Fiscal Year:	FY 2009	**Task Last Updated:**	FY 12/30/2009
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		
PI Email:	not available	**Fax:**	FY
PI Organization Type:	NASA CENTER	**Phone:**	(702) 895-4320
Organization Name:	University of Nevada, Las Vegas		
PI Address 1:	Health Physics & Diagnostic Sciences / BHS-345		
PI Address 2:	4505 Maryland Parkway		
PI Web Page:			
City:	Las Vegas	**State:**	NV
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:	4	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**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:**	NASA JSC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	Dr. Deepa Sridharan joined the project as a Post-doc at LBNL. Dr Zarana Patel left the project from USRA in Houston		
COI Name (Institution):	Pluth, Janice (LBNL) Cornforth, Michael (U TX Medical Branch) Ponomarev, Artem (USRA) Kim, Myung-Hee (USRA) Qualles, Garry (NASA Langley) Carra, Claudio (USRA Division of Life Sciences)		
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 and supports the development of disease models in general. Models of cancer, CNS, heart disease, 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 translation of research findings into models of risks and their application to the discovery of new biological knowledge, space mission risk estimates, and exploration mission planning was achieved in several areas. In the period of performance a Graphical User Interface (GUI) for the Acute Radiation Risk Body Organ Dose (ARRBOD) model was developed and released as a Beta version. ARRBOD uses the BRYNTRN code to calculate organ doses from solar particle events (SPE) and to evaluate risk of prodromal effects. Efforts to integrate physics and biophysics models of space radiation into a collaborative modeling framework made great progress in the 3rd Year of performance. A stochastic physics model was developed to characterize particle beams and secondaries for experiments at the NASA Space Radiation Laboratory (NSRL). The resulting model called the GCR Event-Based Risk Model (GERMcode) is based on Monte-Carlo algorithms for forward-backward ion transport. This will allow for ray tracing techniques such as the ProE FISHBOWL tool to be seamlessly integrated into a future space version of the GERMcode. Excellent agreement between the GERMcode and NSRL data was found. A beta-version of the GERMcode GUI was released. Cancer risk model updates were completed including: comparison of the BEIR VII, UNSCEAR and NCRP models, development of new tissue weighting factors appropriate for astronauts, preliminary recommendations of new solid cancer and leukemia specific quality factors, and new developments of dose response models for non-targeted effects for heavy ion carcinogenesis. The non-targeted effects model suggest much higher cancer risks at low doses of heavy ions than the conventional model recommended by the NCRP. New probability distribution functions (PDF) to represent the uncertainties in new and existing data sets and knowledge of radiation quality effects, dose-rate modifiers, and the dependecies of risk on age at exposure are being considered from these analyses. Heart disease risk estimates were developed using a triple detriment approach based on US population data for coronary heart disease and stroke and recent meta-analysis of excess relative risks in exposed cohorts. Values of RBEs and dose-rate modifiers for heart disease are being investigated, and suggest a wide range of possibilities for the mortality risks from heart disease with results ranging from negligible to radiation cancer risks to approaching ½ of the cancer risk of males of above age 45 y at the time of exposure. A mathematical representation of the two-hit model of Alzheimer's disease was developed. The model can be used to estimate a shift in the age of appearance of Alzheimer's disease based on the number of neuronal cells with radiation induced hits. Systems biology model developments included new molecular dynamic calculations of the Ku70/80 protein, RecA, and preliminary results for the RPA and Smad protein interactions with DNA. Computational tools to assess DNA repair foci and flow cytometry data for signal transduction phospho-proteins were developed. New flow based assays for dually staining proteins, cell population kinetics and telomere shortening were considered. A stochastic model of ligand-receptor binding to model TGFbeta activation was developed using a Green's function approach. A non-linear model of granulocytopoiesis following acute or chronic irradiation was compared to experimental data for several mammalian species and extended to human exposures including blood level kinetics following exposures to solar particle events. A probabilistic approach to solar particle event organ dose evaluation and shielding design was developed. These models will form the basis for ARRBOD V2.0

Bibliography Type:	Description: (Last Updated: 02/11/2021)
Articles in Peer-reviewed Journals	Cucinotta FA, Kim MH, Willingham V, George KA. "Physical and biological organ dosimetry analysis for International Space Station Astronauts." Radiation Research 2008 Jul;170(1):127-38. http://dx.doi.org/10.1667/RR1330.1 ; PMID: 18582161 , Jul-2008
Articles in Peer-reviewed Journals	Ponomarev AL, Costes SV, Cucinotta FA. "Stochastic properties of radiation induced DSB: DSB distributions in large scale chromatin loops, the HPRT gene and within the visible volumes of DNA repair foci." International Journal of Radiation Biology 2008 Nov;84(11):916-29. http://dx.doi.org/10.1080/09553000802499212 ; PMID: 19016140 , Nov-2008
Articles in Peer-reviewed Journals	Plante I, Cucinotta FA. "Ionization and excitation cross sections for the interaction of HZE particles in liquid water and application to Monte-Carlo simulation of radiation tracks." New Journal of Physics 2008 Dec;10:125020 , 1367-74. https://inis.iaea.org/search/search.aspx?orig_q=RN:41004107 ; http://dx.doi.org/10.1088/1367-2630/10/12/125020 , Dec-2008
Articles in Peer-reviewed Journals	Reitz G, Berger T, Bilski P, Facius R, Hajek M, Petrov V, Puchalska M, Zhou D, Bossler J, Akatov Y, Shurshakov V, Olko P, Ptaszkiewicz M, Bergmann R, Fugger M, Vana N, Beaujean R, Burmeister S, Bartlett D, Hager L, Pálfalvi J, Szabó J, O'Sullivan D, Kitamura H, Uchihori Y, Yasuda N, Nagamatsu A, Tawara H, Benton E, Gaza R, McKeever S, Sawakuchi G, Yukihara E, Cucinotta F, Semones E, Zapp N, Miller J, Dettmann J. "Astronaut's organ doses inferred from measurements in a human phantom outside the International Space Station." Radiation Research 2009 Feb;171(2):225-35. http://dx.doi.org/10.1667/RR1559.1 ; PubMed PMID: 19267549 , Feb-2009
Articles in Peer-reviewed Journals	Valtonen V, Nurmi P, Zheng JQ, Cucinotta FA, Wilson JW, Horneck G, Lindegren L, Melosh J, Rickman H, Mileikowsky C. "Natural transfer of viable microbes in space from planets in extra-solar systems to a planet in our solar system and vice versa." Astrophysical Journal. 2009 Jan 1;690(1):210-5. https://arxiv.org/abs/0809.0378 , Jan-2009
Articles in Peer-reviewed Journals	Kim MH, Hayat MJ, Feiveson AH, Cucinotta FA. "Prediction of frequency and exposure level of solar particle events." Health Physics 2009 Jul;97(1):68-81. http://dx.doi.org/10.1097/01.HP.0000346799.65001.9c ; PubMed PMID: 19509510 , Jul-2009
Articles in Peer-reviewed Journals	Hu S, Kim MH, McClellan GE, Cucinotta FA. "Modeling the acute health effects of astronauts from exposure to large solar particle events" Health Physics 2009 Apr;96(4):465-76. http://dx.doi.org/10.1097/01.HP.0000339020.92837.61 ; PubMed PMID: 19276707 , Apr-2009
Articles in Peer-reviewed Journals	Kim MY, Hayat ML, Feiveson AH, Cucinotta FA. "Using high-energy proton fluence to improve risk prediction for consequences of solar particle events." Advances in Space Research 2009 Dec 15;44(12):1428-32. http://dx.doi.org/10.1016/j.asr.2009.07.028 , Dec-2009
Articles in Peer-reviewed Journals	Carra C, Cucinotta FA. "Binding sites of the E. Coli DNA recombinase protein to the ssDNA: a computational study." J Biomol Struct Dyn. 2010 Feb;27(4):407-28. PubMed PMID: 19916564 , Feb-2010
Articles in Peer-reviewed Journals	Plante I, Cucinotta FA. "Cross sections for the interactions of 1 eV–100 MeV electrons in liquid water and application to Monte-Carlo simulation of HZE radiation tracks." New Journal of Physics 2009 Jun;11(6):063047 , p. 1-24. https://inis.iaea.org/search/search.aspx?orig_q=RN:41041472 ; http://dx.doi.org/10.1088/1367-2630/11/6/063047 , Jun-2009
Articles in Peer-reviewed Journals	Chappell LJ, Whalen MK, Gurai S, Ponomarev A, Cucinotta FA, Pluth JM. "Analysis of flow cytometry DNA damage response protein activation kinetics after exposure to X rays and high-energy iron nuclei." Radiation Research. Submitted January 2010. , Jan-2010
Articles in Peer-reviewed Journals	Plante I, Cucinotta FA. "Energy deposition and relative frequency of hits of cylindrical nanovolume in medium irradiated by ions: Monte Carlo simulation of tracks structure." Radiat Environ Biophys. 2010 Mar;49(1):5-13. http://dx.doi.org/10.1007/s00411-009-0255-7 ; PMID: 19916014 (originally reported as 2009 Nov 15. [Epub ahead of print] in December 2009) , Mar-2010
Articles in Peer-reviewed Journals	Cucinotta FA, Chappell LJ. "Non-targeted effects and the dose response for heavy ion tumor induction." Mutation Research. In press, January 2010. , Jan-2010
Articles in Peer-reviewed Journals	Kim MH, Qualls GD, Slaba TC, Cucinotta FA. "Comparison of organ dose and dose equivalent for human phantoms of CAM vs. MAX." Advances in Space Research. In press, January 2010. , Jan-2010
Articles in Peer-reviewed Journals	Ponomarev AL, Huff J, Cucinotta FA. "The analysis of the densely populated patterns of radiation-induced foci by a stochastic, Monte Carlo model of DNA double-strand breaks induction by heavy ions." Int J Radiat Biol. Submitted, December 2009. , Dec-2009
Articles in Peer-reviewed Journals	Hu S, Cucinotta FA. "A cell kinetic model of granulopoiesis under radiation exposure: Extension from rodents to canines and humans." Radiation Protection Dosimetry. Submitted January 2010. , Jan-2010
NASA Technical Documents	Nounu HN, Kim MY, Ponomarev AL, Cucinotta FA. "The Use of Pro/ENGINEER CAD Software and Fishbowl Toolkit in Ray-tracing Analysis." Washington, DC : NASA, 2009. NASA technical paper ; 2009-214788. NASA TP-2009-214788 , Jun-2009