Fiscal Year:	FY 2019	**Task Last Updated:**	FY 02/08/2019
PI Name:	Chung, Caroline M.D.		
Project Title:	Quantitative Imaging and Biofluid Biomarkers Predictive of Neurocognitive Toxicity from Brain Irradiation		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (2) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Houston	**State:**	TX
Zip Code:	77030	**Congressional District:**	9
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	03/15/2019	**End Date:**	03/14/2022
No. of Post Docs:		**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:	Simonsen, Lisa	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: Period of performance is now 3/15/2019-3/14/2022 per NSSC information since now goes through NSSC; original POP was 1/14/2019-1/13/2022 (Ed., 5/29/19)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Wefel, Jeffrey Ph.D. (Co-PI: University of Texas MD Anderson Cancer Center) Sulman, Erik M.D., Ph.D. (NYU Langone Health (formerly University of Texas MD Anderson Cancer Center))		
Grant/Contract No.:	80NSSC19K0659		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	NASA is concerned about the functional consequences of inflight acute exposure to space radiation and the probability of radiation exposure enhancing or accelerating late neurodegenerative conditions post-mission. This proposed research aims to acquire data on neurocognitive/behavioral impairments and associated biomarkers observed in patients who are undergoing cranial exposure to ionizing radiation with an emphasis on non-invasive imaging modalities and serum biomarkers to quantify predictive changes linked to acute and late neurocognitive impairment and radiation dose. This work will provide benchmark data on structural and functional changes in patients resulting from photon (X-ray) and proton exposures during radiotherapy of head and neck and intracranial neoplasms. Existing research data suggest that animals and humans may share similar pathophysiological mechanisms following brain radiation exposure that lead to adverse cognitive or behavioral conditions or the exacerbation or acceleration of late degenerative conditions. To establish thresholds of permissible exposure for effects on the central nervous system, it is crucial to understand scaling relationships between humans and animals. In the proposed research, the broader range in radiation dose exposure in a more neurocognitively vulnerable population will facilitate more rapid signal finding investigations of these biomarkers that can be further refined for subsequent investigation in astronauts. There is complementary overlap between this work and proposed directed work at MD Anderson involving radiation-induced cardiotoxicities that will tie in common pathways between CVD (cardiovascular) and CNS (central nervous system) decrements through the investigation of common biomarkers. The gaps Degen-2 and -3 and CNS-1, -2, and -6 involve identification of adverse outcome pathways, progression rates and latency periods, and early surrogate markers for radiation-induced cardiovascular/cerebrovascular disease and early and late CNS decrements. Research deliverables from this work will help close the above gaps and serve as quantifiable measures of response to guide countermeasure development and validation in animal studies with HZE (high energy) exposures. Results will also drive predictive model development (Degen-5 and CNS-5). Specific Aims: Aim 1: In patients receiving proton and photon radiotherapy involving radiation exposure to the brain, evaluate serial multidimensional, multimodal tests of neurocognitive function (clinical neurocognitive testing and digital testing including NASA Cognition, CogState C3), biofluid biomarkers (including markers associated with vascular dysfunction and cardiotoxicity following radiation exposure), and quantitative multiparametric magnetic resonance imaging data. Aim 2: Identify brain subregions vulnerable to radiation toxicity using quantitative multiparametric magnetic resonance images that are associated with changes in neurocognitive function and characterize changes in specific neurocognitive domains in relation to radiation dosimetry. Aim 3: Establish predictive models of neurocognitive decline integrating clinical characteristics, quantitative multiparametric magnetic resonance imaging parameters, and biofluid biomarkers pre- and post-irradiation.
Rationale for HRP Directed Research:	Highly constrained research. Time constraint: There is insufficient time for competitive solicitation through a NASA Research Announcement (NRA) due to the Degen Risk accelerated schedule and milestone delivery. The early results from this clinical pilot study will be used in the formulation of the FY22 CVD/CNS NASA Specialized Center of Research (NSCOR) solicitation which needs to be released in early FY21 in order to meet our PRR (Path to Risk Reduction) schedule (which has the studies selected from the FY22 NSCOR commencing at the beginning of FY22). This NSCOR feeds into the 2026 PRR milestone of “Identify Late CNS Countermeasures.” Research constraint: This work is also highly constrained research involving a pilot study with human radiotherapy cohorts and the advanced imaging expertise available at MD Anderson. In addition to the FY22 NSCOR, the findings from this pilot study are expected to inform future solicited animal studies. Retrospective studies are not possible because the biomarkers are newly identified and are not yet fully validated, which this study will help to do.
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2019.
Bibliography Type:	Description: (Last Updated: 08/07/2023)