| | | | |
|---|---|---|---|
| **Fiscal Year:** | FY 2012 | **Task Last Updated:** | FY 08/23/2012 |
| **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<br>(2) **Renal Stone**:Risk of Renal Stone Formation | | |
| **Space Biology Element:** | None | | |
| **Space Biology Cross-Element Discipline:** | None | | |
| **Space Biology Special Category:** | None | | |
| **PI Email:** | mohammad.kassemi@nasa.gov | **Fax:** | FY 216-433-5033 |
| **PI Organization Type:** | NASA CENTER | **Phone:** | 216-433-5031 |
| **Organization Name:** | NASA Glenn Research Center/Case Western Reserve University | | |
| **PI Address 1:** | NASA Glenn Research Center | | |
| **PI Address 2:** | 21000 Brookpark Road, MS110-3 | | |
| **PI Web Page:** | | | |
| **City:** | Cleveland | **State:** | OH |
| **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 |
| **Contact Monitor:** | Watkins, Sharmi1a | **Contact Phone:** | 281.483.0395 |
| **Contact Email:** | sharmila.watkins@nasa.gov | | |
| **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<br>NOTE: End date shows as 5/31/2015 per JSC MTL dtd 12/28/12 (Ed. 1/25/13)<br>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."<br>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.<br><br>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:<br><br>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.<br><br>2) The probabilistic model demonstrates identical sensitivity for Calcium and Oxalate, suggesting that a more detailed surface chemistry simulation needs to be conducted.<br><br>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.<br><br>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.<br><br>1. Determine expected incidence rate of renal stones during exploration missions and how this rate is affected by new countermeasure activities.<br><br>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.<br><br>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.<br><br>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.<br><br>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.<br>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.<br><br>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:** | The Renal Stone Formation Simulation Module (RSFSM) developed as part of this task will provide state-of-the-art computational capability to directly investigate the renal stone size distributions and the statistical propensities for developing a critical stone incident for future mission scenarios and also to help to devise and evaluate different systematic chemical or physical intervention countermeasures for preventing their occurrence in future. The probabilistic risk assessment wrapper of RSFSM is driven by a series of coupled deterministic models that simulate the formation and transport of the renal stones.<br>The deterministic model has four important components: (i) nucleation and crystal growth from supersaturated solution; (ii) agglomeration to form larger stones; (iii) inhibition to growth and agglomeration by the urinary inhibitors; and (iv) transit and passage through the nephron. During the first 1.5 years of this task, the team developed the nucleation and growth model together with a preliminary phenomenological inhibition model. These models have been numerically verified for solution methodology's uniqueness and stability, and validated against archival experimental data published in the literature.<br><br>However, the renal stone problem is not a single stone phenomena but a multiple interacting calculi event. Therefore, in order to be able to consider the size distribution of renal calculi that can interact with each other during growth and to properly capture the aggregation, agglomeration and breakage components of renal stone development, the team implemented a mathematical framework based on the Population Balance Equation (PBE) methodology used extensively by chemical engineers to model continuous chemical crystallizer operations. The preliminary development of the PBE mathematical framework is also completed and partially validated. This PBE model for renal stone includes the nucleation and growth component and the agglomeration and breakage components are currently being incorporated in the PBE.<br><br>The chemical speciation code, JESS has also been acquired through communications with its developers, Dr. Peter May (Murdoch University, Australia) and Dr. Kevin Murray (Insight Modeling Services, South Africa). JESS will be primarily used to account for changes in the kidney's relative supersaturation due to natural or augmented inhibition chemistry of the urine. It has been demonstrated to be more comprehensive in describing renal biochemical speciation than other existing speciation codes. Currently, the MATLAB sampling utility implemented in the probabilistic model, JESS, and the encoded deterministic renal stone growth model (written in C) are being coupled for preliminary simulations using MATLAB as the integrator.<br><br>Preliminary simulation results generated by model have pointed to two quite interesting and important trends:<br><br>1. The adverse effect of microgravity conditions seems to be relatively greater for a normal subject than an inherent stone-former - a finding that may prove important to the astronaut screening protocols. 2. Administration of natural chemical inhibitors such as citrates may provide an effective countermeasure to CaOx stone growth and reduce the risk of renal stone development in space even for inherent stone-formers. Although care must be taken that chemical inhibition of one type of crystal does not lead to other adverse effects such as promotion of other types of renal stone precipitation.<br><br>The above conclusions are, however, preliminary as important effects of agglomeration, inhibition, transport, and wall adhesion that may change the present predictions have not yet been fully incorporated. It is hoped that the future enhancements of the computational module can enable it to paint a broader and more complete picture of renal stone development in micro- and partial gravity environments. |
| **Bibliography Type:** | Description: (Last Updated: 03/08/2022) |
| **Abstracts for Journals and Proceedings** | Kassemi M, Iskovits I, Brock R. "A Combined Transport-Kinetics Model for Growth of Renal Calculi in 1G and Microgravity." 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. , Feb-2012 |
| **Articles in Peer-reviewed Journals** | Kassemi M, Brock R, Nemeth N. "A combined transport-kinetics model for the growth of renal calculi." Journal of Crystal Growth. 2011 Oct;332(1):48-57. http://dx.doi.org/10.1016/j.jcrysgro.2011.07.009 , Oct-2011 |