Fiscal Year:	FY 2013	**Task Last Updated:**	FY 05/28/2013
PI Name:	Kassemi, Mohammad Ph.D.		
Project Title:	Integrated Medical Model		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Operational and clinical research		
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	(1) **ExMC**:Exploration Medical Capabilities		
Human Research Program Risks:	(1) **Medical Conditions**:Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures (2) **Renal Stone**:Risk of Renal Stone Formation		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	44135	**Congressional District:**	10
Comments:	NOTE (Dec 2019): former affiliation included National Center for Space Exploration Research (NCSER), per information from J. McQuillen/GRC		
Project Type:	GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	01/01/2011	**End Date:**	05/31/2015
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA JSC
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Flight Program:			
Flight Assignment:	NOTE: Title change to "Integrated Medical Model - Renal Stone Module" per M. Urbina/JSC (Previous title "Probabilistic Analysis of Renal Stones in US Astronauts")--Ed., 10/8/15 NOTE: End date shows as 5/31/2015 per JSC MTL dtd 12/28/12 (Ed. 1/25/13) NOTE: End date is 8/8/2014, per D. Griffin/GRC (Ed., 5/30/12)		
Key Personnel Changes/Previous PI:	NOTE: Previous PI was Jerry Myers until January 2011. See project with title "Probabilistic Analysis of Renal Stones in US Astronauts" and PI=Myers for previous information		
COI Name (Institution):	Myers, Jerry (NASA Glenn Research Center)		
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The Exploration Medical Capability Element of the Human Research Program carries the risk of not being able to treat ill or injured crewmembers. Gap 4.13 in the Exploration Medical Capability Research Plan is the "Lack of lithotripsy or other capability to treat a renal stone." The description of this gap states that, "Given the high probability of kidney stone formation in crew members during long duration missions the capability to perform Lithotripsy is highly desirable." During all spaceflight missions to date, renal stone incidence is actually lower than what would be expected in the general population or in the analog population utilized by the Longitudinal Study of Astronaut Health. (LSAH). After astronauts return to Earth, however, the incidence rate increases and surpasses both the rate of the general population and the LSAH analog population, with the astronaut incidence rate of calcium oxalate stones approximately doubling that of the general US population. If these trends persist with the reintroduction of even fractional gravity, renal stones during a Mars mission could become a serious problem, not only in terms of astronaut health, but also in terms of the resources required to adequately treat the condition. A Bayesian update analysis of the data above suggested an approximately 5% probability of at least one crewmember developing a renal stone during a Mars mission. Given the nature of these data, the GRC IMM team developed a proof of concept probabilistic simulation of renal stone formation during a long duration exploration mission. While somewhat limited in scope, this simulation included both probabilistic and deterministic components. The deterministic components were developed to support the probabilistic analysis. Key findings from this work included: 1) As the stone grows larger, the governing equation says the rate of growth will increase, which is why the probabilistic analysis picks up the seed size as being influential. 2) The probabilistic model demonstrates identical sensitivity for Calcium and Oxalate, suggesting that a more detailed surface chemistry simulation needs to be conducted. 3) The sensitivities for the dwell time of a stone show pronounced differences between the 2.0L/day and 2.5L/day cases resulting in a 68.6% change in the probability of one stone reaching the effective diameter of a nephron from heterogeneous growth only. This result has a standard deviation of 0.237. As part of the validation process for this module, the task underwent a subject matter expert review of the work done to date. The review was favorable with indication that an increase model fidelity was required, as outlined in Steps 1-3 below. 1. Determine expected incidence rate of renal stones during exploration missions and how this rate is affected by new countermeasure activities. 2. Provide a probabilistic simulation that allows the Exploration Medical Capabilities Element of the Human Research Program to develop medical kits appropriate to the level of risk of renal stone formation. 3. Provide a probabilistic simulation that allows the Exploration Medical Capabilities Element of the Human Research Program the ability to quantitatively evaluate the effect of different operations scenarios on the ability of a given medical kit to adequately treat an ill or injured crew member. The GRC IMM task team is currently working to extend the capabilities of the deterministic model used as the parameter integration function to include both promoters, inhibitors, agglomeration, wall interaction effects and gravity components. Once this is matured, it will be wrapped with a probabilistic simulation representing the scenarios and physiological parameter variation typical of space flight to assess the likelihood of renal stone formation. Once completed, The Renal Stone Formation Simulation Module (RSFSM) will provide a state-of-the-art computational capability that can not only be used to more directly investigate the renal stone size distributions and the statistical propensities for developing a critical stone incident for future mission scenarios but also help to devise and evaluate different systematic chemical or physical intervention countermeasures for preventing their occurrence in future.
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research, which requires focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal.
Research Impact/Earth Benefits:	Nephrolithiasis constitutes as one of the most common diseases that has afflicted man for centuries. Indeed, one of the first evidences of renal stones in humans was found in an Egyptian mummy at El- Amrah dating back to 4800 B.C. Today, approximately 5% of the U.S. population develops clinically significant urinary calculi in their lifetime. However, renal stone disease is not only a concern on Earth, but could conceivably pose as a serious risk to the astronauts' health and safety in space. The physiological, environmental, and dietary conditions imposed by space travel and weightlessness can easily increase this risk as a recent survey of renal stone formation in US astronauts has revealed 14 recorded episodes. Russian medical science investigators have also noted multiple stone events among the Soviet cosmonauts. The most serious one was an in-flight renal stone occurrence that nearly caused the abortion of the Russian mission. The Renal Stone Formation Simulation Module (RSFSM) developed as part of this task is designed to inform NASA's Integrated Medical Model (IMM) with the likelihood and associated uncertainty of astronauts developing kidney stones upon long-term exposure to microgravity, as well as, upon re-entry to a gravitational field. The computational module will be able to assess the effects of various design reference mission scenarios, thus allow mission planners, medical kit designers, and clinicians to compare the efficacy of various countermeasures devised to reduce the probability of developing renal stone incident during the mission. The understanding that these simulations provide will also help to improve the astronauts' screening protocols. The benefits of developing this computational capability is not limited to space applications but will extend back to impact clinical and scientific medicine on Earth. As a state-of-the-art research tool and virtual hypothesis-tester, RSFSM will expand the current level of understanding of renal stone disease. It will also serve as a tool to help improve clinical procedures for screening and treating nephrolithiasis on Earth and devise physical and/or pharmaceutical interventions to help the nearly 15 million Americans who currently suffer from this ailment today.

Task Progress:	In this year of the project, the Population Balance Equation model for renal stone formation involving nucleation and growth was developed. An agglomeration model was also developed and linked with the CFD code fluent for parametric analyses. Front and back end statistical wrapper models were also developed and used to analyze the risk of renal stone for the astronauts based on microgravity biochemistry profiles/data. The deterministic PBE model will be linked with the probabilistic front and back end models for unified simulations in the next phase of the research. In this year of the project, the previously developed combined transport-kinetics model for growth of calcium oxalate crystals is cast in the framework of the Population Balance Equation whereupon the nephron is treated as a continuous crystallizer. This report describes the present model formulations and some interesting results obtained during the preliminary parametric simulations. The model is used to investigate the growth rates and size distributions of renal calculi in the nephron based on parametric simulation case studies for normal and stone-forming subjects in 1G and microgravity. Simulation results seem to suggest that as a result of the shift in renal biochemistry upon exposure to microgravity, a normal subject in space can exhibit stone growth rates and size distributions that are comparable to a stone-former on Earth. Thus, the adverse effects of microgravity conditions may be relatively as consequential for a normal subject than an inherent stone former - a finding that may prove important to the astronaut screening protocols. Numerical results also suggest that while a typical stone former on Earth or in Space may form a considerably larger number of renal stones in the range of 2-8 microns, the normal subject in microgravity tends to make significantly more stones below the 2 microns range. This may lead to an undesirable possibility for future long-duration missions, where the modified renal biochemistry of the astronauts in microgravity during space travel can instigate the formation of a large number of smaller stones that may become problematic upon reentry into a partial gravitational field.
Bibliography Type:	Description: (Last Updated: 03/08/2022)
Abstracts for Journals and Proceedings	Kassemi M, Iskovitz I. "Renal Stone Formation Module (RSFM): Predicting Renal Stone Size Distribution in Microgravity Using a Population Balance Approach." 2013 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-14, 2013. 2013 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 12-14, 2013. , Feb-2013
Papers from Meeting Proceedings	Kassemi M, Iskovitz I. "Prediction of Renal Stone Development and Size Distribution in Microgravity Using Population Balance Equation." 43rd International Conference on Environmental Systems, Vail, CO, July 14-18, 2013. To be presented in Computational Modeling for Human Health and Performance Analysis session. 43rd International Conference on Environmental Systems, Vail, CO, July 14-18, 2013. Paper 1574858, Session: ICES513, Computational Modeling for Human Health and Performance Analysis. , Jul-2013
Papers from Meeting Proceedings	Kassemi M, Iskovitz I. "Role of Transport and Kinetics in Growth of Renal Stones." 42nd International Conference on Environmental Systems, San Diego, CA, July 15-19, 2012. Paper AIAA-2012-3449. 42nd International Conference on Environmental Systems, San Diego, CA, July 15-19, 2012. http://dx.doi.org/10.2514/6.2012-3449 , Jul-2012