INTRODUCTION: A stress fracture represents the failure of a bone to withstand repetitive bouts of mechanical loading. Despite the clinical significance of stress fractures in terms of loss of training and competition time, there are few effective preventative strategies. One hypothesized method is to use an exercise program to alter the material and structural properties of an at risk bone. Bone is inherently mechanosensitive and adapts its properties in response to the prevailing mechanical environment. By inducing adaptation through a mechanical loading program, a bone’s resistance to fatigue may be enhanced resulting in a subsequent reduction in stress fracture risk. However, the ability of a loading program to reduce stress fracture risk has not been established. The aim of this study was to investigate whether the material and structural adaptation of bone to a mechanical loading program can improve skeletal fatigue resistance in an animal model.

METHODS: Adult female Sprague-Dawley rats (250-300g) were used, and all procedures were approved by an Institutional Animal Care and Use Committee. Site-specific mechanical loading was achieved using the ulna axial compression loading model, with the animals under isoflurane anesthesia (Abbott Laboratories, North Chicago, IL). This mode of loading accentuates the mediolateral curvature of the ulna and translates most (approximately 90%) of the axial load into a bending moment to create a strain distribution similar to that resulting from normal limb usage during locomotion. Loading was applied using a 2 Hz haversine waveform for 360 cycles/day, three days per week for five consecutive weeks. The peak load magnitude was 17 N, which elicits a compressive strain of approximately 3600 µε on the medial surface of the ulna midshaft. Left ulnas served as an internal control and were not loaded. Normal cage activity was allowed between loading sessions. Animals were killed five weeks following the final loading session.

Adaptation to mechanical loading was determined by assessing both the material and structural properties of each ulna. Material properties were assessed using dual energy X-ray absorptiometry (DXA) and peripheral quantitative tomography (pQCT). DXA was performed to collect whole ulna bone mineral content (BMC; mg) and areal bone mineral density (aBMD; g.cm⁻²) data, whereas pQCT was performed to determine ulna midshaft BMC (mg.cm⁻³) and volumetric BMD (vBMD; mg.cm⁻³). Structural properties of each ulna midshaft were derived from micro-computed tomography (µCT) slices. Slice images were imported into Scion Image wherein ulna midshaft cortical area (Cl.A; mm²), and the maximum (Iₘ₉₉; mm⁴) and minimum (Iₐ₀₉; mm⁴) second moments of area were determined. In addition, the section diameter (Se.Dm; mm) of each ulna was determined as the largest diameter of the bone in the plane parallel to the Iₐ₀₉ axis.

To permit the calculation of microstrain (µε), right (loaded) and left (non-loaded) ulnas from four animals chosen at random were used for a load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the site of loading. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load-strain calibration experiment. A single element strain gauge (EA-06-015DJ-120; Measurements Group, Inc., Raleigh, NC) was bonded at the load

The mechanical loading program had predictable and consistent effects on the material and structural properties of the ulna, with loaded ulnas having significantly greater values for all measurements compared to the contralateral non-loaded ulnas (Fig. 1). The largest difference was observed for Iₐ₀₉, which was near two-fold greater in exercised ulnas. As a result of the adaptation in loaded ulnas, they experienced only 3614 ± 409 µε when loaded at 25 N during fatigue testing, which compared to the 5361 ± 618 µε experienced by nonloaded ulnas (p < 0.05, paired t-test).

DISCUSSION: By inducing adaptation of its material and structural properties, a mechanical loading program increased the fatigue resistance of the rat ulna by 80-fold. This large increase occurred despite relatively low gains in aBMD and BMC because load-induced new bone was localized to biomechanically relevant sites. Axial compression of the rat ulna accentuates its mediolateral curvature to generate strain and subsequent adaptation in the mediolateral plane. As this plane corresponds with the plane of Iₐ₀₉, adaptation to the mechanical loading program was predominantly observed as an increase in Iₐ₀₉. By fatigue loading the ulnas in the same direction as they were adapted, the two-fold increase in Iₐ₀₉ resulted in a substantial increase in fatigue resistance.

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