Fiscal Year:	FY 2020	**Task Last Updated:**	FY 03/20/2020
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Project Title:	Protracted Exposure to NASA's GCR-Simulator: Cytogenetic Validation and Beam Time Optimization		
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Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
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Human Research Program Risks:	(1) **Cancer**:Risk of Radiation Carcinogenesis		
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Zip Code:	77555-5302	**Congressional District:**	14
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA LaRC
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Flight Program:			
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Key Personnel Changes/Previous PI:			
COI Name (Institution):	Cornforth, Michael Ph.D. (University of Texas Medical Branch, Galveston)		
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Task Description:	Exposure to galactic cosmic rays (GCR) presents a health risk to astronauts on deep space missions. To study these risks, NASA is developing the GCR simulator that will be able to irradiate cell or animal samples with combinations of ions known to be present in GCR. This device will, by necessity, irradiate these samples at doses and dose rates considerably high than that found in space in order to produce statistically meaningful results. To produce the best simulations, dose rates and exposure sequences will need to be optimized. This proposal will endeavor to optimize these parameters by measuring the induction of chromosome aberrations. Most of these aberrations are exchanges of chromosomal segments that come about when radiation damage severs chromosomes. Normally, cells can repair these breaks, but on occasion, if two or more breaks are close to one another, a mistake can be made whereby the cell joins break ends to inappropriate partners causing an exchange of chromosomal segments. The damage forming these breaks is caused by ionizations along the paths (tracks) that ions take as they pass through a medium. While in some cases all the breaks necessary for an exchange to form occur along a single particle track, in other circumstances, breaks are formed along separate and independent tracks in a process referred to as track interaction. Track interaction events become important at higher doses when the number of tracks produce damage that is sufficiently close to interact increases. Track interactions are not likely to occur at the doses thought to be found in space but will certainly happen at the higher doses required for GCR simulations and potentially skew the results. One strategy to avoid track interactions is to lower the dose rate. By spacing out the time over which ions pass through a cell, breaks forming early in the time frame have an opportunity to be repaired before other breaks forming spatially close enough to interact with them arrive on the scene. This produces a reduction in the frequency of chromosome exchanges. As the dose rate decreases further a point is reached where virtually all the exchanges result from single track action. At this “limiting low dose rate” no additional reduction in chromosome exchange frequency is possible by further reduction in the dose rate. These results will be directly scalable to the low doses and dose rates present in space. Specific aim 1 of our proposal will endeavor to determine the limiting low dose rate for protons at the energy stated in the NRA (NASA Research Announcement). This will be accomplished by irradiating cells with a series of doses at dose rates we estimate will be close to the limiting low dose rate and looking for chromosome exchanges. When additional reduction in doses rate fails to produce any further decrease in exchanges as a function of dose we will be at the limiting low dose rate. The GCR simulator will be irradiating samples with a number of different ion beams in order to better simulate the nature of the mixed ion field found in space. The heavier ions in the GCR spectrum will behave differently from the lighter ions. The heavy ions produce more damage along their tracks--so much so that virtually all chromosome exchanges are formed via single track action. In this case we will need to determine the optimal time needed for repair to occur between irradiations with the subsequent ion beams to avoid track interaction. Specific aim 2 will address these concerns by varying the time between ion beams. Much like the dose rate experiments, as we extend the time between irradiations, the probability for track interaction should be reduced. Once we reach a level where no further chromosome exchange frequency reductions are observed, we will have reached the optimal point for irradiation delay. Sequence may also be important in that regard and additional experiment will search for the best sequence that minimizes track interaction.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our project will endeavor to help optimize exposure protocols for NASA's GCR simulator by determining the limiting low dose rate for chromosome aberration induction. This will allow investigators to optimize their experimental protocols in ways that will better simulate the low doses and dose rates found in the space radiation environment. These results may impact how low dose and dose rate experiments are conducted in the future and might provide better risk estimates for low radiation doses both in space and here on Earth.
Task Progress:	Astronauts on deep space missions will be exposed to galactic cosmic rays (GCR) that are composed of a collection of ions (atoms with their electron stripped away) traveling at speeds close to that of light. The types of ions involved and the speeds at which they travel are quite variable. Some, such as iron ions, are rather massive and these exist side by side with much smaller ions such as high energy (very fast moving) protons (hydrogen nuclei). As these ions encounter atoms, for example, inside a space ship or an astronaut’s body, they can pull off electrons from these atoms in a process known as ionization. Ionization events can ultimately produce chemical reactions that can damage vital structures within the cells of an astronaut such as DNA. This ionization damage can break DNA strands or in other ways eliminate important genetic information. Such changes can lead to mutation, cancer, or can even kill the cell. A key factor in nature and severity of the effects produced is the spacing of the ionizations along the path or track that the ion takes through a cell. This is dependent on the mass and charge (the number of positively charged protons making up the ion) of the particle as well as the speed at which the ion is traveling. This spacing we refer to as linear energy transfer (LET) or the amount of energy that is used to produce ionizations along a specific length of the ion’s track. Ionizations are spaced far apart with low LET radiation but become increasingly closer together as LET increases. A key concern to NASA is how dangerous is radiation to space flight crews. Most of the epidemiological data we have is from low LET radiations such as the X-rays used for radiation therapy or from the exposures received by the survivors the atomic bomb attacks in 1945. High LET data is harder to come by and derives largely from experiments using cells or animal model systems. These experiments use ground-based particle accelerators to accelerate ions to energies found in space and simulate potential space radiation exposures. Nearly all of this data come from experiments using a single ion at a solitary energy. As mentioned above, the space radiation environment is far more complex with many ions traveling with large ranges of energies all of which could impact an astronaut’s health, particularly since the probability of a cell in an astronaut’s body being hit sequentially by a small number of different ion species over a Mars mission lasting 600 to 900 days is quite high. In order to provide more realistic simulations of the space radiation environment, NASA is developing the GCR Simulator which has the potential to irradiate samples with multiple ion species within the shortest period of time allowed by ion switching, in order to mimic the effects of coincident (simultaneous) exposure. For the GCR simulator to best duplicate the natural space radiation environment, it is important to optimize dose delivery in ways that allow the results to be directly scalable to the low doses and dose rates that are encountered in deep space. It will be difficult to match the low doses and dose rates directly. From a practical sense higher doses will need to be used in order to obtain statistically meaningful results. Likewise, higher dose rates are also required as exposing samples over long periods of time is just not feasible. Classically, the dose problem has been resolved by exposing samples to a series of higher doses then extrapolating the results back to the doses of interest. Similarly, it has long been known that as the dose rate declines the yield of biological endpoints is also diminished. This diminishment, however, only occurs

to a point beyond which no additional decline in the dose response is detectable. The dose rate at which this point occurs has been termed the limiting low dose rate (LLDR). We plan to determine the LLDR for chromosome aberration induction by first measuring the dose response at high dose rate then using a mathematical model estimate the LLDR. The derived value for the LLDR will be tested in subsequent experiments. If we have achieved the LLDR the dose response will be strictly linear making extrapolations back to the conditions in the space radiation environment relatively straightforward. Future experiment will determine how best to fractionate the dose (deliver the dose in small increments with periods of time between each exposure) in a way that will achieve the same result as a continuous low dose rate exposure.

During the last year we were able conduct our high dose rate experiments which we will use to estimate the LLDR through use of the G-function. We irradiated both human lymphocytes (white blood cells) and fibroblasts (skin cells) with 1 GeV protons or 250 MeV/n Helium ions. We collected mitotic cells (cells undergoing mitosis when the chromosomes are visible) from these populations and analyzed them for the presence of chromosome aberrations. These were tabulated and dose responses were constructed. We then applied a mathematical model to these results and came up with estimates for the LLDR. Based on our model, we estimate the LLDR for protons will be about 0.01 cGy/min. As this rate is likely to be too low to deliver experimentally, we will be using a rate of 0.1 cGy/min for tests scheduled for May of 2020. Analysis of the Helium ion results is on-going, and we hope to have these completed soon.

Bibliography Type:	Description: (Last Updated: 10/29/2023)
Abstracts for Journals and Proceedings	Loucas BD, Cornforth MN. "Galactic cosmic ray simulator: Determining the limiting low dose rate." Presented at the 65th Annual Meeting of the Radiation Research Society, San Diego, CA, November 3-6, 2019. Conference Abstracts. 65th Annual Meeting of the Radiation Research Society, San Diego, CA, November 3-6, 2019. , Nov-2019
Abstracts for Journals and Proceedings	Loucas BD, Cornforth MN. "Predicting the limiting low dose rate for chromosomal exchanges from high dose rate data through the use of the G function." Presented at the 2020 NASA Human Research Program Investigators’ Workshop, Galveston, TX, January 27-30, 2020. Meeting Abstracts. 2020 NASA Human Research Program Investigators’ Workshop, Galveston, TX, January 27-30, 2020. , Jan-2020