

<b>Fiscal Year:</b>	FY 2013	<b>Task Last Updated:</b>	FY 04/04/2013
<b>PI Name:</b>	Qin, Yi-Xian Ph.D.		
<b>Project Title:</b>	Combined Scanning Confocal Ultrasound Diagnostic and Treatment System for Bone Quality Assessment and Fracture Healing		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>	NSBRI		
<b>Program/Discipline--Element/Subdiscipline:</b>	NSBRI--Smart Medical Systems and Technology Team		
<b>Joint Agency Name:</b>		<b>TechPort:</b>	Yes
<b>Human Research Program Elements:</b>	(1) <b>ExMC</b> :Exploration Medical Capabilities		
<b>Human Research Program Risks:</b>	(1) <b>Bone Fracture</b> :Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (2) <b>Medical Conditions</b> :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 (3) <b>Osteo</b> :Risk Of Early Onset Osteoporosis Due To Spaceflight (4) <b>Renal Stone</b> :Risk of Renal Stone Formation		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Zip Code:</b>	11794-5281	<b>Congressional District:</b>	1
<b>Comments:</b>			
<b>Project Type:</b>	Ground	<b>Solicitation / Funding Source:</b>	2007 Crew Health NNJ07ZSA002N
<b>Start Date:</b>	11/01/2008	<b>End Date:</b>	08/31/2013
<b>No. of Post Docs:</b>	3	<b>No. of PhD Degrees:</b>	2
<b>No. of PhD Candidates:</b>	3	<b>No. of Master' Degrees:</b>	2
<b>No. of Master's Candidates:</b>	2	<b>No. of Bachelor's Degrees:</b>	3
<b>No. of Bachelor's Candidates:</b>	3	<b>Monitoring Center:</b>	NSBRI
<b>Contact Monitor:</b>	<b>Contact Phone:</b>		
<b>Contact Email:</b>			
<b>Flight Program:</b>			
<b>Flight Assignment:</b>	NOTE: End date changed to 8/31/2013 (from 10/31/2013) per NSBRI (Ed., 5/14/2013) NOTE: Extended to 10/31/2013 per NSBRI (Ed., 2/22/2013)		
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Rubin, Clinton ( Research Foundation of SUNY ) Lin, Wei ( SUNY- The State University of New York ) Mirza, Naureen ( University of Kentucky ) Gelato, Marie ( University of Kentucky )		
<b>Grant/Contract No.:</b>	NCC 9-58-SMST01603		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>			

Bone loss induced under microgravity environment is one of major health problems during long term space missions, resulting in high risk of fracture. Lack of onboard monitoring methods makes it difficult to evaluate such risk and guide treatment. Using a developing noninvasive Scanning Confocal Acoustic Navigation (SCAN) technology, strong correlations between SCAN determined data and bone's structural and strength parameters were observed. Ultrasound has also been shown therapeutic potentials to accelerate fracture healing. The objectives of this study are to develop 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. The technology will target to the critical skeletal sites, where may be significantly affected by disuse osteopenia and potentially at the risk of fracture. The research team has been focused on the technology development of the (SCAN) system and on determining interrelationship between ultrasound parameters and bone's structural and strength properties in a quantitative manner. The results have demonstrated the feasibility and efficacy of SCAN for assessing bone's quality in animal, human cadaver bone samples, and in vivo human subjects (e.g., bed rest). 13 peer-reviewed journal papers and more than 36 conference short papers were published in this period directly derived from this work. SCAN has shown its ability in bone quality assessment in heel and wrist regions and demonstrated strong correlation between SCAN determined data and microCT identified bone mineral density (BMD), porosity, trabecular space and trabecular width, as well as modulus. These data have provided a foundation for further development of the technology and the clinical application in this continuing research (Technology Readiness Level-TRL 6).

In this period, the technology development of a new generation of the SCAN device is significantly advanced as a portable device to access the bone quality at wrist and heel sites, and to use ultrasound for guided treatment for controlled bone fracture. A demo of the technology was performed at the new National Space Biomedical Research Institute (NSBRI) headquarters in April of 2012. A combined mechanical and electrical array scan modality has been initiated and achieved, which can complete the SCAN time at the particular skeletal site less in than 2 minutes. The new development is capable of generating non-invasive, high-resolution quantitative ultrasound (QUS) attenuation and velocity maps of bone for determining the relationship between ultrasonic specific parameters and bone mineral density (BMD) and bone's physical properties (i.e., stiffness). Several example studies were briefly described.

#### Task Description:

1) Developing a SCAN system for bone quality assessment: A real time rapid acoustic mapping system is developed for evaluation of bone density, structural and mechanical properties, and defect using a patented technology developed in the Principal Investigator's lab. Phased arrays using a linear array of elements, emitted with different delays, generate a focal ultrasonic beam in X-direction by controlled programming. Combined mechanical scanning will be performed in the Y-direction. Such design greatly reduces scan time (less than 30 sec) and maintains resolution and image quality. Beams are generated and received with the use of focal laws, in which software models the programs to spatially control confocal points and scanning. Setup of pulse wizards will be controlled by a house designed 16-bit microprocessor. Phased array transducers will be designed and built with 120 linear elements with the frequency range of 0.5~2.5 MHz. Each phase of excitation is approximately 2 micros. Each focal point will take approximately 0.1 ms. A 2-D electro-mechanic scanning region may take about 20 sec. Thus, the influences of soft tissue, cortical bone, and irregular shape surfaces can be greatly reduced. In this confocal scanning mode, ultrasound parameters, i.e., broadband ultrasound attenuation (BUA) and ultrasound-UV, can generate a spatial acoustic map at the region of interest.

2) Noninvasive prediction of bone internal and principal structural orientation using SCAN: Bone has the ability to adapt its structure in response to the mechanical environment as defined as Wolff's Law. The alignment of trabecular structure is intended to adapt to the particular mechanical milieu applied to it. Due to the absence of normal mechanical loading, it will be extremely important to assess the anisotropic deterioration of bone during the extreme conditions, i.e., long term space mission and disease orientated disuse, to predict risk of fractures. In this work, 7 bovine trabecular bone balls were used for rotational ultrasound measurement around 3 anatomical axes to elucidate the ability of ultrasound to identify trabecular orientation. By comparing to the mean intercept length (MIL) tensor obtained from  $\mu$ CT, the angle difference of the prediction by UV was 4.45°, while it resulted in 11.67° angle difference between direction predicted by  $\mu$ CT and the prediction by Achilles tendon thickness (ATT). This result demonstrates the ability of ultrasound as a non-invasive measurement tool for the principal structural orientation of the trabecular bone.

3) Development of mechano-electronic array SCAN imaging for bone quality assessment: New hardware and software are developed to synchronize mechanical fine scan with electrical phase delay scan, and sequential data transaction. Computer algorithms are designed to perform data analysis and imaging forming. An accelerated continuous scan mode is further designed and built including rapid A/D (amplitude-dependent) data acquisition, microprocessor control synchronizing (for scanning, transmit signal, and A/D trigger), and control algorithm. A high-resolution ultrasound image array with 0.5 mm resolution results in scan times of less than 2 minutes is achieved in the region of interest (ROI).

#### 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 24 million people suffer from osteoporosis in the United States, with an estimated annual direct cost of over \$18 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 Bioastronautics 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 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:	<p>The objectives of this study are to develop 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. The technology will target to the critical skeletal sites, where may be significantly affected by disuse osteopenia and potentially at the risk of fracture. The research team has been focused on the technology development of the SCAN system and on determining interrelationship between ultrasound parameters and bone's structural and strength properties in a quantitative manner. The results have demonstrated the feasibility and efficacy of SCAN for assessing bone's quality in animal, human cadaver bone samples, and in vivo human subjects (e.g., bed rest). 13 peer-reviewed journal papers and more than 36 conference short papers were published in this period directly derived from this work. 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 critic 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. Developed prototype of SCAN is successfully used in the bedrest subjects and clinical test (Stony Brook University). A fast scan mode (~2.5 min) and a surface topology mapping technology using scanning ultrasound are developed and capable of determining calcaneus bone thickness accurately and hence enhancing the accuracy of UV measurement. Ultrasound treatment for progressive bone loss is also initiated in this year's research.</p>
Bibliography Type:	Description: (Last Updated: 02/17/2021)
Articles in Peer-reviewed Journals	<p>Cheng J, Serra-Hsu F, Tian Y, Lin W, Qin YX. "Effects of phase cancellation and receiver aperture size on broadband ultrasonic attenuation for trabecular bone in vitro." <i>Ultrasound Med Biol.</i> 2011 Dec;37(12):2116-25. Epub 2011 Oct 26. <a href="http://dx.doi.org/10.1016/j.ultrasmedbio.2011.08.009">http://dx.doi.org/10.1016/j.ultrasmedbio.2011.08.009</a> ; PubMed <a href="#">PMID: 22033134</a> , Dec-2011</p>
Articles in Peer-reviewed Journals	<p>Lin L, Cheng J, Lin W, Qin YX. "Prediction of trabecular bone principal structural orientation using quantitative ultrasound scanning." <i>J Biomech.</i> 2012 Jun 26;45(10):1790-5. Epub 2012 May 5. <a href="http://dx.doi.org/10.1016/j.jbiomech.2012.04.022">http://dx.doi.org/10.1016/j.jbiomech.2012.04.022</a> ; PubMed <a href="#">PMID: 22560370</a> , Jun-2012</p>
Articles in Peer-reviewed Journals	<p>Lin W, Serra-Hsu F, Cheng J, Qin YX. "Frequency specific ultrasound attenuation is sensitive to trabecular bone structure." <i>Ultrasound Med Biol.</i> 2012 Dec;38(12):2198-207. Epub 2012 Sep 10. <a href="http://dx.doi.org/10.1016/j.ultrasmedbio.2012.07.020">http://dx.doi.org/10.1016/j.ultrasmedbio.2012.07.020</a> ; PubMed <a href="#">PMID: 22975035</a> , Dec-2012</p>
Articles in Peer-reviewed Journals	<p>Qin YX, Lin W, Mittra E, Xia Y, Cheng J, Judex S, Rubin C, Muller R. "Prediction of trabecular bone qualitative properties using scanning quantitative ultrasound." <i>Acta Astronautica.</i> 2013 Nov;92(1):79-88. <a href="http://dx.doi.org/10.1016/j.actaastro.2012.08.032">http://dx.doi.org/10.1016/j.actaastro.2012.08.032</a> (originally reported as Available online 5 October 2012.), Nov-2013</p>
Articles in Peer-reviewed Journals	<p>Zhang S, Cheng J, Qin YX. "Mechanobiological modulation of cytoskeleton and calcium influx in osteoblastic cells by short-term focused acoustic radiation force." <i>PLoS One.</i> 2012;7(6):e38343. <a href="http://dx.doi.org/10.1371/journal.pone.0038343">http://dx.doi.org/10.1371/journal.pone.0038343</a> ; PubMed <a href="#">PMID: 22701628</a> , Jun-2012</p>
Articles in Peer-reviewed Journals	<p>Hu M, Cheng J, Qin YX. "Dynamic hydraulic flow stimulation on mitigation of trabecular bone loss in a rat functional disuse model." <i>Bone.</i> 2012 Oct;51(4):819-25. Epub 2012 Jul 20. <a href="http://dx.doi.org/10.1016/j.bone.2012.06.030">http://dx.doi.org/10.1016/j.bone.2012.06.030</a> ; PubMed <a href="#">PMID: 22820398</a> , Oct-2012</p>
Articles in Peer-reviewed Journals	<p>Zhang ZK, Guo X, Lao J, Qin YX. "Effect of capsaicin-sensitive sensory neurons on bone architecture and mechanical properties in the rat hindlimb suspension model." <i>J Orthop Translat.</i> 2017 Jul 27;10:12-7. eCollection 2017 Jul. <a href="https://doi.org/10.1016/j.jot.2017.03.001">https://doi.org/10.1016/j.jot.2017.03.001</a> ; PubMed <a href="#">PMID: 29662756</a>; PubMed Central <a href="#">PMCID: PMC5822959</a> , Jul-2017</p>
Articles in Peer-reviewed Journals	<p>Qin YX, Xia Y, Muir J, Lin W, Rubin CT. "Quantitative ultrasound imaging monitoring progressive disuse osteopenia and mechanical stimulation mitigation in calcaneus region through a 90-day bed rest human study." <i>J Orthop Translat.</i> 2019 Jul;18:48-58. <a href="https://doi.org/10.1016/j.jot.2018.11.004">https://doi.org/10.1016/j.jot.2018.11.004</a> ; PubMed <a href="#">PMID: 31508307</a>; PubMed Central <a href="#">PMCID: PMC6718925</a> , Jul-2019</p>
Articles in Peer-reviewed Journals	<p>Grover K, Hu M, Lin L, Muir J, Qin YX. "Functional disuse initiates medullary endosteal micro-architectural impairment in cortical bone characterized by nanoindentation." <i>J Bone Miner Metab.</i> 2019 Nov;37(6):1048-57. Epub 2019 Jul 10. <a href="https://doi.org/10.1007/s00774-019-01011-1">https://doi.org/10.1007/s00774-019-01011-1</a> ; <a href="#">PMID: 31292723</a> , Nov-2019</p>
Awards	Qin Y-X. "Elected Corresponding Member, International Academy of Astronautics (IAA), May 2012." May-2012
Awards	Qin Y-X. "First patent award, Brookhaven Town, NY, July 2012." Jul-2012