Fiscal Year:	FY 2011	**Task Last Updated:**	FY 12/06/2011
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
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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 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 and subsequent clearance. Studies by us using computational fluid dynamics (CFD) in realistic central airway trees show that ventilation varies widely at the lobar		

Task Description:	bronchiole level. However, typical boundary conditions for deposition simulations assume that lung expansion is uniform, which we know to be incorrect. We developed a MRI technique that allows the quantification of regional specific ventilation in the human lung providing realistic boundary conditions and an accurate prediction of particle deposition. 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 the data collected in 1G with data from low-gravity, the magnitude of the gravitational effect can be assessed. 2) Key findings: In this first year we have successfully developed a Magnetic Resonance Imaging technique for quantifying specific ventilation in the human lung - Specific Ventilation Imaging. We have thus completed point a) of the initial project aims. We are now capable of routine mapping the spatial pattern of specific ventilation in humans. We have used this technique to quantify the vertical, gravitational induced, gradient in specific ventilation that is present on the human lung on earth, in a total of 8 subjects. An article describing the technique is currently under review with the Journal of Applied Physiology. Moreover, we have completed the integration of hardware and software required for the completion of aim b) and we have completed ground tests of the system. The completion of this specific goal is dependent on the availability of parabolic flights. We are currently waiting for NASA to provide such opportunity. 3) Impact of key findings on original project: The successful completion of aim a) was essential to the rest of the project. 4) Research plan for the coming year: Deposition and clearance: the parabolic flight campaign is likely to happen in March or April 2011. The constraints imposed by parabolic flights render the existing deposition and clearance analysis software inadequate. Based on preliminary 1G data of deposition and clearance, I am developing new software tools for the analysis of deposition and clearance. These tools will allow us, for example, to triage events by gravity level, but also to correct for subject movement or misalignment. Specific Ventilation Imaging (SVI) allows to measure realistic boundary conditions for lobar ventilation. During this year, we will simulate deposition using computational fluid dynamics models, based on these realistic boundary conditions. Comparison with 1G supine and low-gravity deposition will follow, once the low-gravity data is available.
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 affects 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 surface), and thus better characterize the risks of exposure to potentially toxic, aggressive dust. This improved risk assessment is important both for future lunar 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), as well as in earth's gravity, where many people are exposed to airborne dust. From a different and more long-term perspective, a better understanding of the individual variability in deposition might also help optimize aerosols drug delivery, aerosols that will more accurately target specific portions of the lung. 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 can be applied repetitively. This can be of particular importance in patient populations suffering from chronic respiratory diseases, such as chronic obstructive pulmonary disease (COPD). Patients with chronic disease could benefit from a noninvasive, zero radiation dose assessment of their lung function, allowing for a more regular follow up than the existing techniques.
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 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 the data collected in 1G with data from low-gravity, the magnitude of the gravitational effect can be assessed. In this first year we have successfully developed a Magnetic Resonance Imaging technique for quantifying specific ventilation in the human lung - Specific Ventilation Imaging. We have thus completed point a) of the initial project aims. We are now capable of routine mapping the spatial pattern of specific ventilation in humans. We have used this technique to quantify the vertical, gravitational induced, gradient in specific ventilation that is present on the human lung on earth, in a total of 8 subjects. An article describing the technique and presenting the first results obtained with it is currently under review with the Journal of Applied Physiology. The data thus obtained allowed us to determine the realistic boundary conditions required for addressing aim c). Moreover, in this year we have completed the integration of hardware and software required for the completion of aim b) and we have completed ground tests of the system. The completion of this specific aim (b) is dependent on the availability of parabolic flights. We are currently waiting for NASA to provide such opportunity; the parabolic flight campaign is likely to take place in March or April 2011. The constraints imposed by parabolic flights render the existing deposition and clearance analysis software inadequate.

	Based on preliminary 1G data of deposition and clearance acquired in 3 subjects, I have started developing new software tools for the analysis of deposition and clearance. These tools will allow us, for example, to triage events by gravity level, but also to correct for subject movement or misalignment induced by the parabolic profile. This is an ongoing work that will continue through the second year.
Bibliography Type:	Description: (Last Updated: 01/11/2021)
Articles in Peer-reviewed Journals	Sa RC, Cronin MV, Henderson AC, Holverda S, Theilmann RJ, Arai TJ, Dubowitz DJ, Hopkins SR, Buxton RB, Prisk GK. "Vertical distribution of specific ventilation in normal supine humans measured using oxygen-enhanced proton MRI." J Appl Physiol. In press, February 2010. , Feb-2010