Fiscal Year:	FY 2008	**Task Last Updated:**	FY 08/26/2008
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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
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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:			
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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, 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:

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.

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.

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.

Nearing the completion of year 3 of this project we have flown the human studies aboard the NASA Reduced Gravity Aircraft in lunar gravity and the results have been presented as a publication now In Press 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. 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. These results are documented in a publication In Press in the Journal of Aerosol Medicine.

In the latest year we have built and successfully tested the flight system for 4 rats. However due to unavailability of the NASA Reduced Gravity Aircraft in the last quarter flights have not yet occurred and have been delayed to the first quarter of Year 4 of the project. As part of the testing activities we have been refining the MRI techniques for measuring deposition and have made two abstract presentations of these results, on at the International Society for Magnetic Resonance in Medicine focusing on detection of particulates, and the second at the International Conference of the American Thoracic Society focusing on the airway morphometry of the rat derived from MRI. CFD modeling (SA #3) has progressed and we have shown that adequate transport estimates for particles can be made based on convective flow patterns, a result which greatly simplifies modeling in the central airways, as convective flow patterns are largely independent of gravity level. These results were also presented late last year in abstract form at the International Conference of the American Thoracic Society. Leveraging off the NIH funding of Dr. Darquenne we have shown that our CFD models are fully-valid in a bifurcating alveolated duct system by comparing those results with results from a physical model using particle imaging velocimetry (PIV).

In the upcoming year we plan the flights of the rat plehysmograph system with aerosol exposure in low gravity. The human studies will be expanded to examine synergistic effects of low gravity and low-density gas on aerosol deposition, a new factor previously not appreciated.

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. Ground studies 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 now plan to directly investigate the effects of both reduced gravity and a low-density carrier gas to better assess deposition likely in a lunar outpost. 2. Develop rat models to assess deposition patterns that can subsequently be used to directly assess lung damage. We have now constructed and successfully ground-tested the multi-animal exposure system to be flown in the Reduced Gravity Aircraft. We had planned to fly this in the second quarter of CY-2008, but NASA was unable to provide us with access to the Reduced Gravity Aircraft. As a consequence these flights are now in the process of being scheduled for the third quarter of CY-2008. All necessary approval paperwork has been submitted and we are essentially ready to fly. As a part of the ground-testing we have been refining our MRI techniques for lung imaging of particulate-laden lungs. 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, the latter being a directly relevant model for the studies performed here.
Bibliography Type:	Description: (Last Updated: 03/11/2021)
Articles in Peer-reviewed Journals	Peterson JB, Prisk GK, Darquenne C. "Aerosol deposition in the human lung periphery is increased by reduced-density gas breathing." Journal of Aerosol Medicine. In press, 2008. , Jun-2008