Extracorporeal Shock Wave Application Stimulates Bone Apposition and Mitigates Bone Loss in Rat Hindlimb Suspension Model

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Introduction: This study aims to develop and optimize a countermeasure for prevention of osteopenia, e.g. loss of bone through lack of weight bearing activity, based on exogenous application of acoustic energy. Ultrasound, a high frequency acoustic energy, has been applied clinically and shown to be efficacious for the treatment of difficult to heal fractures (nonunions) [1]. Our data suggest that this effect stems from an increase in fluid flow and concomitant mass transport of nutrients, minerals, cytokines, and growth factors to and waste products from the fracture callus. Based on these data, the application of acoustic energy to augment bony apposition and prevent disuse osteopenia in space seems logical. However, the application of ultrasound to prevent osteopenia has shown equivocal results in human trials, presumably due to lack of effective penetration through the bony cortex [2]. At the other extreme, acoustic shock waves (extracorporeal shock wave therapy) are implemented clinically to fragment kidney stones in order to facilitate their passage out of the body; typically, during such procedures care is taken to prevent damage to the mineralized matrix of bone tissue. Interestingly, naturally occurring microdamage in bone has been shown to trigger the initiation of the remodeling cycle [3]. The aforementioned data and observations have led us to explore a previously unexploited avenue for preventing disuse osteopenia, i.e. the application of acoustic energy to produce low-level, diffuse microdamage similar to that ensuing from normal physiological activity on Earth. In contrast to phar- 

Materials and Methods: Lithotripsy (Lithotripsy Modulith® SLX) was administered to skeletally mature Sprague Dawley rats (350–400g, approx. 2 years post retirement from breeding). Different lithotripsy energy regimes were applied to the anterior surface of the middiaphysis of the femur under isofluorane (0.5-3%) anaesthesia. Prior to and after the procedure, intravital fluorochromes were administered to monitor the dynamics of remodeling. Ten groups of five animals were used to assess effects of independent variables including number of lithotripsy pulses (500 vs. 1500 at energy density 1.06 mJ/mm^2), disuse prior to and/or after treatment, and time after treatment (immediately post treatment vs. 4 wks. post). Two additional groups of 5 animals served as baseline controls for rats allowed normal cage activity and rats exposed to disuse via hindlimb suspension. After treatment with lithotripsy, animals received 0.05 mg/kg Buprenorphine (Buprenex) administered SQ every 12 hours during the first 72 hours post-treatment.

Discussion: Extracorporeal shock wave application stimulates bone apposition and mitigates disuse osteopenia. Interestingly, lithotripsy appears to exert systemic effects on bone remodeling, as contralateral limbs (not exposed directly to lithotripsy) also showed an increase in bone apposition compared to baseline controls. Although rats were observed in normal cage activity immediately after lithotripsy, further studies should be conducted to insure safety of the method prior to clinical implementation.


Acknowledgements: This study was funded through the NASA John Glenn Bioscience and Engineering Consortium.

Results: Hindlimb suspension resulted in a significant increase in bone resorption area. Bone resorption was observed predominantly within the cortex, as cavities emanating from cortical vascular spaces. Treatment with lithotripsy was associated with a significant decrease in area of bone resorption and a significant increase in bone apposition, in groups exposed to disuse prior and/or after treatment. Bone apposition was observed predominantly on the periosteal surface of the bone, and was increased in the contralateral limb of lithotripsy rats compared to untreated controls. Bone apposition was significantly higher in groups exposed to 1500 lithotripsy pulses compared to 500 pulses. Bone apposition was not significantly different in hindlimb suspended or baseline controls. One non-displaced fracture was observed in a rat treated with lithotripsy and subsequently allowed normal cage activity.

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