

Fiscal Year:	FY 2017	Task Last Updated:	FY 03/13/2018
PI Name:	Qin, Yi-Xian Ph.D.		
Project Title:	Portable Quantitative Ultrasound with DXA/QCT and FEA Integration for Human Longitudinal Critical Bone Quality Assessment		
Division Name:	Human Research		
Program/Discipline:	NSBRI		
Program/Discipline--Element/Subdiscipline:	NSBRI--Smart Medical Systems and Technology Team		
Joint Agency Name:	TechPort:	Yes	
Human Research Program Elements:	(1) ExMC :Exploration Medical Capabilities		
Human Research Program Risks:	(1) Medical Conditions :Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures (2) Renal Stone :Risk of Renal Stone Formation		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	11794-5281	Congressional District:	1
Comments:			
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Contact Email:			
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Key Personnel Changes/Previous PI:			
COI Name (Institution):	Gelato, Marie M.D. (University of Kentucky) Lin, Wei Ph.D. (SUNY- The State University of New York)		
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Task Description:

Project Overview: Skeletal complications, i.e., osteoporosis, induced by microgravity during extended space missions represent a key astronaut health problem. Lack of on-board diagnosis has increased significant risk in astronauts' bone loss during long term space flight. Early diagnosis of such disorders can lead to prompt and optimized treatment that will dramatically reduce the risk of fracture and longitudinal monitoring microgravity and countermeasure effects. Advances in quantitative ultrasound (QUS) techniques provide a method for characterizing the material properties of bone in a manner for predicting both BMD (bone mineral density) and mechanical strength. We have developed a scanning confocal acoustic navigation (SCAN) system capable of generating noninvasive ultrasound images at the site of interest. Both animal and human tests indicated strong correlations between SCAN determined data and microCT determined BMD, and bone strength, as well as monitoring fracture healing with guided ultrasound. The objectives of this study are to develop a portable broadband SCAN for critical skeletal quality assessment, to monitor bone alteration in disuse osteopenia, and to integrate ultrasound with DXA for human subject in multiple skeleton sites. In vivo human tests are evaluated at Stony Brook Osteoporosis Center. Human cadaver and animal samples will be used for testing feasibility of identifying bone loss, microstructural and mechanical strength properties. Development of a noninvasive diagnostic and treatment technology using noninvasive ultrasound with new crystal transducer technology will have a great potential to perform longitudinal measurement of bone alteration and prevent the risk of fracture.

Technical Summary: Non-invasive assessment of trabecular bone strength and density is extremely important in predicting the risk of fracture in space and ground operation. Quantitative ultrasound (QUS) has emerged with the potential to directly detect trabecular bone strength. To overcome the current hurdles such as soft tissue and cortical shell interference, improving the quality of QUS and applying the technology for future clinical applications, this phase of the development of image based SCAN system will concentrate on several main areas: (1) increasing the resolution, sensitivity, and accuracy in diagnosing osteoporosis through confocal acoustics to improve signal/noise ratio, and through extracting surface topology to accurately calculate ultrasound speed of sound; (2) minimizing the scanning time while maintaining reasonable resolution via micro-processor controlled and phased array electronic confocal scanning, e.g., in deep bone tissue scan; (3) developing broadband ultrasound system to measure deep bone tissue density and structural parameters in the critical regions; (4) developing hardware and software interface with flexible ultrasound platform (FUS), and therapeutic ultrasound for acceleration of fracture healing; (5) assessment of the capability of the SCAN system of imaging scan for human wrist and calcaneus for bone density assessment in normal and osteoporosis subjects. The proposed work will develop a portable rapid SCAN system combined with imaging capability, and test its efficacy in human, which will ultimately provide a portable, noninvasive device for bone loss assessment in space.

Earth Applications: Skeletal decay complications are major health problems on Earth, i.e., osteoporosis, and delayed healing of fractures. Development of a low mass, compact, noninvasive diagnostic and treatment technology, i.e., using ultrasound, will have a great potential to prevent and treat bone fracture. Our principal goal is to develop a portable quantitative ultrasound system with therapeutic capability, not only for determination of bone's physical properties, but also for predicting subtle changes of bone during extended flights and diseased condition, which will impact both diagnosis and noninvasive treatment for musculoskeletal disorders. Use of a desktop based non-ionizing bone assessment device has great clinical applications as an in-office quantitative assessment of fracture risk in the general and at-risk populations.

Key findings and milestones: In this study, the team is able to continue development of a scanning confocal acoustic diagnostic combined with therapeutic system capable of generating acoustic images at the regions of interest for identifying the strength of trabecular bone with high-resolution QUS attenuation and velocity maps, and thus determining the relationship between ultrasonic parameters and bone mineral density (BMD), and bone's physical properties, as well as providing treatment for fracture healing. Ultrasound has been used in an OVX (ovariectomy) and femur fracture animal model to mitigate bone loss and acceleration of fracture healing. Phase array transducer and system are built and successfully tested in initial normal control and osteoporotic human subjects in multiple skeletal sites. The team is able to work with TRS Transducers, Inc. for evaluation of a wideband frequency ultrasound transducers in range of 0.5MHz - 7.0MHz, and with GE Research Center for flexible ultrasound platform (FUS) system in system requirement specifics, user-interface software evaluation and 2-D array transducer design. The results have shown that ultrasound can mitigate bone loss and promote fracture healing under disuse osteopenia condition.

Rationale for HRP Directed Research:**Research Impact/Earth Benefits:**

Musculoskeletal decay due to a microgravity environment has greatly impacted the nation's civil space missions and ground operations. Such musculoskeletal complications are also major health problems on Earth, i.e., osteoporosis, and the delayed healing of fractures. About 13 to 18 percent of women aged 50 years and older and 3 to 6 percent of men aged 50 years and older have osteoporosis in the US alone. One-third of women over 65 will have vertebral fractures and 90% of women aged 75 and older have radiographic evidence of osteoporosis. Thus, approximately a total of 28 million people suffer from osteoporosis in the United States, with an estimated annual direct cost of over \$30 billion to national health programs. Hence, an early diagnosis that can predict fracture risk and result in prompt treatment is extremely important. Ultrasound has also demonstrated its therapeutic potentials to accelerate fracture healing. The objectives of this study are focused on developing a combined diagnostic and treatment ultrasound technology for early prediction of bone disorder and guided acceleration of fracture healing, using SCAN imaging and low-intensity pulse ultrasound. Development of a low mass, compact, noninvasive diagnostic and treatment modality will have great impacts as early diagnostic to prevent bone loss and accelerate fracture healing. This research will address critical questions in the Bioastronauts Roadmap related to non-invasive assessment of the acceleration of age-related osteoporosis and the monitoring of fractures and impaired fracture healing. The results have demonstrated the feasibility and efficacy of SCAN for assessing bone's quality in bone. We have been able to demonstrate that the bone quality is predictable via non-invasive scanning ultrasound imaging in the region of interests (ROI), and to demonstrate the strong correlation between SCAN determined data and microCT identified BMD, structural index, and mechanical modulus. These data have provided a foundation for further development of the technology and the clinical application in this research.

Task Progress:	Musculoskeletal complications induced by age-related diseases like osteoporosis, and in long-term disuse osteopenia such as a lack of microgravity during extended space missions and long-term bed rest, represent a key health problem. Such a skeletal disorder changes both the structural and strength properties of bone, and the latter plays a critical role in ultimately leading to fracture. Early diagnosis of progressive bone loss or poor bone quality would allow prompt treatment and thus will dramatically reduce the risk of bone fracture. While most of the osteoporotic fractures occur in cancellous bone, non-invasive assessment of trabecular strength and stiffness is extremely important in evaluating bone quality. Ultrasound has also been shown therapeutic potentials to accelerate fracture healing. We are able to develop a SCAN system combined with therapeutic ultrasound capable of generating acoustic images at the regions of interest for identifying the strength of trabecular bone, in which the system is capable of generating non-invasive, high-resolution ultrasound (US) attenuation and velocity maps of bone, and thus determining the relationship between ultrasonic specific parameters and bone mineral density (BMD), and bone strength and bone's physical properties (i.e., stiffness and modulus). The ultrasound resolution and sensitivity are significantly improved by its configuration, compared to the existing technology. The new generation of SCAN devices greatly improves the practical use of ultrasound imaging. The issue of free water in microgravity has been solved by the development of a self-contained transducer tank, which would also allow for the replacement of water with a more ideal liquid such as mineral oil. Additionally, the development of a hand-held scanner requiring only a thin coating of ultrasound gel on the skin greatly improves the mobility of the device as well as allowing for the QUS assessment of additional regions of interest.
Bibliography Type:	Description: (Last Updated: 02/17/2021)
Articles in Peer-reviewed Journals	Hu M, Lam H, Yeh R, Teeratananon M, Qin Y-X. "Comparison of morphological changes of muscle fibers in response to dynamic electrical muscle contraction and dynamic hydraulic stimulation in a rat hindlimb disuse model." <i>Physiol Res.</i> 2017 Jul 18;66(3):519-30. Epub 2017 Feb 28. PubMed PMID: 28248540 , Jul-2017
Articles in Peer-reviewed Journals	Uddin SM, Richbrough B, Ding Y, Hettinghouse A, Komatsu DE, Qin Y-X, Liu CJ. "Chondro-protective effects of low intensity pulsed ultrasound." <i>Osteoarthritis Cartilage.</i> 2016 Nov;24(11):1989-98. Epub 2016 Jun 27. https://doi.org/10.1016/j.joca.2016.06.014 ; PubMed PMID: 27364595 ; PubMed Central PMCID: PMC5071131 , Nov-2016
Articles in Peer-reviewed Journals	Zhang D, Hu M, Chu T, Lin L, Wang J, Li X, Ke HZ, Qin Y-X. "Sclerostin antibody prevented progressive bone loss in combined ovariectomized and concurrent functional disuse." <i>Bone.</i> 2016 Jun;87:161-8. Epub 2016 Feb 8. https://doi.org/10.1016/j.bone.2016.02.005 ; PubMed PMID: 26868528 ; PubMed Central PMCID: PMC4862887 [Erratum in: <i>Bone.</i> 2016 Aug;89:86. PMID: 27262889] , Jun-2016
Articles in Peer-reviewed Journals	Wu L, Lin L, Qin YX. "Enhancement of cell ingrowth, proliferation, and early differentiation in a three-dimensional silicon carbide scaffold using low-intensity pulsed ultrasound." <i>Tissue Eng Part A.</i> 2015 Jan;21(1-2):53-61. Epub 2014 Jul 24. https://doi.org/10.1089/ten.TEA.2013.0597 ; PubMed PMID: 24935158 ; PubMed Central PMCID: PMC4293095 , Jan-2015
Articles in Peer-reviewed Journals	Gadomski BC, McGilvray KC, Easley JT, Palmer RH, Jiao J, Li X, Qin YX, Puttlitz CM. "An investigation of shock wave therapy and low-intensity pulsed ultrasound on fracture healing under reduced loading conditions in an ovine model." <i>J Orthop Res.</i> 2018 Mar;36(3):921-9. Epub 2017 Aug 11. https://doi.org/10.1002/jor.23666 ; PubMed PMID: 28762588 , Mar-2018
Articles in Peer-reviewed Journals	Moonga SS, Qin YX. "MC3T3 infiltration and proliferation in bovine trabecular scaffold regulated by dynamic flow bioreactor and augmented by low-intensity pulsed ultrasound." <i>J Orthop Translat.</i> 2018 Jul;14:16-22. https://doi.org/10.1016/j.jot.2018.02.002 ; PubMed PMID: 30035029 ; PubMed Central PMCID: PMC6042526 , Jul-2018
Articles in Peer-reviewed Journals	Liu J, Li X, Zhang D, Jiao J, Wu L, Hao F, Qin YX. "Acceleration of bone defect healing and regeneration by low-intensity ultrasound radiation force in a rat tibial model." <i>Ultrasound Med Biol.</i> 2018 Dec;44(12):2646-54. https://doi.org/10.1016/j.ultrasmedbio.2018.08.002 ; PMID: 30286949 , Dec-2018
Articles in Peer-reviewed Journals	Li X, Sun Y, Zhou Z, Zhang D, Jiao J, Hu M, Hassan CR, Qin YX. "Mitigation of articular cartilage degeneration and subchondral bone sclerosis in osteoarthritis progression using low-intensity ultrasound stimulation." <i>Ultrasound Med Biol.</i> 2019 Jan;45(1):148-59. Epub 2018 Oct 12. https://doi.org/10.1016/j.ultrasmedbio.2018.08.022 ; PMID: 30322672 ; PMCID: PMC6289639 , Jan-2019
Books/Book Chapters	Qin YX, Hu M, Li X. "Biomechanics of bone and cartilage." in "Frontiers in Orthopaedic Biomechanics." Ed. C.K. Cheng, S.L.Y. Woo. Singapore: Springer, 2020. p. 1-35. https://link.springer.com/chapter/10.1007/978-981-15-3159-0_1 , May-2020
Books/Book Chapters	Qin YX, Hu M. "In vivo models of muscle stimulation and mechanical loading in bone mechanobiology." in "Mechanobiology: From Molecular Sensing to Disease." Ed. G.L. Niebur. [S.l.]: Elsevier, 2020. p. 117-136. https://doi.org/10.1016/B978-0-12-817931-4.00007-8 , Dec-2019