Fiscal Year:	FY 2007	**Task Last Updated:**	FY 08/03/2006
PI Name:	Burma, Sandeep Ph.D.		
Project Title:	Molecular and Cellular Effects of Heavy Ion Fragmentation due to Shielding		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation Biology		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **ARS**:Risk of Acute Radiation Syndromes Due to Solar Particle Events (SPEs) (2) **Cancer**:Risk of Radiation Carcinogenesis (3) **CNS**:Risk of Acute (In-flight) and Late Central Nervous System Effects from Radiation Exposure (4) **Degen**:Risk of Cardiovascular Disease and Other Degenerative Tissue Effects From Radiation Exposure and Secondary Spaceflight Stressors		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	burma@uthscsa.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	210-450-8981
Organization Name:	University of Texas Health San Antonio		
PI Address 1:	Department of Neurosurgery, Department of Biochemistry and Structural Biology		
PI Address 2:	7703 Floyd Curl Drive, MC7843, Room 102F		
PI Web Page:			
City:	San Antonio	**State:**	TX
Zip Code:	78229	**Congressional District:**	21
Comments:	NOTE: Formerly at University of Texas Southwestern Medical Center at Dallas until fall 2019.		
Project Type:	Ground	**Solicitation / Funding Source:**	2004 Radiation Biology NNH04ZUU005N
Start Date:	10/01/2005	**End Date:**	09/30/2009
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA ARC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: Changed Division and Discipline/Program to HRP as of FY2006, per program changes at that time, per JSC/A. Chu-ARC (jvp 4/2009)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	NNA05CS97G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Galactic cosmic rays (GCRs) represent a major risk to human crews on long-term missions outside the Earth's magnetic field. The GCR consists of protons, helium nuclei and HZE (High Z and Energy) particles such as iron. Understanding the radiobiology HZE particles is of enormous interest as the energy of these particles can be sufficient in many cases to penetrate the spacecraft hull and interior materials. While traversing through matter, high energy radiation fragments into a large number of secondary particles with generally lower energy but with higher ranges and biological effects than the incident cosmic rays. Therefore, an exact knowledge of the biological effects of shielding is important not only for understanding the risks to humans on space flights but also for determining optimal shielding for space crafts. Previous studies have used relatively late end points such as chromosome aberrations and cells survival to elucidate the biological consequences of fragmentation due to shielding. The early response of a mammalian cell to ionizing radiation has recently been very clearly elucidated at the molecular level in the context of the relocation and modification of damage-responsive factors and these very early events have a very important bearing on the repair of DNA damage and the ultimate fate of the cell. In this proposal we aim to study the biological effects of shielding using these pertinent early molecular responses as end points. Specific Aims are: 1) To test the hypothesis that shielded heavy ions may result in more complex DNA damage to the cells as compared to unshielded heavy ions, 2) To test the hypothesis that the molecular response to shielded radiation is different from that induced by unshielded radiation, and 3) To test the hypothesis that shielded radiation may have more deleterious effects on the cell as compared to unshielded radiation and to elucidate the mechanisms involved in repair of DNA damage. Preliminary studies carried out during the first experimental run at Brookhaven National Laboratory (NSRL-6A) indicate that significant differences exist between DNA damage caused by unshielded Fe particles versus particles that have passed through different shielding materials. Future studies will be aimed at elucidating the molecular and cellular consequences of HZE-induced DNA damage of differing complexities.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Galactic cosmic rays (GCRs) represent a major risk to human crews on long-term missions outside the Earth's magnetic field. The GCR consists of protons, helium nuclei and HZE (High Z and Energy) particles such as iron ions. Understanding the radiobiology of HZE particles is of enormous interest as the energy of these particles can be sufficient in many cases to penetrate the spacecraft hull and interior materials. While traversing through matter, HZE particles fragment into a large number of secondary particles with generally lower energy but with higher ranges and biological effects than the incident cosmic rays. Therefore, an exact knowledge of the biological effects of shielding is important not only for understanding the risks to humans on space flights but also for determining optimal shielding for space crafts. Previous studies have used relatively late end points such as chromosome aberrations and cells survival to elucidate the biological consequences of fragmentation due to shielding. The early response of a mammalian cell to ionizing radiation has recently been very clearly elucidated at the molecular level especially, the relocation and modification of damage-responsive factors at DNA-damage sites and these very early events have a very important bearing on the repair of DNA damage and the ultimate fate of the cell. In this proposal, we are studying the biological effects of shielding using these pertinent early molecular responses as end points. With these approaches, we can not only verify the immediate biological effects of beam fragmentation through shielding but can also estimate the efficacy of shielding materials.
Task Progress:	Summary of progress. Preliminary studies carried out during the first two experimental runs at Brookhaven National Laboratory (NSRL-6A and 6B) indicate that significant differences exist between DNA damage caused by unshielded Fe particles versus particles that have passed through different shielding materials. Future studies will be aimed at elucidating the molecular and cellular consequences of HZE-induced DNA damage of differing complexities. We have used two early DNA damage-response proteins (H2AX and 53BP1) to 3D model DNA damage induced by 1 GeV Fe particles after traversal through space shielding materials and to quantify its repair. With these approaches, we can not only verify the immediate biological effects of beam fragmentation through shielding but can also estimate the efficacy of shielding materials. Detailed progress: 1. DNA damage induced by Fe particles in comparison to gamma-rays. As a first step we have sought to establish the extent of DNA damage induced by 1 GeV Fe and to compare this with damage induced by gamma rays. We chose to irradiate primary, early passage human skin fibroblasts (HSFs) as these cells exhibit very low levels of background DNA double-strand breaks (DSBs). To examine the induction of DSBs and its repair we used two early DNA damage response proteins as end points: gamma-H2AX (the phosphorylated version of histone H2AX, modified specifically at the sites of DSBs) and p53BP1 (the DNA-damage signaling protein that is recruited specifically to DSBs). We immunofluorescence (IF) stained HSF cells irradiated with gamma-rays or with 1 GeV Fe ions. The damage induced was visualized by laser confocal scanning microscopy of irradiated cells co-immunostained with antibodies to H2AX (red) and BP1 (green). While X-rays resulted in discrete but diffuse DSBs, Fe particles resulted in tracks of DNA damage presumably corresponding to the path of particle traversal. 2. 3D reconstruction of DNA damage induced by Fe particles compared to gamma-rays. Optical slices (Z-stacks) taken of these images were reconstructed to generate 3D images of the DNA damage-tracks. The extensive nature of DNA damage induced by Fe particles, as compared to X-rays, is clearly evident from these reconstructions. 3. Detection of fragmentation of Fe particles through shielding material. In collaboration with Dr. Jack Miller (Lawrence Berkeley National Laboratory), we are comparing the two consequences of traversal of Fe particles through shielding material – 1) fragmentation into smaller particles with generally less deleterious effects than the parent ion and 2) retardation of an unfragmented particle through matter resulting in more deleterious particles with higher LET (linear energy tranfer). In preliminary studies, we used two shielding materials: 1) 3 cm Pb (which retarded the incident Fe ion increasing its LET from 150 keV/micron to approximately 200 keV/micron and 2) 19 cm polyethylene (PE) (which fragmented the majority of incident ions into smaller particles; the unfragmented minority had an LET of 200 keV/micron). 4. Visualization of the effects of traversal of Fe particles through shielding material. We sought to visualize DNA damage induced by Fe particles that have traversed through these shielding materials and to use these end points to

estimate the efficacy of space shielding materials. 3D images clearly indicate that while Pb exacerbates the DNA damage induced by Fe, PE results in the fragmentation of the incident ion into smaller particles as evident by the replacement of discrete DNA-damage tracks with diffuse DNA damage. 5. Repair of DNA damage induced by Fe particles after traversal through shielding materials. Based upon our 3D models of DNA damage and beam fragmentation studies, we concluded that beam fragmentation through PE may alleviate the effects of Fe particle irradiation. Thus, we hypothesized that PE may be a better shielding material as compared to Aluminum (the existing shielding material in space crafts and space stations). We attempted to verify this by quantifying the kinetics of DNA damage induced by Fe particles after traversal through shielding materials (using the dissolution of H2AX and 53BP1 foci as end points). Indeed, we find that DNA damage induced by Fe particles is more deleterious to the cell as a large fraction of this damage is unrepaired (in contrast to X-ray induced damage) even at 24h. While 3 cm Al shielding has no beneficial effects, PE shielding results in apparently less complex DNA damage taht is repaired with faster kinetics by the cells with less residual DNA damage at 24hrs. These results confirm the efficacy of PE shielding and affirm that these end points can be successfully used to evaluate the efficacy of futuristic shielding materials.

Future plans. The immediate future goal is to examine if the observed (beneficial) effects of PE shielding is due to fragmentation into smaller particles with lower Z and into protons. For this purpose we will quantify and model DNA damage induced by particles with lower Z than Fe (such as chlorine) and by protons to see if the damage induced is less complex and easily repairable. Data from protons obtained during the last run are currently being evaluated and future experiments will involve chlorine and other ions with lower Z. The long term goal would be evaluate the contribution of Fe particles with or without shielding to carcinogenesis using models currently being developed in my laboratory.

Bibliography Type:	Description: (Last Updated: 06/24/2025)