OVERVIEW AND EVALUATION OF A COMPUTATIONAL BONE PHYSIOLOGY MODELING TOOLCHAIN AND ITS APPLICATION TO TESTING OF EXERCISE COUNTERMEASURES

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INTRODUCTION: Prolonged microgravity exposure disrupts natural bone remodeling processes and can lead to a significant loss of bone strength, increasing injury risk during missions and placing astronauts at a greater risk of bone fracture later in life. Resistance-based exercise during missions is used to combat bone loss, but current exercise countermeasures do not completely mitigate the effects of microgravity. To address this concern, we are working to develop a personalizable, site-specific computational modeling toolchain of bone remodeling dynamics to understand and estimate changes in volumetric bone mineral density (vBMD) in response to microgravity-induced bone unloading and in-flight exercise.

MODEL APPROACH: The toolchain combines probabilistic classification methods, a computational bone model, and finite element (FE) analysis to simulate the effects of microgravity on bone. Individualized bone FE models are first procedurally generated from computed tomography (CT) scans that are processed using a Gaussian Naïve Bayes classifier. CT scan information is also used to initialize the computational bone model that simulates bone dynamics at the bone remodeling unit level. Bone dynamics are mathematically formulated as the difference between the rate of bone formation and resorption, and include the removal and replacement of structural units in both cortical and trabecular bone, as well as the cellular dynamics of the RANK, RANKL, and OPG pathway. The computational model uses Frost's mechanostat theory to capture the effect of strain stimulus resulting from skeletal loading. Skeletal loading is simulated using FE software that calculates stresses and strains based on cortical and trabecular vBMD and moduli of elasticity. A sensing level, defined as being proportional to the expression of NO and PGE_2, weights the level of cellular response to mechanical stimulus. This is used to determine if the stimulus is sufficient for maintaining bone health. The computational bone and FE models are executed iteratively throughout the simulation to update and propagate model parameters.

CURRENT PROGRESS: We evaluated the toolchain against data collected from subjects in a 70-day bedrest study, using it to predict individual decline of femoral vBMD for subjects based on body anthropometry, pre-study bone mineral density, study duration, and the amount of exercise performed. We find that it captures bone remodeling trends in the test dataset, quantitatively predicting post-study vBMDs of control group subjects who did not perform exercise, as well as qualitatively predicting the mitigating effects of exercise in microgravity (Fig. 1).

CONCLUSION: The toolchain provides insight into the amount of exercise stimulus needed to minimize bone loss, and can create subject-specific bone models that are potentially useful for quantifying the amount of exercise stimulus needed to mitigate vBMD decline during spaceflight. Specifically, the toolchain predicts post-study vBMDs of control subjects who did not perform exercise with a relative error of $-0.61 \pm 3.53\%$. The toolchain also qualitatively predicts the effect of exercise in mitigating bone loss, showing that post-study vBMD values can be achieved when non-zero forces are applied to the femur, though the magnitude of these forces is lower than expected. This behavior likely results from systematic error of vBMD values in our dataset. These findings inform future work, demonstrating how the toolchain could be improved and further validated with additional test data, as well as how it could be used to develop customized in-flight exercise regimens and predict exercise effectiveness.
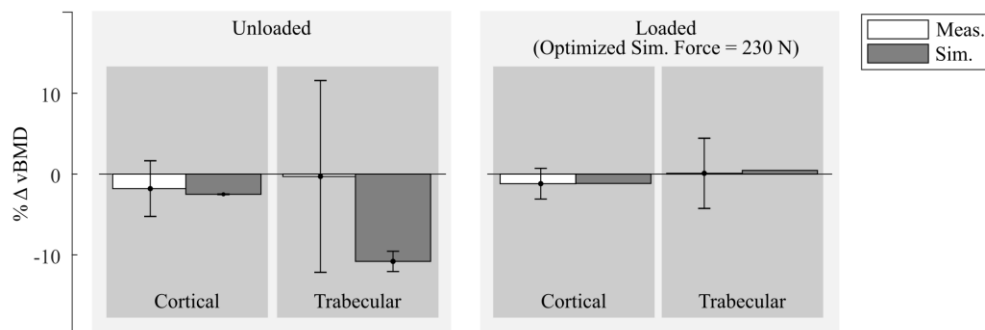

Figure 1. Measured and predicted vBMD change. Loaded simulation used mean anthropometry and vBMD data of all subjects.