Elucidating the Effects of Microgravity on Osteoblast and Osteoclast Activity

Isaiah T Taylor[1], Sardar MZ Uddin[1], David E Komatsu[1]
[1]Stony Brook University, Stony Brook, NY, 11794

Disclosures: Isaiah T Taylor (N), Sardar MZ Uddin (N), David E Komatsu (N)

INTRODUCTION: With the Artemis missions rapidly approaching, and despite recent breakthroughs in space biology, sending the first humans to the moon remains a significant challenge. During space flight, astronauts lose 1-1.5% of their bone mass per month. Because of our inadequate understanding of the mechanisms causing microgravity-induced bone loss, as well as the difficulties in developing effective remedies, NASA has designated microgravity-induced bone loss as a high-priority knowledge gap. Bone quality and quantity are maintained through the complex process of bone remodeling. Osteoblast-osteoclast coupling is a dynamic process in which osteoblasts, bone forming cells, and osteoclasts, bone-resorbing cells, tightly regulate resorption and formation of new bone. Lack of gravity-induced mechanical stress decouples osteoclasts and osteoblasts, increasing osteoclastic bone resorption and decreasing osteoblastic bone formation. Unfortunately, there are not yet any comprehensive studies describing effects of microgravity on osteoblast-osteoclast communication. Our hypothesis is that simulated microgravity will disrupt the activity of osteoblasts and osteoclasts.

METHODS: Primary human osteoblasts and osteoclasts were cultured on ilium tricortical chips in simulated microgravity (SMG) using a rotary cell culture system. The NASA approved commercially available Synthecon® Rotary Culture System- 4HD (RCCS) with slow turning lateral vessels at 30-40 rpm were used to generate simulated microgravity. Osteoblasts or osteoclasts (25,00 cells/chip) were seeded on tricortical human blocks and subjected to either microgravity or gravity in RCCS for 28 days. The mechanical integrity of tricortical blocks was then assessed using unconstrained uniaxial compression as described by Komatsu et al. (Komatsu, Hadjiargyrou et al. 2015).[1] Briefly, a monotonic load was applied at a rate of 5 mm/min, under displacement control, using a single column testing machine (MTESTQuattro, Admet) equipped with a 225lb/ft load cell (SMT2–225, Interface). Load and displacement data were sampled at 100 Hz using the MTESTQuattro software package (Version 3.13.01, Admet). Data were analyzed for ultimate force, energy to failure and stiffness.

RESULTS SECTION: The biomechanical integrity of chips seeded with osteoblasts was significantly reduced in MG-exposed samples compared to samples experiencing normal gravity. Specifically, stiffness was 140% lower, energy to failure was 419% lower, yield force was 274% lower, ultimate force was 269% lower, and failure force was 269% lower in microgravity conditions compared to gravity. The biomechanical results for osteoclast-seeded chips were also decreased as osteoclasts were presumably more active, therefore, resorbing bone at a faster rate than gravity controls.

DISCUSSION: This project only targets cell-cell communication between osteoblasts and osteoclasts which represent only one aspect of the complex process of bone remodeling. To fully understand the effects microgravity on bone remodeling it is essential to study the effects of microgravity on osteocytes and mesenchymal cells in tandem with osteoclast-osteoblast communication. The results of the current study will be pivotal to proceed with studies involving osteocytes and mesenchymal stem cells. In the near future, osteoblast-osteoclast co-cultures will be used to identify the direct and indirect cell communication pathways disrupted by microgravity (MG).

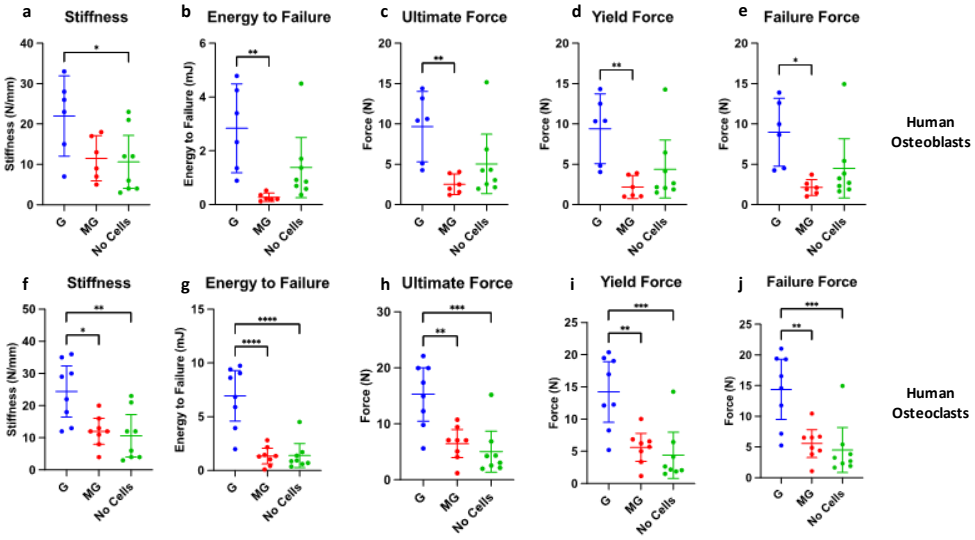

Figure 1: *Mechanical integrity of primary human osteoblasts (a-e) and osteoclasts (f-j) seeded on tricortical blocks. Bone chips were tested for (a, f) stiffness [N/mm], (b, g) energy to failure [mJ], (c, h) ultimate force [N], (d, i) yield force [N], and (e, j) failure force [N]. (n=10, *p<0.05)*

SIGNIFICANCE/CLINICAL RELEVANCE: The use of primary human cells in their physiological environment makes our study highly translational. Subsequent signaling pathway analyses will allow us to determine the effects of microgravity on osteoblast-osteoclast communication leading to osteoblast-osteoclast decoupling and bone remodeling. The functional analysis will show effects of osteoblast-osteoclast decoupling on bone structure and mechanical integrity.

REFERENCES: [1]Komatsu, D. E., M. Hadjiargyrou, S. M. Udin, N. A. Trasolini and S. Pentyala (2015). "Identification and Characterization of a Synthetic Osteogenic Peptide." Calcif Tissue Int 97(6): 611-623.

ACKNOWLEDGEMENTS: Funding for the study was provided by the 2016-17 Space Biology NASA grant (ROSBio) 80NSSC18K1479.