Fiscal Year:	FY 2015	**Task Last Updated:**	FY 11/17/2014
PI Name:	Deymier, Alix C. Ph.D.		
Project Title:	Effect of Unloading on the Structure and Mechanics of the Rotator Cuff Tendon-to-Bone Insertion		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Musculoskeletal Alterations Team		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Bone Fracture**:Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (2) **Osteo**:Risk Of Early Onset Osteoporosis Due To Spaceflight		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	10032-3702	**Congressional District:**	13
Comments:	NOTE: Also known as Alix Deymier-Black; former affiliation Washington University School of Medicine (Ed., 3/8/17)		
Project Type:	GROUND	**Solicitation / Funding Source:**	2013 NSBRI-RFA-13-01 Postdoctoral Fellowships
Start Date:	11/01/2013	**End Date:**	10/31/2016
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**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:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date is now 10/31/2016 per NSBRI (Ed., 10/13/15)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Thomopoulos, Stavros Ph.D. (MENTOR/ Washington University)		
Grant/Contract No.:	NCC 9-58-PF03503		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	POSTDOCTORAL FELLOWSHIP Rotator cuff injuries often occur at the site of the tendon-to-bone attachment. The sensitivity of the musculoskeletal system to its loading environment may augment the risk of injury at insertion sites due to extended periods of microgravity or unloading. Long-term changes in mechanical loading on joints, such as may be experienced during extended space travel, will lead to modifications in the tissues' structural and therefore mechanical properties. The goal of this study is to investigate the effect of unloading on the microstructure and mechanics of the tendon-to-bone attachment at the nanometer and micrometer scale. At the nanometer scale, I proposed to determine the location of mineral relative to the collagen fibril using Scanning Transmission Electron Microscopy (STEM) and identify load-transfer behavior between the two phases via synchrotron x-ray diffraction (XRD). At the micrometer scale, I proposed to study the mineral organization across the attachment site using synchrotron XRD and measure the micromechanics using a novel scanning electron microscopy-atomic force microscopy (SEM/AFM) system. Unloading of the tissue was done by injection of Botulinum Toxin (BtxA) which causes local paralysis. In the past year, I have focused on developing the techniques and acquiring data related to the micrometer scale structure and mechanics. Synchrotron XRD was used to examine mineral organization in supraspinatus-humerus tendon-to-bone attachments. Mineral orientation, size, strain, and strain distribution were calculated from the XRD patterns taken across the attachment. Moving from the unmineralized to the mineralized tissue the mineral orientation became more aligned. The crystal size increased with mineralization while the strain and strain distribution decreased. These changes in crystal organization suggest that as mineralization increases the crystals become more organized within the collagen matrix and form a continuous mineral matrix. With this baseline established, preliminary data examining only the mineralized region of unloaded shoulders were obtained. They indicated that BtxA treatment has significant effects on crystal size, strain, and orientation. To test the micromechanics of the tendon-to-bone attachment, I used a novel technique which combines SEM for imaging and AFM for mechanical testing. This technique has been previously used on mineralized tissues and polymer fibers, but never for unmineralized or graded tissues. A fair amount of time has been dedicated to identifying the issues and challenges associated with testing attachment samples and developing a new testing protocol. The new completed protocol uses Laser capture microscopy and cryo-focused ion beam to prepare small beams of the tendon-to-bone insertion. These small beams are then tested mechanically until failure using an AFM system mounted within an SEM. The SEM allow for the visualization of the sample deformation. Data from the SEM and AFM can then be analyzed to obtain stress-strain and local strain information. All of the current findings support the original research plan; as a result the original specific aims will continue to be pursued. Both techniques for the micrometer scale testing have now been validated. I have applied for access to the synchrotron beam line and hope to obtain data for the Btx treated samples in spring 2015. A new batch of samples was recently sent to London for micro-mechanical testing according to the new protocol. I hope to obtain a full set of mechanical data by December 2014. At the nanoscale I expect to begin the STEM experiments in October 2014 and complete them by January 2015. Preliminary tests for the synchrotron loading experiments will be performed at the Spring 2015 synchrotron access. Further access in the summer/fall 2015 will be requested to complete the experiments.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Rotator cuff tears are extremely prevalent, especially in the elderly population (~50% prevalence in individuals over 80 years). Even in the best of situations these tears are difficult to repair with a failure rate for repaired rotator cuffs as high as 94%. Rotator cuff tears tend to occur at the interface between tendon and bone. Such interfaces between dissimilar materials are prone to stress concentrations and increased failure risk. In healthy tissue, a number of structural mechanisms such as gradients in mineral content, collagen orientation, and matrix composition serve to dissipate these stress concentrations. The increased occurrence of rotator cuff injuries in the elderly population suggests that there may be changes in the interfacial structure due to unloading as a result of disuse or decreased use of the shoulder. Understanding how changes in the enthesis structure affect the mechanics of the insertion in loaded and unloaded systems will help us to develop enhanced techniques for treatment and repair. Therefore, the research performed in this project will not only help the astronaut population, but will also provide essential information in regards to the mechanics of rotator cuff tissues and how they respond to use and disuse.
Task Progress:	The goal of this study was to investigate the effect of unloading on the microstructure and mechanics of the tendon-to-bone attachment at the nanometer and micrometer scale. At the nanometer scale, I proposed to determine the location of mineral relative to the collagen fibril using Scanning Transmission Electron Microscopy and identify load-transfer behavior between the two phases via synchrotron x-ray diffraction (XRD). At the micrometer scale, I proposed to study the mineral organization across the attachment site using synchrotron XRD and measure the micromechanics using a novel scanning electron microscopy-atomic force microscopy (SEM/AFM) system. Unloading of the tissue was done by injection of Botulinum Toxin (BtxA) which causes local paralysis. In the past year, I have focused on developing the techniques and acquiring data related to the micrometer scale structure and mechanics. Sections of healthy tendon-to-bone attachments were examined using nano-scale synchrotron XRD at Argonne National Laboratory. XRD patterns were obtained across the attachment from the unmineralized to the mineralized fibrocartilage. Mineral orientation, size, strain, and strain distribution were calculated from the XRD patterns. Moving from the unmineralized to the mineralized tissue the mineral orientation became more aligned. The crystal size increased with mineralization while the strain and strain distribution decreased. These changes in crystal organization suggest that as mineralization increases the crystals become more organized within the collagen matrix and form a continuous mineral matrix. Preliminary data examining only the mineralized region of unloaded shoulders indicate the BtxA treatment has significant effects on crystal size, strain, and orientation. Access to the synchrotron has been requested to obtain additional data on the BtxA treated samples. To test the micromechanics of the tendon-to-bone attachment, I used a novel technique which combines SEM for imaging and AFM for mechanical testing. This technique has been previously used on mineralized tissues and polymer fibers, but never for unmineralized or graded tissues. A fair amount of time has been dedicated to identifying the issues and challenges associated with testing attachment samples and developing a new testing protocol. The new completed protocol uses Laser capture microscopy and cryo-focused ion beam to prepare small beams of the tendon-to-bone insertion. These small beams are then tested mechanically until failure using and AFM system mounted within an SEM.

	The SEM allow for the visualization of the sample deformation. Data from the SEM and AFM can then be analyzed to obtain stress-strain and local strain information. New beams of the attachment have recently been sent to London to be tested.
Bibliography Type:	Description: (Last Updated: 10/19/2020)
Abstracts for Journals and Proceedings	Deymier-Black AC, Schwartz AG, Cai Z, Genin GM, Thomopoulos S. "Role of Mineral Organization on the Mechanics of the Tendon-to-Bone Interface Examined via High Energy X-ray Diffraction." 4th Annual Winter Symposium of the Musculoskeletal Research Center, Washington University Musculoskeletal Research Center, St Louis, MO, February 12, 2014. 4th Annual Winter Symposium of the Musculoskeletal Research Center, Washington University Musculoskeletal Research Center, St Louis, MO, February 12, 2014. , Feb-2014
Abstracts for Journals and Proceedings	Deymier-Black AC, Schwartz AG, Cai Z, Genin GM, Thomopoulos S. "Role of Mineral Organization on the Mechanics of the Tendon-To-Bone Interface Examined via High Energy X-Ray Diffraction." ORS (Orthopaedic Research Society) Annual Meeting 2014, New Orleans, LA, March 15-18, 2014. ORS (Orthopaedic Research Society) Annual Meeting 2014, New Orleans, LA, March 15-18, 2014. Poster 490. http://www.ors.org/Transactions/60/0490.pdf ; accessed 12/11/14. , Mar-2014