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Characterizing the Acoustic Output of an Ultrasonic Propulsion Device for Urinary Stones

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Abstract

A non-invasive ultrasound system to facilitate the passage of small kidney stones has been developed. The device incorporates a software based ultrasound platform programmed with B-mode and Doppler for visualizing stones, plus long duration focused pulses for repositioning stones using the same transducer. This paper characterizes the acoustic outputs of the ultrasonic propulsion device. Though the application and outputs are unique, measurements were performed based on regulatory standards for both diagnostic ultrasound and extracorporeal lithotripters. The extended length of the pulse, time varying pressure output over the pulse, use of focused targeting, and the need to regulate the output at shallow depths, however, required modifications to the traditional acoustic measurement methods. Output parameters included: spatial peak intensities, mechanical index, thermal index, pulse energy, focal geometry, and target accuracy. The imaging and Doppler operating modes of the system meet the Food and Drug Administration (FDA) acoustic power and intensity limits for diagnostic ultrasound device. Push mode operates at a maximum mechanical index of 2.2, which is above the limit of 1.9 for diagnostic ultrasound, but well below any lithotripsy device and an ISPTA of 548 mW/cm² which is below the 720 mW/cm² limit for diagnostic ultrasound.

Index Terms

acoustic power and intensity; kidney stone; renal calculi; reposition; ultrasonic propulsion; ultrasound; lithotripsy

I. Introduction

A novel non-invasive system has been developed for the ultrasonic propulsion of kidney stones to facilitate stone passage [1-7]. The device incorporates conventional brightness mode (B-mode) and Doppler mode for imaging the kidney and kidney stones, plus a Push mode, which uniquely applies focused ultrasound to reposition the stone. The same

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Declaration of Conflicting Interests

All of the authors involved in this publication have financial interest in the company, Sonomotion, Inc. that is commercializing the ultrasonic propulsion technology.

transducer is used for both imaging and pushing. This work reports on the acoustic output of the investigational ultrasonic propulsion device.

The characterization of B-mode and Doppler outputs was based on the federal guidelines for diagnostic ultrasound (US) [8-11]. These same guidelines, however, were not necessarily appropriate for the Push output. Push mode is most similar to acoustic radiation techniques, such as elastography, shear wave imaging, and acoustic radiation force impulse imaging (ARFI) [12-16]. These technologies differ from most diagnostic ultrasound applications in that they employ long duration focused output bursts in order to measurably displace tissue or induce acoustic streaming. The bursts can range from a millisecond to hundreds of milliseconds, or even seconds. The bursts are also only applied intermittently.

The development of long duration burst techniques has prompted reevaluation of the standardized safety parameters and their appropriateness to these technologies [13-15]. Derivation of the FDA test parameters assumes the operation is continuous. In addition, the calculation of the thermal index utilizes the temporal-average intensity by assuming that the temperature rise during the on-time is insignificant; this may not hold true for long duration pulses. A system could be designed such that the off-time between the longer radiation force bursts is sufficient for the temporal average intensity (and thus thermal index) to be within the FDA requirements, but potentially causes significant transient temperature increases during the actual burst [14]. Herman and Harris [14-15], introduced a conservative model to address this concern, but no formal guidelines have been established.

Characterization of the Push output parameters was instead based upon the federal lithotripsy guidelines [17-19]. As a therapeutic application, the use of focused ultrasound to manipulate kidney stones to facilitate stone passage mimics the application of lithotripters; extracorporeal shock wave lithotripsy (ESWL) uses focused ultrasonic shock waves to facilitate stone passage by noninvasively fragmenting the calculi. The output of the Push pulse though is significantly longer than a conventional lithotripsy pulse and it is time varying. This required modifications to the conventional acoustic output acquisition methods to account for the change in output pressures over the pulse length. Modifications were also needed for evaluating the target accuracy over the entire image field and improving the low signal to noise ratio (SNR) in the fiber optic hydrophone instrumentation. Lastly, the acoustic output was governed such that the peak pressure occurred at 7 cm depth, the clinically relevant treatment depth for kidney stones. This paper describes the implementation of these modifications and the resulting acoustic output parameters compared with both diagnostic US and extracorporeal lithotripters.

II. Materials and Methods

A. Ultrasound System

1) Hardware—This system (Fig. 1) is a Verasonics data acquisition system (VDAS) equipped with an extended transmit burst option (model V-1, Verasonics Inc., Redmond, WA, USA). The unit has two 12-bit data acquisition boards, permitting operation of 128 transmit channels and 64 receive channels simultaneously. The device is programmed and controlled through a host personal computer (HP Z820, Hewlett Packard, Palo Alto, CA,

USA) using MATLAB 2011b (Mathworks, Waltham, MA, USA). A graphical user interface (GUI) is displayed on a touch screen monitor allowing easy control of the ultrasound system parameters. The ultrasound image is displayed on the same monitor. The system is programmed to work with an ATL HDI C5-2 abdominal probe (Philips Ultrasound, Andover, MA, USA). To simplify testing of the diagnostic system, the user can only change the output voltage of either the B-mode or the Doppler imaging. All other controls are for adjusting backend image processing or are used for data collection and measurement tools. Once the operator enables Push mode they can select 50% or 100% power output.

2) Diagnostic Modes

a. B-mode: the B-mode imaging sequence consisting of seven plane waves angled evenly from -12° to $+12^\circ$ that are then spatially compounded. The excitation pulse for each wave is a single transmit cycle. The VDAS hardware can only receive on 64 channels simultaneously, so a synthetic aperture sequence is utilized to receive on all 128 elements of the probe. Therefore, there are two transmit pulses for each of the seven different angles. The center frequency for the B-mode is 2.9MHz

b. Doppler: The excitation for Doppler mode is a 3.1MHz, 14 pulse ensemble where each pulse contains three transmit cycles. The Doppler transmit is a plane wave angled 12° from the probe axis. The received Doppler data are processed with color-flow, power, or custom algorithms designed to enhance a “twinkling artifact” commonly seen when viewing kidney stones with Doppler ultrasound [20-22].

3) Push Mode—The Push transmit sequence was developed and optimized to work with a conventional imaging probe and provide enough force to move a kidney stone from the lower pole to the urinary pelvic junction. The burst is constructed from of a series of pulses (Figs. 2 and 3). Each pulse consists of $450\ \mu\text{s}$ of on time followed by $165\ \mu\text{s}$ of off time (73% duty cycle). This is repeated 81 times for a total burst duration of 50 ms. The target location is spatially dithered with each pulse in discrete step sizes of $\pm 0.25\ \text{mm}$ out to $\pm 2\ \text{mm}$ from center (e.g. 0, $+0.25$, -0.25 , $+0.5$, -0.5 , ... $+2.0$, -2.0). This occurs sequentially starting with the first pulse of the Push burst. At the end of the dithering cycle, the process repeats. So for the 50 ms burst, there are close to 5 cycles of the 17 position dithering cycle. This was done to spread the radiation force over the width of the stone and lower the exposure at any one tissue location.

The total duration and duty cycle of the Push sequence was established as a balance between utilizing all the energy stored in the power supply capacitor, but of short enough duration to fit between two imaging frames. Pulse duration was fixed at $450\ \mu\text{s}$ based on the maximum number of programmable cycles in a transmit pulse of the VDAS hardware. The delay of $165\ \mu\text{s}$ empirically gave the highest pulse intensity integral and appeared to balance the draining and recharging of the capacitor best. We used PII as a surrogate for the acoustic force delivered to the stone. A transmit frequency of 2.3MHz was chosen for Push mode based on empirical measurements of the maximum output force on a stone target.

4) System Operation—The same probe is used to both image the kidney and stone, and generate the acoustic radiation force to push the stone. A typical procedure involves placing the probe in contact with the patient's skin to image the stone following standard ultrasound imaging procedures using both the B-mode and Doppler user interfaces. The operator then switches to Push mode, and targets the stone (under B-mode guidance) with the screen cursor using either a mouse or by touching directly on the screen; this action activates the Push sequence effectively instantaneously. The Push sequence is short enough in duration that it occurs between two B-mode imaging frames without affecting frame rate (30 fps), giving real-time imaging feedback of stone motion. The Push can be applied to any location and any depth within the image, though the effective force and direction vary as a function of target location. To prevent overheating ($> 10\text{ }^{\circ}\text{C}$ rise) of the probe surface, a programmed delay occurs after each Push sequence.

B. Acoustic Output

The parameters to be reported under diagnostic ultrasound guidelines are the frequency, bandwidth, peak positive pressure, peak rarefactional pressure, temporal average intensity, pulse average intensity, mechanical index, and thermal index. The parameters to be reported under ESWL guidelines are the peak positive pressure, peak rarefactional pressure, rise time, and compressional pulse for describing the shock front, focus geometry, acoustic pulse energy, and target accuracy. All measurements were made using hydrophones.

1) Scanning System—The custom, in-house scanning system for diagnostic output measurements included a polyvinylidene fluoride (PVDF) hydrophone (HGL-0085 with a AH-2010-25 preamplifier, Onda Corp., Sunnyvale, CA, USA), Cleverscope (CS320A, Cleverscope Ltd., Epsom, Auckland, NZ), 3-axis positioning system (Velmex, Bloomfield, NY, USA), and water tank (Fig. 4). A custom fixture allows the probe to be tilted in three independent axes (pitch, yaw and roll) for setting the imaging plane parallel with the YZ plane of the motion stage. The hydrophone is mounted to an arm which is connected to the 3-axis positioner system. The tank is filled with room temperature deionized water. The water is degassed using a custom in-house portable degassing system.

Waveform acquisition was triggered by the VDAS through the trigger input of the oscilloscope. Only one of fourteen waveforms was captured for both B-mode and Doppler. A trigger delay was implemented with B-mode to capture the first flash output with no angular beam steering. The peak-pressure map and target accuracy for Push mode were conducted at low amplitude (6 V_p) under the assumption that the beam geometry is the same at low and high output, so the PVDF hydrophone was used for this acquisition as well. For the high amplitude Push measurements (90 V_p), a fiber optic hydrophone (FOPH 2000, RP Acoustics, Leutenbach, Germany) was used for the acoustic outputs. The FOPH is capable of withstanding the greater pressures associated with higher amplitude acoustic pulses without compromising bandwidth, though the decreased sensitivity requires more signal averaging to improve SNR. An Agilent scope (DSO-X3034A, Santa Clara, CA, USA), was substituted for the Push measurements for its combination of bandwidth, sequential acquisition mode, and large memory.

2) AP&I for Diagnostic Modes—The free-field pulse intensity integral (PII) and peak derated pulse intensity integral ($PII_{.3}$) were determined [8]:

$$P I I = \frac{\int_{t_1}^{t_2} p^2(t) dt'}{\rho c} \quad (1)$$

$$P I I_{.3} = \exp(-2 * 0.115 * 0.3 * f_c * z_{.3}) * P I I, \quad (2)$$

where ρ is density, c is speed of sound, p is the pressure in Pa, and z is the distance from the ultrasound probe along the beam axis to the location of the peak derated pulse intensity integral. The integral is performed over a single pulse (t_1 to t_2). The constant 0.115 provides the conversion from decibals (dB) to nepers and 0.3 is the assumed tissue attenuation for derating (0.3 dB/cm/MHz). The subscript .3 denotes the term is derated and by what value

[9]. For the PVDF hydrophone, $p_r = \frac{V_h}{M_L(f_c)}$, where $M_L(f_c)$ is the cable loaded sensitivity for the hydrophone at the center frequency, f_c , and $v_h(t)$ is the voltage from the hydrophone. The derated spatial-peak pulse-average intensity ($I_{SPPA.3}$), derated spatial-peak temporal-average intensity ($I_{SPTA.3}$), and derated peak rarefactional pressure ($P_{r.3}$) were then calculated from the peak intensity integral:

$$I_{S P P A.3} = P I I_{.3} / P D, \quad (3)$$

$$I_{S P T A.3} = 14 * P I I_{.3} * P R F, \quad (4)$$

$$P_{r.3} = P_r * \exp(-0.115 * 0.3 * f_c * z_{.3}). \quad (5)$$

PD corresponds to the pulse duration and PRF corresponds to the pulse repetition frequency. The multiplicative factor of 14 is included in equation (4) to correct for only one of 14 waveforms being captured.

The mechanical index (MI) and thermal index (TI) are calculated as [10]:

$$M I = P_{r.3} / \sqrt{f_c}, \quad (6)$$

$$T I S(V_p) = \frac{\min[W_{.3}; I_{S P T A.3} \times 1 \text{ cm}^2]}{\left(\frac{210}{f_c}\right)} \quad (7)$$

$$TIB(V_p) = \min\left\{\frac{\sqrt{W_{.3(z_{B.3})} * I_{SPTA.3(z_{B.3})}}}{50}, \frac{W_{.3(z_{B.3})}}{4.4}\right\} \quad (8)$$

The thermal index equation, TIS, is for soft tissue applications while TIB is for bone. TIB was included since we are imaging kidney stones, which may act more like bone than tissue. V_p is the temporal-peak amplitude of the electrical drive waveform, and $W_{.3}$ is the derated time average acoustic power at depth z . z_{bp} is the minimum depth of intensity measurements equal to $1.5 * \pi \sqrt{4/(aperture)}$. For TIB, the power and intensity are still derated by a factor of 0.3, but at the depth where the pulse intensity integral is a maximum when derated by a factor of 0.6, ($z_{B.3}$). The equations assume the system is operating under unscanned mode (emission of ultrasound pulses in a single direction) and the aperture is greater than 1 cm².

3) Push Mode -Peak Pressure Map and Target Accuracy—The peak-positive pressure, and hence the focal intensity, depends on the target location within the image field. Recall in Push mode the ultrasound beam can be focused anywhere in the image plane. Therefore, to characterize the peak positive pressure for Push mode, a localized (16 mm × 4 mm) field scan was performed across the 2D space with the ultrasound beam focused on the hydrophone at each location.

Within the same field scan, the target accuracy at each location was verified. Target accuracy is a measure of any offset between a point selected in the B-mode image and the Push acoustic focus. In this case the hydrophone represented the target on B-mode. The localized field scan provided a measure of the location of peak pressure relative to the initial location of the hydrophone. The final result is a measurement of the peak positive pressure for every potential focal position within the image plane and the amount of offset between the target and measured focal region

4) AP&I Push Mode - Lithotripsy Guidelines—The purpose of this task was to compare the maximum acoustic output of the investigational device operating in Push mode to that of a typical lithotripter output. Slight modifications to the guideline [17]. were needed to account for the long duration waveforms. It was critical to acquire the complete waveform for two reasons. The first reason is that since the focus is spatially dithered, the measured acoustic field will vary over the entire burst depending upon the focal location of the pulse (Fig. 5a). For example, at (0, 0) the first pulse will be maximum amplitude. But the second and third pulses, which are a dithered step size away from the origin (+0.25 mm and -0.25 mm), will have a lower measured amplitude, and so on. Second, there is also a change in the pressure amplitude due to a decay in the supply current of the system hardware. This Push sequence draws significant energy from the power supply's capacitor causing the amplitude to drop to nearly zero over the duration of the output.

Because of limits in the memory size and acquisition rate of the oscilloscope though, only 50 μ s out of the 450 μ s could be acquired (Fig. 5b). The 50 μ s window was placed 200 μ s into

the waveform and represents the equivalent constant pressure across the entire 450 μ s pulse, as verified by separate test measurements. The scope was set in sequential acquisition mode with the same trigger delay for each acquisition. This signal was transmitted with each of the 81 output pulses of the Push burst.

5) AP&I Push Mode - Ultrasound Burst Average—Derivation of the FDA test parameters, such as thermal index, assumes the operation is continuous, i.e. a steady state temperature rise is achieved. In addition, the calculation of the thermal index utilizes the temporal-average intensity by assuming that the temperature rise during the on-time is insignificant, i.e. short pulses. This may not hold true for long duration pulses such as those used in acoustic radiation techniques and, as proposed here, ultrasonic propulsion. Herman and Harris [14, 15]. introduced a conservative model to address this concern.

Their model is based upon the spatial peak burst average intensity (I_{SPBA}) (Fig. 6):

$$I_{SPBA.3} = I_{SPPA.3} * P D * P R F, \quad (9)$$

$$I_{SPBA.3} = I_{SPTA.3} / (t_B * P R F_B), \quad (10)$$

where the peak average and temporal average intensities are defined by (3) and (4), t_B represents the burst length, and PRF_B corresponds to the pulse repetition frequency of the burst. Since the FDA does not specify the time range over which the intensity is averaged to determine I_{SPTA} , a time can be chosen (t_{pause}) to ensure that $I_{SPTA.3} \leq 720 \text{ mW/cm}^2$.

$$\Delta t = P R F_B^{-1} \geq (I_{SPBA.3} / 0.72) * t_B \quad (11)$$

where $t = t_B + t_{pause}$.

III. Results

A. Diagnostic Ultrasound Comparison

The results of the AP&I measurements for B-mode and Doppler are listed in Table 1. For our device, the peak derated pressure occurred at 4.9 cm for B-mode and 5.1 cm for Doppler. TIB measurements were taken at $z_{\min} = 4.9 \text{ cm}$, based on the aperture of the transducer. The results are well below the FDA limits because of the use of flash (plane wave) imaging. Also included in Table 1 are the results for Push mode calculated from the burst average, presented in Results section D.

B. 2D Pressure Map and Target Accuracy for Push Mode

To reduce the total scan time, the field was checked for symmetry, and data were captured for only half the plane. The focus was programmed at each location, and then a localized YZ scan was performed over $\pm 8 \text{ mm}$ in depth with a resolution of 2 mm and $\pm 2 \text{ mm}$ laterally

with a step size of 0.2 mm. The peak pressure of this scan was recorded along with a measurement of displacement from the intended target location. Focal dithering would obfuscate this measurement; so therefore, it is ignored by only measuring the first pulse in the entire Push burst.

The 2D pressure map is shown in Fig. 7. The color scale represents the relative pressure in decibels. Recall the data was acquired by moving the target of the Push with the hydrophone. Thus, the image is not a snap shot of the instantaneous pressure field, but the result of overlaying the pressure map for each targeted location. The arrow associated with each sub-scan indicates the target accuracy. The length of the arrow corresponds to the magnitude of the offset and the direction of the arrow corresponds to the direction of the true target location.

This is better illustrated in the two sub-scans taken along the centerline at 7 cm, and 7 cm laterally at a depth of 10 cm. Each local subplot is scaled to its own peak pressure and the true target location is at (0, 0). For the on-axis position, the target error is zero in both the depth and lateral direction. For the 7 cm lateral position, the peak pressure is (-1.8, -4) mm relative to the expected target position. However, because of the size of the focal spot at this position, as indicated by the -6 dB contour lines, the difference in pressure between the expected and true target location is negligible and the vector of the force is still in the same direction. Overall, the targeting error is minimal on axis and increases with depth and lateral extent. For all the positions, the true target location lies within the -6 dB contour of the expected location.

C. AP&I Push Mode - Lithotripsy Guidelines

The results of the measurements based on the lithotripsy guidelines are provided in Table 2. The focal location for all measurements was on axis at a depth of 7 cm. This was not the depth of peak pressure for Push mode - that occurred at 5.5 cm. Seven centimeters was, however, believed to be the clinically relevant treatment depth for kidney stones. To account for this discrepancy, a software control was implemented to cap the acoustic outputs to the maximum at 7 cm. The depth on mean in the clinical trial was close to expected and was 6.5 cm [3].

Because of the poor sensitivity of the FOPH the noise floor rises above the signal for the later pulses in the 50 ms burst (Fig. 8). Typically with the FOPH, the SNR is improved through averaging of waveforms on the oscilloscope. This is not practical with our measurements due to the lengthy acquisitions and number of positions to be acquired. Instead, the SNR was improved by averaging the individual cycles within each sampling window, assuming the waveform for each cycle is identical. Each 50 μ s window contains 10,000 data points covering approximately 115 cycles. This is sufficient to resolve and average the cycles, but includes an alignment uncertainty of 5 ns. To minimize this potential error in the averaging process, the data is up-sampled, and then divided into cycles, where each cycles now consists of approximately 2000 data points, resulting in an alignment uncertainty of 0.2 ns.

The free-field pulse intensity integral was calculated for each pulse at each position using (1), where $p(t)$ is the calibrated and deconvolved signal from the fiber optic hydrophone. The results from the 81 pulses were then summed and scaled, PII_{corr} , to account for the windowing, where $t_{pulse} = 450 \mu s$ and $t_{acq} = 50 \mu s$:

$$PII_{corr} = \sum PII * (t_{pulse}/t_{acq}). \quad (12)$$

The derived focal acoustic pulse energy, E_f and derived acoustic pulse energy, E_R , were then calculated as:

$$E = \int_S PII_{corr}(r, \theta) dS, \quad (13)$$

E_f is derived over the focal cross-sectional area, S , defined by the -6 dB contours in the XY plane. E_R is derived over the cross-sectional area of a stone defined by radius $R = 5$ mm.

The focal geometry (Table 2) was calculated by measuring the -6 dB contour relative to the peak positive pressure in all three dimensions. Fig. 9 shows the geometry for the XY plane taken at high power, as well as the XZ and YZ planes taken at low power. The focal width in the two planes orthogonal to the beam axis are similar (3.54 mm and 4.97 mm) with the implementation of dithering in the lateral plane. The focal extent in the depth direction is three to four times greater. The focal area and volume were approximated from the focal width measurements, versus the entire scan of the volume. Focal area (17.6 mm^2) was calculated assuming a rectangular geometry. Focal volume (151 mm^3) was calculated assuming an ellipse. The regional energy was derived over the circular cross-section of a stone defined by radius $R = 5$ mm. The two pulse energies are similar (1.24 J and 1.26 J) since the focal cross-sectional area is approximately the same as the area of a 5 mm stone.

The temporal measurements were taken from an acoustic waveform at (0, 0) after averaging all the waveforms within the $50 \mu s$ window (Fig. 10). The rise time is defined as the time for the pressure to increase from 10% to 90% of the peak-positive pressure. This is represented by the green line in Fig. 10. Compressional pulse duration is defined as the time integral between when the pressure first exceeds 50% of the peak pressure and when it falls back below 50% of the peak pressure. This is indicated with a red line on Fig. 10.

The pulse intensity integral from which the acoustic pulse energies are derived is shown in Fig. 11. Compared with the peak pressure map (Fig. 7), the energy is tightly localized. This suggests that the dithering process is not distributing the energy as evenly as anticipated. Both pulse energies are similar since the focal cross-section area is approximately the same as the area of a stone.

D. Acoustic Burst Average

The illustration by Hermon and Harris [14] (Fig. 6) assumes the intensity of each pulse is constant. The spatial peak intensity is then calculated for one pulse, and averaged across the entire burst. For this device, the amplitude of the pulses decreases with time due to the

dithering process and capacitance drainage (Fig. 12). As a result, the free-field pressure, and thus I_{SPPA} , is not captured over a single pulse but assembled from all 81 pulses and then averaged:

$$I_{SPPA.3} = \frac{P I_{I.3}(81)}{P D}, \quad (14)$$

where $PD = 450 \mu s$.

Applying equation (14) in combination with equations (9-11) results in an $I_{SPTA.3}$ below the FDA limits with a 3.2 second pause between bursts. The thermal index though at a t_{pause} of 3.2 s is 7.9. This can be reduced to 6.0 by changing the pause time to 4.2 seconds. The peak rarefactional pressure was close to 6 MPa. At 2.3 MHz, this results in a MI of 2.23, which is just above the FDA limits for mechanical index. Because of the transient nature of the Push burst, the potential temperature rise is more appropriately calculated using the thermal dose limit rather than the thermal index. We followed equations (20) and (21) from Herman and Harris [14], to establish a limit in $I_{SBPA.3}$ representing renal calculi as bone. Substituting $t_{43} = 20$ min for a kidney [23], resulted in $I_{SBPA.3}$ for bone 48.4 W/cm^2 , which we satisfy (46.4 W/cm^2).

IV. Discussion

Imaging Modes

The spatial compounding (flash angles) imaging B-mode and Doppler imaging mode have been evaluated as prescribed by the diagnostic ultrasound standards [8-11]. The values for $I_{SPTA.3}$, $I_{SPPA.3}$, MI & TI are all within the FDA's regulatory limit, including probe surface heating measurements (not discussed in this paper), meaning that it is safe for clinical use. The system has been used for imaging kidney stones in humans with success [24].

Focal accuracy and peak pressure variability

This set of measurements were developed independently of the HITU standards that were emerging at the time. It is the feeling of the authors that these are crucial measurements to any ultrasound system that has a variable focal location requiring a high degree of accuracy. For example, in the development of the system, there were errors in the phase calculations relating to differences in frequency (wavelength) between the imaging and the pushing modes. Though the error was slight, the push efficacy improved significantly when this difference was accounted for. Other sources of targeting error could include incorrect position and dimensions of the elements, lens effects, and diffraction effects. In our case, the measurements showed that even with targeting error, the measured target was in-line with the intended focus and within -6 dB of the true target.

Also of significance is the peak pressure map, which essentially depicts where the Push will have the greatest effective force. The techniques described for these measurements could be used for other applications, such as characterization of HIFU arrays. Variability of the output intensity at the focus throughout a field would need to be corrected for to give an appropriate

dose to a treatment location. Additional measurements and calculations have been made of the nonlinear distortion of the waveforms relevant to HIFU and imaging [25].

Comparison to diagnostic ultrasound transiently increased output (burst average)

Though ultrasonic propulsion is a therapeutic and not a diagnostic tool, it is still valuable to compare the acoustic outputs to diagnostic devices and limits. It is understood that diagnostic devices are effective without causing adverse effects, whereas a therapeutic device, such as ESWL can have collateral damage along with its therapeutic benefits. Therefore, meeting the safety limits of a diagnostic system greatly improves confidence that there will be a low possibility of tissue damage. As discussed earlier, I_{SPTA} and MI for P-mode are time averaged values that includes a required pause between user activated push pulses. It was determined that a 4.2 second pause between pulses would reduce the output to within the FDA's $I_{SPTA,3}$ and TI limits, with MI just above the FDA's upper limit.

Though some may see this 5 second pause as an impediment to a treatment procedure, there are other processes that are occurring simultaneously that need time to complete. These include a recharge of the Push capacitor and a cooling period for the surface of the probe. In addition, time is needed to adjust the patient, probe, and image settings. Though MI is slightly greater than the allowed FDA limit, there is low risk of mechanical damage to the tissue. Injury studies [26-28] found no evidence of cavitation in the kidney tissue (with the same energy delivered, but over 1 s versus 50 ms) and an injury threshold for the kidney at significantly greater intensity amplitudes than presented here. Also, 0.3dB/cm/MHz is used as the derating factor, which is a conservative value for the attenuation of tissue. If it is desired to lower the MI to FDA limits, the peak pressure could be reduced while still maintaining the magnitude of the effective radiation force by increasing the duty cycle of the burst.

Comparison to ESWL

With the absence of any predicate devices, lithotripsy appeared the most similar existing therapeutic application. In both cases, ultrasound energy is being delivered to a kidney stone. A lithotripter fragments a stone for the purposes of facilitating stone clearance. This device is intended to reposition the stone for the purposes of facilitating stone clearance. Although we note that ultrasonic propulsion could also have other uses including moving an obstructing stone to relieve pain [29]. A comparison of key parameters between the two devices is shown in Table 3. Because of the long pulse length, the ultrasonic propulsion device does deliver more energy per pulse than a lithotripter. The total energy delivered over the course of a treatment though is on the low end of lithotripter devices because thousands of shock waves are needed to fragment the stone while only tens of pushes are expected to be required to move the stone. If the attenuation is also considered, the decrease in total energy delivered with the investigational device is greater than that of most lithotripters. This is because the center frequency (F_c) of most lithotripters is on the order of 0.5 - 1 MHz, compared to 2 MHz for our device.

Future directions

Since the characterization and first clinical trial of the system described here, the team has developed a technique for designing and fabricating transducers and amplifiers [30-32]. A new design incorporates a single element annular therapy array with a P4-2 imaging probe looking through a central opening [33, 34]. The new design includes several other advances including real-time Doppler guidance using the twinkling artifact. That system is currently in clinical trials and is compatible with a new technology to comminute kidney stones called Burst Wave Lithotripsy (BWL) [35].

V. Conclusion

The acoustic output of an ultrasound based system for pushing kidney stones was presented. An ultimate goal of the device is to improve the natural passage of small stones and stone fragments, reducing the need for surgical intervention. The method was implemented on a software based engine, facilitating the implementation of novel transmit and receive algorithms. The design for the Push mode was a 50 ms long burst at a transmit voltage out of the Verasonics of $50 V_p - 90 V_p$. The individual pulses within the burst were dithered ± 2 mm laterally to reduce the local peak pressure, while still delivering the acoustic force over the entire stone. B-mode and Doppler mode were both shown to operate within the FDA limits for diagnostic ultrasound systems. Using a burst average approach, Push mode could also be delivered in a way that satisfies the FDA's I_{SPTA} requirements, but slightly above the MI requirement. The peak pressures and total energy delivered is below of a traditional lithotripsy treatment.

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Biographies

Bryan Cunitz received a BA in Physics from Colby College in 1999 and a BS in Electrical Engineering from Dartmouth College in 2000. After his under-graduate degrees he has worked at the University of Washington where he also earned an MS degree in electrical engineering in 2005. His work as a Senior Research Engineer includes improving ultrasound systems for the detection of kidney stones, therapeutic applications of focused ultrasound for the breaking and repositioning of kidney stones, image guided acoustic hemostasis, transducer development, and acoustic output measurements.

Barbrina Dunmire received her B.S. and M.S. degrees in Aeronautical and Astronautical engineering in 1989 and 1991, respectively, from the University of Washington (UW). Ms. Dunmire joined the UW Applied Physics Laboratory in 1994, where she is currently a Senior Research Engineer. During this time, Ms. Dunmire completed a second M.S. degree in Bioengineering (1998). Her research activities include tissue mimicking materials and phantoms, vector Doppler ultrasound, acoustic hemostasis, FDA regulatory compliance, and ultrasound based methods for kidney stone management.

Michael R. Bailey received his B.S. degree in 1991 from Yale and his M.S. and Ph.D. degrees in 1994 and 1997, respectively, from the University of Texas at Austin, all in mechanical engineering. He is currently a Senior Principal Engineer at the Applied Physics Laboratory and Associate Professor of Mechanical Engineering and Adjunct Associate Professor of Urology at the University of Washington. His research interests include cavitation, shock wave lithotripsy, HIFU, and ultrasound imaging; currently his energy is focused on developing ultrasound-based technology to reposition kidney stones. He has been a Fellow of the Acoustical Society of America (ASA) since 2007 and currently serves on the ASA Executive Council. He served on the Board of the International Society for Therapeutic Ultrasound (ISTU) from 2009 to 2012, the Bioeffects Committee of the American Institute for Ultrasound in Medicine from 2006 to 2012, and the Biomedical Acoustics Technical Committee of the ASA from 2005 to 2008. He received Early Career Awards from ASA in 2004 and ISTU in 2008.

Fig. 1. Ultrasonic propulsion system hardware. The ultrasound system (left) consists of the Verasonics data acquisition system, computer, keyboard, touchscreen monitor, and a C5-2 curved linear array (right).

Fig. 2.

Schematic of the Push burst. A 50 ms burst consists of 81 pulses. Each pulse is 4500 μs long followed by 165 μs of off time; a duty cycle of 73%.

Fig. 3.

Lateral dithering of the Push burst. A dithering cycle consists of 17 pulses. The initial pulse is centered at the user selected focal position. Each pair of pulses after is delivered at alternating increasing lateral distance from the axis in ± 0.25 mm steps. After the 17th pulse, at - 2.0 mm, the dithering cycle repeats starting on axis. The dithering sequence is applied over the 81 pulses of a single 50 ms Push burst.

Fig. 4.
Block diagram of the custom assembled scanning tank and system for the AP&I measurements.

Fig. 5.

Illustration of the modified acquisition of a 50 ms burst. (a) The decrease in amplitude associated with the capacitor drain across the five dithering cycles. Within each dithering sequence there is an additional decrease as the treatment focus moves away from the hydrophone with dithering. (b) Acquisition across one dithering cycle (17/81 pulses); the entire 50 ms pulse is not shown. The red boxes illustrate the portion of the waveform that is acquired by the oscilloscope. The average cycle amplitude measured within the acquisition window is applied across the 450 μ s pulse.

Fig. 6.

Replica of the figure used to illustrate I_{SPBA} in Herman and Harris [14].

Fig. 7.

The peak positive pressure map showing the relative pressure and target error over the acoustic field. The length of the arrow represents the error in distance between the true and measured peak location. The direction of the arrow represents the location of the expected (true) target location relative to the measured target location. The local pressure maps shown to the right provide an amplified view of the target accuracy. At 7 cm on axis there is no error. At 10 cm depth, 7 cm off axis the peak positive pressure is at $(-1.8, -4)$ relative to the expected location $(0, 0)$.

Fig. 8.
 (top) True pressure waveform without (blue) and with (green) the FOPH noise reduction.
 (bottom) View of several cycles in a low signal section. The nonlinearity of the waveform are discussed in detail in Ref. 24.

Fig. 9.

Peak positive and negative pressure at 7 cm. (a) Low power - XZ plane. (b) Low power - YZ plane. (c) Maximum output - XY plane. The color scale is in units of MPa. The black line is the -6 dB contour.

Fig. 10.

Peak positive acoustic pressure. The waveform was obtained by averaging the 115 waveforms captured in a windowed $50 \mu s$ acquisition. The green line represents the rise time and the red line represents the compressional pulse duration

Fig. 11.

Pulse intensity integral in the XY plane at a depth of 7 cm. The results are after correction and summation of the 81 pulses. The units for the color scale are J/cm^2 .

Fig. 12.

Illustration of the burst average calculation for the ultrasonic propulsion device. Herman and Harris [14] assume each pulse is the same amplitude, which is not the case for the investigational device.

TABLE I

Acoustic Output Parameters based on Diagnostic Ultrasound Methods

Mode	F_c (MHz)	BW (MHz)	$I_{SPPA,3}$ (W/cm ²)	$I_{SPBA,3}$ (W/cm ²)	t_{pause} (s)	$I_{SPTA,3}$ (mW/cm ²)	MI	TIS	TIB
B-mode	2.90	0.69	31.67	-	-	9.90	0.60	0.14	0.34
Doppler	3.11	0.33	24.76	-	-	14.50	0.38	0.21	0.51
P-mode [*]	2.30	2.50	63.36	46.36	3.9	720	2.2	7.9	-
P-mode ^{**}	2.30	2.50	63.36	46.36	4.2	548	2.2	6.0	-
FDA Limit			190			720	1.9	6	6

^{*} P-mode : Push mode with a 3.9 second pause between pushes,

^{**}

P-mode Push mode with a 4.2 second pause between pushes. This pause time effects both the $I_{SPTA,3}$ and TI. A pause time of 3.9 s satisfies the $I_{SPTA,3}$ requirement of 720 mW/cm², but TI is over 6. A pause time of 4.2 s is required to satisfy both regulatory limits of $I_{SPTA,3}$ 720 mW/cm² and TI 6.

TABLE II

AP&I Measurements, Push mode, lithotripsy guidelines

Parameter	Units	C5-2
$V_{\max}$	V_p	90
F_c	MHz	2.3
Focal depth	cm	7.0
Focal width x, maximum	mm	3.54
Focal width y, orthogonal	mm	4.97
Focal extent (z)	mm	16.42
Focal x-sect Area (XY plane)	mm^2	17.59
Focal Volume	mm^3	151
P_{peak}^+	Mpa	19.2
P_{peak}^-	Mpa	-5.9
Rise Time	nsec	5.4
Compressional pulse duration	nsec	29.6
E_f^*	J	1.24
E_R (R = 2.5 mm)*	J	1.26

Focal measurements are defined by the -6 dB isobar of the peak positive pressure. Energy measurements are per 50 ms burst.

TABLE III

Comparison of Acoustic Output between ultrasonic propulsion and lithotripsy

Device	P ⁺ (Mpa)	P (Mpa)	E _T / pulse (mJ)	Total Energy $n \cdot E_T$ (J)	Total Energy $n \cdot E_{T3}$ (J)
Clinical Lithotripter [25]	37-115	-10	4 - 90	4 - 270 ¹	3.2 - 220 ¹
P-mode (@ 90 V _p)	19.2	-5.9	1260	25-50 ²	8 - 17 ²

¹ Assumes approximately 1000 - 3000 shock waves, F_C of 0.5 MHz and z of 7 cm

² Assumes a total 20 - 40 pulses, F_C of 2.3 MHz and z of 7cm.