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Project Title:	A Low Intensity Mechanical Countermeasure to Prohibit Osteoporosis in Astronauts During Long-Term Spaceflight		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
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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		
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Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	11794-2580	**Congressional District:**	1
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Flight Program:			
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COI Name (Institution):	Judex, Stefan (State University of New York at Stony Brook) Qin, Yi-Xian (State University of New York at Stony Brook)		
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Task Description:

Osteoporosis, the progressive loss of bone density and strength that cripples tens of millions on our planet, distinguishes itself as perhaps the greatest physiologic obstacle to an extended human presence in space. The principal objectives of this proposal are to establish the efficacy of a unique, mechanical countermeasure to inhibit bone loss - and muscle strength- in the lower appendicular skeleton of astronauts and payload specialists during International Space Station missions. Using a ground based model of microgravity, the tail-suspended rat, we have shown that brief exposure (10 minutes) to extremely low magnitude (0.25g, engendering <5 microstrain), high frequency (30-90 Hz) mechanical signals will inhibit the bone loss which typically parallels disuse, even though 10 minutes of full weightbearing failed to curb this loss. Longer-term experiments in sheep have shown this stimulus to be strongly anabolic, increasing bone mineral density, trabecular number and connectivity, and improving bone strength. Preliminary results in post-menopausal women and children with cerebral palsy indicate that this intervention can inhibit, and perhaps reverse, osteoporosis. To determine this intervention's ability to inhibit bone loss - and muscle strength - in people during prolonged space missions, we will subject astronauts, in single let stance, to brief exposures to the low level stimulus (10 minutes at 30 Hz, 0.3g), allowing the contralateral limb to serve as an intra-subject control. The proposal is structured to "piggy-back" onto ongoing flight studies, and thus the assays for efficacy will be determined by collaborative decisions between NASA teams studying the musculoskeletal system. At a minimum, DXA, QCT, and muscle strength measurements will be made both pre- and post- flight. This work represents a critical step in establishing a physiologically based, non-pharmacologic, non-invasive treatment for osteoporosis, for use on Earth or in space.

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

Two clinical studies, evaluating the efficacy of the device, are to be published in the March issue of J. Bone & Mineral Research. In the first study, the intervention is shown to prevent osteoporosis in a group of post-menopausal women. In the second study, the intervention is shown to stimulate bone formation in children with cerebral palsy.

NASA Status Report, Jan 1 2004 through Dec 31, 2004
PI: Clinton Rubin Graduate Students: Jesse Muir, Beney Lee Lab Technician: Ben Adler

1. Background Summary

This project is focused on studying the anabolic effect of low magnitude, high frequency mechanical stimulation on the load bearing bones of astronauts. A vibrating plate which generates accelerations of 0.3 g peak-to-peak, at a rate of 30 Hz is being used as the source of mechanical stimulation. Exercise and resistance training the have been put in place on MIR and the ISS over the years to help reduce muscle wasting have not stopped the loss of bone that is seen in astronauts (~2%/Month). By having astronauts stand on the plate for 10 minutes per day we hope to show a significant inhibition of the loss of bone due to the lack of gravity.

2. Harness System

The mechanical stimulation is applied to the human body via a harness wore by the subject. Two harnesses were tested in the past year. The main difference between harness one and two was the increased padding in the second harness, and the Velcro adjustability of the first harness. Both harnesses loaded the body in the same manner; two attachment points to the harness along the side of the body, directly under the armpits, at about the level of the waist. Harness one was designed to place a load of 30% of the subject’s body weight when standing and lying down. Harness two was designed to place a load varying from 30% to 60% of the subject’s body weight when lying down. The subjects testing the harnesses ranged in height from 5’0” to 6’4” and in weight from 108lbs to 185lbs. The subject pool of 8 males and 4 females tested harness two for comfort and ease of use. The former had a mixed response from the subjects in terms of comfort. The latter was not an issue for any of the participants; the harness was worn as a jacket, and secured with a front strap. For both of the harnesses, subjects of both genders mentioned an uncomfortable, but not unbearable, pressure mainly in their shoulders and indicated that they would be fine wearing the harness with the load in the 30% and 60% loading conditions. However, several of the women expressed severe discomfort with the harnesses, due to the compression of the chest by the front strap. Similar comments were made about harness one with a 30% load. This discomfort was not present in any of the male subjects. In the two loading conditions we tested, the Velcro adjustment in the back wasn’t used in the various body types of the subjects. In all subjects, the harness only made contact in the back along the top third of the harness. The extra padding in harness two was a definite improvement. One concern that noted was that in zero-g, there will be greater propensity for the body to bend under the application of the load. It may be better to use a hip/shoulder combo harness, such as the TVIS, to decrease the likelihood of bowing under the load in zero g, and it would also remove the need for a separate harness for this countermeasure. We would like to test the TVIS harness to compare it to the other two harnesses in terms of comfort, ease of use, and ensuring the transmission of the signal with a hip/shoulder loading combination versus a shoulder loading combination. Minimizing the mass and volume of equipment needed in the space station is a priority, due to the heavy restriction on payload mass availability and free space in the ISS.

3. Change of protocol from one-leg to two-leg stance

The initial plans for the protocol of the bed rest and astronaut studies had the intervention applied to one leg of the subjects, with the other leg being used as a contra lateral control. By placing an accelerometer on the top plate between the heels of the subject and measuring the acceleration at the head using an accelerometer attached to a bite bar, we could measure the transmission of the signal through the body. When the subject changed from two to one legged stance, there was a drop in transmission of 60% (Figure 1). The protocol has since been changed so that the subjects will be standing with both legs on the plate, and controls will be done with subjects who do not use the plate. Another reason for this is that we wish to look at effects of the vibration on the bones of the spine, and there is no left/right spine to compare. It was also found that the transmission of vibration was dependant on the stance of the subject (Figure 2). When the subject stood with straight legs (locked or relaxed) there was high transmission, but if the legs were bent at a 20 degree angle, or if only one leg was stood on, the transmission dropped dramatically. 4. Measurement of Transmission of Vibration in through the Body To determine how the application of mechanical vibration to the foot of a subject propagates through the body, we attached accelerometers to different points of the body. When the plate was activated, the peak to peak accelerations were measured using tri-axial accelerometers (crossbow inc). Acceleration was measured at the surface of the top plate, and at the shin, hip, and head of the subject. Shin and hip measurements were made by attaching the accelerometer using double sided tape to the skin 5 inches below the knee where the tibia is near the surface, and to the skin above the iliac crest. In both cases, athletic tape was wrapped around the accelerometer and

Task Progress:

body, making the connection more secure. Measurement at the head was performed using a bite-bar. Percent transmission was defined as the ratio of acceleration at a point in the body to the acceleration of the top plate. The subjects were told to stand on the plate with their feet at shoulder width, and their arms at their sides. There was a large variation between the 10 subjects tested (Figure 3). At the bite bar, there was an average transmission of 68.56% (SD = 20.48). At the hip, transmission was 30.25% (SD = 10.2). At the tibia, transmission was 148.39% with an SD of 61.62. The large variation is contributed to the variation in body types of the subjects. At the hip, there is not a solid interaction between the accelerometer and the bone due to muscle and/or body fat, causing the measured acceleration to be lower than the acceleration of the bone itself.

5. Change in transmission in supine subjects

In the original experimental design, the astronauts were to stand on the plate with one leg, with a load of 30% of their total body weight placed at their shoulders. To simulate microgravity we had the subjects lie on their backs. When the subjects were in a supine position, there was a 50% drop in transmission with both feet on the plate. The drop was smaller in one-legged stance. Our previous work has shown the benefits to a subject who stands freely on the plate for 10 minutes a day. The loss in transmission indicates that a subject in a microgravity environment will be undergoing stimulation of half the magnitude that the standing subjects were under. The magnitude of the stimulation must be increased to levels closer to those seen in a standing subject before the device can be successfully tested in a microgravity environment.

6. Determination of Correct Loading Condition

The application of low magnitude, high frequency mechanical stress to the load bearing bones is being expanded to astronauts in a low to zero-gravity environment. Before the device is to be brought into space, we needed to verify that the application of LMMS to the feet of the subject in a 0g environment would have the same mechanical effect on the body as when standing. To show this, we using a simulated microgravity simulation of a subject in bed rest. The stimulation plate was suspended by a 2 foot chain vertically. The subject was fitted with a harness system which could attach to the plate via springs. These springs applied a force normal to the surface of the plate to the shoulders of the subject, pulling them to the plate. The force applied could be adjusted by adding length to the end of the springs. The subject lay on a moving platform, with their feet on the plate. The applied load to the subject was varied from approximately 30% to 70% of the total weight of the subject. At load intervals, acceleration measurements were taken with the plate activated. Percent Transmission was defined as the ratio of measured acceleration at the body to the acceleration of the plate (set to 0.3 g peak to peak). The percent transmission of the signal varied across subject group (n = 10), though this is expected due to differences in body types and genders. What was found was that as the applied load increased, the transmission of signal increased (Figure 5). When 30% of the subject’s body weight is applied to them, there was approximately 30% transmission. When this load was increased to 60% body weight, the transmission increased to 50%. When the plate was placed on the floor and the subject stood on it under the effects of gravity, there was an average transmission of 62%. This means that with 60% applied body weight to a supine subject, there is 80% of the stresses applied to the body compared to standing. According to the test subject, they would feel comfortable using a 60% BW loading for 10 minutes a day, while higher loads caused discomfort with several subjects. For this reason, we are preceding using 60% body weight at our applied load to supine subjects.

7. Future Studies On February 20th, the first pair of subjects for a 90 day bed rest study will enter the facility at the University of Texas Medical Branch (UTMB) in Galveston Texas. Day 0 of bed rest will be March 4th. We will be involved with four other research teams, studying the effects of unloading as an analog for prolonged space flight. Subjects in the experimental group will be exposed to 10 minutes of vibration each day for the length of the study. Measurements of bone quantity/quality will be performed with DXA, qCT, and ultrasound. Posture control will be determined with a Kistler force plate. Data collected from the other research teams including muscle strength and neurological changes will also be analyzed. The experimental group will be compared to the control group, which is not subjected to the mechanical stimulation. Another study we will be performing will be evaluating the plate and harness system on the KC-135 plane, to study how the plate works in actual microgravity. We will study the effects of microgravity on the transmission of vibration through the body, as well as the ease of use of the device in a micro-g environment. It must be verified that the mechanical stimulation will propagate through the body of the astronauts in microgravity before we can place a plate on the ISS for a long term study.

Bibliography Type: Description: (Last Updated: 10/22/2009)