r \geq 8$ mm), which correlates to their higher $P_{+(avg)}$ at these locations. Based on the $P_{+(avg)}$ thresholds (≈ 7.6 and 5.3 MPa for hard and soft BegoStone phantoms, respectively) for initiating fragmentation, the new lens possesses a much wider effective area (determined by $r_{threshold}$) than the original lens, which may contribute to its enhanced performance *in vivo* (Mancini *et al.*, 2010). The correlation between stone comminution and $P_{+(avg)}$ shown in this and our recent study (Smith and Zhong, 2012) provides a practical basis for guiding the design improvement of EM shock wave lithotripters and potentially other lithotripter technologies.

Subsequently, an *in vitro* respiratory motion model is introduced for stone fragmentation experiments using both lenses. The results confirm previous observations that translational motion negatively affects stone fragmentation in the absence of renal stone tracking systems (Orkisz *et al.*, 1998; Chang *et al.*, 2001), especially for high peak pressure, narrow focus lithotripters (Cleveland *et al.*, 2004). Furthermore, the simulated motion histograms are utilized for the prediction of stone comminution efficiencies from both lenses through the heuristic model. A comparison of the model-calculated predictions vs experimental results has revealed a similar pattern in stone comminution produced by the two lenses overall, illustrating the predictive capability of the heuristic model. Modest discrepancies between the model and experimental stone comminution efficiencies may be a result of current model limitations in capturing complex cavitation phenomena caused by simulated respiratory movement. Additionally, the effective fragmentation region of each lens may contract as stones

begin to fragment and reduce in size, an effect that requires further investigation.

All in all, although there are other parameters such as size and geometry of the stone, PRF, peak negative pressure (P_-), and pulse duration that have yet to be incorporated in the heuristic model, it is not an intention to diminish their importance to SWL. In particular, PRF, as it relates directly to cavitation activity (Pishchalnikov *et al.*, 2006), may play an important role in affecting the shape and scale parameters of the heuristic model of stone comminution. Similarly, stone composition (i.e., flaw distribution) has been identified as influencing the shape and scale parameters of the model in a manner similar to variations in Weibull parameters, though uncovering its precise role within the model requires additional experimentation. The artificial kidney stones used in this study have demonstrated clinical relevance (Esch *et al.*, 2010), but do not necessarily mimic the Weibull parameters of all renal and ureteral stones. Determination of Weibull parameters for kidney stones and correlation with parameters of artificial stones may improve applicability of the model. Despite its simplicity, the heuristic model developed in this study is useful in elucidating the roles of two critical parameters of SWL (i.e., $P_{+(avg)}$ and dose), and the influence of fluid viscosity (and thus a particular facet of cavitation) in stone comminution outcome. More importantly, the heuristic model has demonstrated its value in clarifying the physical basis for improved performance of a newly designed acoustic lens for EM shock wave lithotripters, and may provide valuable guidance in the future improvements of lithotripter technologies.

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- Bierkens, A. F., Hendriks, A. J., de Kort, V. J., de Reyke, T., Bruynen, C. A., Bouve, E. R., Beek, T. V., Vos, P., and Berkel, H. V. (1992). "Efficacy of second generation lithotripters: a multicenter comparative study of 2,206 extracorporeal shock wave lithotripsy treatments with the Siemens Lithostar, Dornier HM4, Wolf Piezolith 2300, Direx Tripter X-1 and Breakstone lithotripters," *J. Urol.* **148**:1052–1056, discussion 1056–1057.
- Bromage, P. R., Bonsu, A. K., el-Faqih, S. R., and Husain, I. (1989). "Influence of Dornier HM3 system on respiration during extracorporeal shock-wave lithotripsy," *Anesth. Analg.* **68**, 363–367.
- Chang, C. C., Liang, S. M., Pu, Y. R., Chen, C. H., Manousakas, I., Chen, T. S., Kuo, C. L., Yu, F. M., and Chu, Z. F. (2001). "In vitro study of ultrasound based real-time tracking of renal stones for shock wave lithotripsy: Part 1," *J. Urol.* **166**, 28–32.
- Cleveland, R. O., Anglade, R., and Babayan, R. K. (2004). "Effect of stone motion on in vitro comminution efficiency of Storz Modulith SLX," *J. Endourol./Endourol. Soc.* **18**, 629–633.
- Cleveland, R. O., and McAteer, J. A. (2007). "The physics of shock wave lithotripsy," in *Smith's Textbook on Endourology*, edited by G. H. Badlani, D. H. Bagley, R. V. Clayman, S. G. Docimo, G. H. Jordan, L. R. Kavoussi, B. R. Lee, J. E. Lingeman, G. M. Preminger, and J. W. Segura (BC Decker, Inc., Ontario, Canada), pp. 317–332.

- Cleveland, R. O., and Sapozhnikov, O. A. (2005). "Modeling elastic wave propagation in kidney stones with application to shock wave lithotripsy," *J. Acoust. Soc. Am.* **118**, 2667–2676.
- Coleman, A. J., Saunders, J. E., Crum, L. A., and Dyson, M. (1987). "Acoustic cavitation generated by an extracorporeal shockwave lithotripter," *Ultrasound Med. Biol.* **13**, 69–76.
- Coloma, M., Chiu, J. W., White, P. F., Tongier, W. K., Duffy, L. L., and Armbruster, S. C. (2000). "Fast-tracking after immersion lithotripsy: general anesthesia versus monitored anesthesia care," *Anesth. Analg.* **91**, 92–96.
- Davies, S. C., Hill, A. L., Holmes, R. B., Halliwell, M., and Jackson, P. C. (1994). "Ultrasound quantitation of respiratory organ motion in the upper abdomen," *Br. J. Radiol.* **67**, 1096–1102.
- Eisenmenger, W. (2001). "The mechanisms of stone fragmentation in ESWL," *Ultrasound Med. Biol.* **27**, 683–693.
- Esch, E., Simmons, W. N., Sankin, G., Cocks, H. F., Preminger, G. M., and Zhong, P. (2010). "A simple method for fabricating artificial kidney stones of different physical properties," *Urol. Res.* **38**, 315–319.
- Forquin, P., and Hild, F. (2010). "A probabilistic damage model of the dynamic fragmentation process in brittle materials," *Adv. Appl. Mech.* **44**, 1–72.
- Gerber, R., Studer, U. E., and Danuser, H. (2005). "Is newer always better? A comparative study of 3 lithotripter generations," *J. Urol.* **173**, 2013–2016.
- Graber, S. F., Danuser, H., Hochreiter, W. W., and Studer, U. E. (2003). "A prospective randomized trial comparing 2 lithotripters for stone disintegration and induced renal trauma," *J. Urol.* **169**, 54–57.
- Gracewski, S. M., Dahake, G., Ding, Z., Burns, S. J., and Everbach, E. C. (1993). "Internal-stress wave measurements in solids subjected to lithotripter pulses," *J. Acoust. Soc. Am.* **94**, 652–661.
- Granz, B. (1994). "Measurement of shock wave properties after the passage through a tissue mimicking material," in *Proceedings of 1994 IEEE Ultrasonics Symposium*, pp. 1847–1851.
- Granz, B., and Kohler, G. (1992). "What makes a shock wave efficient in lithotripsy?," *J. Stone Disease* **4**, 123–128.
- Leighton, T. G., Fedele, F., Coleman, A. J., McCarthy, C., Ryves, S., Hurrell, A. M., De Stefano, A., and White, P. R. (2008). "A passive acoustic device for real-time monitoring of the efficacy of shockwave lithotripsy treatment," *Ultrasound Med. Biol.* **34**, 1651–1665.
- Lingeman, J. E., McAteer, J. A., Gnassin, E., and Evan, A. P. (2009). "Shock wave lithotripsy: advances in technology and technique," *Nat. Rev. Urol.* **6**, 660–670.
- Lokhandwalla, M., and Sturtevant, B. (2000). "Fracture mechanics model of stone comminution in ESWL and implications for tissue damage," *Phys. Med. Biol.* **45**, 1923–1940.
- Lubock, P. (1989). "The physics and mechanics of lithotripters," *Dig. Dis. Sci.* **34**, 999–1005.
- Mancini, J. G., Simmons, W. N., and Raymundo, M. E. (2010). "In vivo stone fragmentation and tissue injury produced by a new acoustic lens for a Siemens lithotripter," *J. Endourol.* **24**, A20–A20.
- Moerland, M. A., van den Bergh, A. C., Bhagwandien, R., Janssen, W. M., Bakker, C. J., Lagendijk, J. J., and Battermann, J. J. (1994). "The influence of respiration induced motion of the kidneys on the accuracy of radiotherapy treatment planning, a magnetic resonance imaging study," *Radiother. Oncol.* **30**, 150–154.
- Mota, A., Knap, J., and Ortiz, M. (2006). "Three-dimensional fracture and fragmentation of artificial kidney stones," *SciDAC 2006: Scientific Discovery Through Advanced Computing* **46**, 299–303.
- Ng, C. F., Thompson, T., and Tolley, D. (2007). "Characteristics and treatment outcome of patients requiring additional intravenous analgesia during extracorporeal shockwave lithotripsy with Dornier Compact Delta Lithotripter," *Int. Urol. Nephrol.* **39**, 731–735.
- Orkisz, M., Farchtchian, T., Saighi, D., Bourlion, M., Thiounn, N., Gimenez, G., Debre, B., and Flam, T. A. (1998). "Image based renal stone tracking to improve efficacy in extracorporeal lithotripsy," *J. Urol.* **160**, 1237–1240.
- Ortiz, M. (1988). "Microcrack coalescence and macroscopic crack-growth initiation in brittle solids," *Int. J. Solids Struct.* **24**, 231–250.
- Philipp, A., and Lauterborn, W. (1998). "Cavitation erosion by single laser-produced bubbles," *J. Fluid Mech.* **361**, 75–116.
- Pishchalnikov, Y. A., McAteer, J. A., Williams, J. C., Jr., Pishchalnikova, I. V., and Vonderhaar, R. J. (2006). "Why stones break better at slow shock-wave rates than at fast rates: in vitro study with a research electrohydraulic lithotripter," *J. Endourol./Endourolog. Soc.* **20**, 537–541.
- Quinn, J. B., and Quinn, G. D. (2010). "A practical and systematic review of Weibull statistics for reporting strengths of dental materials," *Dent. Mater.* **26**, 135–147.
- Rassweiler, J. J., Knoll, T., Kohrmann, K. U., McAteer, J. A., Lingeman, J. E., Cleveland, R. O., Bailey, M. R., and Chaussy, C. (2011). "Shock wave technology and application: An update," *Eur. Urol.* **59**, 784–796.
- Rinne, H. (2009). *The Weibull Distribution: A Handbook* (CRC Press, Boca Raton, FL), p. 784.
- Rosin, P., and Rammler, E. (1933). "The laws governing the fineness of powdered coal," *J. Inst. Fuel* **7**, 29–36.
- Sapozhnikov, O. A., Maxwell, A. D., MacConaghy, B., and Bailey, M. R. (2007). "A mechanistic analysis of stone fracture in lithotripsy," *J. Acoust. Soc. Am.* **121**, 1190–1202.
- Sass, W., Braunlich, M., Dreyer, H. P., Matura, E., Folberth, W., Preismeyer, H. G., and Seifert, J. (1991). "The mechanisms of stone disintegration by shock waves," *Ultrasound Med. Biol.* **17**, 239–243.
- Simmons, W. N., Cocks, F. H., Zhong, P., and Preminger, G. (2010). "A composite kidney stone phantom with mechanical properties controllable over the range of human kidney stones," *J. Mech. Behave. Biomed. Mater.* **3**, 130–133.
- Smith, N., Sankin, G. N., Simmons, W. N., Nanke, R., Fehre, J., and Zhong, P. (2012). "A comparison of light spot hydrophone and fiber optic probe hydrophone for lithotripter field characterization," *Rev. Sci. Instrum.* **83**, 014301.
- Smith, N., and Zhong, P. (2012). "Stone comminution correlates with the average peak pressure incident on a stone during shock wave lithotripsy," *J. Biomech.* **45**, 2520–2525.
- Sorensen, M. D., Bailey, M. R., Shah, A. R., Hsi, R. S., Paun, M., and Harper, J. D. (2012). "Quantitative assessment of shockwave lithotripsy accuracy and the effect of respiratory motion," *J. Endourol./Endourolog. Soc.* **26**, 1070–1074.
- Weibull, W. (1939). "A statistical theory on the strength of materials," *Proc. Roy. Swed. Inst. Eng. Res.*, No. 151.
- Weibull, W. (1951). "A statistical distribution function of wide applicability," *J. Appl. Mech.* **18**, 293–297.
- Xi, X., and Zhong, P. (2000). "Improvement of stone fragmentation during shock-wave lithotripsy using a combined EH/PEAA shock-wave generator-in vitro experiments," *Ultrasound Med. Biol.* **26**, 457–467.
- Xi, X. F., and Zhong, P. (2001). "Dynamic photoelastic study of the transient stress field in solids during shock wave lithotripsy," *J. Acoust. Soc. Am.* **109**, 1226–1239.
- Zhong, P. (2013). "Shock wave lithotripsy," *Bubble Dynamics and Shock Waves, in the Series of Shock Wave Science and Technology Reference Library* **8**, edited by C. F. Delale (Springer-Verlag, Berlin), pp. 291–338.
- Zhu, S., Cocks, F. H., Preminger, G. M., and Zhong, P. (2002). "The role of stress waves and cavitation in stone comminution in shock wave lithotripsy," *Ultrasound Med. Biol.* **28**, 661–671.
- Zohdi, T. I., and Szeri, A. J. (2005). "Fatigue of kidney stones with heterogeneous microstructure subjected to shock-wave lithotripsy," *J. Biomed. Mater. Res., Part B: Appl. Biomater.* **75**, 351–358.