Published in final edited form as:

Urology. 2018 January ; 111: 225–229. doi:10.1016/j.urology.2017.09.013.

Effect of Stone Size and Composition on Ultrasonic Propulsion Ex Vivo

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Abstract

OBJECTIVE—To evaluate in more detail the effectiveness of a new designed more efficient ultrasonic propulsion for large stones and specific stone compositions in a tissue phantom model. In the first clinical trial of noninvasive ultrasonic propulsion, urinary stones of unknown compositions and sizes up to 10 mm were successfully repositioned.

MATERIALS AND METHODS—The study included 8- to 12-mm stones of 4 different primary compositions (calcium oxalate monohydrate, ammonium acid urate, calcium phosphate, and struvite) and a renal calyx phantom consisting of a 12 mm × 30 mm well in a 10-cm block of tissue-mimicking material. Primary outcome was the number of times a stone was expelled over 10 attempts, with ultrasonic propulsion burst duration varying from 0.5 seconds to 5 seconds.

RESULTS—Overall success rate at expelling stones was 95%. All calcium oxalate monohydrate and ammonium acid urate stones were expelled 100% of the time. The largest stone (12 mm) became lodged within the 12-mm phantom calyx 25% of the time regardless of the burst duration. With the 0.5-second burst, there was insufficient energy to expel the heaviest stone (0.88 g), but there was sufficient energy at the longer burst durations.

CONCLUSION—With a single burst, ultrasonic propulsion successfully moved most stones at least 3 cm and, regardless of size or composition, expelled them from the calyx. Ultrasonic propulsion is limited to the stones smaller than the calyceal space, and for each burst duration, related to maximum stone mass.

Ultrasonic propulsion offers a noninvasive option to move stones in the kidney and ureter.^{1–8} This technique might be used clinically to facilitate passage by expelling small stones from the kidney, to relieve an obstruction in the ureter by repositioning the stone into the bladder

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The references and statements made in the work are accurate. There are fairly few references with a sizable percentage being self references because of the nature of the topic. This paper compares a new way to reposition stones to the way we previously developed and no one else is moving stones with ultrasound.

Financial Disclosure: Michael R. Bailey, Barbrina Dunmire, Mathew D. Sorensen, and Bryan W. Cunitz have equity in and consulting relationships with SonoMotion, Inc., which has licensed this technology from the University of Washington.

or back into the renal pelvis, or to facilitate access and stone clearance by repositioning a stone at the time of surgery. Ultrasonic propulsion has been successfully demonstrated in a human clinical trial to move stones of various sizes and compositions.² Clinical results included moving an obstructing stone as large as 10 mm, but in a limited number of cases and with no statistical evaluation of stone size or composition possible.²

A new custom ultrasonic propulsion probe has been developed since the first-in-human trial and shown more effective than the trial probe at stone repositioning in a tissue-mimicking phantom.⁹ The purpose of this study was to evaluate potential limits of this new ultrasonic propulsion probe with regard to stone size and composition within a calyx model.

MATERIAL AND METHODS

System

Ultrasonic propulsion was conducted using a dedicated therapy probe (Sonic Concepts, Bothell, WA) with a coaxially aligned P4-2 imaging probe (Philips Ultrasound, Andover, MA). Real-time imaging was achieved using a Verasonics Data Acquisition System (VDAS-1, Verasonics Inc., Kirkland, WA) and supporting personal computer. The excitation pulse for the ultrasonic propulsion probe was programmed through a function generator (Agilent 33250, Santa Clara, CA) and amplified through a radiofrequency power amplifier (ENI AP400B, Electronic Navigation Instruments, Rochester, NY). The triggering of each ultrasonic propulsion burst and the duration of the burst was controlled through a LabView (National Instruments, Austin, TX) graphical user interface. The probe and exposures tested in this study were demonstrated safe in animals.⁹

Calyx Phantom

The phantom consisted of a truncated 12 mm × 30 mm cylindrical pipette bulb embedded in a tissue-mimicking material at 10-cm depth, simulating the calyx within the kidney (Fig. 1). The stone was “pushed” from below to move the stone up and out of the calyx. The phantom was tilted 15° from vertical so the stone did not just fall back into the calyx.

Stone Model

Three representative large human stones (all 8–12 mm in maximum dimension) of each of 4 different compositions were used. Stone composition (average weight) included calcium oxalate monohydrate (0.26 g), ammonium acid urate (0.16 g), calcium phosphate (0.28 g), and struvite (0.62 g) (Fig. 2). Stone type was established from spectroscopic analysis, with the dominant component composing at least 80% of the stone.¹⁰

Study Protocol

The stones were hydrated at least 48 hours before the study, and the weight of the hydrated stone was taken on the day of the study. An ultrasonic propulsion burst was applied to each stone 10 times, attempting to reposition the stone up and out of the phantom calyx, a distance of 30 mm. If the stone became trapped within the calyx, 2 additional ultrasonic propulsion bursts were applied. Each time the stone moved out of the calyx, it was manually replaced in the dependent portion of the calyx. The ultrasonic propulsion burst duration

varied from 0.5 seconds to 5 seconds, where the maximum duration of 5 seconds is the maximum expected clinical duration. The experiment was repeated 4 times for every stone, resulting in 480 data points (10 attempts $\times$ 3 individual stones of each compositions $\times$ 4 compositions $\times$ 4 burst durations).

RESULTS

Overall ultrasonic propulsion was successful at expelling the stone 95% of the time (456 of 480 attempts) (Fig. 3). The calcium oxalate monohydrate and ammonium acid stones were expelled 100% of the time over all burst durations regardless of stone size or weight. The stone with the largest dimension (12 $\times$ 9 mm), a calcium phosphate stone, frequently became lodged at the orifice of the phantom calyx, independent of burst duration, and was successfully expelled only 73% of the time (29 of 40 bursts). At the shortest burst duration of 0.5 seconds, a low mass (0.12 g) calcium phosphate stone in the shape of a thin disk was expelled only 70% of the time. This same stone was expelled 100% of the time for push durations 1 second and longer. Rotation of the stone in the acoustic field could potentially account for this. When positioned with a large cross section, there was sufficient radiation force to move the stone, but also high drag force. When rotated to lower cross section, there was lower drag but also insufficient radiation force applied to the small cross-sectional area. Also, at the shortest burst duration, the heaviest single stone (0.88 g), a struvite stone, could not be lifted far enough to be expelled from the calyx. However, increasing the burst duration to 1 second or longer expelled all struvite stones 100% of the time.

DISCUSSION

Ultrasonic propulsion succeeded in moving stones across 4 primary stone types with complete expulsion, defined as the movement of the stone, the full height of the phantom calyx (30 mm) with 1 propulsion burst, in 95% of the cases. The 5% of non-successes included 0% success (0 of 10) in attempting to expel the heaviest stone (0.88 g) at the shortest burst duration (0.5 seconds). This was overcome when the burst duration was increased. Also, in 30% of cases (3 of 10), at the lowest burst duration, 1 low mass, disk-shaped stone would rotate on its end, experiencing reduced radiation force as its cross-sectional profile was minimized, and not reach the exit of the 30-mm deep calyx. Lastly, regardless of burst duration, in 27% (11 of 40) of cases, a stone with a dimension equal to or greater than the diameter of the calyx became lodged within the orifice of the calyx. Our conclusion is ultrasonic propulsion was able to reposition stones up to the size of the space in which they are moving and was insensitive to stone type.

Observed sensitivity to stone shape and insensitivity to composition are supported by theory. The exact acoustic beam, stone properties, and stone shape can be measured, and from those, the acoustic force and motion of the stone in water can be calculated numerically.¹¹ As a first approximation, the radiation force must overcome the gravitational weight of the stone, which is offset by approximately half because of buoyancy within the fluid space. Stone composition can impact this, as a denser stone would require greater force for the same stone size. But research has shown there is no significant difference in density across stone types.^{12,13} Note this is true density vs radio-opacity on computed tomography, which is

often also referred to as density. Radio-opacity is quantified using the Hounsfield unit, which has been shown to differ among stone types.^{14,15}

The radiation force can be estimated as the wave intensity times the stone cross-sectional area divided by the sound speed of the fluid. The force can stem from the acoustic energy being “caught” (absorbed) by the stone or reflected. If all the energy is reflected 180° directly back to the source, the force doubles because the energy was not only temporarily caught but returned in the opposite direction.¹⁶ Thus, a shape that reflects at angles away from the source or with a smaller cross section, such as that a stone-shaped like a disk positioned edge on, receives less radiation force. Note a strong backscattered reflection also makes the stone bright and easy to target on the ultrasound image. Properties of the stone, such as density and sound speed, affect the degree reflection, and the stone material’s attenuation coefficient describes the degree of absorption. However, from stone to stone among our range of target stones, material properties have less impact on the net force than do stone shape and particularly mass, because the material properties vary less.^{12,13}

The maximum stone mass in the experiment was $m = 0.88$ g, which was displaced less than 3 cm with a 0.5-second burst and more than 3 cm with a 1-second burst. The maximum displacement d , as a function of burst duration t , is the second time integral of the acceleration $d = \frac{1}{2}at^2$. Acceleration is the force divided by the mass m of the stone, where the net force, neglecting drag and friction by the calyx walls, can be approximated as the radiation force above minus the difference of gravity and buoyancy ($\sim \frac{1}{2}mg$ where g is 9.8 m/s²). Given a 6 W/cm² intensity, a 10 mm $\times$ 11 mm stone cross section, and a sound speed of 1500 m/s, the 0.88 g stone travels approximately 1 cm with a 0.5-second burst and 5 cm with a 1-second burst, in agreement with experiment. Alternatively, a 0.83 -g stone would be displaced 3 cm with a 0.5-second burst.

The primary limitations of the study were the phantom model did not capture the potential compliance of the calyx, was not a closed system, and did not account for variability in the angle of approach to the stone through the body. The phantom material did not stretch. True kidney collecting space might be more compliant and stretch to allow a stone equal to the size of the passage through. Then, perhaps stones slightly larger than the calyx could possibly be repositioned. Note the force is enough to just flick a stone 3 cm; the stone does not move like a bullet. We have never observed tissue injury from motion of the stone in animal models, and when the stone became stuck in the phantom, it was easily released with a tap of the phantom. Similarly, the phantom was open, whereas the urinary tract is a closed space and thus the drag forces likely differ. It is not known how similar the friction force is between the smooth sinus tissue and the smooth-walled phantom. The phantom design did align the force with the direction of the path the stone could move and against gravity. For carefulness of measurement but not necessarily for accurate simulation of the collecting space, the force was applied only along the basis of a narrow channel in the phantom, and stones were not free to move laterally.

With a patient, it might not be possible to obtain this perfect alignment, and thus the stone would receive less force (the component of the force in the direction of the path) and travel a shorter distance. The limitations of this model design could possibly be overcome in human

clinical trials by identifying the proper patient positioning. With this specific type of technology, the patient is ideally awake and therefore can participate and allow for real-time probe and patient adjustments.

Despite the limitations in completely and accurately simulating the patient condition, this phantom study found ultrasonic propulsion was able to expel stones as large as the calyx space and that its performance was not dependent on stone composition. These results simplify the application of ultrasonic propulsion as stone composition can be mixed and is often not known. The results also broaden the application of ultrasonic propulsion beyond facilitating the passage of small stones to potentially repositioning a large stone from the ureteropelvic junction into the pelvis or a calyx to relieve pain or to reposition a large stone from a calyx to the pelvis before shock wave lithotripsy or ureteroscopy.⁴ It was not tested, but there may be sufficient force to dislodge an obstructing stone in the ureter or to detach a stone forming on tissue or Randall plaque.⁶

CONCLUSION

Ultrasonic propulsion has been shown to reposition stones and assist with spontaneous passage of residual fragments in humans. In this study, we successfully demonstrated that ultrasonic propulsion is robust to stone size and composition. Stone displacement was limited to stone diameters narrower than the “calyx,” and stone mass was found limiting only as it was dependent on propulsion burst duration. The results of this study support investigation of the use of ultrasonic propulsion as a potential noninvasive treatment for relief of pain associated with acute obstruction.

Acknowledgments

Funding Support: This work was supported by the National Space Biomedical Research Institute through NASA NCC 9-58, National Institute of Diabetes and Digestive and Kidney Diseases grant P01 DK043881, and the Madigan Army Health System Department of Urology residency program. Some of this material is the result of work supported by resources from the VA Puget Sound Health Care System, Seattle, WA. IACUC Approval: All animal studies were approved by the Institutional Animal Care and Use Committee at the University of Washington under protocol 4200-01.

We appreciate the help of our colleagues at the UW Center for Industrial and Medical Ultrasound, UW and Madigan Urology Departments, and the NIH NIDDK Program Project DK043881.

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Figure 1.

(A) Diagrams of the calyx phantom model. A pipette bulb was used to create a phantom calyx measuring 12 mm × 30 mm in a 10-cm block of tissue-mimicking material. (B) Ultrasonic propulsion bursts were delivered from below to work against gravity with the ultrasonic propulsion probe coupled using ultrasound gel through a 1.5-mm silicone sheet to mimic human skin. The ability to expel a stone from the phantom calyx was assessed over 10 attempts. (Color version available online.)

Figure 2.

Image of each stone used in the study: (A) calcium oxalate monohydrate, (B) ammonium acid urate, (C) calcium phosphate, and (D) struvite. The 2 largest dimensions and hydrated weight of each stone are shown next to the stone. The ruler scale represents centimeters. (Color version available online.)

Figure 3.

Percent expulsions of a single stone as a function of burst duration (seconds) within each stone composition group. Within each graph are the 3 individual stones (weight and size). (Color version available online.)