Fiscal Year:	FY 2007	**Task Last Updated:**	FY 01/04/2008
PI Name:	Cucinotta, Francis A Ph.D.		
Project Title:	Space Radiation Risk Assessment		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:		**TechPort:**	Yes
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) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (3) **Cancer**:Risk of Radiation Carcinogenesis (4) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes (5) **CNS**:Risk of Acute (In-flight) and Late Central Nervous System Effects from Radiation Exposure (6) **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		
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Zip Code:	89154-3037	**Congressional District:**	1
Comments:	Formerly at NASA Johnson Space Center, until summer 2013 (Ed., Oct 2013)		
Project Type:	GROUND	**Solicitation / Funding Source:**	Directed Research
Start Date:	06/01/2006	**End Date:**	05/31/2011
No. of Post Docs:	3	**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:		**Monitoring Center:**	NASA JSC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Pluth, Janice (LBNL) Cornforth, Michael (U TX Medical Branch) George, Kerry (Wyle Labs) Ponomarev, Artem (USRA) Nikjoo, Hooshang (USRA) Huff, Janice (USRA) Kim, Myung-Hee (USRA) Qualles, Garry (NASA Langley) Clowdsley, Martha (NASA Langley)		
Grant/Contract No.:			

Performance Goal No.:	
Performance Goal Text:	
Task Description:	The Risk Assessment Project at Johnson Space Center is responsible for the integration of results from NASA space radiobiology research into computational models used for astronaut radiation risk assessments. The purpose of the Project is fourfold: (1) evaluate the extent to which ongoing research leads to reduction in the uncertainty of risk assessments and provide, as a metric of program progress, the number of days in space during which the radiation exposure of astronauts remains below NASA limits within a 95% confidence interval ("safe days in space"); (2) perform mission planning studies to predict the number of safe days for any mission; (3) assess the radiation risk to astronauts for ongoing missions in real time; and, (4) provide recommendations for research directions most likely to reduce risk or improve the accuracy of risk predictions. The four categories of risks from radiation in space are defined by the NASA Bioastronautics Roadmap (BR). They are: 1) Carcinogenesis, 2) Acute and late effects to the Central Nervous System (CNS), 3) Degenerative Tissue Effects such as heart disease and cataracts, and 4) Acute Radiation risks. The number of safe days currently predicted for an astronaut's career is less than required by mission planning, due to the large uncertainties in risk prediction. In particular, a projection uncertainty below + or - 50% is the goal for the 1000-day Mars mission because the high level of risk will require high precision risk evaluations. The current approach used to project risk is based on epidemiology data and on phenomenological models used to derive risk prediction from them. This approach cannot lead to improvements in the accuracy of risk prediction beyond a factor of approximately 2. New approaches using molecular biology and genetics are the only viable ones for achieving the level of accuracy required by space exploration and a robust program to obtain the required data is supported by the Space Radiation Program. However, how to incorporate these data into risk prediction and assessment models is not well understood. This Project Plan describes the approaches that will be used to develop models of risk assessment based on mechanistic space radiobiology research funded by the Space Radiation Program, leading to incremental uncertainty reduction based on new experimental data, and to the development of application software to be used in the NASA operational radiation protection program. To accomplish these goals, we will establish new molecular based models of risk. The molecular pathways that are the hallmarks of genomic instability and cancer, and the perturbation of these pathways by radiation will be described using systems biology approaches and Monte-Carlo simulation. We will develop descriptive models of such pathways utilizing track structure models of biomolecular damage, and deterministic and stochastic kinetic models of dominant molecular pathways causative of BR radiation risks. These simulations will make maximum use of results from mechanistic space radiobiology, and will replace traditional hazard functions and their inherent uncertainties due to reliance on epidemiological or phenomenological approaches.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Radiobiology research provides many important qualitative descriptions of biological effects of radiation on biomolecules, cells, and tissues. The Space Radiation Risk Assessment Project provides an important link that integrates qualitative experimental observations into detailed quantitative biophysical models of radiations risks. This research benefits all humans that will be exposed to ionizing radiation. Models of cancer, acute and other risks developed by the Space Radiation Risk Assessment Project provide NASA with the ability to project risks and develop cost-effective mitigation approaches for future exploration missions.
Task Progress:	The NASA cancer risk projection model was updated with new excess relative risks and excess additive risk coefficients recommended by the BEIR VII report and in recent publications from the RERF in Hiroshima. The age at exposure dependence of cancer risks is a critical factor in these newer models, and displays a much slower change with age than the models described in NCRP Report No. 132. A cancer incidence data base was developed and a publication is in preparation. Uncertainty analysis for the new Dose and dose-rate reduction effectiveness factors (DDREF) and age dependence of cancer risks are being updated for the NASA model. Progress was made in developing systems biology models of the double strand break repair (DSB). In mammalian cells there are two mechanisms of DNA double strand break repair: Non-homologous end-joining (NHEJ) and homologous recombination (HR). The error-prone NHEJ is the main mechanism in resting cells and the G1 phase of the cell cycle. A systems biology model (Cucinotta et al., in press) of the NHEJ pathway was developed and used to make quantitative descriptions of the gamma-H2AX foci and DSB rejoining experiments. The model includes a kinetics description of several DNA repair proteins including the Ku70/80 hetero-dimer, the catalytic sub-unit of the DNA-PK repair complex denoted DNA-PKcs, and the Ligase-IV/XRCC4 complex. The regulation of DNA-PKcs by autophosphorylation for simple and complex DSB was described. The model is being extended to consider the radiation quality dependence of the relative fraction of simple and complex DSB, rejoining and associated repair defects, and the kinetics of various radiation induced foci (RIF). In further work, the addition of ATM and the MRN complex to the model was achieved and the role of processing of damaged ends by the Artemis and WRN proteins are being modeled For biophysical understanding of sub-tissue structures a description of cell size and shape, and geometry of multiple cell lineages is needed. A "tissue box" model (Ponomarev and Cucinotta, 2006) was developed to represent heterogeneous tissue architecture and to score HZE tracks and nuclear reactions in 2D and 3D tissues. Accurate segmentation of imaging data from 2D or 3D from a variety of imaging methodologies is possible. The tissue box model will be applied to represent experimental models used by SRP funded investigators. Nuclear reactions were shown to be rare in a small tissue sample (<100 cubic-micron), however the possibility of a large imparted dose at such sites is a continuing concern. A random walk polymer model of whole chromosomes was extended to include description of all human chromosomes within a typical cellular volume and to predict the role of DNA loops and attachment points on the spatial distributions of DSB (Ponomarev and Cucinotta, 2006) To overcome the background DSB inherent in experimental methodologies a subtraction technique was formulated and applied to several data sets in collaboration with the Tufts U. NSCOR (PI. L. Hlatky) (Ponomarev et al., 2007). Also these models were used in an imaging approach to study DNA repair foci (Costes et al., 2007) in collaboration with the LBNL NSCOR (PI. M. Barcellos-Hoff). A more detailed model of DNA damage and mutation using Monte-Carlo scoring of energy deposition in atomistic models of DNA and chromosomes is also under development (Nikjoo et al. 2007). Work on the transmission of specific chromosomal aberrations in subsequent cell cycles was initiated using basic

	cytogenetic theories. A modeling project to predict the initial yield of terminal and interstitial deletions was begun. Differences between normal cells and specific DNA repair defects are also under study and the role of longer times for open breaks in ATM and MRN deficient cells will be studied to consider the increases in overall and specific types of aberrations and the potential impacts on transmission frequencies. New statistical models of the probability of SPE frequency and size were developed using our data base of historical SPE and solar cycles (Kim et al., 2006, 2007). The model was extended back to the 15th century for the >30 MeV proton fluences using ice-core data on nitrate concentrations normalized to modern events as reported by McCracken and collaborators. The time dependence of dose-rate for the 30 largest SPE's was also evaluated. These studies indicate that acute radiation risks will only occur with a realistic probability under EVA conditions, and therefore the focus of acute risk models should be on the so-called prodromal risks (nausea, vomiting, fatigue, etc.) that may occur during EVA in deep-space or on the lunar surface. The DoD based, RIPD model was adapted for a description of risks from SPE. A computer code of the model was developed ab-initio at JSC. This model uses a logistic scale to assign performance degradation probabilities and time-courses for the acute risks. Using the BRYNTRN code and initial estimates of RBEs from the scientific literature, application of the model to the 1972 SPE for EVA conditions was made. (Hu et al., 2007 and in preparation). Work in collaboration with Dr. Smirnova of Moscow State U. was begun to study the probabilities of mortality from one or more, large SPE's, including the role of an adaptive response due to simulation of granulocytes by a first SPE, leading to protection against a second SPE within the ensuing next few months.

Bibliography Type:	Description: (Last Updated: 02/11/2021)
Articles in Peer-reviewed Journals	Cucinotta FA, Durante M. "Cancer risk from exposure to galactic cosmic rays: implications for space exploration by human beings." Lancet Oncol. 2006 May;7(5):431-5. PMID: 16648048 , May-2006
Articles in Peer-reviewed Journals	Ponomarev AL, Cucinotta FA. "Chromatin loops are responsible for higher counts of small DNA fragments induced by high-LET radiation, while chromosomal domains do not affect the fragment sizes." Int J Radiat Biol. 2006 Apr;82(4):293-305. PMID: 16690597 , Apr-2006
Articles in Peer-reviewed Journals	Kim M-HY, George KA, Cucinotta FA. "Evaluation of skin cancer risks from lunar and Mars missions. " Advances in Space Research 2006;37(9):1798-803. http://dx.doi.org/10.1016/j.asr.2006.03.032 , Aug-2006
Articles in Peer-reviewed Journals	Cucinotta FA, Kim M-HY, Ren L. "Evaluating shielding effectiveness for reducing space radiation cancer risks." Radiation Measurements 2006 Oct-Nov;41(9-10):1173-85. http://dx.doi.org/10.1016/j.radmeas.2006.03.011 , Nov-2006
Articles in Peer-reviewed Journals	Cucinotta FA, Wilson JW, Saganti P, Hu X, Kim M-HY, Cleghorn T, Zeitlin C, Tripathi RK. "Isotopic dependence of GCR fluence behind shielding." Radiation Measurements 2006 Oct-Nov;41(9-10):1235-49. http://dx.doi.org/10.1016/j.radmeas.2006.03.012 , Nov-2006
Articles in Peer-reviewed Journals	Ponomarev AL, Belli M, Hahnfeldt PJ, Hlatky L, Sachs RK, Cucinotta FA. "A robust procedure for removing background damage in assays of radiation-induced DNA fragment distributions." Radiat Res. 2006 Dec;166(6):908-16. PMID: 17149980 , Dec-2006
Articles in Peer-reviewed Journals	Cucinotta FA, Kim MH, Schneider SI, Hassler DM. "Description of light ion production cross sections and fluxes on the Mars surface using the QMSFRG model." Radiat Environ Biophys. 2007 Jun;46(2):101-6. PMID: 17342547 , Jun-2007
Articles in Peer-reviewed Journals	George K, Cucinotta FA. "The influence of shielding on the biological effectiveness of accelerated particles for the induction of chromosome damage." Advances in Space Research, 2007;39(6):1076-81. http://dx.doi.org/10.1016/j.asr.2007.01.004 , Aug-2007
Articles in Peer-reviewed Journals	Costes SV, Ponomarev A, Chen JL, Nguyen D, Cucinotta FA, Barcellos-Hoff MH. "Image-based modeling reveals dynamic redistribution of DNA damage into nuclear sub-domains." PLoS Comput Biol. 2007 Aug;3(8):e155. PMID: 17676951 , Aug-2007
Articles in Peer-reviewed Journals	Kim MH, Cucinotta FA, Wilson JW. "A temporal forecast of radiation environments for future space exploration missions." Radiat Environ Biophys. 2007 Jun;46(2):95-100. PMID: 17165049 , Jun-2007
Articles in Peer-reviewed Journals	Kim M-HY, Cucinotta FA, Wilson JW. "Mean occurrence frequency and temporal risk analysis of solar particle events." Radiation Measurements 2006 Oct-Nov;41(9-10):1115-22. http://dx.doi.org/10.1016/j.radmeas.2005.11.006 , Nov-2006
Articles in Peer-reviewed Journals	Ponomarev AL, Cucinotta FA. "Nuclear fragmentation and the number of particle tracks in tissue." Radiat Prot Dosimetry. 2006;122(1-4):354-61. PMID: 17261538 , Jul-2006
Articles in Peer-reviewed Journals	Nikjoo H, Uehara S, Emfietzoglou D, Cucinotta FA. "Track-structure codes in radiation research. A review." Radiation Measurements 2006 Oct-Nov;41(9-10):1052-74. http://dx.doi.org/10.1016/j.radmeas.2006.02.001 , Nov-2006