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TITLE: Leg Muscle Usage Effects on Tibial Elasticity During Running

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14. ABSTRACT Tibial stress fractures (TSFs) are a substantial problem in military training, but a means of predicting their occurrence remains elusive. Bone strength is key to the resistance of TSF, but bone density, a determinant of strength, is known not to predict TSF. Elasticity is nearly as important as density in determining bone strength but has not been tested in TSF, or even studied in runners. However, clinical studies of osteoporotic patients given bisphosphonates have shown significant correlations between low elasticity and fracture incidence. These basic validation studies will determine if modulators of tibial stress, such as strike mechanics and surface incline, also modulate bone elasticity during running. Because these modulators may operate on the tibia via muscles, we have combined ultrasound characterization of tibial elasticity with MRI monitoring of muscle recruitment during a running protocol in healthy volunteers.					
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Introduction

Tibial stress fractures (TSFs) are a substantial problem for military recruits, elite athletes, and adults transitioning from a sedentary lifestyle to an exercise regimen. Bone strength is key to the resistance of TSF, but it is evident that a better method of evaluating bone quality is needed, as the gold standard method (bone mineral densitometry) is known not to predict TSF risk. Furthermore, there is growing evidence that the influence of muscles on bone may be an important determinant of bone properties. This school of thought is embodied in Frost's Utah paradigm of skeletal physiology [1] where the load-bearing skeleton adapts to the voluntary mechanical loads induced by muscles. Ultrasound critical-angle reflectometry (UCR) is a novel modality developed in laboratory of Dr. Peter Antich that allows the complete anisotropic elastic properties of bone to be measured in vivo [2]. This modality does appear to show an association between low elasticity and fracture incidence in osteoporotic patients treated with bisphosphonate [3]. In this study, tibial stress will be modulated in subjects by varying running styles and treadmill inclination. Changes in bone elasticity will then be analyzed in relation to the muscle recruitment patterns as determined using magnetic resonance imaging (MRI).

Body

In September 2003, the Principle Investigator status for this study was transferred to Dr. Peter Antich. This was in response to the departure of the original PI for a position in private practice. At that time, it was learned that the Study Protocol and Consent Form had outstanding issues with the Human Subjects Safety Review Board (HSSRB) and had not been approved. In summary, it was determined by the members of the HSSRB that this study was Greater than Minimal Risk. For the time period December 2003 to May 2004, the Study Protocol and Consent Form were scrutinized by all parties, and significant revisions were submitted on several occasions.

After all changes were submitted in written form, the Protocol and Consent Form were provisionally accepted by the HSSRB in July 2004, provided that local IRB approval for changes was obtained. Documentation for all changes was prepared in August 2004 and submitted to the UT Southwestern IRB in September 2004 at the time of annual review. Acceptance of all changes was received on 28 October 2004 and communicated to the HSSRB. Final HSSRB approval was dated 1 November 2004.

Recruitment of subjects was re-started in January 2005, with postings of flyers again on the campus of UT Southwestern Medical Center at Dallas. Subject recruitment showed us the existence of difficulties in recruiting a sufficient number of subjects satisfying the criteria agreed to from this University (both staff and students are very health- and exercise-conscious) and we decided to attempt recruiting subjects from other Institutions and corporations within the Dallas City boundaries. Advertisements were made at both Southern Methodist University and the University of Texas at Arlington, leading to 4 additional subjects.

Key Research Accomplishments

Subject recruitment, training, and data collection is on-going. As per the original protocol, 40 subjects will be enrolled in total, with 5 groups of 8 subjects grouped for training efficiency. Recruitment of subjects but was discontinued in August 2006 due to low enrollment numbers in the restricted local community. We now have 12 subjects recruited and ready to start studies by June 2006. We will continue recruitment efforts and complete the studies in December 2006.

In 2005, we identified a subject exercising under the supervision of one of the co-Investigators (PS) as a prototypical forefoot runner. We have obtained a video showing well-defined forefoot-running without coaching and have developed a short training video for subjects assigned to that research arm. This video is available upon request.

Reportable Outcomes

No directly reportable outcomes are available at this time.

Although not directly supported by this grant, one paper based on data collected with the third generation clinical UCR device used in this study has been published [3].

Conclusions

No conclusions can be drawn at this time. Data analysis will be complete in the next study year.

References

- [1] HM Frost. "The Utah paradigm of skeletal physiology: an overview of its insights for bone, cartilage and collagenous tissue organs." J Bone Miner Metab, 18:305-316, 2000.
- [2] PP Antich and S Mehta. "Ultrasound critical-angle reflectometry (UCR): a new modality for functional elastometric imaging." Phys Med Bio, 42:1763-1777, 1997.
- [3] E Richer, MA Lewis, CV Odvina, MA Vazquez, BJ Smith, RD Peterson, JR Poindexter, PP Antich, CYC Pak. "Reduction in Normalized Bone Elasticity Following Long-Term Bisphosphonate Treatment as Measured by Ultrasound Critical-Angle Reflectometry." Osteoporosis International, 16:1384-1392, 2005

Appendices

Up-to-date letter of approval from UT Southwestern IRB.

SOUTHWESTERN
THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

Institutional Review Board

TO: Pietro Antich, PhD
c/o Irma Dobbins
Radiology - 9058
Jan Harrell for

FROM: John Sadler, MD
Institutional Review Board 3 – Chairperson
IRB - 8843

DATE: January 12, 2006

SUBJECT: **Continuing IRB Review – Expedited Approval**
IRB File Number: 1101-555
Project Title: Leg Muscle Usage Effects on Tibial Elasticity During Running

The Institutional Review Board reviewed this research activity on an expedited basis. Your protocol and consent form(s) were approved for continuation for the period beginning November 6, 2005 and expiring on November 5, 2006.

Please report to the IRB any unexpected or serious adverse events that occur during the study. Any proposed changes in this research must be submitted to the IRB for review and approval prior to implementation, except for immediate changes necessary to assure research subject safety, which must be reported to the IRB within two days.

This study will require continuing review from the IRB and a reminder will be mailed to you 60 days prior to the **expiration date of November 5, 2006.**

Important Note: You must use a photocopy of the attached IRB-approved and stamped consent form(s). Use of a copy of any consent form on which the IRB-stamped approval and expiration dates are replaced by typescript or handwriting is prohibited.

Please note the enclosed notice regarding the mandatory consent wording change to conform with HIPAA policies; specifically, item #1 remains incomplete (the paragraph headed, "Publication of the results of the research" remains in the consent form and should be deleted), and item #5 has not been done.

Should you have any questions, please telephone Jan Harrell in the IRB office at 214.648.9453.

JS/iw