Fiscal Year:	FY 2012	**Task Last Updated:**	FY 11/14/2011
PI Name:	Sa, Rui Carlos Ph.D.		
Project Title:	Variability in Flow Distribution within the Lung and Its Effects on Deposition and Clearance of Inhaled Particles in Normal and Reduced Gravity		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Human Factors and Performance Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SHFH**:Space Human Factors & Habitability (archival in 2017)		
Human Research Program Risks:	(1) **Dust**:Risk of Adverse Health and Performance Effects of Celestial Dust Exposure		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	Last name ometimes seen as “Pereira de Sa” "		
Project Type:	GROUND	**Solicitation / Funding Source:**	2009 NSBRI-RFA-09-01 Postdoctoral Fellowships
Start Date:	11/01/2009	**End Date:**	10/31/2012
No. of Post Docs:	1	**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:	0	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Prisk, G. Kim (MENTOR/University of California, San Diego)		
Grant/Contract No.:	NCC 9-58-PF02103		
Performance Goal No.:			
Performance Goal Text:			

POSTDOCTORAL FELLOWSHIP
1) Original project aims and objectives: Our goal is to provide a better understanding of how variability in convective flow patterns in the lung affects aerosol deposition, and thus subsequent clearance between individuals. Such an understanding will allow better characterization of the normal variability in deposition and clearance rates both in 1G, and in low-gravity such as on the lunar surface. Three key factors define the toxicological risk to the lung of exposure to airborne lunar dust which is believed to be highly reactive: 1) the degree of deposition, 2) the toxicological properties of the material itself, and 3) the residence time within the lung of the particles once they have been deposited. The distribution of ventilation within the lung determines deposition. Studies by us using computational fluid dynamics (CFD) in realistic central airway trees show that ventilation varies widely at the lobar level. However, typical boundary

Task Description:	conditions for deposition simulations assume that lung expansion is uniform, which we know to be incorrect. We have developed a Magnetic Resonance Imaging (MRI) technique that allows the quantification of regional specific ventilation in the human lung, providing realistic boundary conditions. In this proposal we will: a) map the spatial pattern of specific ventilation; b) map deposition in the supine position at 1G; and combine these with data on the spatial pattern of deposition of inhaled particles collected in low-gravity as part of our existing NSBRI studies; c) The measured pattern of aerosol deposition will be compared with the CFD predictions, using uniform and the more realistic boundary conditions. By comparing across a number of subjects, the mechanisms underlying the observed variability in deposition and regional ventilation can be elucidated. By comparing 1G and low-gravity deposition, the magnitude of the gravitational effect can be assessed. 2) Key findings: We have successfully applied the MRI technique for quantifying specific ventilation in the human lung- Specific Ventilation Imaging- completing aim a). We have used this technique to quantify the vertical, gravitational induced, gradient in specific ventilation that is present on the human lung on earth. Our findings are in accordance with previous radiation based techniques for quantifying specific ventilation. An article describing the technique was published during the second year in the Journal of Applied Physiology. A patent, protecting the intellectual property of this and two other MRI methodologies developed at our lab is currently actively pursued. During the second year we have mapped particle deposition for 4µm particles, when inhalation occurs in the supine position (10 subjects) and recently in low-gravity (6 subjects), addressing aim b). 3) Impact of key findings on original project: The successful completion of aim a) was essential to completion the project. The data for addressing aim b was recently collected for 4µm particles. Data analysis is under way. These results allow us to start CFD modeling, addressing aim c). 4) Research plan for the coming year: We have collected deposition data for 4µm particles (aim b). A second parabolic flight campaign (1µm particles) is expected in the spring 2012. MATLAB based software tools for the analysis of this data developed by the fellow are in use for the analysis of ground (1-G) data. Further development and optimization of these tools for application to low-gravity acquired data is underway. Computational Fluid Dynamic modeling will begin soon. The third year will be dedicated to the analysis of the outcomes of these models, and establishing a metric for comparison with the measured deposition patterns. We expect that, by imposing realistic instead of idealized boundary conditions, we will significantly improve our ability to predict particle deposition. Time will be dedicated to compiling and writing these results into a scientific publication.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The overall goal of this project is to better understand how variability in convective flow patterns in the lung affect aerosol deposition and subsequent clearance between individuals. Such knowledge will help better characterize the normal variability, both on the ground and in low gravity (the lunar, martian or asteroid surface), and thus better characterize the risks of exposure to potentially toxic, aggressive dust. This improved risk assessment is important both in earth's gravity, where many people are exposed to airborne dust, as well as in future planetary exploration (lunar dust is aggressive, highly reactive, and in low gravity, dust particles are likely to deposit further down in the lung, increasing residence time; little is know at this time on the toxicological properties of martian or asteroid dust). From a different and more long-term perspective, an improved fundamental understanding of the individual spatial variability in particle deposition might also help optimize aerosols drug delivery, helping optimizing aerosols mixes that will more accurately target specific portions of the lung. Individualized targeting of aerosol medication in chronic diseases such as asthma has the potential to increase the efficiency of the drug delivery, decreasing the inhaled dose and minimizing side effects. In the framework of this project, we have developed a novel MRI technique for the quantification of specific ventilation in the human lung. The technique requires a standard proton MRI machine with a 1.5 Tesla field, machines that are widely available in clinical setting. The technique does not require the use of radiation, and is therefore suitable for repeated measures. At a first stage, we are using the technique as a novel research tool, but its repercussions can be extended to the clinical setting. The fact that it does not involve radiation opens a novel diagnostic window, for it can be applied repetitively. This can be of particular importance in patient populations suffering from chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD). Patients with chronic respiratory disease could benefit from a non invasive, zero radiation dose assessment of their lung function, that can thus be repeated time and again, allowing for a more regular follow up than the existing techniques. A patent protecting the intellectual property of this MRI technique as well as two additional MR-sequences developed by our group is currently being pursued (provisional patent application: "New method for imaging ventilation and perfusion in the lung using MRI" - SD2010-320, provisional application number 61420554 - R.B. Buxton, G.K. Prisk, S.R. Hopkins, R.C. Pereira de Sá, R.J. Theilmann, M.V. Cronin).
Task Progress:	The goal of this project is to provide a better understanding of how variability in convective flow patterns in the lung affects aerosol deposition, and thus subsequent clearance between individuals. In order to achieve this goal, three specific aims need to be addressed: a) map the spatial pattern of specific ventilation; b) map deposition in the supine position at 1G; and combine these with data on the spatial pattern of deposition of inhaled particles collected in low-gravity as part of our existing NSBRI studies. c) The measured pattern of aerosol deposition will be compared with Computational Fluid Dynamics (CFD) predictions, using uniform and the more realistic boundary conditions. By comparing across a number of subjects, the mechanisms underlying the observed variability in deposition and regional ventilation can be elucidated. By comparing the data collected in 1G with data from low-gravity, the magnitude of the gravitational effect can be assessed. In the first year we have successfully developed a Magnetic Resonance Imaging technique for quantifying specific ventilation in the human lung - Specific Ventilation Imaging, completing point a) of the initial project aims. We have used this technique to quantify the vertical, gravitational induced, gradient in specific ventilation that is present on the human lung on earth. An article describing the technique and the first physiological results obtained was published in the Journal of Applied Physiology during the second year of the project. This novel MRI technique was included in a provisional patent application: "New method for imaging ventilation and perfusion in the lung using MRI" (provisional application number 61420554). During this second year we quantified specific ventilation in the entire pool of subjects available (parabolic flight certified) for the low-gravity deposition experiments (N=10). The data thus obtained allowed us to determined realistic boundary conditions required for addressing aim c) in a individualized subject by subject basis. We have mapped the deposition of 4µm particles (1G supine) in the same pool of subjects (N=10). A subset of these

	subjects (N=6) participated in a recent NASA parabolic flight campaign, where maps of particle deposition in low gravity were obtained for the first time, thus completing data acquisition for 4µm particles. Low-gravity deposition maps for 1µm particles, and the corresponding post-flight controls are expected to occur during a parabolic flight campaign tentatively scheduled for the spring 2012. The analysis of the acquired data is ongoing using MATLAB based software analysis tools developed during the first and second year of the project. The constraints of parabolic-flight acquired data imposed, as expected, additional customization and optimization. The implementation of the necessary changes is currently underway. We expect to start the CFD modeling component of the project shortly.
Bibliography Type:	Description: (Last Updated: 01/11/2021)
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Abstracts for Journals and Proceedings	Prisk GK, Sa RC, Bennett WD, Darquenne C. "Deposition and subsequent clearance of aerosols in reduced gravity." 18th International Academy of Astronautics (IAA) Humans in Space Symposium, Houston, TX, April 11-15, 2011. 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011. , Apr-2011
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