

Fiscal Year:	FY 2006	Task Last Updated:	FY 01/08/2007
PI Name:	Prisk, G. Kim Ph.D., D.Sc.		
Project Title:	Aerosol Deposition in the Lung in Fractional Gravity: Risk Mitigation for Lunar and Martian Habitats		
Division Name:	Human Research		
Program/Discipline:	NSBRI Teams		
Program/Discipline--Element/Subdiscipline:	NSBRI Teams--Technology Development 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		
PI Email:	kprisk@ucsd.edu	Fax:	FY 858-534-6046
PI Organization Type:	UNIVERSITY	Phone:	858-534-3233
Organization Name:	University of California, San Diego		
PI Address 1:	Department of Medicine		
PI Address 2:	9500 Gilman Drive		
PI Web Page:			
City:	La Jolla	State:	CA
Zip Code:	92093-0852	Congressional District:	53
Comments:			
Project Type:	GROUND	Solicitation / Funding Source:	2004 NSBRI NNH04ZUU003N Human Health in Space
Start Date:	07/01/2005	End Date:	06/30/2009
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):			
Grant/Contract No.:	NCC 9-58-TD00701		
Performance Goal No.:			
Performance Goal Text:	<p>The deposition of aerosols from the environment in the lung presents a health risk. For particles larger than 0.5 micron, such deposition is strongly influenced by gravitational sedimentation. In microgravity, deposition by gravitational sedimentation is absent, and as a consequence, airway particle concentrations are higher than in 1G, enhancing aerosol transport to the alveolar region of the lung. The presence of previously unaccounted for complex mixing patterns in the periphery of the lung, combined with high alveolar aerosol concentrations, results in high deposition in this sensitive region of the lung in microgravity. Similar effects are expected in the fractional gravity environments of the moon and Mars.</p> <p>The dust on the surface of Mars is highly oxidative in nature, due to the UV environment on the surface, and that on the Moon has properties comparable to that of fresh-fractured quartz on Earth, a highly toxic substance. The dust is also electro-statically charged, and so will tend to stick to the outside of spacesuits, and be tracked into habitats. The lung,</p>		

	<p>with its huge exposed surface area is highly vulnerable to adverse effects resulting from exposure to Mars and Moon dust.</p> <p>We are engaged in a multi-faceted approach involving human and animal experiments, combined with sophisticated modeling, to provide a path to assessing the health risk of dust exposure in habitats on both the Moon and Mars, addressing Risk #7 in the Bioastronautics Critical Path Roadmap. Such an assessment has profound implications on the degree of engineering (and thus cost) that will be required to limit the risk of such exposure to the inhabitants of these habitats. We will address the following hypotheses and objectives:</p> <p>1: That total aerosol deposition in the human lung in fractional gravity will be higher than predicted by existing models (as is the case in microgravity), and that a higher than predicted alveolar deposition will result in these circumstances. Using the NASA Microgravity Research Aircraft, we will non-invasively measure both the total and regional deposition of inert particles (0.5 to 2 micron) in humans in fractional-G corresponding to that on the surface of the Moon and Mars.</p> <p>2: That aerosol deposition in the lungs of spontaneously breathing rats in fractional-G will be more peripheral (closer to the alveoli) than in 1G. We will expose spontaneously breathing rats to fluorescent- and magnetically-labeled particles of varying sizes (between 0.5 and 2 micron) in 1G, and in fractional G corresponding to surface of the Moon and Mars, and measure the specific sites of regional deposition in the lungs using both fluorescent microscopy, and magnetic resonance imaging techniques.</p> <p>3: We will couple existing sophisticated computational fluid dynamics (CFD) models of the upper airways of humans, to our model of the alveolar region of the lung, to predict aerosol deposition under conditions matching those of the experiments performed in humans. In rats we will use detailed 3D images of the rat bronchial tree to develop an upper airway CFD model which used in conjunction with an appropriately scaled alveolar model, will predict aerosol deposition under conditions matching those of the experiments performed in rats.</p> <p>At the completion of year 1 of this project we have flown the first series of human studies aboard the Microgravity Research Aircraft (scheduled for mid-June at time of writing). These will encompass both total and regional deposition experiments (specific aim #1). As the only available flight profiles aboard the Aircraft are presently a mixture of microgravity and fractional-gravity profiles, we will use the microgravity phases of the flights to perform engineering evaluation so the plethysmographic system to be used for studies associated with specific aim #2. In pursuit of specific aim #3 (CFD) we have begun the development of a detailed atlas of the upper airway geometry in rats (using MRI imaging). In parallel, we have begun the coupling of the CFD codes for central and peripheral airways. Limited simulations in fractional gravity have been performed to generate preliminary data and test development progress. We have installed the upgraded CFD processing workstation to support these activities.</p> <p>In the upcoming year we will continue the flights aboard the Microgravity Research Aircraft, to complete the human studies (Specific Aim #1). Flights are currently scheduled for September, with subsequent flight opportunities not yet defined by the Reduced Gravity Office. We will complete engineering evaluations of the rat plethysmographic system and expect to fly the first rat exposure studies in CY 2007. CFD development will be on-going in parallel.</p>
<p>Task Description:</p>	<p>Rationale for HRP Directed Research:</p> <p>The Earth-based applications for this research fall into two areas:</p> <p>First is the development of better models for assessing environmental exposure to particulate matter (PM). Because of its unique structure and function, the lung is a vulnerable target for airborne particulate matter (PM). On Earth, effects of oxidative-induced lung injury are most readily seen in individuals with pre-existing lung disease (i.e. asthma, chronic obstructive pulmonary disease). However, there is little question, that even healthy individuals exposed to PM for extended periods are susceptible to oxidant-induced lung injury. Evidence suggests that short-term exposure is also of considerable risk. Short-term exposure to PM can exacerbate various pulmonary diseases and increase the risk of myocardial infarction. It is also interesting to note that the correlation of exposure with risk factor increases as one considers total suspended particles (TSP), PM smaller than 10 micron (PM10) and then PM2.5, suggesting that the smallest particles may in fact be the most significant in terms of damage.</p> <p>Research Impact/Earth Benefits:</p> <p>Second is a better understanding of the fate of aerosols in the lung may also be beneficial in aerosol drug therapy as many drugs are now administered in aerosolized form. As an example, Beta-2 agonists are used in an aerosolized form for the treatment of asthma. It is long known that the effect of Beta-2 agonists as bronchodilators is enhanced if they can be delivered directly to their intended site of action. This concept of spatial targeting requires knowledge of the nature of the aerosol being delivered, and the behavior of such an aerosol in the lung. Poor spatial targeting is associated with lowered efficacy, and potential side effects. Drugs such as pentamidine or ergotamine have systemic effects that are best achieved if they can be delivered into the alveolar region of the lung, with minimum deposition in other regions. Thus it may be possible to obtain optimal results with small quantities of drugs if spatial targeting puts the drug at exactly the right place in the lung, minimizing harm caused by side effects, and minimizing the use of a potentially expensive drug.</p>
<p>Task Progress:</p>	<p>There are three major tasks. Progress under each is described below</p> <p>1. Use human models to assess deposition patterns.</p> <p>The human studies, which are an extension of previous studies in microgravity performed by us, are ready to fly on the Microgravity Research Aircraft. Actual flight has been delayed by non-availability of the aircraft. First flight is scheduled for mid-June 2006, and will include both total and regional deposition studies in lunar gravity</p> <p>2. Develop rat models to assess deposition patterns that can subsequently be used to directly assess lung damage.</p> <p>As part of the flights scheduled for mid-June an engineering evaluation of the rodent aerosol exposure system will be performed. This system has been developed based on laboratory systems modified for flight and numerous aspects require testing in the flight environment prior to actual rodent flight. As such several key design decisions have been delayed pending engineering evaluation. It is anticipated that flight availability will increase in the next FY and as such the delays experienced this year can be readily compensated for. In parallel we have been developing and refining our high resolution imaging capability in mouse and rat lungs, with a paper recently submitted for publication in this area with Dr Scadeng.</p>

	<p>3. Develop more comprehensive computational models of aerosol deposition under fractional-G consistent with these data.</p> <p>A new workstation dedicated to the computational simulations has been purchased and equipped with Computational Fluid Dynamics software allowing for aerosol transport simulations in the conducting airways as well as in the alveolar region of the lung. In this first year, simulations have focused on the human lung. Flow patterns have been computed in both the conducting airways and a model of a portion of the human acinus for the same breathing conditions as those that will be used in the experimental human studies to be carried during parabolic flights in June 2006. Aerosol transport and deposition in the three-dimensional model of conducting airways have also been simulated both in a microgravity and normal gravity, these gravitational environments representing a lower and upper bound to lunar and Martian gravity. Simulations of aerosol transport in lunar gravity are now being performed.</p>
Bibliography Type:	Description: (Last Updated: 03/11/2021)
Articles in Peer-reviewed Journals	Scadeng M, Rossiter HB, Dubowitz DJ, Breen EC. "High-resolution three-dimensional magnetic resonance imaging of mouse lung in situ." Investigative Radiology. in press, June 2006. , Jun-2006