Is Shear Stress the Anabolic Signal in Bone Marrow During Low-Magnitude High-Frequency Vibration?

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INTRODUCTION:
Low-magnitude high-frequency (LMHF) loading is anabolic to bone, but the mechanism of signal transmission has not been established. LMHF loading for one year resulted in a 32% increase in the trabecular bone volume in sheep [1]. In contrast, no change was seen in cortical bone, suggesting the anabolic effect is limited to the trabecular compartment. Furthermore, rats subjected to 90 Hz vibration developed greater trabecular bone volume and thicker trabeculae than rats subjected to vibration at 45 Hz [2], even though the 90 Hz vibration induced lower strain in the bone. Thus, the anabolic effect is not due to matrix strain. However, the cells in the bone marrow may be subjected to shear stress due to inertial motion within the trabecular pores, which could provide the anabolic signal.

Fluid shear stress in the range of 0.5 to 2.0 Pa affects various cell lineages present in bone marrow in an osteogenic manner [3-5]. As such, shear stress induced during LMHF vibration may affect the marrow cell population. However, the mechanical environment of the bone marrow is poorly understood. Marrow from the distal skeleton, which contains more adipose cells, has lower viscosity than marrow in proximal regions [6] and marrow changes composition with aging and disease [7]. As such, the response to mechanical stimulation of the marrow by LMHF loading may depend on marrow properties.

The goal of this study was to determine the effect of marrow viscosity on the magnitude of mechano-biologic stimuli in bone marrow during LMHF vibration of trabecular bone. Specifically, we quantified the shear stress within the marrow using computational fluid dynamics models, and determined the dependence of shear stress on marrow viscosity and vibration frequency.

METHODS:
A trabecular bone sample from a human lumbar L-5 vertebra was imaged by micro-CT (Scanco μCT-80, Brüttschellen, Switzerland) at 20 μm resolution. The sample was Gaussian filtered, and resampled by cubic interpolation to 35 μm resolution. A 4 mm cubic region of the marrow space was discretized into tetrahedra using marching cubes (VTK, Kitware, Clifton Park, NY). The bone was assumed to be rigid, with a no-slip interface between the bone and marrow. The surface nodes of the bone-marrow interface were assigned a 10 or 30 Hz sinusoidal velocity profile with a peak acceleration of 1 g along the superior-inferior direction. The marrow volume was allowed to move freely with uniform pressure under inertial forces. Newtonian viscosities ranging from 50 to 400 mPa·s [6], and a power-law fluid model, defined by \( \tau = 7.5 (\text{d}t/\text{dt})^{0.796} \text{Pa·s} \), were investigated.

Transient, dynamic solutions were performed in ADINA-F (Watertown, MA). The solution was carried out starting from 0 velocity to 2 cycles. To avoid artifacts from the edges, a 3.6 mm² subregion in the center of the sample was selected for postprocessing. The median, 25th, and 75th percentile shear stress in the marrow volume were determined from histograms at peak acceleration, at the end of the first cycle.

RESULTS:
The shear stress increased with increasing viscosity and frequency (Fig. 1). Increasing the viscosity broadened the distribution of shear stress within the marrow resulting in greater shear stress farther from the bone walls. Increasing the frequency had a similar effect to increasing viscosity (Fig. 2). At all viscosities and frequencies, approximately 75% of the marrow in the lumbar spine model was subjected to shear stress over 0.5 Pa (Fig. 1), which is stimulatory to osteoblasts, osteoclasts, and mesenchymal stem cells (MSCs) [3-5].

DISCUSSION:
This study found that bone marrow viscosity affects the potential shear stress experienced by cells within the marrow. The magnitude of the shear stress at the bone-marrow interface is the most sensitive to changes in both viscosity and frequency. This interface is believed to be occupied primarily by quiescent osteoblasts [3]. However, a more complete understanding of marrow cell location is needed to assign shear stress magnitudes to specific cell types.

A limitation of this study is simplifying the marrow as a homogeneous fluid. Capturing the heterogeneous behavior would require multi-scale modeling that incorporates cell-cell and cell-fluid interaction.

This study provided an estimate of the effect of marrow viscosity and vibration frequency on shear stress in marrow during LMHF loading. In combination with fluid flow studies [5,9], which quantify the response of bone marrow cells to shear stress, understanding the range of shear stress in the marrow will provide improved insight into how cells of specific lineages respond to LMHF loading.

![Figure 1: Affect of viscosity on shear stress at 10 (blue) and 30 Hz (yellow) vibration (bars show the 25th percentile, median, and 75th percentile of the shear stress).](image)

![Figure 2: Shear stress in marrow at 10 and 30 Hz vibration with 50 and 400 mPa·s marrow viscosity (white is bone and blue regions are below 0.5 Pa, the approximate mechanostimulatory threshold).](image)

SIGNIFICANCE:
Understanding the mechanical environment of bone marrow will provide insight into its role in response to mechanical stimuli that are anabolic in bone.

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REFERENCES: