In Vitro Assessment of Three Clinical Lithotripters Employing Different Shock Wave Generators

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Abstract

Objective: To test the hypothesis that shock wave lithotripsy machines vary in their ability to fragment standardized artificial urinary calculi.

Materials and Methods: An *in vitro* test configuration was used to fragment synthetic U-30 Gypsum (U.S. Gypsum, Chicago, IL) stones (mean length 7.1 ± 0.2 mm, mean diameter 6.5 ± 0.07 mm, mean mass 299 ± 16 mg) using the Sonolith i-sys (EDAP TMS, Vaulx-en-Velin, France), Modulith SLX F2 (Storz Medical AG, Tägerwil, Switzerland), and Piezolith 3000 (Richard Wolf GmbH, Knittlingen, Germany) lithotripters. Gypsum stones were placed at the nominal focus and treated with 250, 500, or 1000 shocks. The residual mass following passage through a 2-mm wire mesh was measured and compared using ANOVA and the Tukey–Kramer HSD test.

Results: There was no statistically significant difference between the Modulith SLX F2 and Piezolith 3000 lithotripters for 250 and 1000 shock treatments ($p=0.34$ and 0.31 , respectively). The Piezolith 3000 demonstrated the most favorable stone mass reduction for 500 shock treatments (187.4 ± 45.2 mg). The Sonolith i-sys was found to be significantly less effective than the other lithotripters for all shockwave conditions. Furthermore, performance of the Sonolith i-sys decreased beyond a threshold generator electrode age of 6000 shocks.

Conclusions: This *in vitro* study found considerable variability in the ability of lithotripters to fragment synthetic urinary calculi. Synthetic stones were employed to provide a repeatable means of assessing variability in fragmentation efficiency of lithotripters. The Modulith SLX F2 and Piezolith 3000 are broadly equal and resulted in greater fragmentation efficiencies than the Sonolith i-sys. The performance of the Sonolith i-sys deteriorates at 6000 shocks, before the specified lifetime of 20,000 shocks.

Introduction

THE INTRODUCTION OF EXTRACORPOREAL shock wave lithotripsy (SWL) in the early 1980s transformed the treatment of urinary lithiasis.¹ Over the last three decades, SWL has been widely adopted as the preferred treatment for urinary tract stones <20 mm in size. During this time, a number of technologies have emerged as viable methods for shock wave generation. Early electrohydraulic lithotripters, such as the Dornier HM3, demonstrated effectiveness, but were superseded by second- and third-generation electromagnetic, piezoelectric, and electroconductive lithotripters, which removed the need for spark plug replacement.^{2,3} However, studies directly comparing the available technologies are rare, display contradictory results, and often employ an equipment that is no longer in the market.⁴

Sofras and colleagues⁵ compared the Dornier HM3 (electrohydraulic) and EDAP LT01 (piezoelectric) lithotripters in 1000 patients with renal stones up to 3 cm in diameter by assessing stone-free rate (SFR) at 3 months. No difference in SFR was observed for stones <10 mm (87.5% vs 90.4%), while the electrohydraulic lithotripter was superior for stones >30 mm in size (77.2% vs 42.5%). In a randomized study of 694 patients comparing electrohydraulic (Dornier MFL 5000) and electromagnetic (Dornier Lithotripter S) lithotripters, Sheir and colleagues⁶ saw no difference in success rate for ureteral calculi and for all stones >10 mm ($p>0.05$), but a higher success rate for renal stones ≤ 10 mm with the electromagnetic device. Conversely, however, Ng and colleagues⁷ reported superior performance of an electrohydraulic lithotripter (Dornier MPL 9000) in comparison to both piezoelectric (Wolf Piezolith 2300) and electromagnetic

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(Dornier Compact Delta) lithotripters in a retrospective study of 3123 patients at a single center.

Comparison of such studies is difficult given inherent differences in operator experience, patient group characteristics, and treatment regimes within each center. Teichman and colleagues⁸ sought to address these issues in an *in vitro* setting using seven electrohydraulic and electromagnetic lithotripters to fragment human urinary calculi. Outcomes were determined by measuring the percentage of fragments <2 mm and were superior with the Dornier HM3 (electrohydraulic), Storz Modulith SLX (electromagnetic), and Siemens Lithostar C (electromagnetic) lithotripters. The use of human urinary stones demonstrated clinical relevance, but added variability to the assessment of each device and limited group sizes for comparison.

In this study, three current lithotripters are investigated, each relying on a different energy source, using standardized *in vitro* targets to provide repeatable results. Three different energy sources (electromagnetic, piezoelectric, and electroconductive) are compared to give an accurate representation of the performance of the range of lithotripters currently available.

Materials and Methods

An *in vitro* test configuration was designed to minimize the variables present during the clinical use of SWL machines. Each data set was gathered by a single operator (SRF) using the Sonolith i-sys (EDAP TMS, Vaulx-en-Velin, France), Modulith SLX F2 (Storz Medical AG, Tägerwil, Switzerland), and Piezolith 3000 (Richard Wolf GmbH, Knittlingen, Germany) lithotripters based at three clinical centers in the United Kingdom (Table 1).

Experiments were conducted within a Perspex tank filled with filtered degassed water and coupling was achieved through a low-density polyethylene window. Separate tanks were designed for each lithotripter to accommodate the varying geometries of each device as indicated in Figure 1. Figure 2 shows a photograph of the tank used with the Piezolith 3000.

Stone variability was minimized by employing homogeneous, artificial Ultracal-30 gypsum stones (U.S. Gypsum, Chicago, IL),^{9–12} the benefits and limitations of which are described in the discussion. Each stone cylinder (mean length 7.1 ± 0.2 mm, mean diameter 6.5 ± 0.07 mm, mean mass 299 ± 16 mg) was hydrated in filtered, deionized, and degassed water for at least 96 hours before shock wave exposure as advised by McAteer and colleagues¹¹ Stones were placed in 4 mL of filtered, deionized, and degassed water within a finger cot tied using 4.0 Vicryl sutures and suspended in the test configuration by a rigid gantry. Each finger cot was held in place protruding from the end of a plastic tube to reduce

movement during experiments. The stones lay outside of the tubing and thus the acoustic field was not disturbed by the tubing itself. Finger cots were not lubricated and did not contain talc.

Each stone was targeted using the predominant imaging modality used at the center—either ultrasonography or fluoroscopy (Table 1). Each stone was aligned in two imaging planes to achieve accurate focal positioning. Stones were then exposed to a treatment regime of 250, 500, or 1000 shock waves at a pulse repetition frequency of 2 Hz using the typical focal size and power settings in clinical use at each center (Table 1). The values for focal pressure and dimensions of the focal zones are those that are specified by each manufacturer in their supporting literature.

After lithotripsy was complete, the finger cot was removed from the tank, opened, and fragments were collected and dried within an absorbent paper envelope for a minimum of 7 days. Subsequently, fragments were passed through a custom-made 2-mm wire mesh and the residual mass measured. This 2-mm threshold represents a size below which fragments may be freely passed without significant discomfort.^{8,11,13,14} For each lithotripter and treatment regime (250, 500, or 1000 shock waves) a minimum of eight stones were treated. In the case of the Sonolith i-sys lithotripter, it became clear that performance varied significantly throughout the life of the generator electrode and so a lifetime study was conducted.

Data were analyzed using Matlab (Mathworks, Natick, MA) and mean values were compared using ANOVA and the Tukey–Kramer HSD test. Differences were considered significant for *p*-values <0.05 and data are displayed as mean $\pm$ standard deviation unless otherwise stated.

Results

The performance of each lithotripter is expressed in terms of the mass reduction when compared to a sample of eight untreated, hydrated, and dried stones with mean mass 299 ± 16 mg. Figure 3 shows the mass reduction as a function of number of shock waves. It can be seen that for all lithotripters, the mass reduction of the synthetic stones increased with shock wave number.

The results of Tukey–Kramer HSD tests are displayed in Tables 2 and 3. For 250 shock waves, the Sonolith i-sys produced no significant mass reduction (-4.7 ± 22.0 mg). However, the Modulith SLX F2 and Piezolith 3000 significantly reduced stone mass (62.6 ± 23.7 and 82.0 ± 33.6 mg, respectively), but there was no statistically significant difference between the two lithotripters (*p* = 0.34). At 500 shock waves, the Piezolith 3000 resulted in a significantly higher mean mass reduction compared to the Sonolith i-sys (mean difference of 152.3 mg, 95% confidence interval [CI] 106.7, 197.8 mg) and Modulith SLX F2 (mean difference of 111.1 mg,

TABLE 1. SHOCK WAVE LITHOTRIPSY MACHINES AND PARAMETERS, INCLUDING SETTINGS ON EACH LITHOTRIPTER ALONG WITH PEAK PRESSURE AND FOCAL SIZE AS REPORTED BY THE MANUFACTURERS

Model	Energy source	Imaging modality	Energy level (%)	Pulse repetition frequency (Hz)	Peak focal pressure (MPa)	Focal zone width $\times$ length (mm)
Sonolith i-sys	Electroconductive	Fluoroscopy	100	2	129	6×22
Modulith SLX F2	Electromagnetic	Fluoroscopy	6	2	60	9×50
Piezolith 3000	Piezoelectric	Ultrasonography	20	2	120	2.3×37

FIG. 1. Schematic of the experimental setup for (a) the Modulith SLX F2, (b) the Piezolith 3000, and (c) the Sonolith i-sys. Experiments were conducted within custom-made Perspex tanks filled with filtered and degassed water. Coupling was achieved through a polyethylene window angled to accommodate the geometry of each lithotripter. Stones were targeted using the predominant imaging modality at each center (summarized in Table 1).

95% CI 65.6, 156.7 mg). For 1000 shock waves, both the Modulith SLX F2 and Piezolith 3000 significantly outperformed the Sonolith i-sys. There was no significant difference between the Modulith SLX F2 and Piezolith 3000.

There was a notable deterioration in performance of the Sonolith i-sys, which correlated with the age of the generator electrode before it reached a nominal lifetime of 20,000 shock waves. To investigate the ageing of the Sonolith i-sys generator electrode further, at total of 59 synthetic stones were exposed to 1000 shock waves throughout the life cycle of four separate generator electrodes (Fig. 4). The resultant

plot demonstrates a use-related decrease in performance of the Sonolith i-sys, with a threshold age of around 6000 shocks at which point the lithotripter failed to produce a statistically significant mass reduction.

Data from these studies were separated into those above or below the 6000-shock age threshold. Figure 5 compares the fragmentation efficiency for 1000 shock waves above and below this threshold. There was no statistically significant difference in performance of the Modulith SLX and Piezolith

FIG. 2. Photograph of the experimental setup for the Piezolith 3000 lithotripter (Fig. 1b). Stones were placed in 4 mL of filtered and degassed water within a finger cot tied using 4.0 Vicryl sutures and suspended within a plastic tube in the test configuration by a rigid gantry.

FIG. 3. Mass reduction of synthetic stones for 250, 500, and 1000 shock treatments. Error bars indicate 95% confidence intervals. For all lithotripters, the mass reduction increased with increasing shock numbers. At 250 shocks, the Sonolith i-sys produced no significant mass reduction. Five hundred shock treatments with the Piezolith 3000 resulted in significantly greater mass reduction, while for 1000 shock treatments, the Modulith SLX F2 and Piezolith 3000 significantly outperformed the Sonolith i-sys.

TABLE 2. TUKEY–KRAMER HSD COMPARISON OF MEAN MASS REDUCTIONS FOR 250 AND 500 SHOCK WAVES

Comparison	250 shock waves			500 shock waves		
	Estimated mass difference (mg)	95% CI (mg)	p	Estimated mass difference (mg)	95% CI (mg)	p
SI vs SLX	−67.3	−101.2, −33.3	1.73×10^{-4}	−41.2	−85.4, −3.0	0.071
SI vs P3000	−86.6	−120.6, −52.6	6.57×10^{-6}	−152.3	−197.8, −106.7	5.83×10^{-8}
SLX vs P3000	−19.4	−53.3, 14.6	0.34	−111.1	−156.7, −65.6	9.08×10^{-6}

The table displays results for comparisons between the Sonolith i-sys (SI), Modulith SLX F2 (SLX), and Piezolith 3000 (P3000). CI=confidence interval.

3000 for 1000 shock waves. For those treatments above the 6000-shock age threshold, the Sonolith i-sys produced no significant mass reduction, while below this threshold there was a mean mass reduction of 105.6 ± 57.9 mg. Even below this threshold, the Sonolith i-sys was not as effective as either of the other two lithotripters.

Discussion

SWL aims to achieve stone comminution, producing small enough fragments to be passed through the urinary tract without significant discomfort. The data presented herein show that lithotripters vary in their ability to fragment artificial stones into pieces small enough to pass. This is a key given that, in a clinical setting, the reduction of fragment size not only reduces the time to pass a stone but also minimizes risk of future symptomatic episodes.^{14,15}

The data showed that, for each of the lithotripters tested, the mass reduction of synthetic stones increased with the number of shocks delivered in a treatment. The Sonolith i-sys (electroconductive) failed to produce a statistically significant mass reduction at 250 shock waves, was outperformed by the Piezolith 3000 (piezoelectric) at 500 shock waves, and produced a significantly smaller mass reduction than both the Piezolith 3000 and Modulith SLX F2 (electromagnetic) at 1000 shock waves. This difference in performance may, in part, be accounted for by degradation of the Sonolith i-sys generator electrode. There was a statistically significant difference in mean mass reduction for 1000 shock treatments beyond a threshold generator electrode age of 6000 shocks. Current manufacturer guidelines suggest electrode replacement after 20,000 shocks; however, the data here suggest that improved performance may be achieved with more regular electrode replacement. Importantly, even when comparisons were restricted to tests below a 6000-shock generator elec-

trode age threshold, the Sonolith i-sys produced a significantly smaller mass reduction than the Modulith SLX F2 and Piezolith 3000 in 1000 shock treatments.

The data indicate that the mean stone mass reduction for treatments with the Modulith SLX F2 and Piezolith 3000 is comparable, particularly at the 1000 shock level. Given that the majority of clinical treatments involve a total of around 3000 to 4000 shocks, there appears to be little difference that can be extrapolated to clinical practice. Of note, the Piezolith 3000 produced a near linear increase in mass reduction with the number of shocks delivered. Conversely, the Modulith SLX F2 showed a marked increase in performance between 500 and 1000 shock treatments. We speculate that this difference is indicative of the mechanism by which each lithotripter affects stone comminution. For example, the Piezolith 3000 may gradually erode the stone, producing increasing numbers of passable fragments with the delivery of further shock waves, while the Modulith SLX F2 may create internal fractures in the stone that result in dramatic fragmentation above a threshold number of shocks delivered—between 500 and 1000 shocks in this case. Computer simulations suggest that lithotripters with a larger focal volume (in this case the Modulith SLX F2) are more likely to generate high internal stresses that result in such fractures.¹⁶

Our study does exhibit limitations. The inherent variability in structure, composition, mineral properties, and fragility of natural kidney stones clearly influences their response to treatment with SWL.⁹ This heterogeneity introduces an additional source of variability, further complicating the comparison of lithotripter performance.

In an attempt to limit variability and provide a more accurate means of directly comparing lithotripters, synthetic renal stones were used. Despite beneficial homogeneity, these targets are less clinically relevant than human urinary

TABLE 3. TUKEY–KRAMER HSD COMPARISON OF MEAN MASS REDUCTIONS FOR 1000 SHOCK WAVES

Comparison	Estimated mass difference (mg)	95% CI (mg)	p
SI >6000 vs SI <6000	−93.9	−133.0, −54.9	1.15×10^{-7}
SI >6000 vs SLX	−201.9	−251.8, −152.0	3.77×10^{-9}
SI >6000 vs P3000	−245.8	−298.2, −193.4	3.77×10^{-9}
SI <6000 vs SLX	−108.0	−164.0, −52.0	1.73×10^{-5}
SI <6000 vs P3000	−151.9	−210.1, −93.6	1.57×10^{-8}
SLX vs P3000	−43.9	−109.9, 22.1	0.31

Data from the Sonolith i-sys (SI) have been separated to those treatments where the generator electrode age falls above or below a threshold of 6000 shock waves. A statistically significant difference in performance exists either side of this threshold. Comparisons are with the Modulith SLX F2 (SLX) and Piezolith 3000 (P3000).

FIG. 4. Mass reduction of synthetic stones for 1000 shock treatments with increasing age of four different Sonolith i-sys generator electrodes. There is a clear age-related decrease in performance of the Sonolith i-sys, with a threshold of around 6000 shocks beyond which the lithotripter fails to produce a statistically significant mass reduction.

calculi as it has not been shown that they fragment by the same process. Furthermore, the test configuration positioned stones within the focal zone for the duration of the treatment. In clinical practice, movement of the target, particularly with respiration, leads to stones occupying the focal zone for a smaller proportion of the treatment.¹⁷ Thus, mass reductions observed in this *in vitro* setting may be of greater magnitude than seen clinically.

FIG. 5. Mass reduction of synthetic stones for 1000 shock waves using the Sonolith i-sys, Modulith SLX F2, and Piezolith 3000. Error bars indicate 95% confidence intervals. A statistically significant difference in fragmentation efficiency was observed between the Sonolith i-sys and both the Modulith SLX F2 and Piezolith 3000 using Tukey–Kramer HSD multiple comparison tests with a threshold of $p < 0.05$. Data for the Sonolith i-sys are separated into those treatments above and below a 6000-shock generator electrode age threshold. There was a statistically significant increased mass reduction for treatment with the Sonolith i-sys below the 6000-shock threshold.

This study has only assessed the comparative performance of three clinical lithotripters. While we believe this gives a useful cross section of the range of technologies available, a more extensive study of available lithotripters would be beneficial. Moreover, we have only addressed the ability of a lithotripter to fragment synthetic calculi and drawn no inferences regarding imaging and targeting capabilities of each lithotripter. However, at each center, targeting was achieved in the same manner used in clinical practice and we therefore believe that the test configuration accurately simulates the clinical setting.

Conclusion

Our *in vitro* test configuration provides an unbiased means of evaluating the performance of a range of lithotripters. The results give an assessment of fragmentation efficiencies of the current generation of clinical lithotripters, allowing direct comparison of three alternative shock wave generation technologies. The data suggest that there is considerable variability in the ability of lithotripters to fragment synthetic urinary calculi. In this study, the Modulith SLX F2 and Piezolith 3000 exhibited superior fragmentation characteristics when compared to the Sonolith i-sys. Moreover, there appears to be a significant reduction in performance of the Sonolith i-sys above a threshold generator electrode age of 6000 shock waves.

Acknowledgments

We gratefully acknowledge Mandy Spencer, Cathy O'Neill, Mark Wynn, and Jane Collier for their assistance in configuring the lithotripters and imaging systems at each clinical center. We also thank Professor James A. McAteer and Dr. Guangyan Li, Indiana University School of Medicine, for furnishing the U30 stones employed in this study. R.O.C. acknowledges the support of the National Institutes of Health through grant DK43881. B.W.T. is supported by funding from the NIHR Oxford Biomedical Research Center program and the Bernard Fund.

Author Disclosure Statement

No competing financial interests exist.

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Abbreviation Used

ANOVA = analysis of variance
 CI = confidence interval
 SFR = stone-free rate
 SWL = shock wave lithotripsy

DOI: 10.1089/end.2016.0158

Editorial Comment for Faragher *et al.*

Khaled Z. Sheir, MD

THIS IS AN EXCELLENT well-designed experimental study with a thorough analysis of the data, nice presentation of the results, and good interpretation of the findings.

The use of artificial stones is very important in such an experimental study as it limits variability and provides a more accurate means of directly comparing lithotripters. In contrast to the opinion of the authors that these targets are less clinically relevant than human urinary calculi, I think they give a better and more accurate assessment of the lithotripters' efficiency, which in the clinical situation will be less efficacious because of patient's and stones' characteristics. I mean that, in general, the power of the lithotripters will be lower in a clinical situation than in an *in vitro* experiment, so the findings of experimental

studies could be applied to a clinical situation after correction according to variations in patient's and stones' characteristics.

Application of lithotripter parameters in clinical use (as regard the power and frequency) in this study is of utmost importance to be comparable to a clinical situation. Many other experimental studies in the literature used high parameters that could not be applied clinically.

The findings of this study give important messages for both the clinicians and manufacturers.

For the clinicians:

- (1) The piezoelectric and electromagnetic lithotripters are comparable and both of them are far better than