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Break Wave Lithotripsy for Urolithiasis: Results of the First-in-Human International Multi-Institutional Clinical Trial

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Study Need and Importance: Urolithiasis is a global health care burden with increasing incidence rates annually. Many patients who experience a stone episode visit the emergency department, with some visiting more than once while awaiting treatment. Shock wave lithotripsy (SWL) is a standard treatment for stones < 10 mm according to international guidelines. A modality that can treat urolithiasis without anesthesia or sedation in a clinic setting has the potential to reduce patient suffering and health care costs. Break Wave lithotripsy (BWL) is a new technology utilizing focused ultrasound to fragment stones and may address this unmet need.

What We Found: In this first-in-human trial, we evaluated the efficacy and safety of BWL in treating stones indicated for SWL in 44 patients. Mean ± SD stone size was 6.1 ± 1.5 mm. The majority were performed without anesthesia or sedation in a clinical office setting. Stone fragmentation occurred in 88% of patients, with 70% and 51% having residual fragments ≤ 4 mm and ≤ 2 mm, respectively. Forty-nine percent were completely stone free, improving to 58% when using the optimal therapy dose (Figure). BWL was safe and well tolerated, with all complications being Clavien-Dindo grade 1. Eighty-six percent of patients underwent BWL with no medications (22/44, 50%) or with mild analgesia (16/44, 36%). Repeat treatment following BWL was 7% at 90 days post procedure.

Limitations: Patients included in this trial had relatively smaller stones (albeit indicated for SWL), BMI, and skin-to-stone distances. As BWL is ultrasound based, certain stone locations were not treatable (due to air, bone, etc).

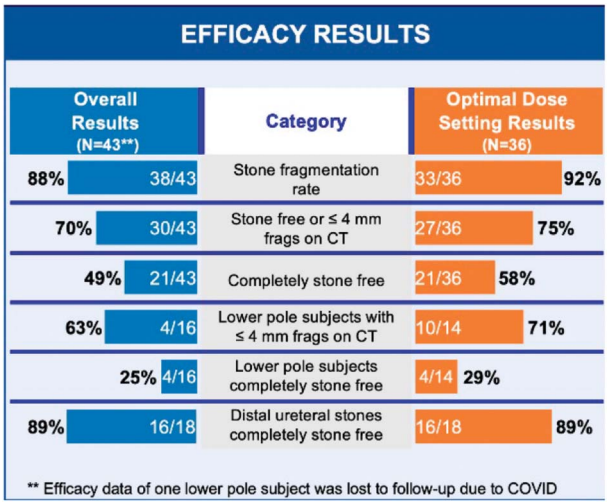

Figure. Procedural efficacy results following Break Wave lithotripsy treatment of renal and ureteral stones. Optimal dose settings = maximum 8 MPa with a broadened focus beam.

Interpretation for Patient Care: This study represents a treatment for urolithiasis that can be performed in a clinic setting without anesthesia or sedation, with comparable outcomes to SWL. These results indicate that BWL can play a role in treating patients outside the normal lithotripsy suite or operating room. The BWL pivotal trial is currently underway.

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Break Wave Lithotripsy for Urolithiasis: Results of the First-in-Human International Multi-Institutional Clinical Trial

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Purpose: This study reports on a prospective, multicenter, single-arm, clinical trial utilizing the SonoMotion (San Mateo, California) Break Wave lithotripsy (BWL) device to fragment urinary stones.

Materials and Methods: Patients with a urinary stone underwent a single treatment of 30 minutes and peak negative pressure of 4.5 to 8 MPa. Subjects were contacted and outcomes assessed at 7, 14, and 35 days after treatment, with clinical

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Ethics Statement: This study received Institutional Review Board approval (University of British Columbia IRB No. H18-02988).

Author Contributions:

Conception and design: Chew, Chi, Buckley, Wong, Forbes, Schuler, Sorensen, Harper.
Data analysis and interpretation: Sur, Chi, Buckley, Paterson, Wong, Forbes, Hall, Bechis, Bochinski, Schuler, Sorensen.
Data acquisition: Chi, Buckley, Wong, Forbes, Hall, Kessler, Woo, Wang, Bayne, Bochinski, Samji, Sorensen, De, Harper.
Drafting the manuscript: Chew, Buckley, Wong, Schuler, Wollin, De.
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Statistical analysis: Chew, Wong, Kessler.
Supervision: Chew, Chi, Buckley, Paterson, Forbes, Hall, Bechis, Woo, Wang, Bayne, Bochinski, Schuler, Samji, Sorensen, De, Harper.

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follow-up and CT imaging 70 ± 14 days postprocedure. The primary objectives were to assess the safety (hematomas, complications, etc) and effectiveness of BWL (any fragmentation, residual fragments ≤4 mm or ≤2 mm, and completely stone-free rate) as assessed via noncontrast CT–kidneys, ureters, and bladder.

Results: Forty-four patients with a ureteral (43%) or renal (57%) stone were treated across 5 centers. Stone fragmentation occurred in 88% of cases; 70% had fragments ≤ 4 and 51% ≤ 2 mm, while 49% were completely stone free on CT; no serious adverse events were reported. Eighty-six percent of patients received either no analgesic medication at all (50%) or minor analgesia (36%). After determining optimal therapy settings, 36 patients were treated and the effectiveness improved exhibiting fragmentation in 92% (33/36), residual fragments ≤ 4 mm in 75% and 58% with fragments ≤ 2 mm with 58% completely stone free. Effectiveness was less in subjects with lower pole stones with 81% fragmentation, 71% having fragments ≤ 4 mm, 29% with fragments ≤ 2 mm, and 29% completely stone free; of distal ureteral stone patients, 89% were completely stone free.

Conclusions: BWL offered safe and effective noninvasive stone therapy requiring little to no anesthesia and was carried out successfully in nonoperative environments.

Trial Registration: ClinicalTrials.gov identifier: NCT03811171

Key Words: urolithiasis, lithotripsy, calculi, ultrasound

Urolithiasis is a significant health care burden with annual prevalence and incidence rates increasing globally.[1] In this study, we report the safety and efficacy from the first-in-human clinical trial of the Break Wave lithotripsy (BWL) system (SonoMotion, San Mateo, California), a standalone mobile ultrasound unit using low-amplitude focused ultrasound waves to fragment kidney stones. This new technology addresses an unmet need for a system to fragment stones without anesthesia or sedation with minimal pain and complications.

MATERIALS AND METHODS

This prospective, nonrandomized, multi-institutional clinical trial (clinicaltrials.gov, NCT03811171) was conducted at 5 North American centers: University of British Columbia (Vancouver, British Columbia, Canada), University of Washington (Seattle, Washington), University of California San Diego (California), University of California San Francisco (California), and University of Alberta (Edmonton, Alberta, Canada). Approval for research ethics was obtained from each institution.

Patients with a single renal or ureteral stone who met the AUA guidelines for shock wave lithotripsy (SWL) were recruited. Key study inclusion and exclusion criteria are listed in Table 1. Pre-BWL CT–kidneys, ureters, and bladder (CT-KUB) was performed within 90 days prior to the BWL procedure to confirm target stone location, density, and dimensions. Basic metabolic panel, urinalysis with reflex urine culture, pregnancy test, and continuous intraprocedural cardiac monitoring were performed according to standard SWL treatment protocols. Patients were treated in either a standard SWL suite, operating room, emergency department (ED), or clinical office setting. The primary objectives were to assess the safety and effectiveness of BWL.

All patients with distal ureteral stones had a period of observation, remained symptomatic or failed conservative management, and had elected to pursue traditional treatment (ureteroscopy or SWL) when approached and offered the research procedure as an alternative, with the exception of 4 patients who were offered BWL in the ED for their symptomatic acute obstructing ureteral stone. All study patients with renal stones had the option of undergoing stone treatment with ureteroscopy or SWL but chose to receive BWL instead.

Immediately prior to BWL, a screening ultrasound with the BWL system's therapy/imaging probe was performed to confirm the visualization and ability to target the stone (Figure 1, A-E) within the acoustic window. One of 3 treatment probes was used based on skin-to-stone

Table 1. *Key Inclusion/Exclusion Criteria*

Inclusion criteria	Exclusion criteria
>18 y of age	Acute untreated urinary tract infection or urosepsis or untreated urinary tract infection
Kidney stone visible on CT within the upper urinary tract	Uncorrected bleeding disorders or coagulopathies (including patients receiving anticoagulants and are unable to interrupt the medication)
Stone would meet the criteria for SWL treatment as per the AUA 2016 guidelines	Uncorrected obstruction distal to the stone
Stone must be visible with ultrasound and the Break Wave probe	Target stone or patient anatomy preventing adequate positioning or delivery of the Break Wave therapy
	Calcified abdominal aortic aneurysms or calcified renal artery aneurysms
	Pregnancy
	Solitary kidney
	Comorbidity risks which, at the discretion of the clinician, would make the patient a poor candidate for the Break Wave procedure (eg, anatomical abnormalities that may not be conducive to adequate stone fragment passage)

Abbreviations: SWL, shock wave lithotripsy.

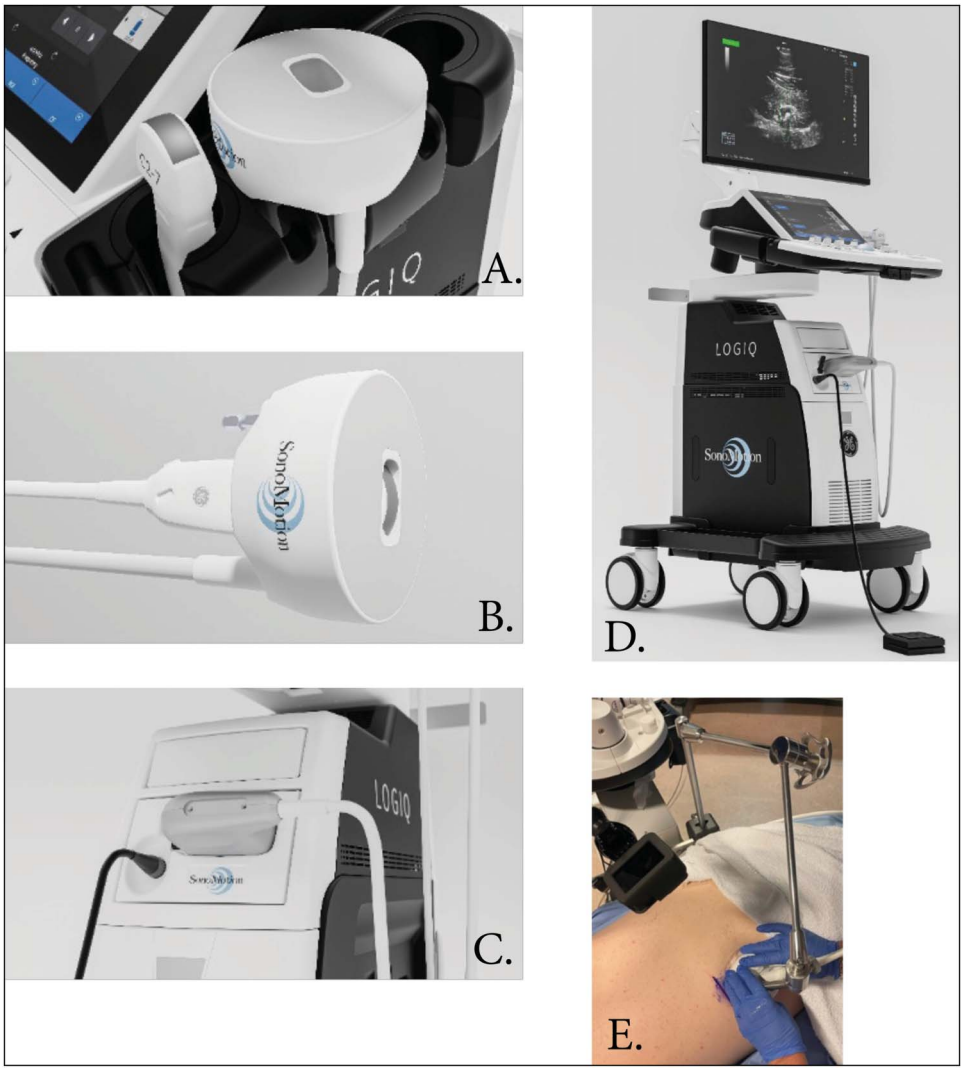

Figure 1. Break Wave device. A, The imaging probe (left) and therapy probe (right). B, The imaging probe clicks into the center of therapy probe for treatment. C, The therapy probe and foot pedal are plugged into the therapy generator. D, The entire device required for treatment. E, An optional positioning arm may be attached to the clinic bed and used to assist in positioning.

depth. These 3 options allow treatment of stones across a broad range of depth (4-14 cm) and the pressure at the focus is optimized to account for attenuation of the acoustic energy through the corresponding tissue depth. BWL was delivered under real-time sonographic guidance by a physician or sonographer trained on the device.

Procedures were conducted under general anesthesia, conscious sedation, minor analgesia, or no medication. One of the secondary objectives of the study was to determine the degree of discomfort associated with the procedure. Initial subjects had anesthesia and/or sedation according to SWL protocols at the study site. In a subsequent phase, subjects received monitored anesthesia care to allow minimal anesthesia and escalation as necessary. After determining that no anesthesia or sedation was necessary, procedures were transitioned to an outpatient setting with no anesthesia or sedation. Only analgesia was given preoperatively to some patients and subjects therefore no longer had to be NPO (nil per mouth) prior to the procedure.

All target stones received a total of 30 minutes of delivered therapy under real-time ultrasonography targeting. All treatments were directed by the treating physician, either operating the treatment device directly or supervising a radiologist or sonographer trained in BWL. During treatment, the BWL therapy probe was either held manually by the operator or by an adjustable surgical arm fixed to the bed rail. Initial regulatory approved (Food and Drug Administration/Health Canada) BWL therapy dose levels were between 4.5 to 7 MPa of acoustic negative pressure with a narrow focus beam. Subsequent regulatory approved amendments allowed for the optimized therapy dose of a maximum 8 MPa with a broadened focus beam. These optimal dose settings were previously determined to be safe in porcine and bench testing and the higher pressure and wider focus allowed for treatment of larger stones. BWL treatment was monitored in real time, allowing the operator to temporarily pause BWL if sustained (>5 seconds) cavitation (echogenicity) was visualized in tissue (cavitation bubbles may shield the target stone from effective energy delivery and potentially injure tissue). The skin at the location of therapy probe placement was examined for injury and

Table 2. *Patient Demographics and Results*

Characteristics	Values N = 44
Mean age ± SD, y	50 ± 14
Gender, No. (%)	
Male	32 (73)
Female	12 (27)
BMI ± SD, kg/m^2	28 ± 5
Stone size (longest diameter)	
Mean ± SD, mm	6.1 ± 1.5
Median (IQR)	6.0 (5.0-7.0)
Stone density	
Mean ± SD, HU	847 ± 238
Range	450-1346
Skin-to-stone distance by CT	
Mean ± SD, mm	10.4 ± 1.7
Median (IQR)	10.2 (9.2-11.5)
Laterality, No. (%)	
Right	20 (45)
Left	24 (55)

Abbreviations: IQR, interquartile range.

photographed immediately prior to, after BWL, and at hospital discharge. Postoperative medications were prescribed at each physician's discretion.

Patient-reported pain scores (0 [No Pain]-10 [Maximum Pain]) were recorded prior to, throughout BWL, and at discharge. Descriptors of discomfort or pain by the patient were documented, if reported. Adverse events, medications, ED visits, and stone passage were recorded during patient follow-up 7, 14, and 35 days post-BWL, along with patient chart reviews up to 90 days post-BWL.

Adverse events were captured and included all patient-reported issues over the follow-up period. Serious adverse events were predefined and included cardiac arrhythmias, symptomatic perinephric hematoma, renal injury, urinary tract infection, urinary obstruction requiring admission or intervention, while other adverse events included transient hematuria, renal colic, fever, nausea/vomiting, and pain, redness, or bruising at the site of treatment.

Effectiveness was graded as any stone fragmentation, residual fragments (≤4 and ≤2 mm), and stone free as assessed via noncontrast CT (CT-KUB) obtained at 10 ± 2 weeks postprocedure. The established Food and Drug Administration benchmark for success after lithotripsy is residual fragments ≤ 4 mm for approval of shock wave lithotripters; the authors recognize that these are not "clinically insignificant residual fragments," and thus this study also reports outcomes of subjects as entirely stone free and with smaller residual fragments (≤4 and ≤2 mm) consistent with how current literature is reported. All posttreatment imaging was reviewed by a radiologist independent from the study according to standard-of-care reporting procedures. All study data and adverse events reported were reviewed and verified by a data safety monitoring board.

Descriptive statistics were used to tabulate demographic and clinical variables, which were summarized by count and percentage. Mean and standard deviations were reported when data were normally distributed and median with IQR were reported for data that were skewed. Subgroup analyses were performed to assess adverse events and outcomes in subjects with lower pole stones (expected lower success rate), ureteral stones (expected higher success rate), small stones ≤ 4 mm (expected higher success) and those treated with optimal dose settings after regulatory approval amendment (expected higher success rate).

RESULTS

Patient Demographics, Stone Characteristics, and Procedural Time

The study accrued 44 patients who met criteria for SWL according to the AUA SWL guidelines between August 2019 and February 2022. A total of 75 patients were consented, and 44 patients completed all study procedures (Table 2). Thirty-one consented patients failed to meet study eligibility criteria and did not receive BWL due to: embedded stone found upon pre-BWL CT-KUB (n = 12), poor acoustic window during pre-BWL ultrasound screening (thus precluding delivery of BWL; n = 12), stone passage prior to procedure (n = 6), stone movement to location unamenable by ultrasound (n = 2), consent withdrawal (n = 1), adjacent stones (n = 1; exclusion criteria). No follow-up imaging was obtained in 1 patient due to COVID-19 restrictions.

Forty-four (n = 44) patients were included in this study. Table 2 lists the patient and stone characteristics. Mean maximal diameter for ureteral stones treated was 5.7 ± 1.3 mm and 6.4 ± 1.5 mm for renal stones. Overall, 88% (39/44) of stones were larger than 4 mm, 4 stones were 4 mm, and 1 stone was 3 mm. The median time between patient presentation to BWL treatment for distal ureteral stones was 12.0 days (IQR: 0.3-30.0). Four subjects were treated acutely in the ED during their acute presentation. All other ureteral stone subjects had a period of observation, in most cases with medical therapy, and had failed to pass their ureteral stone before undergoing the BWL procedure.

The overall mean procedural time was 41 ± 9 minutes in the operating room setting, and 35 ± 3 minutes in the clinic setting. Mean procedural time for renal stones was 44 ± 10 minutes, and 38 ± 8 minutes for ureteral stones. Time accrued in addition to the 30 minutes of therapy was due to procedural pauses (patient repositioning, changes to therapy dose settings, visualization changes, etc).

Efficacy: Overall and Optimal Dose Settings

Fragmentation and success rates according to location are noted in Table 3. There was evidence of fragmentation in 88% (38/43) of stones on CT-KUB. Overall, 70% of patients had residual fragments ≤ 4 mm (30/43), 51% had residual fragments ≤ 2 mm (22/43), and 49% (21/43) were completely stone free.

As expected, subgroup analyses (Table 3) revealed efficacy and fragment clearance was lower in subjects with lower pole stones, while success was higher for

Table 3. *Results*

Location	No. subjects	Fragmentation evidence, %	≤4 mm, %	≤2 mm, %	Stone free, %
Upper pole	1	0	0	0	0
Mid pole	6	83	67	33	17
Lower pole	17	81	63	25	25
Renal pelvis	1	100	100	100	100
Ureteropelvic junction	1	100	0	0	0
Distal ureter	1	100	100	100	100
Ureterovesical junction	17	100	88	88	88
Total	43	88	70	51	49

subjects with distal ureteral stones (89% stone free), small stones ≤ 4 mm (3 of 5 subjects were stone free), and after optimal dose settings (max 8 MPa with broad focus beam) were utilized. Specifically, the remaining 36 patients were treated using these settings and had higher rates of fragmentation (33/36, 92%), residual fragments ≤ 4 mm (27/36, 75%), and completely stone free (21/36, 58%; Figure 2). With these optimized settings, lower pole stone-free rate also improved (4/14, 29% compared to 4/16, 25%).

Anesthesia and Sedation Requirements

The procedure was tolerated well and over the study period we determined that most patients could be treated in a clinical setting with no anesthesia (Figure 3). During the initial phase of the study, patients were planned to undergo general anesthesia (4/44) or conscious sedation (2/44), and 1 subject transitioned to general anesthesia due to anxiety and procedural discomfort early in the study. However, through the remainder of the study patients were changed to monitored anesthesia care and then transitioned to an outpatient clinical setting: the remaining 86% of subjects underwent the study procedure with no medications (22/44, 50%) or mild analgesia (16/44, 36%) with ketorolac 15 to 30 mg IV prior to treatment. Subjects in the outpatient clinical setting no longer had to be NPO prior to procedure and also could be discharged on their own without requiring responsible adult accompaniment.

Safety Profile and Retreatment

Table 4 lists the adverse events reported and categorized as per the Clavien-Dindo classification. All complications were grade 1. Specifically, there was no urinary tract infection, urosepsis, renal hematoma, or renal injury observed. Postprocedural complications experienced by patients were similar to SWL in character and frequency. No hospitalizations occurred post-BWL, and 3 patients visited the ED without requirement for adjunct procedures.

Postoperative medications were prescribed according to physician discretion. Most patients received nonsteroidal anti-inflammatories and alpha-blockers as per standard SWL protocols. No patients were prescribed opioids.

Within the entire study cohort, retreatment rate within the 90-day follow-up (any stone intervention) was 7% after the target stone was not successfully treated with BWL. The decision for retreatment was determined after shared decision-making between the physician and patient. There were 4 retreatment procedures in 3 patients with patients undergoing SWL (n = 1), ureteroscopy (n = 1), and 1 patient who had a failed SWL underwent a subsequent successful ureteroscopy. Retreatment with BWL was not permitted as per study protocol.

DISCUSSION

To date, SWL is the only noninvasive extracorporeal modality available for the treatment of urolithiasis.[2] Various barriers to access are associated with SWL, as this modality requires expensive equipment to be mobilized to either an operating room or placed permanently in a lithotripsy suite.[3] The cost to purchase and maintain an SWL system can be onerous and requires significant dedicated human capital (radiation and biomedical technologists, nursing staff, anesthesiologists, and urologists) for its operation.

In this study, the first-in-human data of the Break Wave system demonstrate a novel modality that is efficacious and safe for extracorporeal

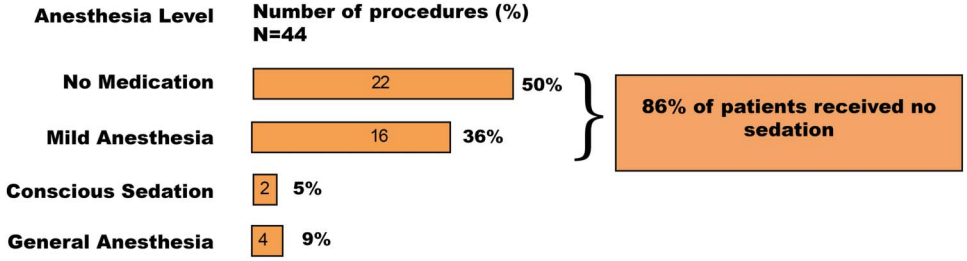

Figure 2. Efficacy success rates.

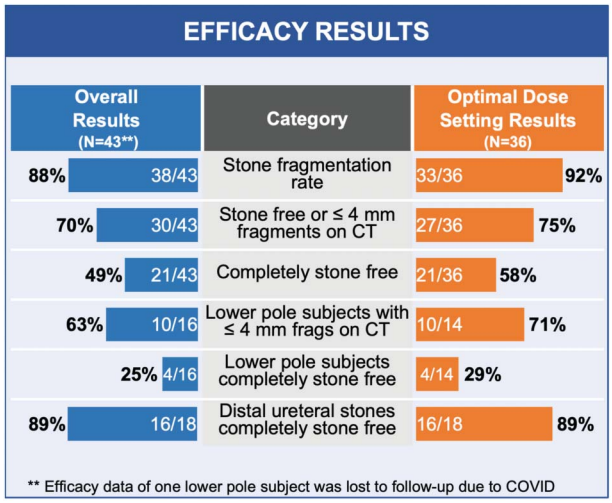

Figure 3. Anesthesia usage.

lithotripsy, without the need for anesthesia or sedation, and can be performed in the ED or office setting. Such a modality could potentially reduce resource burdens and provide more timely care.

Lower pole and distal ureteral stones can be challenging for SWL,[4,5] with SWL guidelines indicating lower stone-free rates in these regions when treated with SWL compared to ureteroscopy (URS).[2,6,7] Current AUA guidelines recommend URS as primary management of distal ureteral stones, with SWL being a secondary option. For distal ureteral stones, BWL outcomes (89% completely stone free) were comparable to URS (up to 94%).[2,6,7] In addition, no distal ureteral stone patients who received BWL required anesthesia or ureteral stenting. Most of the ureteral stones had a period of attempted stone passage, but it is conceivable that the stone-free rate achieved with BWL was augmented by stones that may have passed spontaneously if observed for longer.

Intraoperative pain experienced during SWL is cutaneous, somatic, and visceral in nature.[8] As such, a wide variety of anesthetic techniques have been employed for SWL to manage pain and patient movement.[9,10] General anesthesia is a commonly used anesthetic technique for SWL.[11] Patient respiration inhibits the effectiveness of SWL, as up to 40% of shock wave pulses are potentially mistargeted due to respiration-mediated stone motion.[12,13] This mistargeting is further exacerbated by the lack of real-time guidance available for SWL systems. There have been multiple attempts to synchronize respiratory motions in SWL machines,[14] but none have reached common usage. In our study, most patients were fully awake, with 50% receiving no medications and 36% receiving only mild analgesia. In most cases, the awake patient was helpful as they viewed the ultrasound monitor in real time and quickly learned to modulate their breathing to maximize the time the stone was in the BWL target area. Lower pain levels experienced by patients during BWL can be explained by the significantly lower acoustic peak pressures needed for stone fragmentation compared to SWL.[15-19]

Table 4. *Post–Break Wave Lithotripsy Complications (Clavien-Dindo Grade)*

Adverse event type (Clavien-Dindo grade)	Total No. adverse events (N = 44)
Grade 1, No. (%)	
Transient hematuria (self-limiting)	41 (93.2)
Pain/renal colic (treated with analgesics)	25 (56.8)
Skin redness at treatment site	4 (9.1)
Skin bruising at treatment site	1 (2.3)
Fever (self-limiting)	1 (2.3)
Nausea/vomiting	3 (6.8)
Grade 2	0
Grade 3	0
Grade 4	0
Grade 5	0

No serious adverse events or intraoperative complications associated with the Break Wave system or procedure occurred as all complications fell under Clavien-Dindo grade 1. No hematomas occurred in any patients treated with BWL. The significantly lower peak pressure of BWL compared to SWL may lower the risks of hemorrhagic complications and reduce tissue injuries such as subcapsular or perinephric hematomas.[20-22] Targeting with ultrasound is continually performed (compared to intermittent fluoroscopy in SWL) allowing for the immediate recognition of cavitation and immediately pausing the procedure to avoid tissue injury.

From our study, most stone patients who meet the AUA guidelines for SWL (favorable stone location, BMI, skin-to-stone distance, etc) would be suitable candidates for BWL. The greatest barrier in delivering BWL is that stones can only be treated if they can be visualized with ultrasound and not treated through bone or air. Factors that prevent ultrasound detection (and thus treatment) include air (from the lung or bowels), overlying bone (pelvis, ribs), or very deep skin-to-stone distance (>14 cm). A preoperative diagnostic ultrasound with analysis of preprocedural CT provides a high degree of confidence for the ability to deliver BWL treatment as this confirms an acceptable acoustic treatment window. The skin-to-stone distance on ultrasound was often shallower than measured on CT by 2 to 3 cm.

Despite promising initial results, this study has several limitations. Due to the small sample size of this study, extrapolation is limited. Patients included in this study had relatively smaller stone sizes (albeit within the indications for SWL), BMI, and skin-to-stone distances, and limited female (27%) subjects. In the Break Wave pivotal trial (clinicaltrials.gov, NCT05701098) already underway, a concerted effort is being made to enroll a wider range of patients to include varied race/ethnicities and gender. As BWL is an ultrasound-based technology, certain stone locations such as the proximal and midureter, and some upper pole stones, are not amenable to BWL due to inability to identify the

stone with ultrasound, or obstructing anatomical features such as bowel, lung, rib/pelvic bones, and depth. At times, ability to treat with BWL could only be ascertained upon examination with ultrasound even if preoperative CT was available—there were 12 subjects consented and then excluded when their ultrasound determined they were not suitable candidates. These areas are often treatable with SWL due to fluoroscopic targeting, suggesting that SWL and BWL may be complementary modalities. We have gained knowledge about patient anatomy and stone location to further optimize patient selection for BWL. Lastly, like any new technology or technique, a learning curve is associated with BWL, and its deployment requires basic ultrasound skills. The presence of a physician adept at ultrasound or a sonographer will help shorten this learning curve.

CONCLUSIONS

BWL is a novel, noninvasive modality for the safe and effective treatment of kidney stones. In this first-in-human study, fragmentation occurred in 88% of patients, with 70% and 51% having residual fragments ≤ 4 mm and ≤ 2 mm, respectively. Forty-nine percent were completely stone free, which improved to 58% when using the optimal therapy dose. BWL was shown to be safe and well tolerated, with the majority of procedures being performed without anesthesia or sedation in clinical office settings. New technologies on the horizon such as ultrasonic propulsion (SonoMotion) may complement stone therapies allowing for the repositioning of target stones immediately prior to treatment, or to facilitate stone passage using a single device.[23]

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EDITORIAL COMMENTS

Those who can recall the days of open surgery for stones can attest to the transformative effect shock wave lithotripsy (SWL) and ureteroscopy had on the field of urology. Yet despite these innovative feats, an unmet clinical need exists in that convenient office-based therapies have eluded us. It is in this spirit that we should recognize the significance of the work by Chew and colleagues in reporting the results of the first-in-human, international, multi-institutional clinical trial of break wave lithotripsy (BWL) for urolithiasis.[1]

One of the main advantages is the ability to perform BWL without the need for anesthesia as demonstrated in the current study, where 86% patients required minimal or no anesthesia. This is due to the low-amplitude focused ultrasound, which has a lower acoustic peak pressure than SWL, resulting in less discomfort. BWL appears to be safe and efficient with mean ± SD procedure time of 35 ± 3 minutes in the clinic. The awake patient can assist in the BWL by altering their breathing to keep the stone in the target area. BWL may reduce time to treatment and permit stone treatment in patients deemed high risk due to anesthetic concerns.

As we interpret the results of this study, it may be tempting to compare the outcomes of BWL to SWL. However, the average stone size in this trial was smaller (5.7 mm for ureteral stones, 6.4 mm renal stones) than in most SWL trials. This underscores the importance of reporting true stone-free rate (SFR) and not utilizing < 4 mm fragments as a treatment success. While that definition may have been used in the Food and Drug Administration SWL trials, several patients in this trial would have already met that criterion even before BWL treatment, emphasizing why this definition should be abandoned. The use of CT to determine SFR is responsible and should be considered the standard for kidney stone studies. One similarity between BWL and SWL is reduced efficacy for lower pole stones with a 29% SFR.

The main limitations of BWL are due to it being an ultrasound-based therapy, which precludes treatment of some ureteral stones and makes it difficult to target stones when obscured by air, overlying bone, or significant skin-to-stone distance. In the current study, 14 patients were excluded due to limitation in targeting despite having rather low BMI (mean±SD 28±5) and skin-to-stone distance 10.4 ± 1.7 mm. Therefore, it remains to be seen if similar results can be achieved in obese stone formers.

Acknowledgement of these limitations should not detract from the significance of the BWL results. An overall 58% SFR for a short procedure performed in the office is noteworthy. On the contrary, we should consider BWL an emerging technology complementary to our existing treatments. The explosion of ultrasound-based therapeutics such as ultrasonic propulsion and BWL opens the door for fresh innovative stone treatment strategies such as utilizing ultrasonic propulsion to relocate stones for BWL or to assist stone fragment passage following BWL.[2]

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Since the introduction of shock wave lithotripsy (SWL) in 1980,[1] treatment of kidney stone patients has been continuously driven by the innovation, development, and clinical application of new technologies, mostly in ureteroscopy, percutaneous nephrolithotomy, and ancillary devices. Soon, the landscape of lithotripsy will be further altered by Break Wave lithotripsy (BWL)—an ultrasound-based technology for noninvasive fragmentation of kidney stones without the need of fluoroscopy, sedation, or anesthesia in most patients.

The results of this first prospective, multicenter, single-arm clinical study have demonstrated that BWL has the potential to provide a safe, effective, and well-tolerated office-based procedure to manage patients with small stones in the kidney and distal ureter.[2] Specifically, BWL may provide rapid access to treatment for patients with colic. It may also benefit patients with asymptomatic intrarenal stones who would prefer treatment over observation. Furthermore, if the preliminary data reported in this study hold, BWL may offer a safer

option for pediatric patients than SWL when the inclusion criteria for both modalities are satisfied.

Despite these encouraging initial clinical observations, the ideal clinical scenarios where BWL will be most effective still need to be clearly defined. As a complementary modality to SWL, the clinical success of BWL will critically hinge on multiple factors, including the accessible acoustic window to image and target the stone by ultrasound after patient presentation, volume and composition of the stone mass, quality of cavitation monitoring, and patient's body habitus.[3] As discussed by the authors,[2] a Break Wave pivotal trial (clinicaltrials.gov, NCT05701098) is currently underway to optimize the criteria for patient selection best suited for BWL, and to determine the effects of stone size, BMI, skin-to-stone distance, and gender on the treatment outcomes. We eagerly await this and future studies to ultimately determine the clinical impact of this innovative technology.

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