Prevention of Renal Stone Complications in Space Exploration

B.L. Dunmire[1], J.D. Harper[2], M.D. Sorensen[2], H. Wessells.[2] J.E. Lingeman,[3] M. Coburn,[4] B. W. Cunitz[1], Y.-N. Wang[1], J.C. Simon[1], A.D. Maxwell[1], W. Kreider[1], M. Paun[1], L.A. Crum[1], V.A. Khokhlova[1,5], O.A. Sapozhnikov[1,5], M. R. Bailey[1,2]

[1]Center for Industrial and Medical Ultrasound, Applied Physics Laboratory, University of Washington, 1013 NE 40th Street, Seattle, WA, 98105 (bailey@apl.washington.edu); [2]Department of Urology, University of Washington; [3]Department of Urology, Indiana University Health, [4]Department of Urology, Baylor College of Medicine, [5]Physics Faculty, Moscow State University

Our NSBRI projects address the medical condition *Nephrolithiasis* (kidney stones), specifically ExMC Gap 4.13: Limited capability to diagnose and treat a renal stone. Astronauts are at an increased risk of renal stone development because of microgravity, dehydration, and altered bone metabolism associated with space flight. The risk is that a stone, while innocuous when still in the kidney, will cause debilitating pain as it passes or worse, become obstructing, which can lead to urinary tract infection, sepsis, renal failure, and death. Short of surgery there is currently no available technology to affect when the stone moves from the kidney or manipulate the stone once it has begun to move. We report on progress to develop and validate 3 new technologies to provide options to manage stones in space. These technologies have been developed on a Flexible Ultrasound System (FUS).

The first technology is to improve imaging of stones called Stone mode or S-mode, and has two parts detection and sizing. Previous funding led to understanding that twinkling artifact use to detect stones arises from tiny bubbles on the stone surface. We then wrote a detection algorithm based on this knowledge. Stone sizing has been automated, and size is measured from not the image of the stone itself but from the shadow behind the stone. The sensitivity and specificity of S-mode compared to CT was 80% and 100% respectively (9 subjects, 27 stones). S-mode ruled out two false positives identified by B-mode ultrasound alone. In a phantom, stone size overestimation was reduced. and the number of stones over-classified greater than 5 mm, a clinical decision point, was reduced from 25% to 10%.

The second technology is repositioning stones, called ultrasonic propulsion or UP. Using a Verasonics FUS (VFUS), commercial handheld probe, and real-time imaging, the stone and kidney are visualized and, with a touch of the screen, a short burst of ultrasound waves are focused on the stone to reposition (push) the stone to a new location. This technology could, if validated in human studies, provide flight surgeons and astronauts the option to expel a small stone when it is likely to pass safely or to push an obstructing stone back into the kidney to relieve symptoms and avoid emergency surgery. At the time of writing, we have all approvals in place and will soon begin recruiting subjects for the first clinical feasibility test of repositioning stones. With NSBRI funding, we will continue refine the full capabilities of this technology, e.g., can ureteral stones be moved? can all obstructing stones be dislodged? can stones growing on tissue be detached?

The third technology is capability to use sinusoidal ultrasound and not shock waves to fragment stones. We call the technology burst wave lithotripsy (BWL) and operate it with real-time ultrasound image guidance and feedback on fragmentation. Human stones in water were completely fragmented in times of 10 seconds (uric acid) to 20 minutes (cystine) at $p = 6.5$ MPa and a pulse rate of 200 Hz. Stones treated at higher ultrasound frequency generated smaller fragments. Treatment appears safe and effective in preliminary results on 5 pigs.

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