THE EFFECTS OF INTERMITTENT AXIAL COMPRESSION ON BONE HEALING

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INTRODUCTION
Most fractures heal uneventfully using traditional treatment methods, but more than 500,000 of the 5.6 million fractures that occur annually in the United States show evidence of impaired healing. Abundant evidence exists that fracture healing can be influenced by mechanical loading. However, the specific loading parameters that are osteogenic remain unknown. The purpose of this study was to apply noninvasive external compression to mouse tibial osteotomies to determine the effects that timing and load magnitude have on bone healing. In addition, the utility of microcomputed tomography (microCT) in predicting the mechanical properties of callus was assessed.

METHODS
Eighty 12-week old C57BL/J6 mice underwent surgical osteotomy of the left tibia followed by intramedullary nailing with a 27-gauge needle. Mice were divided into six groups (n = 10 to 16 per group) based on the timing and load amplitude during postoperative loading. In five groups, compression was applied to the ends of the tibia with a noninvasive external loading device.[1] Three groups had a 4-day delay prior to initiation of loading ("4d" groups), with load amplitudes of 0.5N, 1N, or 2N. In two additional groups, loading was initiated on the day of surgery ("0d" groups), and load amplitudes of either 0.5N or 1N were applied. The final group, the control group, did not receive any postoperative loading. All loading protocols were performed at 1 Hz for 100 cycles per day using a triangle waveform, for 5 days per week for 2 weeks. Bone healing was first assessed by microCT reconstructed to a resolution of 11.6 µm. To characterize calluses globally and locally, two volumes of interest were selected to determine the total mineralized volume of the callus and to judge the quantity and quality of newly formed bone at the osteotomy site (Fig. 1). Subsequent to microCT scanning, all bones were tested to failure using four-point bending. The bending moment to failure and bending stiffness were calculated. For each measurement, the mean and standard deviation were calculated for each group. One-way ANOVA tests, followed by Bonferroni post hoc tests, were used to compare the means of each group, using a p-value < 0.05. Regressions were examined and Pearson correlation coefficients calculated for each of the microCT measurements compared to the bending moment to failure in each group. The experiment was approved by the institution's Animal Care and Use Committee.

RESULTS
Increased callus strength was found in one loaded group relative to the control group. The group with a 4-day delay prior to loading and 0.5N load amplitude had 39% greater maximum bending moment ($p < 0.05$) compared to the control group ("4d / 0.5N", Fig. 2). Bending stiffness was also significantly greater in this group compared to controls. Despite the increased strength, neither callus bone volume, BMC, nor BMD was significantly different from the control group. The load amplitude affected callus formation among the 4-day delay groups. The 0.5N group was significantly stronger than both the 1N and 2N groups (Fig. 2). In addition, the 2N group had a significantly lower BMC and was less stiff compared to the 0.5N group. Immediate application of loading following surgery (the two "0d" groups) had an adverse effect on callus strength, regardless of the load magnitude. Load amplitudes of 0.5N and 1N led to callus strengths that were reduced by 68% and 57% relative to the control group, respectively, and stiffnesses that were reduced by 70% and 63% (Fig. 2). However, in both groups the callus bone volumes were significantly larger (Fig. 2), and BMC was greater at the osteotomy site than for the controls. No significant correlations were found between microCT parameters measured at the callus and the bending moments to failure in any of the groups.

DISCUSSION
A short delay followed by cyclic application of a relatively low load led to improved fracture healing, as determined by increased callus strength, but this enhancement disappeared as load amplitudes increased. Load initiation immediately following fracture inhibited healing, regardless of the magnitude of load applied. MicroCT measurements of calluses in the early healing stage did not predict the mechanical strength of the fractures. Our finding that mechanical stimulation immediately post-fracture inhibited effective callus formation, regardless of the load magnitude applied, is contrary to previous data.[2, 3] The weaker calluses that resulted from immediate loading may have been caused by disruption of early blood vessel ingrowth into the hematoma.[4] As the loading parameters necessary to enhance fracture healing become refined, external compression may be used as a potent stimulus for treating fractures with decreased biological capacity.

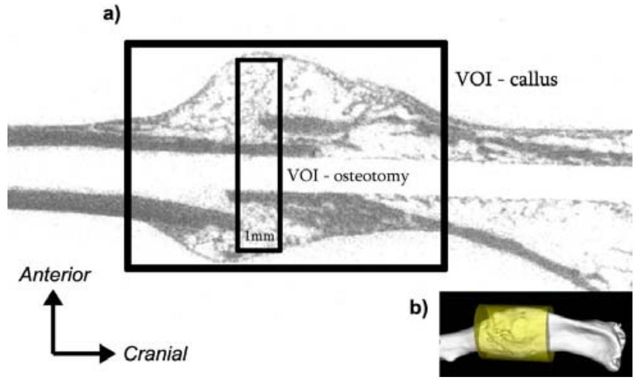

Figure 1: Depiction in a single plane of: (a) the volumes of interest analyzed, and (b) an example of a 3-D reconstruction and elliptical VOI.

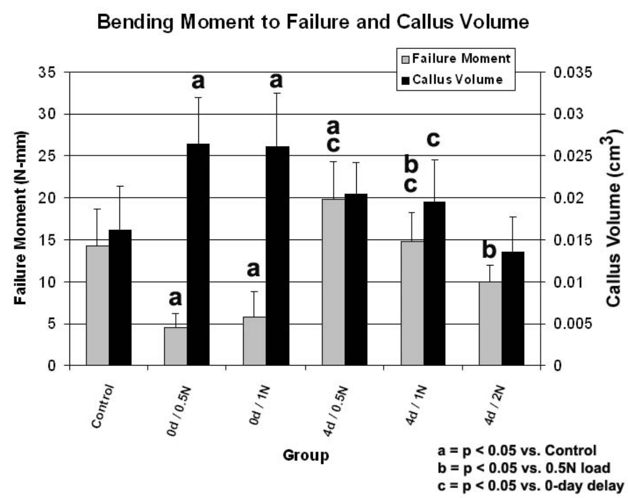

Figure 2: Maximum bending moment to failure and callus volume among the groups. The 0-day groups were both significantly weaker and larger than the controls, and the 4-day, 1N group was stronger than the controls.

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