Intramedullary Pressure Induced by Dynamic Hydraulic Stimulation and its Potential in Attenuation of Bone Loss

INTRODUCTION: Bone fluid flow has been demonstrated as a critical regulator in mechanotransductive signaling and bone adaptation. Intramedullary pressure (ImP) is suggested to initiate bone fluid flow and influence the osteogenic signals within bone. The potential ImP-induced bone fluid flow then triggers the remodeling process in the skeleton [1]. It has been demonstrated that ImP generated by oscillatory electrical stimulations can effectively mitigate disuse osteopenia in a frequency-dependent manner in a disuse rat model [2, 3]. Directly related to translational potentials of ImP, a non-invasive method that couples external stimulation and internal bone fluid flow remains challenge. Therefore, it was hypothesized that noninvasive dynamic hydraulic stimulation (DHS) can induce ImP with minimal strain and initiate adaptive responses in vivo to elicit osteogenic activity. The objectives of this study were: 1) to demonstrate the effects of a novel, non-invasive dynamic external pressure stimuli (3Hz) on bone structural properties in a disuse model; and 2) to evaluate the immediate effects on ImP and bone strain induced by the stimuli over a range of frequencies.

METHODS: All experimental procedures were approved by Stony Brook University IACUC. Five-month old female Sprague-Dawley virgin rats were randomly assigned to 5 groups: baseline controls (n=15), age-matched controls (n=13), hindlimb suspended (HLS, n=13), HLS + static pressure (n=10), and HLS + 3Hz dynamic pressure (n=5). Functional disuse in the rat hindlimbs were introduced via HLS procedure. Pressure stimulations were applied to the right tibia of the experimental rats for 10min on-5min off-10min on/day, 5 days/week for at least three weeks. Ttibial bone samples were sacrificed after 4 weeks and the right tibial bone samples were obtained.

RESULTS: The μCT data showed significant improvements in BV/TV and bone microarchitecture in response to non-invasive oscillatory DHS. Induced ImP at 3Hz loading significantly attenuated disuse bone loss. Direct ImP and bone strain measurements under such stimuli further demonstrated the possible ImP-induced bone fluid flow mechanism for bone adaptation. DHS may build up vessel pressure gradient, triggering blood flow into bones that affects ImP. In contrast to previous dynamic strain stimulation studies, e.g., remodeling was optimized at frequencies of 20-60Hz [3]; we found that the bone adaptation in response to DHS was more effective at the lower frequency range. The viscoelastic nature of surrounding connective tissues may have filtered out high frequency components. This implies that direct hydraulic coupling may influence adaptation in a more physiologic frequency range.

DISCUSSION: The μCT data showed significant improvements in BV/TV and bone microarchitecture in response to non-invasive oscillatory DHS. Induced ImP at 3Hz loading significantly attenuated disuse bone loss. Direct ImP and bone strain measurements under such stimuli further demonstrated the possible ImP-induced bone fluid flow mechanism for bone adaptation. DHS may build up vessel pressure gradient, triggering blood flow into bones that affects ImP. In contrast to previous dynamic strain stimulation studies, e.g., remodeling was optimized at frequencies of 20-60Hz [3]; we found that the bone adaptation in response to DHS was more effective at the lower frequency range. The viscoelastic nature of surrounding connective tissues may have filtered out high frequency components. This implies that direct hydraulic coupling may influence adaptation in a more physiologic frequency range.

ACKNOWLEDGMENT: This work is kindly supported by NIH, US Army Medical Research, and NSBRI.