Fiscal Year:	FY 2020	**Task Last Updated:**	FY 07/10/2020
PI Name:	Chung, Caroline M.D.		
Project Title:	Imaging and Serum Biomarkers to Predict and Identify Early Cardiac Injury from Radiation Exposure		
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) **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		
PI Email:	CChung3@mdanderson.org	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	713-745-5422
Organization Name:	University of Texas MD Anderson Cancer Center		
PI Address 1:	1515 Holcombe Blvd.		
PI Address 2:	Radiation Oncology and Diagnostic Imaging		
PI Web Page:			
City:	Houston	**State:**	TX
Zip Code:	77030	**Congressional District:**	9
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	08/23/2018	**End Date:**	08/22/2021
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:	Zawaski, Janice	**Contact Phone:**	
Contact Email:	janice.zawaski@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: Period of performance is now 8/23/2018-8/22/2021 per NSSC information since now the project goes through NSSC (Ed., 5/29/19)		
Key Personnel Changes/Previous PI:	June 2020 report: Added Dr. Junichi Abe as CoInvestigator (CoI) and removed Dr. Saumil Gandhi as CoI.		
COI Name (Institution):	Dabaja, Bouthaina M.D. (Co-PI: University of Texas MD Anderson Cancer Center) Lopez-Mattei, Juan M.D. (University of Texas MD Anderson Cancer Center) Swamique, Yusuf M.D. (University of Texas MD Anderson Cancer Center) Gladish, Gregory M.D. (University of Texas MD Anderson Cancer Center) Lin, Steven M.D., Ph.D. (Co-PI: University of Texas MD Anderson Cancer Center) Layman, Rick Ph.D. (University of Texas MD Anderson Cancer Center) Abe, Junichi M.D., Ph.D. (University of Texas MD Anderson Cancer Center)		
Grant/Contract No.:	80NSSC18K1639		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	[ED. NOTE November 2018: Principal investigator (PI) changed to Dr. Caroline Chung, from Dr. Sarah Milgrom, due to Dr. Milgrom's change in institution. Period of performance also revised to 8/23/2018-8/22/2021, due to PI change; original period of performance was 7/18/2018-9/30/2021.] Within the "Risk of Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation Exposure and Secondary Spaceflight Stressors," the gaps Degen-2 and -3 involve identification of adverse outcome pathways, progression rates and latency periods, and early surrogate markers for radiation-induced cardiovascular disease. To date, no tasks have included human radiotherapy cohorts to assess those parameters and identify biomarkers. The proposed work will acquire data on cardiovascular impairments and associated biomarkers observed in patients undergoing cardiac exposure to ionizing radiation with emphasis on non-invasive imaging modalities to quantify predictive changes linked to late impairment. Prompt identification of damage may enable interventions to prevent progression to cardiac dysfunction. Furthermore, study of cardiac changes that occur during and soon after radiotherapy would grant insight into the pathophysiology, which may lead to novel therapeutic interventions. The results may then be correlated with other studies performed in animals or in human cohorts with different types of radiation exposure such as astronauts. Research deliverables from this work will help close gaps Degen-2 and -3 as well as feed into countermeasure development and validation in animal studies with space radiation exposures. Results will also drive predictive model development (Degen-5). Specific Aims for the work include: 1) Assess for cardiac toxicity in patients treated with radiotherapy to the chest. 2) Assess for an association between 3D imaging findings suggestive of cardiac injury and radiation dosimetry. 3) Explore the association of radiation exposure with serum biomarker levels. Research Deliverables 1. Evaluation of MRI as noninvasive imaging modality for detection of early indicators of cardiotoxicity following radiotherapy, compared with electrocardiograms. 2. Evaluation of serum markers and other cardiovascular parameters for detection of early indicators of cardiotoxicity following radiotherapy.
Rationale for HRP Directed Research:	There is insufficient time for competitive solicitation through an NRA (NASA Research Announcement) due to Degen Risk accelerated schedule and milestone delivery. This work is also highly constrained research involving a pilot study with human radiotherapy cohorts and the advanced imaging expertise available at MD Anderson. 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:	Within the "Risk of Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation Exposure and Secondary Spaceflight Stressors," the gaps Degen-2 and -3 involve identification of adverse outcome pathways, progression rates and latency periods, and early surrogate markers for radiation-induced cardiovascular disease. To date, no tasks have included human radiotherapy (RT) cohorts to assess those parameters and identify biomarkers. The proposed work will acquire data on cardiovascular impairments and associated biomarkers observed in patients undergoing cardiac exposure to ionizing radiation with emphasis on non-invasive imaging modalities to quantify predictive changes linked to late impairment. Prompt identification of damage may enable interventions to prevent progression to cardiac dysfunction. Furthermore, study of cardiac changes that occur during and soon after RT would grant insight into the pathophysiology, which may lead to novel therapeutic interventions. The results may then be correlated with other studies performed in animals or in human cohorts, such as astronauts, with different types of radiation exposure. Research deliverables from this work will help close gaps Degen-2 and -3 as well as feed into countermeasure development and validation in animal studies with space radiation exposures. Results will also drive predictive model development (Degen-5). This study aims to identify early markers of cardiac injury after radiation exposure, at a time when steps could be taken to prevent progression to irreversible cardiac dysfunction. The results of this study may be correlated with other studies performed in animals or in human cohorts with different types of radiation exposure, such as astronauts during space travel, and the ultimate goal of our work is to develop agents that prevent cardiac toxicity through early detection and intervention.
	This research project aims to identify biomarkers produced when cardiovascular tissue is damaged by ionizing radiation. This study will examine subjects undergoing radiation therapy where their hearts are exposed to ionizing radiation. Non-invasive medical imaging will be used to identify changes in heart tissue that predict later impairment. Prompt identification of damage may allow interventions to prevent progression to cardiac dysfunction. Studying changes to heart tissue that happen during and after radiation therapy would grant insight into the pathophysiology, which may lead to new therapeutic interventions. These results could be correlated with studies performed on animals, or in human cohorts with different types of radiation exposure – such as astronauts. Research deliverables from this work will help close gaps Degen-2 and -3 as well as feed into countermeasure development and validation in animal studies with space radiation exposures. Results will also drive predictive model development (Degen-5). If early biomarkers of cardiac injury after radiation exposure can be identified, steps could be taken to prevent progression to irreversible cardiac dysfunction. The results of this study may be correlated with other studies performed in animals or in human cohorts with different types of radiation exposure, such as astronauts during space travel, and the ultimate goal of our work is to develop agents that prevent cardiac toxicity through early detection and intervention. Our overarching hypothesis is that changes in imaging and serum biomarkers will suggest early cardiac injury after radiation exposure and our specific aims are the following: Aim 1: Assess for cardiac toxicity in cancer patients treated with radiation therapy to the chest. We will assess for cardiac toxicity, looking at a reduction in heart fitness or elevation of damage markers in blood serum. Aim 2: Assess for an association between 3D imaging findings suggestive of cardiac injury and radiation exposure. We will perform side-by-side comparisons of 3D MRI studies and radiation treatment plans. We will map the relationship between regions of early cardiac injury and radiation dose delivered to these areas. These findings may identify threshold radiation doses for cardiac injury.

Task Progress:	Aim 3: Explore the association of radiation exposure with serum biomarker levels. We will collect blood samples from cancer patients receiving standard radiation therapy to the chest and analyse it at different time points for markers of heart tissue damage and inflammation. Approach : Cancer patients receiving radiation therapy will be enrolled in this study following their written informed consent. Their current cardiovascular health will be evaluated before their radiation treatment, during their final week of treatment, and six months after their treatment. Blood will be collected twice during treatment, and 3, 6, 12, and 24 months after treatment. A history and physical examination will be performed before, twice during treatment, and 3, 6, 12, 18, and 24 months after RT. Subsequently, a cardiac history will be taken in person or by phone annually until study termination, disease progression, or patient death. Immune cells will be separated from the blood samples drawn and counted to note any increase of immune cell populations in the blood, indicating inflammation. They will also be stained to see if they are expressing any markers of inflammation. Cardiac MRIs will be performed to measure the strength of heart muscle contraction. Results: Fifteen subjects have been enrolled to the clinical trial to-date. COVID-19 is delaying enrollment and necessary MRI scans. We are working with our clinical team to re-open enrollment as soon as possible. MRI scans scheduled for June are expected to proceed as planned. Blood Biomarkers: Analysis of blood collected before, during, and after RT has identified p90RSK as a potential early marker of tissue injury from radiation therapy. This marker was significantly elevated in blood collected after radiation exposure as compared to before radiation exposure. Imaging Biomarkers: Of the 15 subjects currently enrolled, cardiac MRIs were analyzed for 7 subjects. Changes in heart muscle strength were variable across this group. One subject had regions of the heart with impaired strength measurements prior to radiation treatment but had minimal change after radiation treatment, whereas another subject had generally normal functioning heart muscles but had significant decline in heart muscle strength after radiation treatment. Declines like this were seen in two subjects out of the seven who had cardiac MRI before and after radiation treatment. Discussion: We have enrolled 50% of the total accrual goal, and interesting preliminary data has been found. Despite the delays caused by COVID-19, we anticipate to complete enrollment in the next 12 months, as research operations become fully operational. Further analysis of blood markers, as well as imaging data will be integrated with preliminary results described here.
Bibliography Type:	Description: (Last Updated: 08/07/2023)
Articles in Peer-reviewed Journals	Milgrom SA, Varghese B, Gladish GW, Choi AD, Dong W, Patel ZS, Chung CC, Rao A, Pinnix CC, Gunther JR, Dabaja BS, Lin SH, Hoffman KE, Huff JL, Slagowski J, Abe JI, Iliescu CA, Banchs J, Yusuf SW, Lopez-Mattei JC. "Coronary artery dose-volume parameters predict risk of calcification after radiation therapy." J Cardiovasc Imaging. 2019 Oct;27(4):268-79. https://doi.org/10.4250/jcvi.2019.27.e38 ; PMID: 31614398; PMCID: PMC6795565 , Oct-2019