Fiscal Year:	FY 2014	**Task Last Updated:**	FY 06/06/2014
PI Name:	Bailey, Michael R. Ph.D.		
Project Title:	Prevention of Renal Stone Complications in Space Exploration		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Smart Medical Systems and Technology Team		
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	(1) **ExMC**:Exploration Medical Capabilities		
Human Research Program Risks:	(1) **Medical**:Risk of Adverse Health Outcomes & Decrements in Performance due to Inflight Medical Conditions (IRP Rev I) (2) **Renal**:Risk of Renal Stone Formation		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
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No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	4	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Wang, Yak-Nam (University of Washington) Sorensen, Mathew (University of Washington) Khohklova, Vera (M.V. Lomonosov Moscow State University) Sapozhnikov, Oleg (University of Washington) Crum, Lawrence (University of Washington) Harper, Jonathan David (University of Washington) Kreider, Wayne (University of Washington)		
Grant/Contract No.:	NCC 9-58-SMST03402		
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Task Description:

1. Specific aims. We will refine and validate probes to integrate with the NASA Flexible Ultrasound System to address ExMC Gap 4.02 Nephrolithiasis.
AIM 1. Refine ultrasound probes to detect, reposition, and fragment kidney stones. AIM 2. Validate probes to visualize, reposition, and fragment stones. AIM 3. Refine and validate imaging to guide therapy.

2. Key Findings. A new stone specific imaging mode was developed, reported, and a patent submitted. In the first step the system automatically identifies the location of stones in the image and highlights them with color during real-time scanning. In the second step, the system automatically determines the size of the kidney stone. Published a clinical study showing reduced false positives with S-mode. Submitted a paper showing improved accuracy in stone size determination with our system. Presented and submitted a patent and paper showing stone size measurement across the shadow behind the stone is more accurate than measurement not across the image of the stone itself. Hence anyone can improve his or her stone size measurement. Published several preclinical safety and effectiveness studies of repositioning stones. Published a study of training techniques and outcomes for reposition stones. Initiated first clinical study of repositioning stones and reported preliminary results. In summary, stones were moved in all six subjects. No subjects observed any discomfort associated with the procedure. Invented, reported, patented, and submitted paper on a new method to comminute kidney stones, termed Burst Wave Lithotripsy BWL. Published paper 'Pulse focused ultrasound treatment of muscle mitigates paralysis-induced bone loss in the adjacent bone: a study in a mouse model.' Since the start of the clinical trial we have doubled the effectiveness of ultrasonic propulsion as measured by vertical stone displacement. Simultaneously we have reduced the channels needed. We have published and used a numerical model of radiation force and the acoustic field in tissue to design an improved probe. We have begun implementing BWL on the flexible ultrasound system. We have participated in several meetings with GE and ExMC about NASA's flexible ultrasound system (FUS). We stand by to integrate GE probe into our FUS and refine and validate ultrasonic propulsion on these probes. We await a probe and a probe description (pin-out) from GE. We continue to present demonstrations of ultrasonic propulsion and BWL. We presented at the American Urological Association in 2012, 2013, and 2014 and at NSBRI's Congressional demonstration in 2014.

3. Impact. We have invented a technology to reposition kidney stones and demonstrated it works in people. In 3 of the 6 cases, what appeared as one large stone on x-ray was 2 or 3 small passable stones. This had direct diagnostic benefit to these subjects and changed their course of treatment. In two other subjects we moved stones out of the kidney, which they passed and which was a direct therapeutic benefit to these subjects. We have shown we can produce a working prototype, develop sufficiently high-quality imaging to guide treatment, train new users, and conduct a successful clinical trial. This opens the path to refine the system and repeat, to commercialize the system, to add refined imaging as a software upgrade, and to repeat the process with BWL to demonstrate an improved way to comminute stones in humans. Specifically, we have now implemented our technologies with different probes making it efficient to add the probes NASA selects or to continue to refine the probes we could provide. Our software continues to be refined and validated. The preclinical work funded by NSBRI enables us to pursue demonstration in humans to assess where best this technology fits into care in the clinic and in space exploration.

4. Proposed Research. We have undertaken a retrospective study to see how commonly the shadow is seen and to compare accuracy of stone size from the stone or the shadow. We are beginning a clinical trial of S-mode for automatic stone detection and stone sizing. Our numerical codes and bench top testing will be used to optimize radiation force used to move stones. We will characterize the acoustic and thermal outputs of the new probes. We plan preclinical safety and effectiveness studies of imaging, repositioning, and comminution studies with improved probe outputs. Preclinical data will be resubmitted to FDA for a second clinical trial with the improved probe and outputs. We will work toward clinical trials with BWL. We have used preclinical data generated with NSBRI funds to apply to NIH to pursue additional clinical trials to investigate the benefit of expelling small asymptomatic kidney stones, stone clearance with repositioning, obstructing stone displacement, and stone detachment.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

Kidney stones have long been near the top of NASA's list of concerns; mitigating Gap 4.02 medical condition Nephrolithiasis is a must for all missions beyond the ISS. Likewise, stones have plagued humans since ancient Egypt. Currently, one in eleven Americans has suffered from stones - more than have diabetes or cardiovascular disease. Dehydration, stasis, and bone demineralization are strong contributors to kidney stones, and occur in microgravity, increasing the risk of stones in space. Stones are often debilitating, and pilots cannot fly with stones. Stones occurred on a Russian space mission, and the mission was nearly aborted before the stone passed. Over 30 stones have occurred shortly following even short duration space flights. NASA has collected compelling evidence for concern on its website https:// . Additionally, since the website publication, the total number of astronaut stone episodes has more than doubled, and a drug introduced to combat visual impairment/intracranial pressure has exacerbated the risk. Science, experience, and the negative medical consequences support concern for the risk of stones in space. NASA and NSBRI have focused considerable attention on stones and made progress. However, there are many types of stone disease, and it is unlikely that stone disease will ever be completely prevented on Earth or in space. We propose a way to prevent or minimize the consequences of any stones that form while in space. The treatment for most kidney stones is to encourage natural passage. To quote NASA's expectations in space Based on current Lifetime Surveillance of Astronaut Health (LSAH) data, 80 to 85% of in-flight cases of nephrolithiasis are expected to be best case scenarios (defined as a renal stone that responds to conservative treatment, e.g., analgesics and hydration), and 15 to 20% would be worst case scenarios (defined as a renal stone that does not respond to conservative treatment, e.g., requires lithotripsy or surgical treatment). Even surgery leaves residual fragments that must pass. Our technology provides the capability to reposition stones within the kidney and ureter, which will enhance conservative treatment or surgery by accelerating and facilitating passage of stones or fragments. However, this does not have to be the only use. The technology can also be used to reposition a stone to a non-obstructing location within the kidney to postpone surgery or to accelerate passage through the ureter, as proposed here. Finally, the technology proposed in this grant also provides the capability to comminute the stone as in shock wave lithotripsy (SWL) with what we call burst wave lithotripsy (BWL).

Task Progress:	AIM 1. Refine ultrasound probes to detect, reposition, and fragment kidney stones. Task 1.1. Select imaging probe for stone repositioning. Clinical trials are underway with the C5-2 probe of ISS Ultrasound 1. Awaiting delivery of probe to be used with NASA FUS-GDU. Task 1.2. Custom design probe to image, reposition, and fragment stones. Developed and tested probe. Integrating probe with FUS and modifying imaging portion to be smaller. AIM 2. Validate probes to visualize, reposition, and fragment stones. Task 2.1. Validate capability to displace an obstructing stone. Pursuing initial test in current clinical trial and applying for follow-on trial. Pre-clinical investigations of safety and effectiveness conducted with upgraded outputs. Task 2.2. Validate capability to displace a ureter stone. Followed schedule and did not pursue in year 1. Task 2.3. Validate capability to comminute a stone. Invented, patented, and reported burst wave lithotripsy BWL. Appears to have faster comminution than SWL, comminute stones that are difficult to break with SWL, have effectiveness and safety feedback, and be operable in a safe range. Task 2.4. Validate capability to expel a stone attached to tissue. Enhanced outputs and developed BWL to address this task. Testing underway. AIM 3. Refine and validate imaging to guide therapy. Task 3.1. Refine and validate capability to measure stone size. Reported and patented significant enhancement with our technology and technique. Task 3.2. Refine capability to localize a stone. Initiated clinical validation now at the end of year 1. Task 3.3. Refine and validate capability to detect a ureter stone. Followed schedule and did not pursue in year 1.
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