Fiscal Year:	FY 2009	**Task Last Updated:**	FY 03/12/2009
PI Name:	Qin, Yi-Xian Ph.D.		
Project Title:	A Scanning Confocal Acoustic Diagnostic System for Non-Invasively Assessing Bone Quality		
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) **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:	11794-5281	**Congressional District:**	1
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2003 Biomedical Research & Countermeasures 03-OBPR-04
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No. of Master's Candidates:	3	**No. of Bachelor's Degrees:**	2
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Gruber, Barry (SUNY- The State University of New York) Rubin, Clinton (Research Foundation of SUNY)		
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The bone loss which parallels extended space missions represents a serious threat to astronaut health, both during flight and on return to gravitational fields. Early diagnosis of osteoporosis would enable prompt treatment and thus dramatically reduce the risk of fracture. Currently, the principal method used to diagnose osteoporosis is dual-energy X-ray absorptiometry (DEXA), which provides a 2-D representation of bone mineral density (BMD), but not bone's physical properties per se. Recent advances in quantitative ultrasound have enabled a true characterization of bone quality, including both BMD and mechanical strength. Currently funded by the National Space Biomedical Research Institute (NSBRI), we have developed a scanning confocal acoustic diagnostic (SCAD) system capable of generating acoustic images at the regions of interest. The objectives of this study are to develop an unique diagnostic modality for non-invasively evaluating both human bone's mineral density and stiffness, particularly to improve the resolution, to shorten the ultrasound scanning time (e.g., < 5 min), to validate image based characterization of bone's physical properties with true bone quality as based on material testing, and to initiate human subject testing. In essence, this next phase of research will focus on developing the SCAD prototype as a real-time, high-resolution, and portable bone image modality for determining bone quality. A series of four interrelated specific aims are proposed to achieve the goals. Specific Aims: The aims of the study are to develop and establish the efficacy of a real-time Scanning Confocal Acoustic Diagnosis system for assessing bone status, to identify the complexity of surface morphology, and to correlate image based parameter to bone quality.

S.A. #1: Develop a rapid SCAD system capable of generating high-resolution acoustic images for trabecular structural and strength properties in the region of interest (ROI).

S.A. #2: Develop the system capable of extracting trabecular broadband ultrasound attenuation (BUA) and ultrasound wave velocity (UV) images at multiple skeletal sites, i.e., calcaneus, wrist, and knee, providing evaluation of loss and fracture risk.

S.A. #3: Evaluate the capability of the SCAD system in testing bone's structure and strength in cadavers by micro-CT determined microstructure, nanoindentor tested integrity, and modulus.

S.A. #4: Correlate the degree of osteoporosis and disuse osteopenia in human to determine the relationship to age, gender, degree of bone loss, and rational effects at ROI using SCAD and DXA.

Task Description:

The SCAD system was further developed in this research period. The new system is capable of generating non-invasive, high-resolution quantitative ultrasound (QUS) attenuation and velocity maps of bone, and thus determining the relationship between ultrasonic determined parameters and BMD, bone strength, and bone's physical properties (i.e., stiffness and modulus). The ultrasound resolution and sensitivity are significantly improved in this new configuration. Several milestones are achieved.

(1) Improvement of scanning speed by computer chip and hardware design and time sequence and control in the software design. The goal of this study was to accelerate the bone scan with reduced time and incorporate with identifying 3D surface topology of bone for accurate calculation of ultrasound wave velocity and attenuation. The hardware and programming were successfully developed, in which the scan time for 80 x 80 pixel region of confocal ultrasound was reduced to 5 min with all the surface topology information. The irregular surfaces of calcaneus can be clearly depicted using surface mapping. SCAD parameters were highly correlated to BMD, bone volume fraction, and bone modulus.

(2) Bone surface topology mapping and its role in trabecular bone quality assessment using scanning confocal ultrasound. The goal of this study was to identify 3D surface topology of bone for accurate calculation of ultrasound wave velocity. The irregular surfaces of calcaneus can be clearly depicted using surface mapping and SCAD parameters were highly correlated to BMD, bone volume fraction, and bone modulus.

(3) Automatic region of interests based on the ultrasound broad band attenuation. This feature is capable of determining ultrasonic parameters through bone more accurately and automatically with friendly user-device interface, which can be easily incorporated into future in vivo clinical application.

(4) Explore the capability of ultrasound assessment for bone quality in bedrested subjects. QUS provides a method for characterizing the quality of bone non-invasively. The team continues to conduct the study for longitudinal assessment of bone mass and quality for bedrest subjects. The performance of a scanning confocal QUS system was evaluated in a 90 day microgravity analog study with the comparison to standard DXA in localized regions of interest, e.g., calcaneus. The subject pool included 11 disuse (control) and 18 disuse plus vibration (low magnitude, high frequency treatment) subjects at the University of Texas Medical Branch (UTMB), Galveston, TX. QUS scanning for the calcaneus region showed a unique pattern in the acoustic images. Strong correlation was observed between pooled broadband ultrasound attenuation (BUA) in the heel region and pooled whole body BMD (determined by the DXA), R2=0.7. Longitudinally, subtle changes were significantly predicted by the ultrasound wave velocity (UV) measurements at 0, 60, and 90 days, in which 1.5% UV reduction in 60 days bed rest. These results suggested that BMD is one of the major contributors for bone loss in the skeleton and QUS could be used to longitudinally monitor bone loss in bed rest environment. A manuscript is under review.

(5) Initiation of SCAD assessment in large and critical bone sites, e.g., proximal femur. These works will help to refine a non-invasive diagnosis for bone loss, and may potentiate the development of a flight instrument for the precise determination of bone quality during extended space missions.

Rationale for HRP Directed Research:

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.
Development of a low mass, compact, noninvasive diagnostic tool, i.e., ultrasound bone quality detector, will have a great impact as an early diagnostic to prevent bone fracture. This research will address critical questions in the Critical

Research Impact/Earth Benefits:	Path Roadmap and NASA Human Research Program's (HRP) Risks map 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 SCAD 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 SCAD determined data and micro-CT 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. Our principal goal is to continue the development and evaluation of the SCAD system for ground-based determination of bone's physical properties, and for determining even subtle changes of bone during extended flights, as well as early diagnosis of osteoporosis and prediction of fracture risks.
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. In this year's research, we are able to develop a scanning confocal acoustic diagnostic (SCAD) system capable of generating acoustic images at the regions of interest (e.g., in the human calcaneus) 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 SCAD is successfully used in the bedrest subjects (UTMB, Galveston, TX) 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.
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