Fiscal Year:	FY 2009	**Task Last Updated:**	FY 12/09/2009
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Project Title:	Aerosol Deposition in the Lung in Fractional Gravity: Risk Mitigation for Lunar and Martian Habitats		
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 In-Mission Health and Performance Effects and Long-Term Health Effects Due to Celestial Dust Exposure		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	92093-0852	**Congressional District:**	53
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2004 NSBRI NNH04ZUU003N Human Health in Space
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: Change in end date to 9/30/2009 (from 6/30/2009) per N. Gibbins/NSBRI (5/2009) NOTE: Team changed as of 5/1/08 (formerly was Technology Development Team) per NSBRI (6/18/08)		
Key Personnel Changes/Previous PI:			
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Task Description:

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.
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, with its huge exposed surface area is highly vulnerable to adverse effects resulting from exposure to Mars and Moon dust.

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. We will address the following hypotheses and objectives:

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.

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.

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 and predict aerosol deposition under conditions matching those of the experiments performed in rats. At the completion of the final year of this project we have successfully completed all 3 of the specific aims with some publications still forthcoming.

In the area of human studies of aerosol deposition in fractional gravity (SA #1) an important publication has now appeared in the European Journal of Applied Physiology. These studies showed that while deposition was reduced in fractional (lunar) gravity, that deposition which did occur was much more peripheral in the lung, with likely attendant increases in clearance time. The implications of this finding are that exposure models used for a lunar outpost cannot utilize terrestrial models. In parallel but related ground studies, we showed that breathing a reduced-density gas (in this case heliox), results in more peripheral deposition of particles. This publication has now appeared in the Journal of Aerosol Medicine. As the plans for the lunar outpost habitat are refined this has become a new and important point, as the current atmosphere design calls for a significantly lower density than sea-level air. Based on these studies, in February 2009 we flew an additional (previously unplanned study) on the Microgravity Research Aircraft. This extra set of flights was made possible by our previously more efficient use of aircraft time. In these studies we examined the regional deposition of particles under the combined influence of reduced gravity, and a reduced gas density mimicking for the first time, the lunar habitat environment with high fidelity. These extra studies are still under analysis and will be the subject of a future publication.

For the studies of deposition in rat lungs (SA #2), we flew the rat equipment in July 2008 and in September 2008. The last week of flights was cut short because of Hurricane Ike. Since then, we have not been able to complete our data collection aboard the NASA Reduced Gravity aircraft due to unavailability of flights. As a consequence, while the study of two particle sizes was planned in the original proposal, only one particle size (1 μm) was used in the experiment. Deposition in the rat lungs was assessed by magnetic resonance imaging (MRI). Preliminary MRI results from parabolic flights as well as from ground data have made two abstract presentations, one at the conference of the International Society for Aerosols in Medicine for the flight data, and the second at the International Conference of the American Thoracic Society focusing on the ground data. Future full-length publications are in development.

In the latest year, we have focused on modeling aerosol transport in the alveolar zone of the human lung (SA #3). We have developed models of up to four generations of bifurcating fully alveolated ducts. These models allow for the expansion and contraction of the airspaces during breathing and show that, even in the absence of gravity, substantial amounts of particles deposit in the alveolar cavities. Preliminary data have made an abstract poster presentation at the International Conference of the American Thoracic Society. These results are now being compiled in a manuscript. Leveraging off the NIH funding of Dr. Darquenne we have expanded the validation of our CFD models to both the flow and particle transport predictions. These results have been presented in a poster at the annual fall meeting of the Biomedical Engineering Society and also compiled in a paper published in the Journal of Aerosol Science.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

The Earth-based applications for this research fall into two areas:
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.

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.
Task Progress:	There are three major tasks. Progress under each is described below: 1. Use human models to assess deposition patterns. All planned data collection is complete in lunar gravity and results currently In Press. No data were able to be collected in Martian gravity, but the results collected suggest a largely linear response to gravity, allowing adequate extrapolation to this condition. Results show that earth-based deposition models are inappropriate for use in the lunar environment. A ground study using a reduced density carrier gas (comparable in density to that in the planned lunar habitat) also moves deposition to a more peripheral site. Based on this we investigated the effects of both reduced gravity and a low-density carrier gas to better assess deposition likely in a lunar outpost in a series of "extra" flights made possible by our more efficient use of reduced gravity flight time than initially anticipated. 2. Develop rat models to assess deposition patterns that can subsequently be used to directly assess lung damage. We have now constructed and successfully flown the multi-animal exposure system to be flown in the Reduced Gravity Aircraft. Flights were performed in June 2008 and Sept 2008, although the latter were curtailed due to Hurricane Ike. NASA has been subsequently unable to accommodate this experiment and with the concurrence of NSBRI we have curtailed the scope of this aim to studying only 1-micron particles. As a part of the ground-testing we have been refining our MRI techniques for lung imaging of particulate-laden lungs, and data analysis is ongoing with the excised and preserved rat lungs from flight. 3. Develop more comprehensive computational models of aerosol deposition under fractional-G consistent with these data. Comprehensive studies of aerosol transport in the conducting airways of the human lung have been conducted showing a strong dependence of aerosol transport on convective flow, a useful result in that ground based simulations and studies will be adequate for predicting the transport of aerosol to the periphery of the lung (although based on SA #1, the same cannot be said for peripheral deposition). Leveraging off Dr. Darquenne's NIH funded work, collaborators at the von Karman Institute (VKI) have developed a model of an alveolated bend casted in silicon that can be seen as "half" a bifurcation. In parallel, a computational model was developed at UCSD with the same geometric characteristics as that developed for the experimental study. A more complex multi-bifurcation model with three successive generations of alveolated ducts is being studied both in a physical and an in-silico model. A model of 4 generations of bifurcating alveolar ducts with moving-walls has been developed and shows the important result that even in the absence of gravity, substantial amounts of particles deposit in the alveolar cavities as a direct consequence of wall motion.
Bibliography Type:	Description: (Last Updated: 03/11/2021)
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Significant Media Coverage	Burton A. "Article, 'Lunar lung disease,' about the hazards of lunar dust in respected publications; Dr. Prisk was quoted." Environmental Health Perspectives, 2008 Oct;116(10):A423. PMID: 18941555 , Oct-2008